Functional Limb Salvage

The Multidisciplinary Team Approach

Christopher E. Attinger
John S. Steinberg
Editors

Springer

Functional Limb Salvage

Christopher E. Attinger
John S. Steinberg
Editors

Functional Limb Salvage

The Multidisciplinary Team Approach

Springer

Editors
Christopher E. Attinger
Department of Plastic Surgery
Georgetown University School of Medicine and MedStar Georgetown University Hospital
Washington, DC, USA

John S. Steinberg
Department of Plastic Surgery
Georgetown University School of Medicine and MedStar Georgetown University Hospital
Washington, DC, USA

ISBN 978-3-031-27724-5 ISBN 978-3-031-27725-2 (eBook)
https://doi.org/10.1007/978-3-031-27725-2

© Springer Nature Switzerland AG 2023
This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.
The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.
The publisher, the authors, and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, expressed or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Foreword

Diabetes: The Twenty-First Century Epidemic

It was a few years ago that I had the honour to share the stage at a large Diabetes conference in Bangalore, South India, with the then Prime Minister, Sri Narendra Modi. He spoke passionately about the problems facing the health of the Indian population, but of greatest relevance to this book was his comment that the biggest threat to the health of the Indian population and indeed the world was no longer communicable diseases such as tuberculosis, malaria, and others, but it was now non-communicable diseases such as diabetes. He was, of course, entirely correct in this statement: indeed, lower extremity complications of diabetes contribute greatly to the morbidity, mortality, and costs of diabetes across the world. At the time of writing this introduction early in 2021, the world is in the midst of the COVID-19 pandemic. Understandably, there has been a massive global effort in devising new treatments for this all-too-often fatal viral illness as well as rolling out a mass vaccination programme. My fear is that this might detract from recent increased interest in the importance of non-communicable diseases such as diabetes, cancer, and heart disease across the world. Early during this pandemic in 2020 there was evidence that the management of the numerous very ill patients had necessarily led to the neglect of many conditions, particularly non-communicable diseases [1]. In the area of diabetic lower limb disease, the threat to routine diabetic foot care has been outlined in several publications [2–5].

At the same time, we are experiencing a global epidemic of diabetes with approximately 500 million people with the condition across the world in 2021. The most recent edition of the International Diabetes Federation (IDF) Atlas published at the end of 2019 estimated that this number would increase to more than 700 million in the next 20 years or so [6]. Data from this publication suggest that the prevalence of diabetes in the United States is 13.3%, affecting approximately 34 million individuals. It is well recognized that certain groups such as native Americans, Hispanics, and Blacks have higher prevalences of diabetes, although recent evidence suggests that in certain of these groups, the prevalence has decreased in recent years [7, 8]. The average expenditure on diabetes per patient per year in the USA is approximately $10,000, one of the highest in the world. Other parts of the world have even more frightening prevalences, with Mauritius at 25% and rising in some of

the Polynesian islands to 33% [6]. A recent study from Pakistan [9] reported that 26.3% of all adults in Pakistan had diabetes. Thus, there are a number of reasons why it is vital to raise the global profile and importance of diabetes.

One such reason is the grim statistic that was recorded for diabetes in 2019 when it, for the first time, was listed in the top ten causes of death across the world [10]. At a time when one of the largest declines in the number of deaths witnessed was from infectious diarrhoeal diseases, diabetes entered the top ten with a significant percentage increase of 70% since 2000. Diabetes also represented the largest rise in male deaths among the top ten, with an 80% increase since 2000.

Diabetic foot ulceration (DFU) and its sequelae are associated with significant impairment of quality of life, increased morbidity and mortality, and place a huge drain on healthcare resources [11]. DFU occurs as a consequence of the combination of factors most commonly peripheral neuropathy, peripheral arterial disease, and some form of trauma. Foot problems are amongst the commonest of all the diabetic complications and are associated with very significant morbidity, mortality, and cost to the healthcare system.

Although a decline in the lower extremity amputations (LEA) had been observed in decades before 2010, Gregg et al. recently reported a resurgence of diabetes complications with an increase in diabetes-related LEAs from 2010 to 2015 [12]. Similarly, Harding and colleagues reported a stalling of the progress in non-traumatic LEAs in the very high-risk population of patients with diabetes and end stage renal disease [13]. It should therefore be apparent that the chapters in this book, which emphasize the multidisciplinary team approach to functional limb salvage in diabetes, are of great importance at the beginning of the third decade of the twenty-first century. The editors have assembled an impressive number of authors with true expertise in this area, which will provide the reader with eminently practical information on the diagnosis, medical and surgical management of these all-too-common problems.

References

1. Godlee F. Surviving the long road ahead. BMJ. 2020;369:m1840.
2. Shin L, Bowling FL, Armstrong DG, Boulton AJM. Saving the diabetic foot during the COVID-19 pandemic: a tale of two cities. Diabetes Care. 2020;48:1704–9.
3. Boulton AJM. Diabetic foot disease during the COVID-19 pandemic. Medicina. 2021;57(2):97. https://doi.org/10.3390/Medicina57020097.
4. Rogers LC, Lavery LA, Joseph WS, Armstrong DG. All feet on deck – the role of podiatry during the COVID-19 pandemic: preventing hospitalizations in an overburdened health care system, reducing amputation and death in people with diabetes. J Am Podiatr Med Assoc. 2020. [Epub ahead of print]. https://doi.org/10.7547/20-051.
5. Caruso P, Longo M, Signoriello S, et al. Diabetic foot problems during the COVID-19 pandemic in a tertiary care center: the emergency amongst emergencies. Diabetes Care. 2020;43:e123–4.
6. IDF Diabetes atlas. 9th ed. 2019. www.diabetesatlas.org.
7. Cheng YJ, Kanaya AM, Araneta MRG, et al. Prevalence of diabetes by race and ethnicity in the United States, 2011-2016. JAMA. 2019;322:2389–98.

8. Bullock A, Sheff K, Hora I, et al. Prevalence of diagnosed diabetes in American Indian and Alaska Native adults, 2006-2017. BMJ Open Diabetes Res Care. 2020;8(1):e001218. https://doi.org/10.1136/bmjdrc-2020-001218.
9. Basit A, Fawwad A, Qureshi H, Shera AS. Prevalence of diabetes, pre-diabetes and associated risk factors: second national diabetes survey of Pakistan. BMJ Open. 2018;8:e020961. https://doi.org/10.1136/bmjopen-2017-020961.
10. WHO. The top ten causes of death. 9 December 2020. www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death.
11. Boulton AJM, Whitehouse RW. The diabetic foot. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext 2020. South Dartmouth: MDText.com, Inc; 2020.
12. Gregg EW, Hora I, Benoit SR. Resurgence in diabetes-related complications. JAMA. 2019;321:1867–8.
13. Harding JL, Pavkov ME, Gregg EW, Burrows NR. Trends of nontraumatic lower-extremity amputation in end-stage renal disease and diabetes: United States, 2000-2015. Diabetes Care. 2019;42:1430–5.

Andrew J. M. Boulton

Division of Diabetes,
Endocrinology and Gastroenterology
Manchester Royal Infirmary
University of Manchester
Manchester, UK
University of Miami
Miami, FL, USA

Preface

Functional Limb Salvage has been our professional passion for decades. We have had the great fortune of building and working with a large multidisciplinary team based at MedStar Georgetown University Hospital in Washington DC. We find the work of wound healing, amputation prevention, and limb salvage to be a true privilege and a hidden gem of the healthcare profession. We are truly energized by this work and the motivated people that it attracts.

So why write a textbook on limb salvage? We have published, spoken, taught, and researched on this topic through numerous formats and media… but the missing piece for us has been a true reference text on how limb salvage really works and how to build a team approach to this crucial specialty. We meet around the world several times a year at key meetings and conferences to exchange the latest ideas and innovate together, yet there really is not a foundational text that someone new to the specialty could use as a cornerstone. We hope that this will serve to fill that knowledge gap and can be used as a tool by many who wish to learn more about the challenges that are present in the limb salvage specialty.

Functional limb salvage is an ongoing journey, just like much of medicine and surgery. In our short time doing this work, we have evolved from 'saving length at all costs'...to restoration of function as the key clinical goal. Functional limb salvage is about getting the patient and those around them back to functional capacity. That may mean a well-performed amputation, a surgical wound closure, palliative care to control pain and prevent wound infection, or advanced reconstructive options such as microvascular free tissue transfer, external fixation, and surgical deformity correction. One of the key challenges is to identify the correct course of action for the patient, the problem, and those around them. We must remember that some of our most grateful patients are those with a well-performed amputation and a prosthesis or even those with a wound that we acknowledge we may never heal but that we work to palliate with infection prevention and pain control.

We hope that you enjoy the talented authors we have curated for this unique text. Many are close friends and all are subject matter experts. We hope that this text helps you establish your own multidisciplinary functional limb salvage team, or helps you enhance the one you already have. When done correctly and with the right motivation, this work can be some of the most rewarding in all of healthcare.

Washington, DC, USA — John S. Steinberg
Washington, DC, USA — Christopher E. Attinger

Contents

1 Building It from Scratch: The Team Approach to Functional Diabetic Limb Salvage 1
Areeg A. Abu El Hawa, Kevin G. Kim, John S. Steinberg, Katherine Hubley, Cameron M. Akbari, and Christopher E. Attinger

2 Staffing and Day-to-Day Management: The Nuts and Bolts of Running a Wound Care Center 13
Amara Ellis and Tara Wallace

3 Case Management of the Complex Limb Salvage Admission 35
R. N. Thalia Attinger, M. S. W. Heather Daniels, R. N. Teodora Deperio, and Allen H. Roberts II

4 Integrating Inpatient Care to Your Outpatient Wound Care Center: Key to Successful Patient Management 47
Nancy R. Megas, Katherine S. Hubley, and Margaret C. Kugler

5 Diabetic Foot Ulcers by the Numbers: Epidemiology of Limb Salvage 57
Romina Deldar, Adaah A. Sayyed, Zoe K. Haffner, and John S. Steinberg

6 Unlocking the Mystery of Peripheral Neuropathy in Diabetes 65
Andrew J. M. Boulton

7 The Science and Utility of Offloading the Diabetic Foot 73
Caitlin S. Zarick, Kurtis D. Bertram, and Thomas F. Milisits

8 Medical Management of the Limb Salvage Inpatient 87
Marie M. Alternburg, Jennifer M. Haydek, Sara Kiparizoska, Nina K. Weaver, and Margot G. Wheeler

9 Evaluation and Examination of the Diabetic Foot 107
Michael Edmonds, Rajesh Kesavan, and Arun Bal

10 Frailty and Mobility Degeneration in Diabetes and Diabetic Foot Ulceration 133
Bijan Najafi and Gu Eon Kang

11 Anesthesia for the DLS Patient: Minimizing Risk and Maximizing Safety 147
Kasra Razmjou and Andy Liao

12 Debridement of the Diabetic Foot and Leg 157
Christopher E. Attinger and Jayson N. Atves

13 An Evidence-Based Approach to Treating Osteomyelitis 175
Benjamin A. Lipsky and Suzanne A. V. van Asten

14 Practical Lessons Learned in Managing Diabetic Foot Infections 187
Andrew I. Abadeer, Mark R. Abbruzzese, and William Davis

15 Managing Soft Tissue Infection in the Diabetic Foot: Cultures, Drugs, and Source Control 193
Eric Senneville and Romina Deldar

16 Surgical Management of Diabetic Foot Infection and Osteomyelitis 203
Venu Kavarthapu and Javier Aragón Sánchez

17 Charcot Foot Syndrome: Aetiology and Diagnosis 215
William Jeffcoate and Fran Game

18 Charcot Foot: Conservative Management 227
Armin Koller

19 Charcot Foot: Surgical Management and Reconstruction 237
Dane K. Wukich and Venu Kavarthapu

20 Diagnostic Evaluation of Arterial Disease in Limb Salvage 251
Michael Siah and Cameron M. Akbari

21 Arterial Disease Management in the Limb Salvage Patient: Endovascular and Open Bypass 263
Michael C. Siah, Roberto Ferraresi, Alessandro Ucci, Andrea Casini, Giacomo Clerici, and Cameron Akbari

22 Venous Disease Management in the Limb Salvage Patient: Diagnostics, Compression, and Ablation 285
Bianca Cutler, Nikita Patel, and Misaki Kiguchi

23 Science and Practicality of Tissue Products in Limb Salvage 305
Alexandra N. Verzella, Allyson R. Alfonso, and Ernest Chiu

24 Limb Wounds of Dermatologic Disease: Dermatopathology, Biopsy, and Medical Management 329
Helena B. Pasieka, Nicholas Logemann, Felix Yang, and Alexandra Gosh

25 Prosthetics, Orthotics, and Amputation Rehabilitation 349
Benjamin G. Higgs

26 Surgical Offloading, Tendon Balancing, and Prophylactic Surgery in Diabetic Limb Salvage 359
John S. Steinberg, Paul J. Carroll, Jayson N. Atves, and John D. Miller

27 Negative Pressure Wound Therapy 391
Paul J. Kim

28 Hyperbaric Oxygen Therapy in Functional Limb Salvage 401
Kelly Johnson-Arbor

29 Skin Grafting 415
Adaah Sayyed, Paige K. Dekker, Caitlin S. Zarick, and Karen K. Evans

30 Local Flaps for Reconstruction and Limb Salvage of the Foot and Ankle 429
David Z. Martin and Gabriel Del-Corral

31 Free Tissue Transfer in Diabetic Limb Salvage: Lessons Learned and Best Practices for Functional Salvage 449
Paige K. Dekker, Kevin G. Kim, Kenneth L. Fan, and Karen K. Evans

32 Advanced Plastic Surgical Reconstruction Options in the Lower Extremity 467
John M. Felder and Joon Pio Hong

33 Partial Foot Amputations: Technique and Outcomes 521
Jayson N. Atves, Ali Rahnama, and Tiffany K. Hoh

34 Below Knee Amputation: Techniques to Improve Rehabilitation, Pain Management, and Function 545
Tanvee Singh, Kevin G. Kim, Grant M. Kleiber, and Christopher E. Attinger

35 Complications and Revision Surgery in Complex Limb Salvage 559
Ali Rahnama, Noman Siddiqui, and Janet D. Conway

36 Establishing and Running an Amputee Support Group to Empower Your Patients 587
Firras Garada and Holly Shan

37 Analyzing the Population Dynamics of Limb Salvage 591
Kevin G. Kim, Paige K. Dekker, and Kenneth L. Fan

38 DLS Innovations: Landmark Publications and Innovations from Our Team 603
Samuel S. Huffman, Christopher E. Attinger, John S. Steinberg, Karen K. Evans, and Kenneth L. Fan

Index 615

1 Building It from Scratch: The Team Approach to Functional Diabetic Limb Salvage

Areeg A. Abu El Hawa, Kevin G. Kim, John S. Steinberg, Katherine Hubley, Cameron M. Akbari, and Christopher E. Attinger

Background

Diabetic foot ulcers (DFUs) are a major concern in health care systems. The World Health Organization (WHO) estimates that roughly 8.5% of the global adult population has diabetes, of which one-in-four will develop a DFU within their lifetime [1]. The chronically wounded patient consistently reports lower quality of life, worse physical functioning, and higher levels of pain. The 5-year mortality rate for the diabetic with a foot ulcer is reported to be as high as 43–55%, with rates jumping to 80% after progression to major lower extremity amputation [2, 3]. This rate is concerning, considering that approximately 23% of new DFUs will ultimately result in a lower extremity amputation.[1].

When faced with such sobering statistics, it is essential to treat patients with aggressive wound care to prevent major amputation. Unfortunately, this often proves to be difficult, which may be attributable to several factors. For example, wound care continues to lack standardization, despite the publication of strategies and evidence intended to improve patient outcomes. To illustrate, 70% of chronic leg ulcers have an etiology with a venous component, for which the gold standard of treatment is compressive therapy. Despite these recommendations, only 17% of venous leg ulcers receive compression therapy in the USA [4]. Furthermore, additional reports have shown that diagnostic examinations were only performed in 51% of wounded patients and a diabetic assessment in only 34% of patients with foot ulcers [5].

To optimize wound care treatment and improve patient outcomes, various care models have been proposed, each with their own set of advantages and disadvantages (Fig. 1.1). Within these models, several collaborative approaches can be pursued (Fig. 1.2). The multidisciplinary care team (MDT) model has established a position internationally as the gold standard of treatment for DFU). The MDT model can achieve its highest beneficial potential in treating DFU when utilized within a tertiary referral wound care center housed within an academic medical center.

A. A. Abu El Hawa · K. G. Kim · K. Hubley
Department of Plastic Surgery, MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: aaa495@georgetown.edu; kgk31@rwjms.rutgers.edu

J. S. Steinberg · C. E. Attinger (✉)
Department of Plastic Surgery, Georgetown University School of Medicine and MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: john.steinberg@medstar.net; christopher.attinger@medstar.net

C. M. Akbari
Department of Vascular Surgery, MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: cameron.akbari@medstar.net

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_1

	Advantages	Disadvantages
Private-Practice	Convenience Unintimidating environment	Other practice interests Limited wound-specific resources Outsource for ancillary services Limited communication with other specialists
Stand-Alone Center	Convenience Efficient delivery of care	Outsource for ancillary services Barriers to communication among specialists
Hospital Based	Full range of ancillary services available Shared EMR Continuity between clinic, OR, inpatient	Difficult access Intimidating environment
Academic Hospital Based	Same as above Research and innovation focused	Same as above

Fig. 1.1 Wound center models. (Reproduced from Kim et al. 2016)

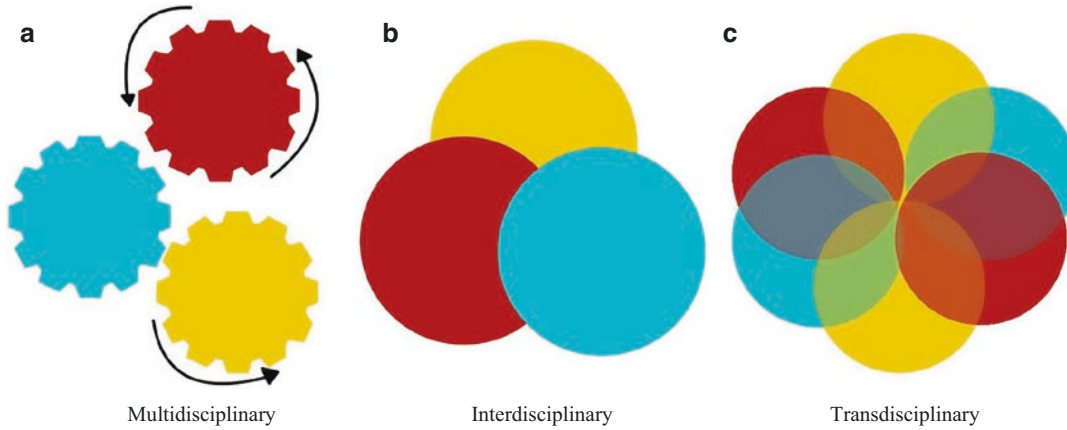


Fig. 1.2 Team working models (**a**) Multidisciplinary care involves various specialties working together as a unit with clearly distinct roles. Information between team members is shared. (**b**) Interdisciplinary care expands upon multidisciplinary care but emphasizes collaborative communication. The roles of team members can extend beyond the confines of their discipline. (**c**) A transdisciplinary model involves sharing of roles across disciplinary boundaries. Roles and responsibilities across the transdisciplinary model are blurred (Attinger et al.; MacRae et al.; Seidu et al.)

Successful implementation of a MDT has led to a greater than 50% improvement in outcomes by reducing both amputation rates and wound related complications [6].

Despite the clear advantages of a MDT), its implementation within an academic institution remains challenging and requires thorough preparation. As such, an organizational framework for the launch of a multidisciplinary diabetic limb salvage team is warranted. Development of such a model will be the focus of this chapter.

The Multidisciplinary Team

Given the complexities of multimodality treatment for DFU), no single professional can possess the knowledge repertoire necessary to make all treatment decisions for any single patient. Recognition of this limitation can be traced back to the turn of the twentieth century. Maurice J. Lewi, MD (1857–1957), founder of the oldest college of podiatric medicine, was vocal on the

need for specialized diabetic foot care and the role of chiropodists as allies in providing care. In agreement was Elliott P. Joslin, MD (1869–1962), whose efforts paved the way for the introduction of the first hospital foot clinic: The New England Deaconess Hospital established in 1928. The multi-dimensional burden of the diabetic foot was beginning to be recognized. Joslin believed that a team approach to foot care, infection management, surgical care, exercise, and nutritional therapy could remedy complications that arose secondary to the diabetic foot. The multidisciplinary team approach to diabetic limb salvage continued to evolve and as early as the mid-1990s, it was recognized that the introduction of these teams, both in Europe and the USA, could reduce the development and progression of diabetic foot ulcers [7].

Benefits of a Multidisciplinary Team Approach: A Global Perspective

In recognition of the complex care needs of the diabetic patient, a multidisciplinary team approach has emerged as an essential component of evidence based chronic wound management. Implementation of multidisciplinary in-hospital teams is globally recognized as a benefit to patients. Although management guidelines for diabetic foot ulcers differ internationally, a multidisciplinary team approach is consistently recommended. Professional organizations that have recommended a team approach include:

- **USA**: American College of Foot and Ankle Surgeons, Association for the Advancement of Wound Care (AAWC), American Diabetes Association [8–10]
- **Europe**: National Institute for Health Care Excellence (NICE), Scottish Intercollegiate Guidelines Network (SIGN), International Diabetes Federation, the Association of British Clinical Diabetologist, and the Primary Care Diabetes Society [11–13]
- **Canada**: Registered Nurses' Association of Ontario (RNAO), Canadian Diabetes Association [14, 15]
- **Australia:** National Health and Medical Research Council (NHMR) [16]

Results of this approach has led to significantly improved clinical outcomes. Studies have reported higher levels of patient satisfaction in institutions that have adopted a multidisciplinary team approach [17]. A comparison of diabetic patients with ulcers in a multidisciplinary teaching hospital setting with those treated in a traditional setting showed a significant improvement in scores pertaining to health-related quality of life [18]. Team interventions in the care of chronic wounds can also lessen the financial burden experienced by the patient. Studies have shown that by reducing clinician time, consolidating services, and the potential for downstream revenue production a multidisciplinary team approach reduces the cost of care [6].

Evidence consistently shows that a MDT approach improves wound healing rates and reduces the rate of amputations, the most feared complication of diabetic foot ulcers. Krishnan et al. reported a 70% and 82% reduction of total and major amputation, respectively, following introduction of a multidisciplinary approach in a hospital-based wound care center in the UK [19]. A significant reduction in major amputations was also associated with a multidisciplinary diabetic foot care team at the Dokuz Eylul University in Turkey [20].

Composition of the Team

Diabetic foot ulcers often arise secondary to a myriad of problems, necessitating management spanning across several disciplines. The strength of a multidisciplinary approach to functional diabetic limb salvage lies within the combined insight of several professions all working toward the overarching goal of improving care and outcomes, specifically for this patient population. The team should consist of healthcare professionals with skills and competencies that reflect the holistic management required for DFU treatment. To achieve functional diabetic limb salvage, the MDT should consist of both a core and

peripheral group of specialists. Although the composition varies between institutions, the core group of specialists often consists of plastic and reconstructive, vascular, and podiatric/orthopedic surgery. The core team should work closely with a peripheral group of specialists which can include infectious disease, internal medicine, rheumatology, hyperbarists, general surgery, wound nurses, nurse practitioners, physician assistants, dieticians, and other essential personnel. A MDT comprised of the aforementioned specialties ensures that each patient receives individualized care tailored to his or her unique medical situation based upon input from all directions; ownership of the patient is disseminated among all team members.

The 1995 definition of multidisciplinary teams includes the concept of a "gatekeeper" [21]. This specialist, a physician within a core specialty, will serve to champion communication between members of the multidisciplinary care team, pose innovative ideas, and serve as the overarching champion fostering collaboration between the team's many members. Additionally, this physician assumes the responsibility of inviting other disciplines into the team and ensuring growth of the MDT program in its home institution. Their commitment is pivotal to the overall success of the MDT program. Without a dedicated pioneering champion, efforts to build a program may be futile; teams in which the team leader lacks a personal commitment struggle to cope and manage difficult situations [22]. While a single member should champion efforts, all team members should be fully committed to the overarching goal and mission of the program. The specifics regarding the roles of individual team members are further described below (Fig. 1.3).

Role of Team Members in Functional Diabetic Limb Salvage:

Plastic and Reconstructive Surgery: Conventional wound healing modalities are often not sufficient to achieve healing by secondary intention for DFUs. In these situations, the reconstructive surgeon is often tasked with the challenge of soft tissue reconstruction, employing free tissue transfer, advancement flaps, or skin grafting.

Podiatric/Orthopedic Surgery / Podiatrist: The expertise of the podiatrist or orthopedic surgeon centers on foot-related risk factors exacerbating wound development or progression, such as peripheral neuropathy, tendon imbalance, and damaged bony architecture. Apart from utilizing local wound care modalities, podiatrists provide treatments to address lower extremity biomechanics, such as total contact casts and other offloading devices. Even with adequate wound healing, DFU) recurrence is common, with roughly 40% of patients having a recurrence within 1 year of ulcer healing [23]. Through expert identification and management of the high-risk diabetic foot, the podiatric and orthopedic specialists can potentially circumvent the issue of recurrence. Those trained in foot and ankle surgery can employ lower extremity skeletal reconstruction, contributing heavily to ambulatory limb salvage, especially if more proximal extremity reconstruction is required.

Vascular Surgery: Diabetic patients are at significantly higher risk for developing a range of both macro- and microvascular complication. There is a reciprocal risk relationship between DM and PAD with PAD being present in up to 30% of diabetics, contributing to both ulceration and failed wound healing in at least one-third of DFU [24, 25]. As such, the role of the vascular surgeon to promote ulcer healing is an essential component of multidisciplinary wound care. Apart from performing and interpreting noninvasive and open vascular studies, bypass and endovascular interventions, the vascular specialist is also able to perform wound debridement, forefoot, guillotine, and major limb amputations [24].

Endocrinologist/Diabetologist: The rising prevalence of diabetes necessitates the involvement of specialists who are well versed in the care of the diabetic patient requiring complex insulin regimens and newer therapies. Within the MDT, diabetes consultants should lead the role of providing comprehensive and long-term management of the patient. Poor glycemic control not

Member	Contribution
Core-Team	
Plastic Surgeon	Soft tissue reconstruction
	Wound coverage
Vascular Surgeon	Vascular assessment
	Open and endovascular Intervention
Podiatric Surgeon	Wound care and diabetic foot risk assessment
/ Podiatrist	Surgical and Biomechanical Management
Peripheral-Team	
Orthopedic Surgeon	Lower extremity skeletal reconstruction
Infectious Disease Specialist	Medical management of infections
Endocrinologist/Diabetologist	Glucose control
Internal Medicine	Management of comorbid conditions (i.e chronic kidney disease, autoimmune conditions etc.)
Hyperbarist	Hyperbaric oxygen therapy
Nutritionist	Nutritional counseling and supplementation to optimize healing
Physical Therapist	Mobility training
	Rehabilitation
Wound Nurse	Wound Care
	Patient education
Medical Assistant	Casting and Dressing application
Nurse Practitioner/Physician	Patient education
Assistant	Perioperative care
	Wound care
Orthotist/Prosthetist	Orthotics
	Prosthetics
Administrative Staff	Clinic and surgery scheduling
Administrator	Human resource management
	Finance Management
	Training of administrative staff

Fig. 1.3 Members of a multidisciplinary wound care team. (Adapted from Kim et al. [6]; Kim et al. (2016); Attinger et al.)

only increases postoperative complications in the surgical DFU patient, but also contributes to delayed wound healing and increases risk of infection [26]. It is therefore imperative to achieve and maintain adequate plasma glucose control during both the operative and wound management period.

Infectious Disease: The diabetic patient may require chronic management of foot infections as up to 30% of infections recur, especially in those with underlying osteomyelitis [27]. The infectious disease specialist offers invaluable expertise in managing infections that often cooccur with DFU. Their expertise on current guidelines for microorganism management of DFUs is essential when empiric antibiotics are required for timely limb salvage and culture and sensitivity results cannot be reasonably obtained. Further, when the patient is not a surgical candidate, infectious disease plays a pivotal role by providing prolonged or intermittent suppressive antibiotic therapy to augment wound healing.

General Surgery: General surgeons that are a part of the diabetic limb salvage MDT should not only be skilled in acute wound management but also display competence in chronic wound healing. The general surgeon experienced in wound management can provide aggressive surgical debridement and lower extremity amputations when necessary.

Other Essential Personnel: Care for the wounded diabetic is complicated and requires additional personnel to achieve optimal outcomes. A prosthetist can modify footwear to aid in healing an ulcer. Their specific role is further detailed in Chap. 25. Hyperbarists offer adjunctive hyperbaric oxygen therapy, which has shown to assist with wound healing in approximately 10–15% of patients [28]. Given that wound care is both time and labor intensive, the wound nurse is

essential in providing multi-dimensional care, assisting in care coordination, and offering wound care education. Similarly, nurse practitioners and physician assistants can be involved in wound care, discharge planning, postoperative care, and patient education. The nutritionist/dietician possesses expertise that can ally the efforts of the diabetologist in preventing abnormal electrolyte excursions and optimizing nutritional status by providing education on adequate nutrition [29].

Wound Management Pathway: Multidisciplinary Framework

Immediately following the identification of a wound, the patient must be referred to the wound care team either through an outpatient clinic or inpatient consultation, depending on the severity of the wound. This first step is heavily reliant on a well-established referral system between providers (Fig. 1.4). In the inpatient setting, wound care service is initiated immediately following consultation by another provider.

Those being referred via an outpatient setting will arrange an appointment to be seen in the wound care center. It is recommended that the initial visit be with a discipline comprising the core wound care team, such as podiatric, plastic, or vascular surgery, to determine the acute severity of the wound. This ensures that examination of the DFU and appropriate therapeutic process are not delayed. Regardless of setting, a DFU should be evaluated and treated accordingly. The initial assessment is followed by further examination; wound measurements are recorded, biomechanical abnormalities are identified, and vasculature is assessed. This is followed by an extensive discussion with the patient to (1) identify factors that can contribute to wound propagation, (2) elucidate patient expectations, and (3) establish shared decision-making necessary for optimal care. Once an extensive history and wound profile are determined, core team members should meet and discuss whether the patient's presentation warrants involvement from peripheral team members. For example, a patient admitted to the inpatient service with poor glycemic control and osteomyelitis will warrant consultation with both an endocrinologist and infectious disease.

Based on the needs of the patient, an individualized care of plan is created and executed with the ultimate goal of wound healing. Once the wound is healed, the patient is recommended to continue ongoing diabetic foot care at intervals of 1–3 months by a podiatrist within the wound care center to assess for any risk of recurrence. In the event of recurrence, the patient will have an already established team of care knowledgeable on the history of their condition and ready to rigorously address their wound.

Pragmatics to Delivery: Ingredients for Success

Although ideal, the implementation of a multidisciplinary wound care team may be hindered by many factors. For example, patients may have limited education on the care required to treat their DFU and may not appreciate the value in seeking out these centers, resulting in a reluctancy to travel to a distant academic medical center. Insurance plans may also restrict access to specialists by requiring preapproved referrals. These factors combined can manifest as delays in presentation, leading to poor clinical outcomes. Unclear referral pathways may confuse both patients and providers on whom to see for wound care. Wound centers offer a variety of services to provide optimal care for the diabetic patient suffering from a lower extremity wound. Unfortunately, despite the clear benefits, a functional gap exists regarding the establishment of an efficient MDT. In the following paragraphs, pragmatics of service delivery will be discussed (Fig. 1.4).

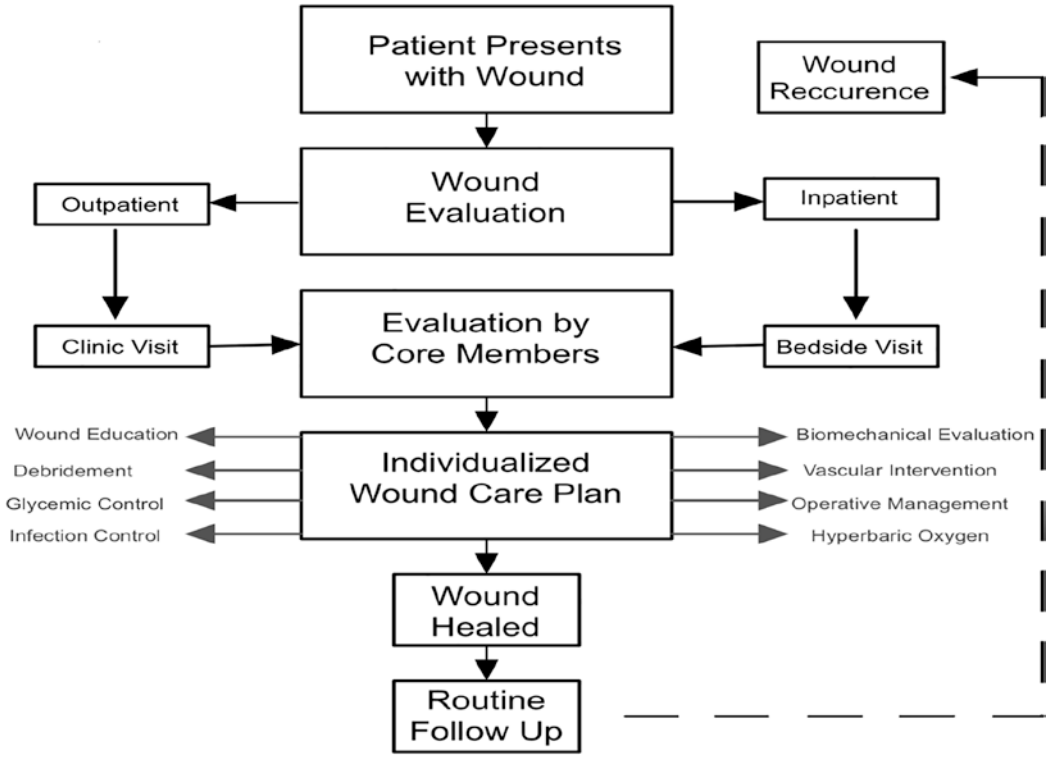


Fig. 1.4 Multidisciplinary wound management framework, which begins with patient referral to wound service, followed by wound evaluation by core specialist, subsequent development of individualized wound care plan that is implemented to achieve wound healing

Identifying the Patient with Multidisciplinary Needs

While the concept of a multidisciplinary approach to DFU healing may seem simple in theory, the delivery of such is complex. It relies on the recognition of the multidisciplinary needs of the DFU patient by a champion physician possessing the leadership qualities to build such a service. In an ideal model this provider, upon identification of a diabetic foot problem, should transfer wound care responsibility off to a multidisciplinary care team within 24 h of presentation [30]. An additional layer of complexity in managing DFU is added when considering comorbid conditions that adversely affect wound healing. In an ideal team approach, the professional will be required to have a broad understanding of the services offered by different personnel. It is imperative that personnel understand the services offered by different professions and are aware of which patient will benefit from them.

Location

Optimal care is heavily reliant on the structure of the MDT which is primarily geographically dependent [5]. The optimal environment for a multidisciplinary team is colocation within a single location, often within a tertiary referral center housed within an academic institution. This model allows for the ability to coordinate inpatient services, diagnostic studies, complex treatment options, and close monitoring. Colocation of facilities readily provides access to team members and communication, both of which are vital to the success of a MDT.

A shared infrastructure facilitates seamless care from either outpatient clinic or inpatient admission to the operative room, postoperative stay, and discharge. Wound care centers housed within an academic hospital often have dedicated inpatient floors with nurses who are skilled in the postoperative needs of the wound patient. Seeing

as the majority of patients with DFU will likely undergo surgery, their postoperative admission within an institution experienced in the care of the chronically wounded patient will undoubtedly be a benefit to the patient [31]. Colocation within a hospital-based center may also provide a scholarly atmosphere that encourages advances in wound care through research. These centers often have infrastructure that enables research, such as internal institutional review boards, that are not easily accessible in other settings.

A common infrastructure not only enhances efficiency of care but also provides logistical benefits to the patient, which are particularly valuable when timely treatment is necessary. When care is provided at a single location, the patient can attend several appointments in one day, reducing transportation costs, time taken from work, and overall number of visits [32]. Colocation also increases timely access to multiple specialties The diabetic patient admitted with an infected or ischemic lower extremity wound often requires a series of surgical intervention, all which can be addressed during a single admission, as opposed to having to be referred to an outside institution. A study performed by Maximillian et al. demonstrated the importance of centralization of wound treatment through a patient's perspective. Their work showed that the adoption of a MDT within a shared facility not only improved patient outcomes but also reduced the cost of treatment [33].

Pearls for Practice: Wound Care in the Rural Setting

Although ideal, colocation of a MDT within an academic institution is not always feasible. Limited access to comprehensive care health resources coupled with a lack of diverse medical specialties complicates the provision of team oriented wound care. Patients with diabetic foot wounds living in rural communities suffer from poorer outcomes [34, 35]. Innovative solutions to widen access to multidisciplinary teams in rural settings have been proposed. The Reducing Amputation in People with Diabetes (RAPID) Study was implemented in the NHS Highlands, UK. By utilizing innovative technology, MacRury et al. established a care pathway in this region allowing for early triage and remote review of diabetic foot problems with a multidisciplinary care team [36]. In this study, two community podiatrists evaluated patients either at their home or in a local clinic. Using a tablet device, the podiatrists were able to capture images and remotely access a clinical database. Face-to-face consultation by community podiatrist with members of a multidisciplinary diabetic foot care team was enabled by an Omnirouter mini™ device, which aided in connectivity. The RAPID team was able to provide patients with timely decision-making around hospital admissions, provide a MDT care plan and wound care education [36].

Team Communication

DFUs presenting with the threat of limb amputation need to be treated swiftly and efficiently. Central to the provision of such care is frequent, continuous, and collaborative communication. A working MDT bears its value from the unique expertise of individuals from varying medical disciplines; having so many different individuals at play requires clarity of roles and responsibilities. Establishing a communications framework that supports interactive participation of key team members at regular frequencies is imperative. Gaining consensus on the responsibilities of the team and meetings aims is required prior to organizing MDT meetings. This should be carried out by a team leader, a member who champions initiatives and is integral in maintaining support for the meetings. The role of this "champion" is especially important during the initial stages of a team's formation. Examples of a potential framework of meetings are described below.

Daily discussions between core team members, residents, and medical students regarding admitted diabetic patient to allow updates and modifications for the plan of care. In addition to the members above, nurses, medical assistants, and administrative staff participate in weekly interdisciplinary problem solving and wound and department grand rounds. These meetings serve to improve the type of care provided by the team and address factors that may hinder the success

of the MDT. Members also participate in monthly department morbidity and mortality conference. Factors that can improve communication:

- **Electronic Medical Record (EMR):** A shared EMR offers easy access to all diagnostic results, photo-documentation, operative reports, and clinical assessments.
- **Set Meeting Times:** Having set times to meet among specialists within the MDT is essential as members are less likely to attend meetings without protected time [37]. This also avoids confusions and facilitates sustainability of the MDT.
- **Personal Commitment:** The most central component to successful communication is possessing a shared purpose and willingness to address the task at hand.

Barriers to Communication

Although many health care professionals claim to work in the best interests of a team, studies have demonstrated that individuals may work autonomously [38]. Other barriers to a collaborative team environment may include perceived loss of autonomy, unawareness of the services of transdisciplinary colleagues, and distrust in decisions of others. Communications and collaboration barriers existing among the clinicals staff can jeopardize efforts to improve health care safety and quality care.

Support from Above

The success of a multidisciplinary care team is reliant on the hospital administration's ability to provide the infrastructure for the development and sustainability of a wound care center. A committee comprised of leaders from team members respective institution facilitates administrative coordination for care organization, resource allocation, and data collection.

Although administrators may be initially hesitant to take on a seemingly financially and resource demanding endeavor, the cost benefits and improved patient outcomes largely recoup, and exceed, any losses from initial investments.

Patient Centered Care and Role of the Patient

The driving force of any decision made by the MDT reflects the patients' needs and preferences. In partnership with core members of the MDT, the patient should be heard and be able to make informed decisions about their care. Having a DFU may be overwhelming for many patients and easing the process of care is necessary. The patient should be assigned a contact personnel who will simplify the pathway of care, offer the patient information about their treatment plan, elucidate their expectations, communicate clinical information, and support them through their wound care. Although any member of the team can fulfill this role, it has been suggested that a clinical nurse specialist is the preferred team member to carry out this duty and represent the patient's views in meetings [37].

Adherence to treatment plays an important role in the clinical outcome of DFU. Wound centers with a focus on multidisciplinary care have been shown to promote patient adherence to treatment recommendations [39, 40]. Patients who do not follow treatment recommendations face significantly worse outcomes than those who do. This should guide clinical practice to identify patients who are at nonadherent and adopt strategies aimed at improving patient adherence.

Conclusion

The implementation of a multidisciplinary team approach to diabetic limb salvage is complex and difficult; however, when successfully initiated in an academic hospital-based wound care center it can significantly improve patient outcomes. Multidisciplinary teams possess the diversity of skills knowledge and expertise necessary to treat the complex diabetic foot ulcer. In the chapters to follow we will attempt to highlight some of the

essential features within a multidisciplinary team that were discussed in this chapter.

Financial Disclosure Statement The authors have no inancial disclosures, commercial associations, or any other conditions posing a conflict of interest to report.

References

1. Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. JAMA. 2005;293:217.
2. Robbins JM, Strauss G, Aron D, Long J, Kuba J, Kaplan Y. Mortality rates and diabetic foot ulcers: is it time to communicate mortality risk to patients with diabetic foot ulceration? J Am Podiatr Med Assoc. 2008;98:489.
3. Oh TS, Lee HS, Hong JP. Diabetic foot reconstruction using free flaps increases 5-year-survival rate. J Plast Reconstr Aesthet Surg. 2013;66:243.
4. Fife CE, Carter MJ, Walker D. Why is it so hard to do the right thing in wound care? Wound Repair Regen. 2010;18:154.
5. Gottrup F, Holstein P, Jørgensen B, Lohmann M, Karlsmark T. A new concept of a multidisciplinary wound healing center and a national expert function of wound healing. Arch Surg. 2001;136:765–72.
6. Kim PJ, Evans KK, Steinberg JS, Pollard ME, Attinger CE. Critical elements to building an effective wound care center. J Vasc Surg. 2013;57:1703–9. https://doi.org/10.1016/j.jvs.2012.11.112.
7. Sanders LJ, Robbins JM, Edmonds ME. History of the team approach to amputation prevention: pioneers and milestones. J Vasc Surg. 2010;52:3S–16S. https://doi.org/10.1016/j.jvs.2010.06.002.
8. Frykberg RG, Zgonis T, Armstrong DG, Driver VR, Giurini JM, Kravitz SR, et al. Diabetic foot disorders: a clinical practice guideline (2006 revision). J Foot Ankle Surg. 2006;45:S1.
9. American Diabetes Association. Standard medical care in diabetes. Diabetes Care. 2018;41(1):S13–S27. https://doi.org/10.2337/dc18-S002.
10. Moore Z, Butcher G, Corbett LQ, McGuiness W, Snyder RJ, Van Acker K. Managing wounds as a team. J Wound Care. 2014;23:S1–38.
11. Moulton C. Putting feet first. Nurs Older People. 2012;24:9.
12. NICE clinical guideline 119. Diabetic foot problems. Inpatient management of diabetic foot problems Diabetic foot problems. 2011. www.nice.org.uk/guidance/CG119.
13. Scottish Intercollegiate Guidelines Network. SIGN 116. Management of diabetes: a national clinical guideline. SIGN 2017.
14. RNAO. Risk assessment & prevention of pressure ulcers. Progr Manga. 2005.
15. The Diabetes Canada Clinical Practice Guidelines Committee. Clinical practice guidelines for the prevention and management of diabetes in Canada. Can J Diabetes. 2018.
16. NHMRC. National evidence-based guideline on prevention, identification and management of foot complications in diabetes (part of the guidelines on management of type 2 diabetes). Natl Health Med Res Counc. 2011.
17. Mickan SM. Evaluating the effectiveness of health care teams. Aust Health Rev. 2005;29:211.
18. Rerkasem K, Kosachunhanun N, Tongprasert S, Guntawongwan K. A multidisciplinary diabetic foot protocol at Chiang Mai university hospital: cost and quality of life. Int J Low Extrem Wounds. 2009;8:153.
19. Krishnan S, Nash F, Baker N, Fowler D, Rayman G. Reduction in diabetic amputations over 11 years in a defined U.K. population: benefits of multidisciplinary team work and continuous prospective audit. Diabetes Care. 2008;31:99.
20. Yesil S, Akinci B, Bayraktar F, Havitcioglu H, Karabay O, Yapar N, et al. Reduction of major amputations after starting a multidisciplinary diabetic foot care team: single centre experience from Turkey. Exp Clin Endocrinol Diabetes. 2009;117:345.
21. MacRae N, Dyer J. Collaborative teaching models for health professionals. Occup Ther Health Care. 2005;19:93–103.
22. Wilson V, Pirrie A. Indicators of good practice spotlights 2000;1–4.
23. Armstrong DG, Boulton AJM, Bus SA. Diabetic foot ulcers and their recurrence. N Engl J Med. 2017;376:2367–75.
24. Rogers LC, Andros G, Caporusso J, Harkless LB, Mills JL, Armstrong DG. Toe and flow: Essential components and structure of the amputation prevention team. J Vasc Surg. 2010;52:23S–7S. https://doi.org/10.1016/j.jvs.2010.06.004.
25. Thiruvoipati T. Peripheral artery disease in patients with diabetes: epidemiology, mechanisms, and outcomes. World J Diabetes. 2015;6:961.
26. Alfonso AR, Kantar RS, Ramly EP, Daar DA, Rifkin WJ, Levine JP, et al. Diabetes is associated with an increased risk of wound complications and readmission in patients with surgically managed pressure ulcers. Wound Repair Regen. 2019;27:249.
27. Lipsky BA. A report from the international consensus on diagnosing and treating the infected diabetic foot. Diabetes Metab Res Rev. 2004;20:S68.
28. Attinger CE, Hoang H, Steinberg J, Couch K, Hubley K, Winger L, et al. How to make a hospital-based wound center financially viable: The Georgetown University Hospital model. Gynecol Oncol. 2008;111:S92–7. https://doi.org/10.1016/j.ygyno.2008.07.044.
29. McMurray SD, Johnson G, Davis S, McDougall K. Diabetes education and care management significantly improve patient outcomes in the dialysis unit. Am J Kidney Dis. 2002;40:566.
30. McIntosh A, Peters J, Young R, Hutchinson A., Chiverton R, Clarkson S, et al. Clinical guidelines for

Type 2 Diabetes: prevention and management of foot problems (Revised version). Management; 2003.
31. Gottrup F. A specialized wound-healing center concept: importance of a multidisciplinary department structure and surgical treatment facilities in the treatment of chronic wounds. Am J Surg. 2004;187:S38–43.
32. Larsson J, Stenström A, Apelqvist J, Agardh CD. Decreasing incidence of major amputation in diabetic patients: a consequence of a multidisciplinary foot care team approach? Diabet Med. 1995;12:770.
33. Joret MO, Osman K, Dean A, Cao C, van der Werf B, Bhamidipaty V. Multidisciplinary clinics reduce treatment costs and improve patient outcomes in diabetic foot disease. J Vasc Surg. 2019;70:806–14. https://doi.org/10.1016/j.jvs.2018.11.032.
34. Sutherland BL, Pecanac K, Bartels CM, Brennan MB. Expect delays: poor connections between rural and urban health systems challenge multidisciplinary care for rural Americans with diabetic foot ulcers. J Foot Ankle Res. 2020;13:1–10.
35. Rose G, Duerksen F, Trepman E, Cheang M, Simonsen JN, Koulack J, et al. Multidisciplinary treatment of diabetic foot ulcers in Canadian Aboriginal and non-Aboriginal people. Foot Ankle Surg. 2008;14:74–81.
36. MacRury S, Stephen K, Main F, Gorman J, Jones S, Macfarlane D. Reducing amputations in people with diabetes (RAPID): evaluation of a new care pathway. Int J Environ Res Public Health. 2018;15:999.
37. Lamb BW, Taylor C, Lamb JN, Strickland SL, Vincent C, Green JSA, et al. Facilitators and barriers to teamworking and patient centeredness in multidisciplinary cancer teams: findings of a national study. Ann Surg Oncol. 2013;20:1408–16.
38. Coles C. Educating the health care team. Patient Educ Couns. 1995;26:239.
39. Bus SA, van Netten JJ. A shift in priority in diabetic foot care and research: 75% of foot ulcers are preventable. Diabetes Metab Res Rev. 2016;32:195.
40. Armstrong DG, Bharara M, White M, Lepow B, Bhatnagar S, Fisher T, et al. The impact and outcomes of establishing an integrated interdisciplinary surgical team to care for the diabetic foot. Diabetes Metab Res Rev. 2012;28:514.

2 Staffing and Day-to-Day Management: The Nuts and Bolts of Running a Wound Care Center

Amara Ellis and Tara Wallace

Page 1: How Clinic Runs	Page 3: Who Does What? Nurse Manager Roles and Responsibilities	Page 5: Why is Co-Management Important? Our Personal Perspectives	Page 7: Staffing Roles: Administrative	Page 9: What Makes for Triage Desk Success	Page 11: Scheduling: Outlook Master Calendar	Page 13: Scheduling: Upcoming Clinic #s	Page 15: Scheduling: Clinical Staff Schedules	Page 17: Associate Engagement
Page 2: CWH/ HBOT Staffing Structure	Page 4: Patient Services Manager Roles and Responsibilities	Page 6: Staffing Roles: Clinical	Page 8: The Triage Desk	10: Scheduling: Clinic Master Calendar	Page 12: Scheduling: Provider and Orthotic/ Prosthetic Coverage Template	Page 14: Scheduling: Plans of the Day	Page 16: Managerial Tracking of Clinic Operations	Page 18: Leadership Philosophies: The Managers' Perspectives

Page 1: How Clinic Runs

Daily Operations, Center for Wound Healing (CWH)

- Open on Weekdays (No Nights, Weekends, or Holidays):
  - Triage Line takes calls from 0800 to 1700.
  - Patient Appointments are booked at 15, 20, or 30-min intervals from 0800 to 1550. Booking intervals are dictated by that Provider's preferred Scheduling Template.
  - Appointment types include New Patient, Post-Operative, or Follow-Up Evaluations.
  - Some Providers also host limited Telehealth (Remote) clinics during the week.
- Staggered Staff Schedules:
  - Earliest associates are scheduled to arrive at 0700; last associates leave at 1730.
  - Registered Nurses (RNs) and Nurse Practitioners (NPs) work 10-hour shifts to ensure the entire clinic day is covered. They have a rotating day off each week.
  - Our Certified Medical Assistants (CMAs) work 8-hour shifts. They stagger start- and end-times to ensure the entire clinic day is covered. First arrival is 0730; last departure is 1700.
- Provider Clinics:
  - We have 10 Exam Rooms and 2 simultaneous clinics running daily.
  - Exam Rooms are split between Providers (5 each).
  - Each clinic is staffed with 1 Attending and/ or NP, 2 RNs, and 2 CMAs.

A. Ellis (✉) · T. Wallace
Center for Wound Healing/Hyperbaric Oxygen Therapy, MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: amara.e.ellis@gunet.georgetown.edu; tara.d.wallace@gunet.georgetown.edu

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*, https://doi.org/10.1007/978-3-031-27725-2_2

  - There is 1 Triage Nurse for the day, 1 on-site Radiology Technician, 1 Clinical Scribe for each Attending, 1 "floating" CMA, and an on-call Orthotist/Prosthetist.
  - We share Wednesday clinics with Vascular Surgery each week (5 Exam Rooms).
- Patient Volumes:
  - Attendings generally see 20–30 patients in AM, 10–15 patients in PM.
  - NPs generally see 10–12 patients in AM, 8–10 patients in PM.

Daily Operations, Hyperbaric Oxygen Therapy (HBOT)

- Hours are Monday–Friday, 0630–1530 (with occasional weekend/inpatient cases).
- Each day is staffed by 1 Covering Attending, 1 Nurse Coordinator, and 2 HBOT Techs (1 of whom is also their Safety Director).
- There are four chambers available, enabling treatment for up to 12 patients per day.
- Authorization for treatments is submitted through each patient's insurance company, who will determine how many total chamber sessions and "dives" for which a patient will be covered.

Attendings/Residents Coverage

- Weekday outpatient clinic visits.
- Daily OR Cases, both inpatient and outpatient cases.
- Inpatient rounds and coordination with other hospital services for ongoing Plans of Care.
- Consultations for other hospital services.

Operating Room (OR)

- Daily OR cases which are published to the team via email and saved in our practice Share Drive.
- These cases involve Attendings, Residents, OR staff, and Observers/Vendors.

Page 2: CWH/HBOT Staffing Structure

Providers	Affiliated
– 2 Plastic Surgeons	– Vascular Surgery
– 2 Podiatric Surgeons	– Infectious Disease
– 2 Outpatient NPs	– Plastic Surgery/Nerve Specialist
– 3 Inpatient NPs	– Radiology Tech (allows for in-clinic X-ray capability)
– 1 Rheumatologist	– Plastics/Podiatric Residents
– 1 Hyperbaric Medicine Specialist	– Physical Medicine and Rehab (Wound Treatment and Lymphedema therapy)
	– Orthotics/Prosthetics Clinics
	– Visiting Nurse Agencies
	– Clinical Scribes
	– Dermatology

Wound Center Staffing (Fig 2.1)

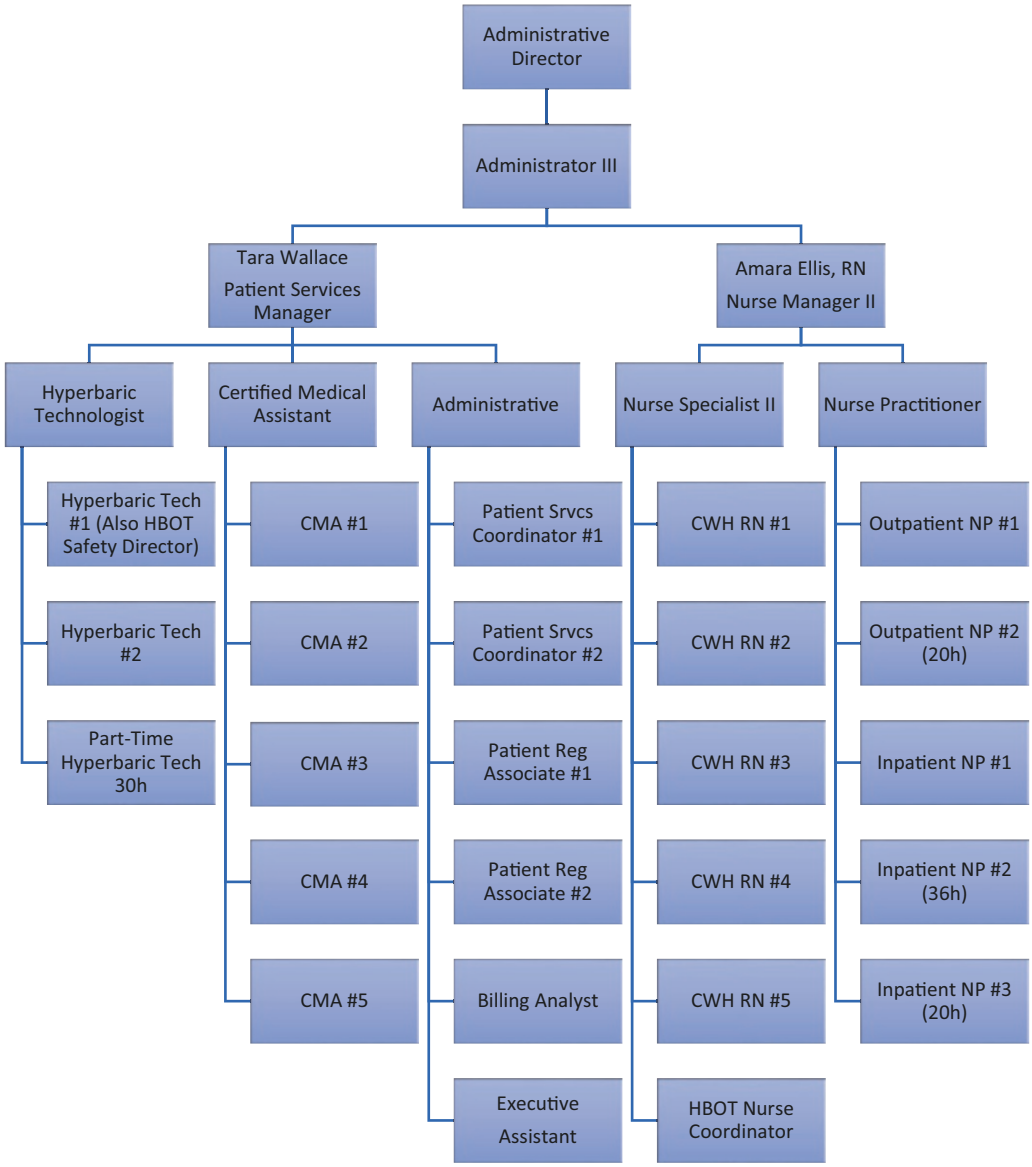


Fig. 2.1 Org Chart

Page 3: Who Does What?

Leadership: Co-Managers

The Clinical Nurse Manager and Patient Services Manager (PSM) work in tandem to oversee the day-to-day Clinical and Administrative operations of the CWH/HBOT. As delineated in the Organizational ("Org") chart in Fig. 2.1, the Nurse Manager's direct reports are all Nursing staff; the PSM's direct reports are the Administrative and Medical Assistant staff.

Nurse Manager Roles and Responsibilities

1. Direct oversight and coordination of day-to-day Clinical operations, staffing, and troubleshooting. Direct oversight and management of the department's RNs and NPs.
2. Updates and maintains clinical staffing and Provider clinic schedules, as well as the CWH Master Calendar. Makes all clinical staffing assignments (daily, weekly, monthly).
3. Performs in simultaneous Nurse Specialist role in Clinic and at the CWH Triage desk, per daily staffing assignment needs. Assists with any other CWH tasks as assigned or indicated.
4. In coordination with the PSM, approves staff leave requests and monitors Time and Attendance. Performs preliminary approval of Nursing/NP staff timesheets in our clocking system, MyTime (PSM does them for Medical Assistant and Administrative staff).
5. In coordination with PSM, site Administrators, Nurse Recruitment, and Human Resources, performs interviewing, hiring, and orientation for new associates, as well as coaching/mentoring or counseling existing staff.
6. Performs monitoring, documentation, clinical education, and follow-up on department Quality and Safety Issues.
   (a) Reports or presents on these issues to Administration as called upon.
   (b) Attends various Hospital/Administrative meetings for these issues as scheduled and/or as appropriate.
   (c) On-site CWH representative and contact point for department audits—Safety, Infection Prevention, Dept of Health, Joint Commission, Magnet, etc.
   (d) Acts, documents, and follows up on all patient-safety related issues with Legal, Risk, Administration, Safety, Patient Advocacy as appropriate.
   (e) Preparation of and follow-through with CWH staff for these audits or issues.
7. Directs and archives weekly all-staff Thursday Meetings. Attends all other Department-related meetings as appropriate.
8. Liaison between CWH/HBOT and Nursing/Hospital Administration.
9. Updates and maintains departmental archives in Shared Drives and Spreadsheets.

Page 4: Patient Services Manager Roles and Responsibilities:

1. Manages the entire patient registration process, ensuring and obtaining complete demographic and insurance information for each patient appointment.
2. Oversees the entire patient scheduling process, including adherence with all established policies, determining, and accurately documenting the appropriate appointment type, referral and/or authorization requirements, and procedure orders.
   (a) Supervises the scheduling of surgical cases, procedures, and admissions for the department, including staff adherence with the appropriate communication of hospital policies and procedures to patients and families.
   (b) Directs implementation and maintenance of approved organization electronic scheduling and billing system, triaging referrals and/or orders to the appropriate physician master scheduling functions. Ensures the performance

of daily schedules edits as necessitated by Provider changes.

3. Manages patient check-in and check-out processes for the department, including patient reception, validation of patient identity, scanning of patient documents to the appropriate system, and resolution of conflicting chart alerts. Ensures immediate updates and resolution for missing or inaccurate information prior to patient arrival, insurance verification, collection, and electronic position of time-of-service payments, and preparation of charge batches.
   (a) Monitors staff adherence to billing procedures and copayment reports on daily reconciliation department activities. Oversees batch management. Monitors encounter form completion and reconciliation and batching process of front- and back-end billing practice, in order to optimize charge capture and Provider reimbursement.
4. Directs referral, pre-certification, and authorization processes to all Managed Care Department requirements and contracts. Ensures managed documentation of referrals and authorizations in the approved organizations' electronic scheduling and billing systems.
5. Ensures medical records meet departmental managed care, Joint Commission, HIPPA, and other regulatory standards.
6. Collaborates with the healthcare team members, patients, Physicians, and Department Administrators to identify and troubleshoot barriers to efficient, quality service.
   (a) Audits staff productivity and utilization of billing systems to include indexing, scanning, phone notes, files in error and other appropriate measures.
7. Actively participates in departmental and hospital meetings, such as Clinical Practice and Managed Care Compliance. Relays relevant information to administrative and clinical staff and provides training and associated documents as appropriate.
8. Implements cross-training schedules between all administrative positions to ensure adequate staff coverage.

Page 5: Why is Co-Management Important? Our Personal Perspectives

In our experience managing the CWH/HBOT, we have come to realize that having two Managers is essential for cohesive and comprehensive coverage of all day-to-day Clinical and Administrative operations. Foremost, the departmental workload and its scope is such that it requires at least two people's involvement, and two differing areas of expertise. The Nurse Manager acts as an available resource, coach, and informational source on the Clinical side, and the Patient Services Manager is able to offer the same on the Administrative side. Managers are also both able to cross-cover any of their associates' duties when needed. Both of us regularly fill in as staff around the clinic - The Nurse Manager as a clinical and Triage nurse, and the Patient Services Manager in any one of our Administrative positions which are vacant on either the short- or long-term.

We have also found that chemistry to the partnership is key - as much as possible, it is important that your Co-Manager possesses shared values, motivations, and goals for the practice and team. We Managers share an office and discuss the minutiae of the day in real time. We can put our heads together to solve any challenges which arise, both small- and big-picture, and we brainstorm together and offer each other different perspectives as to how to best approach these issues. We talk things out and welcome the other's insights and advice - even if we sometimes ignore them, the input is always appreciated. This relationship also allows for the mental security and relief that yours is a shared burden; that someone else appreciates what you are experiencing; that you are supported and championed; and that you are not alone in your responsibilities.

We Managers look at ourselves as a unit. We let all of our associates know, from before hire, that we

work as a team. Our associates and Providers know that we are aligned, and that they can come to either of us at any time for assistance or guidance. They know we approach things in tandem and keep each other updated to the minute, which we feel is necessary for informed and overall management of the team. We have found that the symbiotic nature of this partnership has allowed us to manage our practice effectively and successfully, to recruit, hire, and retain excellent associates, and to ensure continuity and the highest standard of patient care.

Page 6: Staffing Roles: Clinical

This section is meant to provide a consolidated overview of our CWH/HBOT staffing team and their roles in our Clinical setting.

Clinical Associates

Certified Medical Assistants (CWH): Our CMAs see patients with the Providers and Nurses throughout the clinical day. They are responsible for rooming the patients into Exam rooms, getting the patient and exam room prepared for the visit, and removing existing casts and dressings. They also perform the initial patient intake, which includes Vital Signs and general screening for Pain and Fall Risks, Smoking and Allergies, any Specialized Needs, and currently, COVID-related risk factors. The CMAs then conclude the patient visits by cleaning and re-dressing any patient wounds as directed, assisting the patient with their mobility devices, escorting them to where they need to go from there, and then turning over the Exam Rooms for the next visit. The CMAs also coordinate for the retrieval and return of our Sterile Instruments and the ordering and stocking of clinic supplies. They are occasionally called upon to assist with complex Inpatient dressings as well, in order to help expedite patient discharges.

Nurse Specialists (CWH): Trained in a dual Clinical/Triage role.

- **Clinical:** Our RNs see patients with our Providers in the clinic each day, generally alternating each patient assignment (every other exam room). They start the Office Visit note, adding and updating the History of Present Illness (HPI), Review of Systems (ROS), and performing a Medication List Reconciliation. They complete the Wound Assessment documentation and finish with a Visit Summary. This Summary is given to and reviewed with the patient, providing details on all their instructions and ongoing Plan of Care. RNs assist the Providers during the visit with any patient exam or bedside procedural needs. They are also involved in on-site, real-time care coordination for consultations from/referrals to other practices or team members, any diagnostic testing needs, ensuring any orders or updates are sent out to the appropriate parties, and updating anyone involved with the patient's care. Our nurses are also cross-trained with the CMA role and will perform those tasks as well when needed.
- **Triage:** Our nurses assist with anything that comes through our Triage desk, either as their coverage assignment for that day, or in any downtime at the beginning and end of the day. These tasks are all related to patient requests, surgical or admissions planning, patient-related calls and paperwork, and ongoing variable tasks in coordination of patient care and follow-up.

Nurse Practitioners (CWH)

- Outpatient: Our outpatient NPs act in partnership with our Attendings in their clinics and host clinics of their own. They evaluate and examine the patient, assist with or perform any indicated bedside procedures, and recommend and document the Assessment and Plan (A&P) for the patient. They follow up on our specimen results and coordinate with Infectious Disease for any subsequently updated recommendations. They are also cross-trained in the RN, Triage, and CMA roles and will perform those tasks as well when needed.
- Inpatient: Our inpatient NPs work with our Residents and Attendings in ongoing patient

care, monitoring, and discharge coordination from the inpatient side. They round on patients at the bedside and work closely with Case Management for ongoing complex discharge planning and patient follow-up needs. They also compose our Discharge Summaries and stay in constant communication with all of those involved in the patient's care, to ensure streamlining and cohesion to their clinical journey through all systems.

Nurse Coordinator (HBOT): This position is responsible for the safe and effective operation and maintenance of the hyperbaric chambers and related support systems, and oversight of the day-to-day operational activities required to maintain and grow the Hyperbarics Program. Our Nurse Coordinator monitors quality and safety issues and provides nursing care and treatment for incoming patients. They supervise the technicians and assist in specialized clinical and research projects. They also assist in Triage tasks such as insurance authorizations and anything needed in patient follow-up.

Page 7: Staffing Roles: Administrative

This section is meant to provide a consolidated overview of our CWH/HBOT staffing team and their roles in our Administrative setting.

Patient Registration Associates (PRAs): Our two PRAs are responsible for a multitude of tasks at the Front Desk. These associates oversee patient check-in and check-out, insurance verification, and registration updates. Before the patient arrives for their office visit, they verify the appointment type, check eligibility, and contact the patient if a referral is needed. If a patient is within or out of their global period, the correct appointment type is allocated. At check-in, the patient is given a demographic form and asked if any information needs to be updated in our system. The patient's insurance card, ID, and consent to be treated are scanned into their chart at check-in. If the patient's insurance requires a copayment, it is collected before the patient is seated. MedStar also has a virtual appointment verification system called Tavoca, through which patients can cancel their appointments. In the event of cancellation, the PRAs reach out to the patient to reschedule. The Front Desk also scans in new patient paperwork, submits Medical Records Requests, and checks our virtual Administrative Inbox for urgent appointment requests from the clinical staff.

Patient Services Coordinators (PSCs): Though we have two positions with this same title, they encompass completely different roles.

- Patient Services Coordinator (A), sometimes referred to as our Surgical Coordinator, is responsible for booking all inpatient and outpatient surgical procedures for the Providers. When the patient has completed all their pre-surgical requirements, PSC (A) is then tasked with coordinating the surgery booking. If this is an outpatient procedure, PSC (A) is responsible for obtaining authorization for the procedure through the patient's insurance company. For inpatient cases, authorization will already have been obtained and is handled by the inpatient billing team. Once the procedure is authorized, the case is sent to the OR scheduler for posting. PSC (A) will then update the patient's Electronic Medical Record (EMR) and a posting sheet for the Residents, which is located on our practice's Share Drive. Once the surgery has been completed and entered into the surgical billing system, PSC (A) then checks over the submission for errors and makes any needed corrections. When the surgery bills have been committed, a copy is printed and then entered into the patient's EMR for physician billing. PSC (A) is also responsible for communicating with the patient throughout the process of booking their procedure and post-op follow-up appointment and providing instruction and guidance for the day of surgery.
- Patient Services Coordinator (B) is responsible for filtering and navigating all incoming phone calls to our department's Triage line. This direct line is given to all patients in their Visit Summaries, with directions to call if they have any clinical questions or concerns between their appointments. This position is

in partnership with the Triage nurse and involves addressing the patients' needs, directing the calls elsewhere as needed, prioritizing the urgency of the message or request, checking the status of pending outpatient surgery clearances, and coordinating for wound supply orders through the patient's insurance company. PSC (B) either speaks with the Triage Nurse directly throughout the day, or they communicate through the patient's EMR messaging system. PSC (B) is also responsible for collecting and distributing documents from the fax machines, scheduling follow-up appointments for our inpatients on their discharge, and scanning urgent documentation into the EMR system. This position is well-suited to an associate with previous clinical experience in the CWH, as they are often able to address the patients' questions directly without having to route the call elsewhere.

Billing Analyst: Since the CWH is considered an outpatient facility, two bills are issued from each outpatient visit. One is the Physician's charge, and the other is called a Facility Fee, for the usage of the facility and those associated services. It is the responsibility of the Billing Analyst to submit all charges from the Facility Fee to the patient's insurance company. For each patient visit, the Front Desk prints out what is known as a Fee Ticket (Fig. 2.2), which is a list of procedures which may be done in the office. This is completed by the nurse, following the patient's visit. Once the Fee Ticket is completed and turned in, the Billing Analyst will call the patient's insurance company to figure out if Prior Authorization is needed for an outpatient procedure. Once the authorization is either obtained or not needed, the charges are entered into the hospital's billing system. From charge entry a tally is generated, which compares the number of charges with relation to the number of patients seen for the day. A reconciliation spreadsheet is then filled out and submitted to the Outpatient VP of the hospital weekly. This document accounts for missing charges or an abundance of charges vs. the number of patients seen in the clinic. The Billing Analyst is also responsible for the copayment report, which lists the targeted amount vs. the actual amount collected for the day. On the second column of the copayment report, it lists the balances patients have accrued within MedStar and compares it to the total amount collected at that patient's appointment. An outstanding balance sheet is then given to the patient at a subsequent check-in, so the patient is informed of the amount owed. At the end of each business day, once the batches have been closed, the Billing Analyst takes any cash deposits to the Cashier's Office. Other duties include documents scanning, authorization for substitute skin graft materials, code edits, and approvals for single case agreements (Fig. 2.2).

Executive Assistant (EA): The EA acts as our most embedded Provider resource. Their role involves assisting with the needs and requests of all our Attendings and NPs. These tasks are all-encompassing, but include travel coordination, submission and tracking of reimbursements, maintenance and distribution of Provider calendars and the monthly on-call schedules, and meeting coordination. The EA is also responsible for the upkeep of an Excel sheet which details Provider licensing renewals and credentialing updates. The position serves as a backup desk for PSC (A)'s role in scheduling surgeries and submitting the related Provider billing, and other associated CWH-related tasks are substantial. They include, but are not limited to, department key copy and office supplies requests, coordinating staff lunches and potlucks, arranging and execution of staff retreats, and departmental mail distribution. Additionally, our EA coordinates and oversees our monthly Amputee Support Group, which has become an invaluable resource and forum in ongoing support of our patient population.

Hyperbaric Technicians and Safety Director: The Hyperbaric Technician operates the hyperbaric chambers and ensures the safety and close monitoring of the patients throughout their HBOT sessions. They provide instructions and documentation on the details of service and collect data points (e.g., vital signs, blood glucose monitoring, etc.). The Tech is responsible for reporting any abnormal reading or immediate

F95 MedStar Health Date: Appt #: Visit #:
Georgetown University Hospital Patient: Prov: Bill Prov:
The Center For Wound Healing MRN: DOB: Proc:

SVC CODE	MOD	DESCRIPTION	QTY	SVC CODE	MOD	DESCRIPTION	QTY
		** NEW PATIENT **				** FREE SKIN GRAFTS **	
WHC53100004		New Patient Level 1 5-15 pts		WHC25301169		Apligraf per Sq Cm	
WHC53100012		New Patient Level 2 20-35 pts		WHC53101465		Appl Grft Tr/Arm/Lg 1st 25 cm	
WHC53100020		New Patient Level 3 40-60 pts		WHC53101473		Appl Grft Tr/Arm/Lg Add'l 25 cm	
WHC53100038		New Patient Level 4 65-85 pts		WHC53101481		Appl Grft Tr/Arm/Lg 1st 100 cm	
WHC53100046		New Patient Level 5 90+ pts		WHC53101499		Appt Grft Tr/Arm/Lg Add'l 100 cm	
		** ESTABLISHED PATIENT **		WHC53101507		Appl Grft F/N/G/Dig 1st 25 cm	
WHC53100053		Est Patient Level 1 5-15 pts		WHC53101515		Appl Grft F/N/G/Dig Add'l 25 cm	
WHC53100061		Est Patient Level 2 20-35 pts		WHC53101523		Appl Grft F/N/G/Dig 1st 100 cm	
WHC53100079		Est Patient Level 3 40-60 pts		WHC53101531		Appl Grft F/N/G/Dig Add'l 100 cm	
WHC53100087		Est Patient Level 4 65-85 pts		WHC53101580		APPL LC Grft T/A/L 1st 25cm	
WHC53100095		Est Patient Level 5 90+ pts		WHC192306		TISS Grafix PL 16mm 2 sqcm	
		** ACTIVE WOUND CAR,MAN. **		WHC25302134		TISS Grafix 1.5x2cm	
WHC53110227		Selective Debride 20 cm or less		WHC25302142		TISS Grafix 2x3cm	
WHC53110235		Selective Debride Each Additional 20 cm		WHC25302159		TISS Grafix 3x4cm	
WHC53110201		Neg Press Wnd Ther (Vac Ast Drain Coll) Ong Care,Per Sess, Tot Wnd(s) Surf Area<50sq cm		WHC25302167		TISS Grafix 5x5cm	
				WHC191166		GFT Xenogft Porcn Ezderm 3x24	
WHC53110219		Neg Press Wnd Ther (Vac Ast Drain Coll) Ong Care,Per Sess,Tot Wnd(s)Surf Area > 50sq cm				** INCISION & DRAINAGE **	
		** CASTING / STRAPPING **		WHC53100723		I&D Skin Abscess;Simple	
				WHC53101010		I&D Hematoma	
WHC53100921		Appl. of Short Leg Cast(Below knee to toe)		WHC53101028		I&D Post-op Wound Infection	
WHC53100939		Short Leg Cast(Below knee to toes);Walk type		WHC53101036		I&D Bursa Foot	
WHC53100947		Appl. of Short Leg Splint(Calf to foot)		WHC53101424		I&D Below Fascia, Ft Sing Bursal Spc(28002)	
WHC53100954		Strapping; Ankle & Foot		WHC53101432		I&D Below Fascia, Foot, Mul Areas (28003)	
WHC53100384		Appl. of Rigid Total Contact Leg Cast		WHC53101440		Incision Bone Cortex (28005)	
WHC53100798		Strapping; Unna Boot		WHC53101044		Tenotomy, Percut Toe	
WHC53110292		Appl Mult-Layer Comp Sys, leg(below knee) include ankle & foot		WHC53101457		Tenotomy, Percut Toe multiple tendon(28011)	
				WHC53101341		Tarsal or metatarsal bone, except talus	
WHC53110359		Appl Mult-Layer Comp Sys,leg(below knee) include ankle & foot, BiLateral				or calcaneus	
				WHC53101051		Expl Postop Hem,Throm/Inf Diab Training	
		** EXCISION - DEBRIDEMENT **				** INJECTIONS **	
WHC53100624		Debrid, Skin, S. C.		WHC53101093		Inj(s);Single Tendon Sheath/Ligament,	
WHC53100632		Debrid, Skin, Subcu, Tis & Muscle				Aponeurosis	
WHC53100640		Debrid, Skin, Subcu, Tis, Mus & Bone		WHC53101127		Arthro/Aspir/Inj;Intr Jnt/Bursa	
WHC53100681		Debrid, Skin, S.C.; each add'l 20 sq cm		WHC53101143		Inj,Anes Agent;Other Peripheral Nerve/Branch	
WHC53100699		Debid Skin, Subcu. Tis., Musc each additional 20 sq cm				** NAILS **	
				WHC53100764		Debride of nail, Any Metd, 1-5	
WHC53101416		Debrid; Skin, Subcu. Tis., Musc. & Bone; each additional 20 sq cm		WHC53100772		Debride of nail, Any Method, 6 or more	
				WHC53100889		Avulsion of Nail Plate,Partial/Complete, Simple;Single	
WHC53101697		Tangential Biopsy of skin, single lesion					
WHC53101713		Punch Biopsy of skin, single lesion		WHC53100905		Exc Nail Matrixectomy	
WHC53101739		Incisional biopsy of skin, single lesion		WHC53100913		Toenail Wedge	
WHC53101705		Tangntl BX Skin EA Sep/Addl				** HBO RELATED PROCEDURES **	
WHC53101721		Punch BX Skin EA Sep/Addl Les		WHC53110266		HBO2 TX-Per 30 mins.	
WHC53101747		Incisional BX Skin EA Sep/Addl		WHC53110250		Cerumen Removal	
		** DESTRUCTION LESIONS **		WHC53110276		Noninvas Phys Study-Single Lev Bilat	
WHC53100780		Dest. All Benign Les. Exc. Skin Tags 1st Les		WHC53110284		Noninvas Phys Study-Multi Lev Comp Bilat	
WHC53100996		Dest. All Benign Les. Exc. Skin Tags; 2nd - 14 Les. Each				**OTHER**	
				WHC53101200		Removal of Ext. fixator w/o gen anesthesia	
WHC53101333		Dest. (eg, laser surgery, electrosurg (cyrosurg, chemosurg, surgical curettement) of flat wart, molluscum, contagiosum, or milia; up to 14 lesions)		WHC53100749		Removal FB Foot Subcutaneous	
				WHC53101192		Removal of Implant, Superficial	

RN/MA/Tech Signature:_____

Fig. 2.2 Fee ticket

change in the patient's condition to the Attending and Nurse Coordinator. Each accredited Hyperbaric facility also has an on-site Safety Director. The Safety Director is responsible for ensuring the hyperbaric chambers and associated equipment are fully operational, and that the safety guidelines are met daily. Before a patient is permitted inside a chamber, they inspect for and remove any restricted or potentially hazardous materials. The Safety Director also works in collaboration with the Program Director to coordinate all hyperbaric chamber upgrades, modifications, and repairs.

Page 8: The Triage Desk

The CWH Triage desk is an integral operational component of our practice model. This element allows for us to gather and share information, streamline ongoing coordination of patient care, and ensure that our patients' needs are met efficiently and in full. The Triage desk is staffed primarily by our Patient Services Coordinator and the designated Triage RN for that day. There are also backup coverage plans for any associate absences, which involve Triage task designation to various members of our team for that duration.

- **Triage Line:** The CWH Triage line is given to every patient in their Visit Summary at every visit and included in every practice-related communication we send out—to patients, clinical colleagues, referring Providers, etc. Patients (or anyone) are encouraged to call this line if we can assist them in answering any questions, or with anything regarding their clinical needs, with relation to our practice specialty. From 0800 to 1700 this line is answered by either the Patient Services Coordinator or the Triage RN, and the voicemails are checked hourly. Off-hours there is a voicemail directive which reiterates our availability, but which also provides instructions for how to reach the on-call Resident by pager if needed.
- **GUH-CWH Pools:** Triage works out of two electronic Inboxes in our charting system which are designated to and shared by our practice exclusively.
  - **Clinical Pool:** Patient-related requests for action are sent to these Pools at all hours by our own team, by other practices, or by our patients, via our entity's electronic Patient Portal system. The Triage Nurse attends to the task requests and messages in the Clinical inbox throughout the day, updating the notes with details as they go along, and deleting them when the task is complete.
  - **Admin Pool:** Any patient Scheduling requests are sent to the Admin Pool, which is checked on and addressed by our Patient Registration Associates (PRAs) at the Front Desk daily. They will also update these notes as they go along, until the task is completed and the note can be deleted from the Pool.
- **Patient Portal:** Patients are provided with information at each visit as to how to sign up for MedStar's Patient Portal service. This allows them to create an online profile within MedStar from which they can access their medical records, diagnostic imaging and testing reports, appointment information, and laboratory results. They can also use the Portal to send their Provider an "email" communication, which goes directly to that Provider's practice-affiliated Clinical Pool to address. Patients can attach pictures or documents to these messages, and we can Reply to them directly from the Pool. The expectation or Triage is that patients will hear back within 24 h of contacting us, whether via phone call or sending a message to the Pool.

Page 9: What Makes for Triage Desk Success

Staff, Provider, and Patient involvement are the keys to operational success in this aspect of ensuring continued, comprehensive support of our high-risk patient population.

- **Staff:** Much of why our Triage desk is successful is because of our staff's dedicated contributions on the day-to-day. Our on-site team is relatively small (<20 associates), and we stay in constant communication both in-person and electronically throughout the clinic day, via the systems we have established. All our associates are intimately involved in some aspect of the patient's journey through our practice, and thus every member of our team contributes to this desk—by offering insight and updates from the patient's visits or history, by answering the incoming Triage calls to their desks, and by following up on designated Triage-related tasks.
- **Providers:** Our Providers are accessible to our team as resources 24/7. They are diligent about checking their electronic inboxes and returning their messages, they check in personally with the desk to see about any outstanding tasks for which they are needed, and they are at minimum reachable by phone. If you cannot get in touch with one of them, you can absolutely get hold of another. This availability allows us to ensure we are meeting especially the most critically important patient needs in a timely manner and helps to instill a mutually trusting and productive relationship between the Providers and staff, and the Providers and our patients.
- **Patients:** We have been able to cultivate patient buy-in to this desk and to the Portal through a long and consistent history of efficiently and successfully addressing their needs by these routes. We often hear patients say that they call our office first, no matter what their needs, because we are "the ones who pick up" when they call, and because they know at the minimum we can assist them to get in touch with whomever they are trying to reach. Our patients are a high-risk population with multiple and ongoing complex care needs, and it gives them great comfort to know that we are reachable and reliable on the day-to-day.

It is truly not possible to accurately convey the complexity and breadth of our Triage operations. There are so many moving parts, so many variables, and so many people involved, that it would be an incredibly daunting task to try and break it down in a way which could be straightforwardly understood. It is one of the most valuable services that we are able to offer with regard to continuity of patient care, and one of the shining achievements of our practice model.

Page 10: Scheduling

Scheduling coordination is a complex but vital component of our operations. We have several schedules in flux at any given moment, which require constant updating, monitoring, and disseminating. They provide the structural guidelines of our operations and are essential for tracking Provider and staff availability, and in guiding our patient bookings. All of our published calendars and schedules are kept up-to-date by the Nurse Manager and are accessible to our team 24/7 on our practice Share Drive. Any Provider booking template modifications are done electronically by the Patient Services Manager.

Clinic Master Calendar (Fig. 2.3)

This calendar provides an upcoming look at our Provider Clinic Coverage schedules, so that we can see which Provider is available on what date, and where there is alternate coverage if a Provider is out. The Nurse Manager updates and disseminates this schedule to our team at least weekly, and anytime there are changes to Provider coverage. It is posted in every Exam Room and at every workstation to allow for at-a-glance guidance as to how we can book patients in follow-up.

Monday	Tuesday	Wednesday	Thursday	Friday
1/11 ATTINGER AM NICOLE NP PM ATVES BENEDICT	1/12 EVANS ATVES BENEDICT	1/13 ATTINGER AM NICOLE NP PM BENEDICT	1/14 KERRY NP AM/PM STEINBERG AM NICOLE NP PM BENEDICT NO CEA CLINIC/TELE	1/15 STEINBERG AM NO REMOTE PM MOOSE NP
1/18  EVANS ATVES BENEDICT	1/19 EVANS ATVES BENEDICT	1/20 ATTINGER AM NICOLE NP PM (MAX 7 PTS THIS PM) BENEDICT OFF-SITE REMOTE VISITS ONLY	1/21 ATTINGER AM KERRY NP PM STEINBERG BENEDICT CEA TELE 1:40-4:00pm	1/22 MOOSE NP NO STEINBERG
1/25 ATTINGER AM NICOLE NP PM ATVES BENEDICT	1/26 EVANS ATVES BENEDICT	1/27 ATTINGER AM NICOLE NP PM BENEDICT	1/28 STEINBERG KERRY NP AM/PM BENEDICT NO CEA CLINIC/TELE	1/29 STEINBERG AM REMOTE PM NICOLE NP
2/1 ATTINGER AM NICOLE NP PM ATVES BENEDICT	2/2 EVANS ATVES BENEDICT	2/3 ATTINGER AM NICOLE NP PM BENEDICT	2/4 ATTINGER AM KERRY NP PM STEINBERG BENEDICT CEA TELE 1:40-4:00pm	2/5 STEINBERG AM REMOTE PM MOOSE NP
2/8 ATTINGER AM NICOLE NP PM ATVES BENEDICT	2/9 ATVES NICOLE NP BENEDICT NO EVANS	2/10 ATTINGER AM NICOLE NP PM BENEDICT	2/11 ATTINGER AM KERRY NP PM STEINBERG BENEDICT CEA TELE 1:40-4:00pm	2/12 STEINBERG AM REMOTE PM MOOSE NP
2/15 ATTINGER AM NICOLE NP PM ATVES BENEDICT	2/16 EVANS ATVES BENEDICT	2/17 ATTINGER AM NICOLE NP PM BENEDICT	2/18 ATTINGER AM KERRY NP PM STEINBERG BENEDICT CEA TELE 1:40-4:00pm	2/19 STEINBERG AM REMOTE PM MOOSE NP

JAN/FEB 2021

Fig. 2.3 Clinic master calendar

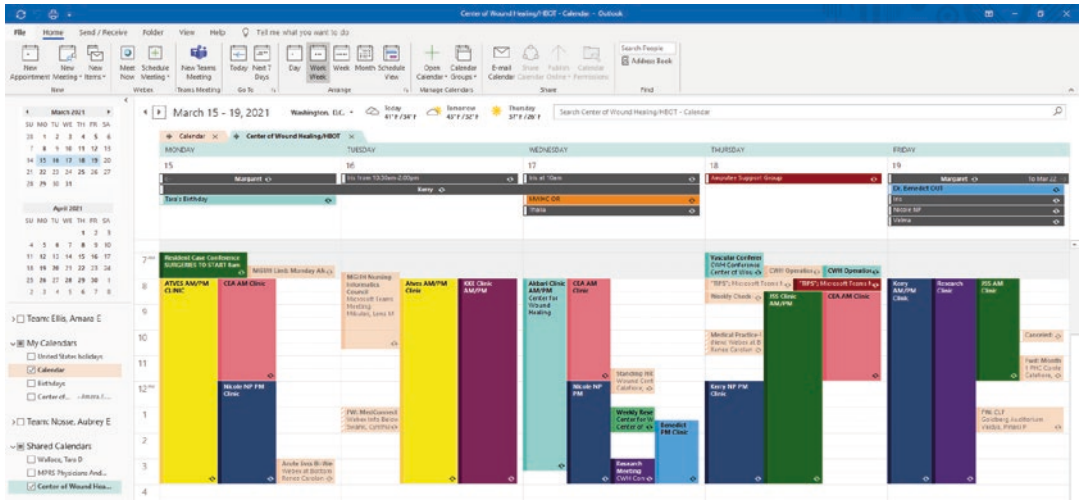


Fig. 2.4 Outlook master calendar

Page 11: Scheduling

Outlook Master Calendar (Fig. 2.4)

This is our shared practice Master Calendar, which our team is all able to access in Microsoft Outlook. It provides a more global overview of Provider coverage plans and clinic breakdowns and includes additional notes for reference. These notes detail staff who are scheduled out, upcoming team or patient-related meetings, shared clinics with other practices, or any anticipated on-site Observers. The Outlook Calendar includes both recurring and one-time events and allows for a look at our clinical operations both historical and upcoming. Managers and varied members of our Administrative staff have editing capability for this calendar, and it is used by the Nurse Manager to guide practice coverage needs in creating the Clinical Staff Schedules.

Page 12: Scheduling

Provider and Orthotic/Prosthetic Coverage Template (Fig. 2.5)

This is another quick-glance reference which lays out our standard, baseline Provider coverage template for the Clinic and OR on the day-to-day. It also includes updated anticipated on-site Orthotic/Prosthetic (Hanger Clinic) associate coverage. This template is available in our Share Drive and posted at the primary workstations around clinic. It is helpful to our associates as a reminder of our Master Template for CWH operations and to see who will be on-call that day for our Orthotic/Prosthetic partners.

Updated Provider Templates as of 1/4/21

	Monday	Tuesday	Wednesday	Thursday	Friday
AM	CEA Clinic	KKE Clinic	CEA Clinic	CEA Clinic	JSS Clinic
	Atves Clinic	Atves Clinic	Akbari Clinic	JSS Clinic	Kerry NP Clinic
	Benedict AM	Benedict		Benedict	
PM	Nicole NP Clinic	KKE Clinic	Nicole NP Clinic	Kerry NP Clinic	JSS Remote/Tele
	Atves Clinic	Atves Clinic	Benedict PM	JSS Clinic	Kerry NP Clinic
		Benedict		Benedict	*(1/4/21, AE)*
				CEA Remote 1:40pm-4:00pm	
OR	JSS/KKE	OR21 CEA AM/PM OR22 CEA AM	KKE	Atves/KKE	OR21 CEA AM/PM OR22 CEA AM/Atves PM (KKE)

Hanger Coverage as of 11/3/20

	Monday	Tuesday	Wednesday	Thursday	Friday
Elisa	8:30-2:30	8:30-2:30	8:30-2:30	8:30-2:30	8:00-5:00
Richard	Fairfax 8-5	MGUH 8-5	MGUH 8-5	Fairfax	MGUH 8-5
CWH	John	x	x	Ben/Charlie (alt)	x

Hanger Schedule for CWH, 2021

Jan 4	John	Jan 7	Charlie
Jan 11	John	Jan 14	Ben
Jan 18	John	Jan 21	Charlie
Jan 25	John	Jan 28	Ben

1.8.21, AE

Fig. 2.5 Provider and orthotic/prosthetic coverage template

Page 13: Scheduling

Upcoming Clinic Numbers (Fig. 2.6)

This is an Internal Document which is published to our Outpatient Team on a once- or twice-weekly basis. One of our nurses will be tasked to do an overview of the upcoming patient numbers on each Providers' schedule, looking ahead about a month forward. The Nurse Manager then does an overview of the numbers and uses a color-coding system to indicate which schedules are full and should be "frozen" from further booking, which schedules are okay to add on for emergencies only, and which schedules are open and available for booking. This schedule also serves as another reference point for upcoming Provider coverage (who is here, who is out, and who is covering alternately). The Nurse Manager sends this out to staff via email and publishes and disseminates color copies for that day to all

AS OF FRIDAY, 1/8/20

- **PLEASE NOTE:**
  - **There is some alternate NP coverage for JSS/CEA clinics in January due to Plastics/Podiatry Resident Interview dates.** ***Please remind the providers!!!***
  - **As of January, Dr. Attinger will ONLY BE DOING TELEHEALTH ON THURSDAYS.**

***CWH Staff – please try to avoid adding on to Red Clinics.** Add-on for emergencies to Yellow.

MON 1/11	TUES 1/12	WED 1/13	THU 1/14	FRI 1/15
CEA CLINIC AM 26 NICOLE NP PM 8 ATVES 27	KKE CLINIC 35 KKE TELE PM 4 ATVES 28	CEA CLINIC AM 28 NICOLE NP PM 4	KERRY NP AM/PM 4 NO CEA CLINIC/TELE JSS CLINIC AM ONLY 20 NICOLE NP PM 0	JSS CLINIC AM 18 NO JSS TELE PM KERRY NP 8
MON 1/18  	**TUES 1/19** KKE CLINIC 13 KKE TELE PM 7 ATVES 28	**WED 1/20** CEA CLINIC AM 28 NICOLE NP PM 4 (MAX 7 PATIENTS)	**THU 1/21** CEA CLINIC AM 25 CEA TELE PM 4 KERRY NP PM 2 JSS CLINIC 33	**FRI 1/22** NO JSS CLINIC/TELE KERRY NP 3
Mon 1/25 CEA CLINIC AM 21 NICOLE NP PM 2 ATVES 15	**Tues 1/26** KKE CLINIC 2 KKE TELE PM 2 ATVES 12	**WEDS 1/27** CEA CLINIC AM 15 NICOLE NP PM 2	**THU 1/28** KERRY NP AM/PM 5 NO CEA CLINIC/TELE JSS 10	**FRI 1/29** JSS CLINIC AM 3 JSS TELE PM 1 NICOLE NP 0
MON 2/1 CEA CLINIC AM 7 NICOLE NP PM 2 ATVES 3	**TUES 2/2** KKE CLINIC 9 KKE TELE PM 3 ATVES 6	**WED 2/3** CEA CLINIC AM 8 NICOLE NP PM 3	**THU 2/4** CEA CLINIC AM 17 CEA TELE PM 2 KERRY NP PM 0 JSS CLINIC 10	**FRI 2/5** JSS CLINIC AM 2 JSS TELE PM 1 KERRY NP 5

Fig. 2.6 Upcoming clinic numbers

schedulers' desks for their reference. Upon receiving that day's schedule, our EA will then "freeze" any provider schedules (red or yellow dates) in the virtual Provider template from further booking by Central Scheduling. Only our staff can add appointments from there. The purpose of this schedule is to assist in getting our patients scheduled evenly across Provider availability, to limit overbooked schedules, and to ensure our team has a quick-reference guideline as to where there is immediate availability for booking.

PLAN FOR THURSDAY, 1/28/21

NOTES:

TIPS at 0800: Patient Case Presentation HK

Dr. Steinberg has room for add-ons today prn.

Amputee Support Group is tonight at 5 via Zoom.

Have a great day everyone!

SCHEDULE/STAFFING

Dr. Attinger has AM (26)
Kerry NP has PM (9)
NP: Kerry
RNs: Sara (7-5:30), Jacqueline (7-5:30)
MAs: Donnell (7:30-4), Iris (8-4:30), Lloyd (8:30-5 float)

Dr. Steinberg has AM (23) and PM (10)
NP: Nicole
RNs: Lauran (7-5:30), Amanda (7-5:30)
MAs: Anna (7-4:30), Amber (8-4:30), Lloyd (8:30-5 float)

Dr. Benedict has AM Clinic (2) and PM Clinic (2)
Dr. Johnson-Arbor has AM (2)

LUNCH:
12:30 – Sara, Lauran, Donnell, Anna
1:00 – Jaqueline, Amanda, Iris, Amber
1:30 –Lloyd

x4-6161: Tynisha (8-4:30)

Triage: Amara (6:30-5)

Hanger coverage/x4-1987: Ben H.

Code Cart: Lauran

Out:
Shinea
Margaret
Thalia

Fig. 2.7 Plans of the day

Page 14: Scheduling

Plans of the Day (Fig. 2.7)

These Plans are sent out daily via Outlook email by the Nurse Manager, or by the designated covering Triage nurse for that day. They are sent to all our inpatient/outpatient team members, as well as to our clinical partners—Radiology, Scribes, Physical Medicine and Rehab, Hanger Clinic, our Chief Resident, and Case Management. The Plan breaks down the clinic setup and assignments for the day, any alternate Provider coverage, any staff outages, and includes any pertinent notes for that day's operations.

Page 15: Scheduling

Clinical Staff Schedules (Fig. 2.8)

These are the weekly clinical staff scheduling assignments, which also include notes about any anticipated alternate Provider coverage, staff outages, and any important upcoming events. They are made and distributed by the Nurse Manager, optimally about a month in advance (i.e., send out the schedules for all of February in early January). These templates are used, in conjunction with the Outlook Master Calendar, to make that day's Plan of the Day. Note here the staggered staff start times for the CMAs, and the longer hours and variable "Out" days for the RNs (as they work four 10-hour shifts).

JAN 2021	Monday	Tuesday	Wednesday	Thursday	Friday
	4 CLINIC **Dr. Attinger (AM)** **with Nicole NP (PM)** **RNs:** Briana (7-5:30) Amanda (7-5:30) **MAs:** Iris (8-4:30), Amber (8-4:30), Lloyd (8:30-5 float) **Dr. Atves** **RNs:** Sara (7-5:30) Jacqueline (7-5:30) **MAs:** Anna (7:30-4), Donnell (8:30-5) Lloyd (8:30-5 float) **Dr. Benedict (AM)** **x46161:** Tynisha (8-4:30) **Triage:** Amara (6:30-5) **Out:** Ebrima Margaret Velma Lauran **Notes:**	**5 CLINIC** **Dr. Evans with** **Nicole NP** **RNs:** Lauran (7-5:30) Amanda (7-5:30) **MAs:** Anna (7:30-4), Amber (8-4:30), Lloyd (8:30-5 float) **Dr. Atves** **RNS:** Sara (7-5:30) Jacqueline (7-5:30) **MAs:** Iris (8-4:30), Donnell (8:30-5) Lloyd (8:30-5 float) **x46161:** Tynisha (8-4:30) **Triage:** Briana (7-5:30) **Admin:** Amara (6:30-5) **Out:** Ebrima Velma **Notes:** Mary Hicks RN (WOCN Student) Shadowing	**6 CLINIC** **Dr. Attinger (AM)** **Nicole NP (PM)** **RNs:** Briana (7-5:30) Lauran (7-5:30) **MAs:** Anna (7:30-4), Amber (8-4:30), Donnell (8:30-5), Lloyd (8:30-5) **Dr. Benedict (PM)** **Desk/Supply** **Orders:** Iris (8-4:30) **x46161:** Tynisha (8-4:30) **Triage:** Sara (7-5:30) **Out:** Ebrima Amanda Amara Jacqueline Thalia **Notes:**	**7 CLINIC** **Dr. Attinger (AM)** **with Kerry NP (PM)** **RNs:** Jacqueline (7-5:30) Lauran (7-5:30) **MAs:** Amber (8-4:30), Donnell (8:30-5), Lloyd (8:30-5 float) **Dr. Steinberg with** **Nicole NP** **RNs:** Amanda (7-5:30) Briana (7-5:30) **MAs:** Anna (7:30-4), Iris (8-4:30), Lloyd (8:30-5 float) **Attinger Remote PM** **x46161:** Tynisha (8-4:30) **Triage:** Sara (7-5:30) **Admin:** Amara (6:30-5) **Out:** Ebrima Margaret **Notes:** Happy Birthday Iris! Mary Hicks RN (WOCN Student) Shadowing Podiatric Residency Interviews in PM	**8 CLINIC** **Dr. Steinberg (AM)** **NO REMOTE PM** **RNs:** Lauran (7-5:30) Amanda (7-5:30) **MAs:** Amber (8-4:30), Donnell (8:30-5), Lloyd (8:30-5 float) **Kerry NP** **RNs:** Jacqueline (7-5:30) **MAs:** Anna (7:30-4), Iris (8-12), Lloyd (8:30-5 float) **Desk:** Iris (1-4) **x46161:** Tynisha (8-4:30) **Triage:** Amara (6:30-5) **Out:** Ebrima Margaret Briana Dr. Benedict Nicole NP Sara Velma **Notes:** No PM Remote visits for Steinberg

Fig. 2.8 Clinical staff schedules

Page 16: Managerial Tracking of Clinic Operations

In order to maintain historical context and stay up-to-date, the CWH Co-Managers keep constant, meticulous track of all small- and wide-ranging clinical operations and events. This is done using shared, secure Google Spreadsheets, which are added to almost daily. These are as follows:

1. CWH/HBOT Manager's List

   This is an informal, voluminous document and an invaluable resource which we use to comprehensively track everything which takes place in the department. We document on all projects, maintain detailed notes on associate or interdepartmental engagements, and add continued updates on any Provider, entity, staff, or administrative requests which cross our desks. We then continuously add notes on any progress, updates, movements on, or conclusions to these events. Current and active items are kept at the top of the list, divided by category; completed items are moved to the bottom of the list to keep on hand for reference.

   This document serves as a comprehensive catalog and history for our department. It helps us to track staffing structures and hiring efforts, associate histories from hiring, clinical scheduling evolutions, timeline histories and next steps for active projects, relevant contact details throughout the hospital and entity, and step-by-step workflow details for future use and ease of return.
2. Time and Attendance

   One of the most persistently frustrating issues we deal with in Management are inconsistencies in our associates' Time and Attendance. Another of our shared spreadsheets is for tracking their lateness, absences, and callouts. This allows for an at-a-glance look at the distribution of any of these patterns among our associates, and for quick access to information when we need to document or refer to the Attendance details in disciplinary documentation or sit-downs. Our associates know we track this performance aspect diligently, and that they will be held to account for any ongoing violations of our hospital and departmental Time and Attendance policies.

   We also make a Google spreadsheet to track our associates' Holiday Requests around Thanksgiving, Christmas, and New Year's. This helps us to ensure adequate staff coverage for clinic and equitable distribution of time out for each staff member during these holidays.
3. Facilities Requests

   This sheet is used to track the timeline and status for any outstanding departmental Facilities-related requests. These include items like department touch-ups, equipment replacement, installation of new electronics or media, and requests for systems upgrades. It is shared with and most regularly updated by our Executive Assistant.

As a practice, we also all utilize the Practice Share Drive ("Limbshare") to preserve, access, maintain, and update all clinic-related documents, resources, workflows, handouts, paperwork templates, etc.

Page 17: Associate Engagement

For our Leadership to ensure a consistently open dialogue and line of communication throughout our practice, several forums are held with consistency.

1. Weekly Operational Meetings: "Ops"

   This meeting takes place every Thursday just before our weekly all-staff meeting. Attendees are, at minimum, our two practice Chiefs/Providers (Dr. Attinger and Dr. Steinberg), the two CWH/HBOT Managers, Tara and Amara, and our department's Practice Administrator. Our other Attending Providers are also invited and make a point to attend when their schedules allow, as does our Administrative Director.

   This brief (30 min) weekly meeting allows for this group to catch up on clinic- and system-wide operations and to address and strategize

on any new or ongoing issues. Constant communication between our leadership teams is essential in keeping our operations up-to-date, forward-moving, and as streamlined as possible from the ground up. It also helps to ensure we are accounting for every perspective in tackling an issue and allows us to maintain a consistently unified lead and messaging to our staff and individual teams.

2. Weekly Thursday Staff Meetings

This meeting is also brief at 30 min and takes place every Thursday just after our Ops Meeting. Under regular circumstances (i.e., pre-pandemic), all present CWH/HBOT staff gather in our department's conference room, before starting the clinic day. These meetings are most often hosted by the Nurse Manager, or by the Patient Services Manager in her absence. Topics vary, and themes include (often a combination of) the following:

(a) **Clinical Operations Updates**: These include overviews on staffing updates, Provider or clinical schedules, any new practice recommendations, and ongoing facilities requests.

(b) **Patient Case Presentations**: These are put together and presented by our Providers or one of our Clinical team. We identify and review an especially challenging patient case for which we are seeking group input and suggestions for any more effective plan of care and treatment.

(c) **Safety and Audit Preparation**: This is a chance to refresh our team on the hot topics and practice recommendations from Regulatory Readiness, the Joint Commission, or the Department of Health, in advance of any known or possible upcoming clinic audit. This helps to keep them feeling prepared and ready to comfortably engage with any surveyors when they arrive.

(d) **Staff Spotlights**: These are generally everyone's favorite sessions. We created a template and forum for each of our team members (and sometimes, an ancillary partner) to give a 10-min-long presentation to the group about their role with our department and themselves as a person. We draw a random name for these at the advance meeting, so they have some notice, and provide a prompter questionnaire/template if needed. It has been a truly enjoyable team-building tool to help people get to know and appreciate each other as colleagues.

(e) **Team Kudos**: This is our chance to acknowledge standout efforts from any of our associates or our team in general. We review complimentary patient letters, details of any earned personal or group awards or accolades, or any significant clinic- or career-related achievements. We also share (with permission) any significant broader success or event in our associates' lives. It gives us a reason to cheer and celebrate and feel proud and happy together.

(f) **Guest Speakers and Multidisciplinary Calls**: Occasionally we will have a Guest Speaker come present to our team on a multitude of topics. These have included Hand Hygiene, Research Updates, Workplace Violence, Associate Wellness, Advancements in Prosthetics, Supplies Vendors, International and Language Services, and many others. We also have a monthly, first-Thursday group video call with our other system-wide Wound Centers, where we alternate case presentations and strategize on patient care on a broader level.

(g) **Education and Conferences**: We take every opportunity to send our team members to relevant, practice-related educational conferences throughout the year. Following their attendance, attendees are asked to present at the next weekly meeting on their takeaways from the experience. This allows for continued gathering and dissemination of current global practices and research updates to the team.

3. Team Huddles and 1:1 Check-Ins

Each Manager hosts regular smaller meetings, or "Huddles," with their direct reports in

their fields (Nurses, CMAs, Admin). This allows for the chance to review any more role-specific practice updates or recommendations and for the gathering of suggestions or input on a more intimate engagement level. These meetings take place approximately every 2 months, or when needed for anything more urgent.

We also meet 1:1, or 2:1 with our associates anytime we feel it is indicated, anytime by associate request, and for formal Mid- and Year-End Performance Evaluations. The informal sit-downs are done to address any immediate issues or concerns. They can also be simply a "check-in" to see how the associate is doing, praise their performance, and see if there is any way we can support or enhance their experience or continued development in our department or their more long-term career goals. If there is any need to formally document or archive these interactions for Human Resources-related or historical reasons, we utilize our entity's "Talent Manager" system to input a Note in that associate's virtual Employee File. This is done as soon as possible after the meeting, and the Notes can be accessed at any time moving forward once saved.

4. Practice "Town Hall" Meetings

   This was an initiative started just before the pandemic, but which has been placed on hold for the time being. The "Town Hall" Meetings were meant to be held twice yearly as an opportunity for all of our staff to sit down with all of our Providers and have their undivided attention for 1–2 h. We envisioned this as an opportunity for our associates to engage in a safe and open dialogue as a collective group and to solicit their insights and suggestions on where they feel we could be more successful on all levels. We were only able to host one of these prior to the pandemic, but from feedback it was much appreciated by the collective whole, and they were already looking forward to the next one. We will absolutely plan to re-initiate this down the road.

5. Staff Team-Building

   One of the best perks our practice offers to our associates has always been the show of appreciation which our Attendings model. They thank us as individuals daily for all of our efforts and support in caring for our patients and making the clinic run successfully. Our Attendings also believe that group engagement, both internal and external, is fundamental to our team's cohesiveness. They treat us to staff meals from a collective fund at least bi-monthly, they sponsor our attendance at Conferences, and they include us in team celebrations like our Residents Graduation ceremonies. Every few months they host a group activity like a Field Day or Happy Hour or an Escape Room event, all of which are usually well-attended. This unwavering support and encouragement, plus the opportunity to have fun together outside work, truly keeps morale boosted and makes us want to do our very best for them, for our patients, and for each other.

Page 18: Leadership Philosophies: The Managers' Perspectives

We would like to close with some of our shared philosophies on what makes for a successful Manager or Management Team. These insights have been gained from our day-to-day observations and experience in the Nurse and Patient Services Manager roles, and from each of our own prior experience under Managers ourselves, from which we sometimes learned what was not effective.

- **Know Your Team's Roles:** We strongly believe that as leaders we should know how to do everyone's jobs, within our specialized fields (i.e., Clinical vs. Administrative). This not only gives us an understanding and appreciation of our associates' task scope and workloads, but also allows us to jump in and cover their role when the need arises. This also enables us to teach the roles when we onboard new associates, and to serve as a constant resource for our associates should they have any questions or need any clarification during the workday. Additionally, if we

need to give any associate feedback, we are well-equipped with an intimate understanding of what is being asked of them on the day-to-day, and how they are performing comparatively. We also have all our associates cross-train within their field and set the expectation that they will be called upon on occasion to cover each other's desks as well. This allows them to learn additional job skills and to feel secure that we will be covered in the event of short-staffing.

- **Lead By Example:** This is modeled from the very top on down. Our Providers have set an admirable and reliable standard for keeping cool heads in challenging situations, maintaining near-constant good cheer and calm, and projecting competence and confidence. They also "praise in public" when they notice an extra or outstanding associate effort and personally say Thank You to their staff every day. As Managers, we try our very best to practice this same approach. This is critical in establishing a trusting relationship with our associates, as they know they can come to us anytime for help in handling a difficult problem. It also engenders pride among the team when they are acknowledged for a job well done. These practices also encourage a "mirror" effect among the team in their interactions with our patients and each other, which of course makes for smooth and positive engagements across the board.
- **Be Available (Open-Door Policy):** Another example our Providers have modeled is constant accessibility. We can reach them at virtually any time, and when they are on-site, their office doors are generally open and welcoming. Our associates also know that they are welcome in the Managers' office, and welcome to call or message us, and we will make ourselves available. We do set boundaries and expectations as appropriate, but have not found in our experience that this has ever been much of a problem. Accessibility ensures that our associates can get the answers that they need in the interests of expediting patient care and services, and this is an essential component of our practice success.
- **Be Present, Be Visible, Be Accountable:** The Managers show up as scheduled, we show up on time, and we make ourselves as visible as possible throughout the day. This lets our associates know that they can rely and depend on us and sets up an expectation that we want to see the same from them. As much as possible, we Managers try to do our jobs from central clinic locations during the day—the clinic hallways from a mobile workstation, or in the Administrative areas where multiple other associates work. This allows us to keep a comprehensive eye and ear on the day's events and interactions and helps encourage our associates to stay on task. We also make sure to let our associates know where they can find us or how they can reach us throughout the day, so they know they can always get a Manager if needed. Keeping in the center of things helps us stay connected to and involved with all aspects of our operations, allows for us to troubleshoot any issues which arise throughout the day in real time, and allows for our staff and Providers to stay in constant engagement with us in every facet of clinic.
- **Constant Communication and Transparency:** Over-communication is both practiced and encouraged by Management. We share information with our team in every way, and as soon as possible—via email, face-to-face communication, team meetings, instant messaging, etc. We feel that as much as possible, our team should have access and insight to the same information we have as leaders (excluding any sensitive HR-related issues). This helps them to understand how we make decisions and to help them feel confident in their own engagements in their workplace and for their entity. They do not feel they are being deceived or withheld from in any way and appreciate that they are being kept up-to-date in real time. We have had many other practices tell us that often they find out about major or minor hospital initiatives from our practice first, since we are so proactive about getting this information out to our team as quickly as possible.

- **No Micromanaging:** We believe that independence and autonomy are key to successful workflow and Manager-Associate relationships. Once our associates have demonstrated sufficient comprehension of and ability to perform well in their role, and understand our expectations of their continued performance, we leave them to it. They know we are available as a supportive resource, and that we will follow up with them if we notice any red flags or coaching opportunities, but generally we let them know that we trust and respect them in their roles.
- **Everyone Has a Voice:** The reason we have so many meetings, huddles, check-ins, and face-to-face engagements with our associates is because we believe an open, constant dialogue is essential, and that every member of our team should have a voice and be encouraged to use it. Everyone's contributions are welcome, considered, and respected. This has led to the development of so many valuable operational modifications and patient experience improvements and is always extremely appreciated.
- **Support Your Team:** As also modeled by our Providers, our team knows the Managers have their backs. We will do anything we can to help them in their success or support them through a challenging situation. We have seen them through school to higher degrees, been their references for continued endeavors, and received many words of gratitude for being strong examples and providing encouragement that was needed. There is truly no greater gift or gratification in this role.
- **Support Yourself:** Lastly, we are huge proponents of self-care and of a healthy work–life balance. We encourage each other and our team to use their Paid Leave, take time for themselves when they need it, find an outside hobby or interest which allows them to escape and relax, and take fulfillment not only from their achievements at work, but from their external successes. Our team talks regularly about strategies for and research findings on self-care in our weekly staff meetings and shares tips with each other on the day-to-day. We also laugh together, all the time, anytime. It truly is the best medicine.

Case Management of the Complex Limb Salvage Admission

3

R. N. Thalia Attinger, M. S. W. Heather Daniels,
R. N. Teodora Deperio, and Allen H. Roberts II

It may be a fair assumption that few, if any, medical schools or residency training programs provide structured education in the art and science of Case Management (CM) and Social Work (SW). Most physicians who speak to CM and SW colleagues during their daily round and routine are unaware that these professional colleagues possess a knowledge base and skill set that would baffle the most accomplished of clinicians; it may be similarly lost on many physicians that, absent of the work of Case Managers and Social Workers, the flow of patients through the hospital to safe discharge destinations would grind precipitously to a halt. Case Managers' and Social Workers' labor is difficult, nuanced, and largely behind the scenes; in many hospitals this work is never presented in Medical Grand Rounds, seldom celebrated in the Admin Suite, and largely inaudible in the Board Room—except, of course, when length-of-stay (LOS) is over budget, or on the occasion when a prominent physician's patient's discharge course is somehow less than perfect! At such times, it seems easier to blame CM/SW than to understand the unique challenges these professionals face, and to commit, at hospital and corporate leadership levels, to the success of their work in meaningful ways. We are fortunate, in our own institution and corporation, that the contributions of all associates across all job descriptions, not least our CM and SW, find recognition and support in all these venues, and that there is corporate commitment to process improvement in these very areas.

In this chapter we shall step behind the curtains into the world and work of Case Managers and Social Workers by way of several hypothetical and composite case studies. The medical issues and a number of the social issues represented here will be all too familiar to medical practitioners and nurses; we will all "recognize" these patients, despite their being fictitious. But the intent of this chapter is to introduce the reader to issues that are at play behind the scenes and to how our CM and SW, in the handling of these complex issues, become the *sine qua non* of the successful transition of complex limb in-patients

R. N. Thalia Attinger (✉)
Center for Wound Healing and Plastic Surgery Services, Medstar Georgetown University Hospital, Washington, DC, USA
e-mail: Thalia.Attinger@gunet.georgetown.edu

M. S. W. Heather Daniels
Department of Case Management, Medstar Georgetown University Hospital, Washington, DC, USA
e-mail: Heather.Y.Daniels@gunet.georgetown.edu

R. N. Teodora Deperio
Limb, Wound-Care, and Orthopedic Services, Medstar Georgetown University Hospital, Washington, DC, USA
e-mail: Teodora.Deperio@gunet.georgetown.edu

A. H. Roberts II
Medstar Georgetown University Hospital, Washington, DC, USA
e-mail: ahr8@gunet.georgetown.edu

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_3

to recovering and rehabilitated outpatients. This chapter will showcase the integrated, multidisciplinary efforts of CM, SW, nursing staff, advanced-care practitioners (such as Nurse Practitioners and Physician Assistants), and Hospital Administration to accomplish these very transitions.

We shall begin with definitions and standard roles of CM and SW, acknowledging that staffing models and roles and responsibilities vary considerably across institutions and corporations.[1] From there we shall consider several cases, moving from the straightforward to the complex, that illustrate the interventions that are undertaken by CM/SW. Finally we shall engage administration-level considerations that are germane to throughput and discharge planning and will comment on several process-improvement interventions which, in our local experience, have proved beneficial.

As of this writing, we are sadly in the midst of the COVID-19 pandemic, which, in addition to its medical and social tolls, has added layer upon layer of additional complexities to the throughput and safe discharge of all our patients, not least of them, those on our limb service. We have learned valuable lessons during this pandemic from which we hope to become better at what we do in the post-COVID era.

The Case Management Society of America defines case management as "a collaborative process of assessment, planning, facilitation, care coordination, evaluation, and advocacy for options and services to meet an individual's and family's comprehensive health needs through communication and available resources to promote patient safety, quality of care, and cost-effective outcomes."[2] At our hospital, the Nurse Case Manager/Discharge Planner (CMDP) works with a Case Manager Associate (CMA), Utilization Review Nurse (UR), and a Social Worker (SW). The Case Manager Associate assists the Case Manager with daily tasks that make the Case Manager be more efficient. Everyone has the same goal—to ensure that patients have a safe and cost-effective discharge plan.

When a diabetic limb patient is admitted to Georgetown, the CMDP is responsible, along with the medical team, for coordinating and facilitating an effective plan of care for discharge. Due to the complexity of the care and treatment of this patient population, discharge planning must begin on admission. The Case Manager meets with the patient within 24–48 h to obtain information such as verifying demographic information, insurance information, and social status**.** The electronic medical records are reviewed to identify patient diagnosis, medical history, surgical plans, Consults from Infectious Disease (ID), General Medicine (GM), Acute Pain Service (APS), etc. It is helpful to know where the patient originated from—home (local or out of state), outside hospital (Medstar or non-Medstar facility), nursing home, rehabilitation facility or from an undomiciled (homeless) situation.

The CMDP collaborates with the Utilization Review (UR) Nurse to ensure patient's hospital stay is authorized by insurance. The UR Nurse reviews clinical information on admission and performs concurrent reviews for continued stay. Interqual Criteria[3] is used as a guide when reviewing clinical information to determine medical necessity. Through written or verbal communication, the Case Manager informs the UR nurse if there are barriers to discharge, i.e., psychological/social issues, expensive medications, lack of rehabilitation days, or type of isolation precautions. When the insurance company issues a denial, the UR Nurse notifies the Attending Physician and provides information for a peer-to-peer review, which may result in the denial being overturned by the payor. If the denial is upheld, many cases may be appealed successfully. It has

[1] See S.K. Powell and H.H. Tahan, *Case Management: A Practical Guide for Education and Practice*, 4th ed., 2019, Wolters Kluwer, Chapter 1.

[2] See https://www.nurse.com/ce/beyond-the-basics-in-case-management accessed 2/5/2021 and https://lms.nurse.com/login.aspx, CE direct, Beyond the Basics in Case Management, Chapter 1.

[3] https://www.priorityhealth.com/provider/manual/standards/utilization-management-program/interqual-loc-criteria, accessed on 2/5/2021.

been our experience that a systematic monthly review of all denials and appeals at the hospital administrative level may result in the identification of documentation or coding issues, or other themes, the correction of which will lend itself to recoupment of significant revenue.

An important innovation in patient throughput was implemented by a MedStar Health Corporate initiative known as the Integrated Model of Care (IMOC) which fosters a collaborative approach to ensuring patient safety, streamlining patient throughput, removing discharge barriers, and ultimately reducing LOS. One of the essential elements of this program is the Multidisciplinary Rounds (MDR), a dedicated, brief session executed on each hospital ward, once daily, in which all patients on that ward are concisely reviewed. These rounds may be held virtually by video- or teleconferencing. At MDR, which is attended by the Physician or Nurse Practitioner, patient's Registered Nurse, Physical Therapist (PT), or Occupational Therapist (OT), Charge Nurse, CM and/or SW, the patient's discharge plan is reviewed in a structured manner that employs checklists and the identification of all discharge barriers. IMOC MDR rounds are held every day to talk about patient/family issues, surgical plans, discharge needs, and expected discharge date. The Physician or NP orders PT and OT consults to help determine patient's level of care for discharge. PT and OT evaluations provide recommendations for durable medical equipment, home care or need for inpatient physical rehabilitation (subacute or acute rehab). IMOC MDR, now a part of the "culture" of the hospital, has proved to be a fundamentally important contributor to safe and efficient throughput.

Once the initial discharge plan is determined, the Case Manager meets with the patient/family to discuss the plan. If PT/OT recommends inpatient acute or subacute rehabilitation, a list of facilities that are in-network with the insurance company is provided. The patient is asked to provide at least three choices to initiate referrals. The patient's family is given sufficient—but not unlimited—time to visit the facilities but due to the COVID-19 pandemic; they are encouraged to research online or call the facilities themselves. When the choices are deferred to the Case Manager, the patient is referred to facilities to which many previous limb patients have been sent. These facilities are familiar with our plastic surgeons' treatment plans and there is a wound care Nurse Practitioner on staff. When an accepting facility is identified, the facility provides bed availability and obtains insurance authorization prior to transfer. If the patient has Medicare, it is important to find out if the patient has available rehab days. Each commercial insurance has a different coverage and benefits must be checked. This is usually done by the facility considering the patient for admission. Depending on type of insurance, the CM is sometimes required to submit clinical information, especially PT/OT notes to the insurance company for approval.

A real-time tracking of the progress of all referrals is kept and updated via task-lists. The CM reviews the task-list with the CMA daily. The CMA sends the referrals out to facilities via a web-based referral platform. He/she is responsible for following up with the facilities, delivering durable medical equipment (DME) to the bedside, setting up medical transport, and providing discharge packets. When referrals are made, it is important to inform the CMA name and duration of intravenous antibiotics, presence of a central line (if applicable), type of isolation, wound care, and discharge date. Both CM and CMA work together in delivering care and services for a timely discharge.

The CM also collaborates with the SW on a regular basis. The Clinical Social Worker in the inpatient hospital setting provides direct services to patients and families related to hospitalization, dealing with illness and post-hospital planning. However, the role of a clinical social worker is complex and is often specialized depending on the setting and population served. As a part of the multidisciplinary team, a clinical social worker is often consulted by the case manager or medical team to address identified barriers to discharge for the complex limb patient. The social worker can help address financial or insurance concerns, assess for home supports, coordinate and collaborate with community agencies and resources, and can also provide support and brief counseling

to the patients who are having a difficult time coping and adjusting to their medical situation.

When consulted, the social worker reviews the patient's chart for current and previous medical and case management documentation, noting interventions and outside resources. The social worker then will conduct a psychosocial assessment with the patient and/or family and collaborate with the case manager, medical team, and outside supports in determining a social work plan.

For patients who are uninsured, the Clinical Social Worker refers the patient to Division of Economic and Community Outreach (DECO)[4] for assistance in applying for Medicaid or Emergency Medicaid. If the patient does not have a secondary insurance, the patient is also referred to DECO to apply for Medicaid as a secondary. In situations when a patient is undocumented and unable to obtain Medicaid, the social worker can then make a referral to charitable sources for assistance with follow-up medical care and will consider and provide for potential discharge needs: clothing, transportation home, or assistance with prescriptions.

The clinical social worker is also consulted to assess and provide needed support regarding patients' living environment. If a patient is particularly vulnerable: homeless, older, and lives alone or has mental health or substance abuse issues, the social worker considers what supports are available in their area based on their insurance and community resources. If the patient has DC Medicaid and is not safe to discharge home alone, they may be eligible for a home health aide through Medicaid. The social worker will collaborate with the limb team in completing paperwork to schedule an assessment for potential home health aid service hours and work with outside case managers and agencies to arrange home care. If the patient needs assisted living facility (ALF) and has some means available to them, the social worker will connect the patient and family with community agencies such as *A Place for Mom*[5] to assist in finding an appropriate ALF. If the patient needs acute rehab or short-term rehab, the case manager takes the lead in making referrals and facilitating rehab discharges with the social worker remaining available as needed. If a limb patient cannot go home with supports and has no payor for rehab, the social worker can request to subsidize a rehab stay with a partnering short-term rehab facility through the case management department.

If the patient does not have insurance, does not qualify for Medicaid, and/or is out of rehab days, the social worker will refer the patient to the case management directors to request a subsidy for home health aides through a local philanthropic source which underwrites proprietary in-home nurse practitioner visits and services and may subsidize necessary medications needed to ensure the patient has a safe and sustainable discharge.

A small population of complex limb patients are homeless and may also have mental health diagnoses and substance abuse issues which require extra coordination between the social worker, case manager, and often outside support agencies. A more traditional discharge plan often does not work out for these patients due to their documented histories of elopement or behaviors, and so the social worker and case manager work together to build rapport with the patients, coordinate with outside agencies and case managers, and communicate with the patients' insurance case managers in order to find the best discharge plan available for the patient. If a complex limb patient needs rehab but is also homeless, most rehab facilities will not accept them without a plan for discharge after rehab. The clinical social worker and case manager work together to explore different options such as discharging from rehab with family members can also make referrals to medical shelters. During the COVID

[4] https://www.decorm.com, accessed 2/3/2021. DECO Recovery Management assists hospitals by providing a full suite of eligibility management services and by guiding patients through the complex process of applying for federal, state, or local programs.

[5] A Place for Mom is a nationally based senior living referral agency that can assist patients and families in finding assisted living, memory care, residential care homes, and non-skilled home care. https://www.aplaceformom.com.

pandemic, some vulnerable patients qualify for a homeless COVID prevention program, PEPV, designed to keep highly vulnerable individuals off the streets to prevent the spread of COVID. The clinical social worker can also refer the complex limb patient to the PEPV program.

The art and science of excellent patient care and optimal patient hospital throughput are centered on collaboration and communication of the clinical team with the CM/SW team. To this end, the discharge plan ideally begins—on the limb services as on all other services—on the day of admission to the hospital. Every patient admitted to the hospital must have a discharge plan and a targeted discharge date (TDD). Limb patients, in particular, are fraught with many unique discharge challenges. We have ideal protocols, but also the reality of what our patients can do physically, mentally, emotionally, and financially. Protocols, it should be remembered, are created for patients, not patients for protocols! A new below- or above-the-knee amputee might best be served by spending time in acute rehabilitation, retraining her brain to avoid falling. A partial-foot amputee will have the best potential for healing by remaining non-weight bearing in a posterior splint. A free-flap patient would benefit from weeks of offloading in an external fixator. But the truth of the matter is that non-weight bearing is often unrealistic for this patient population. They are deconditioned and laden with comorbidities including contralateral weakness or bilateral wounds. As a result, the ideal "discharge" is just a hypothetical "starting point," and each discharge plan, pathway, and strategy must be tailored to the individual. Our inpatient nurse practitioners are uniquely skilled at bridging the gap between the ideal and the realistic discharge. Through extensive collaboration with the physicians, case managers, social workers, and the patients, they are able to create unique, patient-centered care plans. In order to better examine such challenges as we face during the hospitalization and the eventual discharge process, we present three case studies to highlight the nuances of this complex population.

Powell and Tahan, in their magisterial and comprehensive treatment of Case Management, include in their text a section on the Ethics of Case Management, and assert, "Ethics in healthcare is about choices, morals, and the basic rights of free choice, self-determination, independence, and autonomy."[6] In so stating, the authors reflect the ascent, in recent decades, of an individual's autonomy as the ranking determinant for ethical decision making. At Georgetown, we affirm this same principle of autonomy, in addition to the other three principles of ethics, namely the physician's (and health care system's) beneficence, non-maleficence, and distributive justice.[7] We affirm a balanced approach to these four equally weighted principles, inasmuch as the unchecked assertion of autonomy, when taken out of the contexts of community and moral order, inevitably places the most vulnerable of the community at risk.[8] Case Managers are in the line of work of protecting, among others, these most vulnerable. We conclude our introductory section with the acknowledgment that CM and SW thus bear the weight of carrying this ethical balance forward from the in-patient to the out-patient arena. Case Managers and Social Workers are thus the guarantors and sustainers of ethically delivered care through the process of discharge planning. We turn now to exemplar cases.

The Straightforward Discharge: The Amputee

Case

The patient is a 49-year-old male who presented to Emergency Department (ED) with a chronic, non-healing, infected right foot wound. His past medical history (PMH) included insulin dependent diabetes mellitus (IDDM), hypertension

[6] Powell and Tahan, 286.

[7] For an exhaustive presentation of Principlism in Medical Ethics, please see Tom Beauchamp & and James Childress, *Principles of Biomedical Ethics, 8th ed.*, 2019, Oxford University Press.

[8] Allen Roberts, Response to Sulmasy & Snyder, "Ethics and the legalization of physician-assisted suicide: an American College of Physicians position paper." *Annals of Internal Medicine* 2018; 168(11):834.

(HTN), hyperlipidemia (HLD), peripheral vascular disease (PVD), and prior venous bypass to increase blood flow to the leg. He was admitted to the Plastic Surgery (LIMB) service with several consulting specialties: general internal medicine (GIM) for blood pressure and glucose control, infectious disease (ID) for antibiotic therapy, vascular surgery to evaluate blood flow, and acute pain service (APS) for pain management. An angiogram was performed which showed little to no blood flow to the right lower extremity and in light of failed vascular intervention in the past there was no further intervention possible. Given the extent of the wounds and level of infection of both the bone and the tissue the team recommended an amputation. After years of pain, infection, and multiple surgeries to the foot the patient agreed to proceed with a below knee amputation. The patient first underwent a drainage amputation where cultures were taken and then dressed with a negative pressure wound therapy (NWPT) or vacuum assisted closure (VAC) device along with a knee immobilizer to protect the residual limb and prevent contractures, intravenous antibiotics were ordered by ID and physical therapy began to work with the patient to assess his physical abilities. On the third post-operative day the patient returned for his completion BKA along with targeted muscle reinnervation.

Plan

Prior to surgery the patient met with prosthetists, who gave him the opportunity to learn about the process going forward and begin to get a glimpse as to what life was going to look like for him after surgery. Whenever possible, we try to arrange peer support during the hospitalization; sometimes this comes in the form of our monthly virtual amputee support group, other times the prosthetists are able to arrange for one-on-one meetings. These visits/conversations with patients prior to surgery is an invaluable resource we often take advantage of for emotional support during this difficult process. On the day of surgery, or the night prior, APS will place perineural catheters in the operative leg for localized pain management in hopes of decreasing the need for narcotic and improving overall pain control.

The Case Manager met with the patient to perform an initial assessment for discharge needs. During the interview, the patient stated he lived with his spouse in a multi-level home but was able to have first floor set up. He had been receiving wound care from a home health agency three times a week and using a rolling walker for ambulation. Initial physical and occupational therapy evaluation recommended acute rehab (AR) placement. It is generally our recommendation that all new amputees spend at least 7–10 days in an AR to help retrain the mind to acknowledge the missing limb. This helps to reduce falls and in turn reduce risk of dehiscence and hematoma to the residual limb. For those who do not meet criteria for AR (the ability to participate in at least 3 h per day of physical therapy), we recommend a subacute rehab facility (SAR) with eventual upgrade to AR. CM discussed referral process and the patient chose three facilities that are on par (within network) with his insurance. The patient and his wife were informed that he would transfer to the first accepting facility with a bed, authorized by insurance when medically ready for discharge. Typically, patients stay in the hospital for 4–5 days post-surgery at which time the incisional VAC is removed to assess the incision prior to discharge, pain can be well controlled and all surgical drains can be removed. A discharge summary outlining final ID recommendations which were oral antibiotics as the infected tissue was completely removed by nature of an amputation, wound care, patient was placed in a short term, one time use incisional Prevena VAC which stays in place for 7 days and is then changed to a dry sterile dressing, and an effective oral pain regimen was written for AR to follow. A follow-up in the outpatient clinic was scheduled for 10 days from discharge. Additionally, all amputees are invited to attend a virtual support group which meets monthly. This is especially beneficial if the patient happens to still be in-patient at the time of the meeting as they are able to obtain real-time peer support.

The Moderately Complex Discharge: The Free-Flap Patient

Background on Free Flaps

Patients undergoing a free tissue transfer (free flap) have the longest, often most complex hospitalizations. They undergo multiple debridements prior to their final closure, as well as a number of pre-operative clearances and screenings such as angiography, vein mapping, lab studies to assess for any underlying hypercoagulable states, and cardiac clearance given the length of the surgery which often requires over 6 h under anesthesia. Their frequent need for a heparin drip and antibiotics necessitates regular lab draws via a peripherally inserted central catheter (PICC) line early in their hospital course. The sooner we can identify these patients and begin the interdisciplinary coordination of care the better for both mental and physical health. As previously mentioned, remaining non-weight bearing and offloading any pressure to the flap is of the utmost importance whether that be in a mulitpodus boot with strict adherence to non-weight bearing or with the use of external fixation. Whether or not a patient can mentally handle external fixation is always a challenge. Regardless of offloading method these patients require long term IV antibiotics, frequent wound care, and intense physical therapy. The post-operative period is an arduous one. Patients are kept NPO (nothing by mouth) for the first night in case an emergent revision surgery is required. They are kept in bed, under a bair hugger (warming blanket to improve blood flow), with a continuous audible Doppler along with a Vioptix Doppler to assess skin oxygen saturation for 2 days post-op. At that time, they can slowly begin to get out of bed to a chair with continuous leg elevation until they are once week post-op and can begin the dangle protocol where the patient progressively places the limb in a dependent position. Most free-flap patient remain in the hospital for approximately 12–14 days post final surgery.

Case

The patient is a 65-year-old African American male with a past medical history of IDDM HTN, CHF, prior left BKA and CKD Stage III, who presented to the wound center with right plantar heel ulcer. He underwent several debridements in order to get the wound bed clean and the aforementioned screenings prior to receiving the free flap. His post-operative course was uncomplicated but long and mentally taxing.

Case management met with the patient and determined that he lived alone with his small dog in an apartment. The apartment had approximately 20 steps to enter and no elevator access. His treatment regimen required Daptomycin, a notoriously expensive antibiotic, to be administered IV daily for approximately 4 weeks. He refused external fixation and nursing reported he was unable to maintain his non-weight bearing status (“he walks all over that foot”). He had initially agreed to AR; however, due to delays in bed availability he become increasingly dissatisfied and eventually insisted on going home, as he was worried about his dog who was being watched by a neighbor.

Plan

The patient was placed in a total contact cast to offload the flap as best as possible. The cast itself meant that the clothes he has worn into the hospital were not suitable and he had no one to bring him a proper set. Because of the PICC, he was unable to use traditional crutches and so he was ordered a walker and platform crutches as well as rented a knee scooter. Given the high cost of daptomycin, SW was consulted to assess the patient for financial need and submitted a request to the case management department to cover the cost of the daptomycin through our contracted home infusion company. Social work was also able to provide him the necessary clothes for discharge and to help guide him through the application process for medical transportation and community food assistance. Weekly follow-up visits were set up to ensure regular follow-up visits and cast changes.

The Complex Discharge

Case

The patient is a 31-year-old man with a PMH of IDDM and substance abuse who presented to clinic with a right hallux abscess and cellulitis with gangrene, noted at the dorsal aspect of the hallux. Osteomyelitis of the great toe was identified radiographically. He underwent several debridements and ultimately a first metatarsal head resection and amputation of the second to fourth digits. Given the level of infection a 4-week course of outpatient IV antibiotics was initially outlined. Ideally, he would remain non-weight bearing but both nursing and physical therapy documented that he is unable to do so. PT recommended SAR for the immediate post-operative period to help reinforce non-weight bearing and overall strengthening and conditioning along with wound care and antibiotic therapy. He was notably aggressive toward staff throughout his stay, often threatening to leave against medical advice (AMA) and intermittently refusing care. Despite his frequent outbursts and non-compliance, he was deemed competent by psychiatry.

Case management met with the patient and learned that he was undomiciled and lived in his car, delivering food for a living. Patient is adamant that he wants to go home to "deal with things" which was worrisome to the medical team, given that his surgery was on the right foot, and placing a total contact cast to offload the incision would make driving hazardous. To further complicate matters, the patient had no health insurance, so social work helped assist in completing an application for Medicaid or disability; however, sadly, the patient was "over income," that is, his income, while low, was sufficient to disqualify him from Medicare eligibility. The SW, CM, and LIMB team spoke with him several times in order to convince him that going home (i.e., to his car) was not a good option, and he eventually agreed to placement. He was referred to a medical shelter, homeless hotel program, and short-term rehab, but was denied at all facilities due to his substance abuse history and documented combative behaviors.

Plan

This patient had several outside case managers with whom the social worker and case manager collaborated throughout his admission and eventually a safe discharge plan was ultimately agreed upon by all involved. After much deliberation his cousin agreed to let him stay with him temporarily. Our fear was that this welcome may be short lived and therefore sent him home with dressings and medications that were as low maintenance as possible while still providing him the best possible chance to heal. He was placed in a well-padded profore (multilayer compression) dressing[9] with a controlled ankle motion (CAM) boot to offload the forefoot. Given his substance abuse history he was placed on oral antibiotics and set up with weekly follow-up visits to ensure proper wound care and frequent monitoring. Much to everyone's surprise and delight this gentleman went on to heal beautifully.

Other Barriers

Navigating the complex world of health insurance is an unfortunate reality in health care today. The limb salvage patient is, more often than not, a chronically ill patient whose time is spent in and out of hospitals and rehabs. This compounded with the fact that we work with patients from the District of Columbia, Virginia, and Maryland which requires early inquiry on the part of case management and social work to help carve out the best path. Patients having no insurance or being out of rehab days or not qualifying for home health aide can drastically shift the discharge plan at the *n*th hour.

The case manager and social worker review the patient's insurance status. If uninsured, the social worker refers the patient to DECO for assistance in applying for Medicaid or Emergency Medicaid. If the patient does not have a secondary insurance, the patient is also referred to DECO for possible Medicaid for secondary. In

[9] https://www.smith-nephew.com/key-products/advanced-wound-management/profore/.

the case that the patient is undocumented and unable to obtain Medicaid, the social worker can then make a referral to Catholic Charities for assistance with follow-up care and will consider any potential needs: clothing for discharge, transportation, assistance with home medications at discharge.

The social worker is also consulted to help assess the patient's home situation. If the patient is particularly vulnerable, homeless, or older and lives alone, the social worker considers what supports are available. If the patient has DC Medicaid, they may be eligible for a home health aid, and the social worker will collaborate with the limb team in completing paperwork for an assessment for home health aid service hours. If the patient needs assisting living, the social worker will connect the patient and family with agencies like A Place for Mom or Care Patrol. If the patient needs AR or SAR, the case manager takes the lead in making referrals and facilitating rehab discharges with the social worker remaining available as needed. If the patient does not have insurance, does not qualify for Medicaid, and/or is out of rehab days, the social worker will refer the patient to the case management directors for a subsidy for home health aids through Georgetown Home Care, may refer to the subsidized Georgetown NP Program, or subsidize necessary medications needed to ensure the patient has a safe and successful discharge.

No account of the CM/SW aspects of care would be faithful to real-life circumstances, should it fail to acknowledge the infrequent but unfortunate situations when the best efforts and intentions of physicians, nurses, and CM/SW—to treat with medical excellence and to arrange placement with diligence and compassion—are thwarted by a patient's next-of-kin or other surrogate decision maker. A surrogate may suddenly become unavailable to participate, for instance, in AR or SAR site-selection, refuse to make a selection from these sites despite the discharge plan being safe and underwritten by insurance, or fail to be forthcoming on matters financial. Reasons for such disengagement by responsible parties are complex and may be related to cultural, socioeconomic, and demographic disparities. These situations are challenging and require the patience and professionalism of all involved—and the support of hospital administration.

The aforementioned ethics of the care of the patient also pertain to ministry to the greater good, especially when hospital beds are scarce and hospital throughput must be optimized. In circumstances where a family or other surrogate becomes unavailable or uncooperative with discharge planning, it is incumbent upon the hospital—and ethically imperative for the patient's best interests—that the hospital take expeditious measures to obtain a court-appointed guardian to move the patient's care forward. At our facility this (thankfully) rare intervention is initiated by the SW, in consultation with senior administrative physicians, and involves the hospital's or system's legal team and other consultants.

Hospital Administration and the Limb Service

It is a common misconception that Length-of-Stay reduction and patient throughput responsibility is the sole domain of Case Management. As noted previously, it is always easier to blame the "downstream" person, the non-physician, non-nurse members of the team when throughput is suboptimal and LOS, over budget; however, it has been our experience that the persistence of this misunderstanding is at the core of inertia in the effort to ameliorate all aspects of inpatient flow. Experience with throughput enhancement in the COVID-19 era effectively has laid this misconception to rest. In this final section, we shall explore the essential role of a robust and engaged hospital leadership in the provision of responsible and excellent care, while, simultaneously tending to throughput challenges in an effort to "keep the doors open," and thereby to keep the public served.

As noted, staffing and tasking of CM vary broadly across institutions and may be driven by the nature and scope of institution-specific services. For example, hospitals which specialize in cancer treatment or orthopedic procedures may have narrower and more specialized scopes of

CM/SW activities than a full-service facility. Within a full-service facility, the relative number and distribution of service line in-patients may dictate the distribution of CM. Small community hospitals may use a hybrid model wherein a single CM executes both DP and UR actions, whereas larger city hospitals or academic medical centers, such as our own, require dedicated, separate CM and UR specialists to support the volume and complexity of each work-type. And, as in all things organizational, budgetary considerations and constraints may inevitably impact both the number of CM on staff and on how they are deployed. When it comes to the correct staffing model in any hospital, one size does not necessarily fit all.

At our institution we employ differentiated DP and UR case managers, with 50% of our personnel in each group. CMDP is deployed geographically by hospital wards, with each CMDP covering two wards. Several internal Performance Improvement initiatives, all of which maintained this model, resulted in the uncovering of several common discharge barriers, but none in a reduction in LOS. More recently, however, a pilot program in which a single CMDP was dedicated to the Limb Service over a 3-month period resulted in improved internal customer satisfaction among physicians and nursing staff; additionally, a 0.9 day reduction in LOS was realized during this period when compared with a historical control of the same duration.[10] These findings lend themselves to consideration of funding for an extended pilot study of similar metrics which might support augmentation of staffing.

Stepping back from the Limb Service specifically, more generalized efforts to enhance patient throughput bear mention, as all service lines may partake of a collective benefit. Just as the medical and nursing teams collaborate with CM, PT, SW, and others, so to, proactive engagement by the hospital administrative team with all service lines in standardized as well as specific ways brings programmatic unity to the diversity of clinical services. The aforementioned Multidisciplinary Rounding of the Integrated Model of Care initiative is one example of a standardized safety and throughput program that touches all service lines equally.

Recognizing the toll of both COVID 19 disease and other diseases in the early phase of the pandemic, a decision was made to maintain full services at our institution during subsequent waves of the disease. The challenge to hospitals within our network was to develop and sustain an intensive process of safe patient throughput and efficient discharges. The organizational model to accomplish this was the formation of physician, nurse, and case management into *executive leadership triads*, and through these groups, to "connect the dots" of hospital access points, bed tracking, and individual service line throughput processes. Relying heavily on a proprietary electronic system of bed reservation, utilization, cleaning, and reopening, we were able to identify patients who are "ready for discharge today or will be by tomorrow." A list of these patients is disseminated to the appropriate leadership of service lines daily, and live video teleconferencing held thrice weekly. The list of all patients ready or nearly ready for discharge was run daily, discharge barriers identified and escalated promptly. Additionally, Executive Discharge Rounds were conducted by physician, nurse, and CM leadership periodically and these rounds uncovered both barriers and process improvement opportunities.

The result of these interventions was a significant reduction in LOS, in the use of full-capacity beds and the number of ER boarders, and in the amount of time spent on hospital "red-light."

Similar MD, RN, and CM triads were created for our top five service lines, in-patient volume-wise, and the executive triad the leadership triad met with lower-volume service line leadership separately. Procedural and consultative services were engaged and a designation and prioritization of "discharge pending" patients was established for procedure and consultation workflow. The Limb Service, among others, was beneficiary of these enhanced throughput strategies.

Finally, in recent years, we have as a system begun a program of "repatriation" of patients from the tertiary care referral center, back to their

[10] T. Deperio and A. Roberts (unpublished data).

hospital-of-origin. At the time of the original concept development, there was very little, if any, U.S.-based literature on why one might repatriate a patient from a tertiary care hospital back to the more remote community hospital whence he had been transferred. This has not, to date, been a common practice in USA. But repatriation of patients back to their referring hospital has been part of healthcare delivery in the UK, for some time, on the very justification that the practice is necessary to keep the correct number of hospital beds at the correct level of acuity available to the most people.[11]

It has been for this precise reason that our network has adapted a capacity management strategy that includes the repatriation of select patients to their hospital of origin, once the tertiary service has been fulfilled, they are awaiting placement or discharge, and if they consent to the transfer. During the COVID-19 pandemic, this practice has been invaluable to minimizing time on hospital red-light and maintaining patient referral inflow.

Conclusion

The comprehensive, safe, and ethical care of the complex limb patient, like all patients, involves collegial coordination among physicians, nurses, social workers, physical therapists, and others—all in dialogue with the patient or the patient's family. Discharge planning for individual patients should ideally begin on the day of admission, with a projected discharge date set in place up front. Barriers to discharge may be identified and resolved or escalated via standardized interdisciplinary rounds and thrice weekly conference calls. Hospital administrators can facilitate the process by high-level barrier removal; repatriation to referring hospitals is an evolving concept with great potential for regional or system capacity management. A Service Line-dedicated case manager staffing model has been shown dramatically to reduce length-of-stay and to improve internal customer satisfaction.

[11] See, for example, https://sunnybrook.ca/content/?page=discharge-planning-repatriation.

4 Integrating Inpatient Care to Your Outpatient Wound Care Center: Key to Successful Patient Management

Nancy R. Megas, Katherine S. Hubley, and Margaret C. Kugler

Introduction

In 2020 the limb salvage service at MGUH performed over 2000 surgeries. In terms of patient demographics, 34% of their patients required hemodialysis, 79% were diabetic and 20% suffered from congestive heart failure. These were not uncomplicated patients. A rotating team of plastic surgery and podiatric surgery residents is tasked with caring for and discharging these patients. As patient volumes grew to MGUH's current levels it became evident that the resident team needed additional support. Within acute care hospitals, the use of nurse practitioners and physician assistants is an established model of care for acute and critically ill patients [1]. With this in mind, in 2003 a full time nurse practitioner joined the limb service to work exclusively with their inpatients. As volumes continued to increase, two additional nurse practitioners were added resulting in an inpatient care team of three nurse practitioners, six to eight residents, and one fellow. While managing patients' discharges is a key focus, the nurse practitioners function in the same clinical capacity as residents, fielding questions and order requests, being paged to the bedside for emergent developments, interfacing with other services and responding to patient and family concerns.

As soon as an inpatient NP component was added the limb service began to benefit from greater continuity of care given the NPs were permanently part of the service. The NPs also immediately provided unit-based clinical staff with a consistent point of contact for the multidisciplinary team. These are the same benefits identified by Kleinpell and her colleagues in their recent study of the benefits of integrating advanced practice providers in the acute care setting [1].

Discharge Planning Begins on the Day of Admission

When a patient is admitted to the limb service, nurse practitioners begin planning for discharge by rounding on each new patient and discussing certain expectations with them (Fig. 4.1). These guidelines address common barriers to discharge such as: patients wanting to wait for a bed at a preferred rehab or skilled nursing facility, patients wanting to be seen by other services for non-emergent conditions, patients without transportation, and patients without a discharge recommendation from physical therapy. By outlining expectations on the day of admission and reiterating them regularly, the NPs prepare

N. R. Megas (✉) · K. S. Hubley · M. C. Kugler
Plastic Surgery, Medstar Georgetown University Hospital, Washington, DC, USA
e-mail: margaret.c.kugler@gunet.georgetown.edu

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_4

GUIDELINES FOR PATIENTS ADMITTED TO THE HOSPITAL

We understand the enormous burden chronic wounds place on you and your family. We are here to help heal and in turn, to lessen that burden. To do this we need your cooperation. Here are some simple guidelines to maximize your success.

Physical and Occupational Therapy and Your Activity Level – Remaining as active as possible will speed your recovery. You should work with PT and OT therapists whenever they come to see you. If pain is an issue ask them to come back once you've taken pain medication. Without notes in your chart from PT and OT you can't be discharged to rehab. In terms of activity, you should eat at least one of your daily meals sitting up in a chair and spend at least two hours a day out of bed and in a chair.

Prescribed Diets – You'll be prescribed a diet specifically designed to help you heal. Eating foods not on your diet can slow wound healing-especially foods that increase your blood sugar. PLEASE don't ask family and friends to bring you food that isn't on your prescribed diet.

Leaving the Nursing Unit – Smoking/Vaping and use of any tobacco products is prohibited on the entire hospital campus– including outside and parking areas. If desired, patients will be provided with substitutes to help with nicotine withdrawal.

Interaction with Staff-
We strive to cultivate an environment of respect and responsibility. Patients, providers, and staff all have the right to safe, civil, and non-derogatory relations. Failure to maintain these relations may result in referral to an outside practice for continued care, and dismissal from our practice.

Interaction with other MGUH Specialties – During your hospitalization, other specialties may see you. for conditions other than your wounds. You should follow up with these specialties after discharge. Your discharge won't be delayed for you to follow up with them.

Discharge –Depending on your needs, you may be discharged to acute rehabilitation, sub-acute rehabilitation, or home with home care or outpatient therapy. (See descriptions on the back) If discharge to a rehab facility is recommended for you, your Case Manager will help you select 2-3 facilities based on your medical needs, your preferences, and what your insurance covers. You will be discharged to the first of these facilities that accepts you. It's not possible to delay discharge in order to wait for acceptance at a specific facility

Levels of Post-Hospital Care:

- **Acute Rehabilitation**- Provides intensive rehabilitation and nursing services to patients who can tolerate 3 hours of therapy per day.
- **Sub-Acute Rehabilitation** Provides rehabilitation and nursing services to patients who can tolerate 1 hour of therapy a day.
- **Home with Home Therapy and Home Nursing** –For patients who are "home bound" due to medical or functional limitations. Your home care team will teach you and your family how to care for you at home. Home nursing does not provide around-the-clock care.
- **Home with Outpatient Therapy**- This is for patients who are able to go home, and who are medically cleared to travel between their home and physical therapy several times per week.

Fig. 4.1 Guidelines for patients admitted to the hospital

patients to expect to be discharged as soon as their surgeon deems them ready.

Multidisciplinary Discharge Rounds Promote Information Sharing

A second element of the NP led discharge process is attendance at daily multidisciplinary discharge rounds (MDRs). These rounds include case managers, bedside RNs and physical therapists. Multidisciplinary rounds have been demonstrated to improve care coordination including discharge planning [1]. Multidisciplinary rounds have also been shown to be an effective means to facilitate accurate assessments of the social needs of patients and their families, an area often overlooked in the discharge process [2].

At rounds the NPs advise the case management team of each patient's surgical plan and projected date of discharge. The feasibility of various discharge plans is then assessed. For example, despite being recommended for discharge home by the physical therapy team, certain patients requiring complex wound care and/or IV antibiotics may require discharge to a skilled nursing facility. Input from a patient's bedside nurses is crucial in these discussions as they are the most reliable resources regarding a patient's abilities and temperament. The bedside nurse also often provides valuable information regarding variables that can lead to discharge failures such as family dynamics or a change in living arrangements.

When vetting possible discharge options the NPs draw on their experience with particular types of surgery to frequently advocate for disposition to an acute rehabilitation or skilled nursing facility. For example, young healthy patients, status post below knee amputations are often recommended for discharge to their home. Too often, though, these patients experience falls in the home especially after awakening in the middle of the night. Invariably they report they simply forgot about their amputation. NPs will advocate for transition to acute rehab before going home to give these patients the time to develop the mental memory needed to be safe at home. Similarly the NPs advocate for free muscle flap patients to be discharged to a facility instead of home given the initially fragile nature of these flaps and the need for skilled assessment of any changes they exhibit in the postoperative period.

While the benefit of MDRs can be intuited, in 2019 Patel and colleagues developed quantitative analyses of their benefit at the tertiary academic medical center where they practiced. During their study, 1584 patients were discharged from all medicine teams, 825 from teams utilizing MDRs and 759 from control teams. The proportion of patients with discharge before noon (DBN) orders was 41.2% on pilot versus 29.6% on control teams. Length of stay was 92.2 h versus 97.2 h, and 30-day readmission rate was 16.0% versus 18.3% for the pilot versus control teams, respectively. The 30-day readmission rate was 12.6% compared with 18.9% for the pilot versus control teams [3].

One outcome of MDRs is that limb NPs are made aware of barriers to discharge such as a patient who cannot maintain their prescribed weight bearing status. In these cases the NPs will frequently reach out to the patient's surgeon to develop alternative weight bearing restrictions. In some cases a total contact cast (Fig. 4.2) with a walking boot may be applied on the day of discharge and the patient allowed to bear weight for



Fig. 4.2 Total Contact Cast-TCC-EZ®

transfers. In order to expedite discharges an orthotics vendor is on site weekdays at MGUH. In the case of a patient with a heel wound and strict nonweight bearing orders, for example, the orthotics team may be brought in to cast the patient for a custom boot to offload the wound.

Communication Between All Services Is Critical

With rare exception, internal medicine is consulted for the management of all limb patients' comorbidities. As needed, other services such as nephrology, endocrinology, and rheumatology are also consulted. The limb service's NPs serve as critical liaisons with all consulting services. The NPs review progress notes and speak with the residents and attendings of consult services daily to confirm agreement with the planned date of discharge and establish what their requirements are for the patient in terms of new medication/supplies scripts and follow-up appointments. Communication like this is the type of collaboration among providers that is repeatedly called for throughout discussions of improved transitions [4]. Prior to establishing collaboration between limb NPs and consulting services, limb team residents would often issue a discharge order only to have to cancel the order when a consulting service advised that from their point of view the patient was not ready for discharge.

Antibiotic Therapy Requires Early Consideration

An important aspect of discharge planning for limb salvage patients is planning for their antibiotic therapy. MGUH's Musculoskeletal Infectious Disease service is consulted for all limb salvage patients. The limb NP team confers daily with the services' attendings to understand which patients may require IV antibiotics at discharge. They then meet with the patient, advise them of the need for a central line, and then order the appropriate line. Chronic kidney disease patients are not candidates for PICC lines due to the possible need for future dialysis access and will receive alternative access such as a Hickman catheter. These placements require pre-procedure NPO status and sedation which must be taken into consideration in establishing a discharge timeline. Patients already on hemodialysis who require IV antibiotics after discharge can often have their antibiotic administered at their dialysis facility. The NP team interfaces with the patient's hemodialysis facility, ordering the antibiotic and appropriate lab tests. Keeping a close eye on discharge antibiotic plans wards off unexpected surprises such as discovering a patient ready to leave does not have appropriate access for antibiotic infusions.

Provider Involvement Contributes to Successful Transitions

Kripalani and colleagues point out that the effectiveness of a patient transition is often enhanced by the involvement of the attending physician [2]. The limb NPs are in constant communication with the team's attending surgeons, advising them when they need to see a particular patient to pave the way for that patient's discharge. Prior to the NP team serving in this capacity, a well meaning resident would often walk into a patient's room and advise them they were being discharged only to be told, "Absolutely. My doctor didn't say anything about leaving." By alerting patients to their discharge plan and then bringing attending physicians into the discussion the NP team mediates this frequent barrier to discharge.

The limb team's surgeons further contribute to maximizing a patient's potential for successful discharge by identifying those patients at risk for surgical site complications and ordering appropriate interventions. One of these interventions is the use of negative pressure wound therapy (NPWT) on closed incisions. While closed incisions are typically dressed with a sterile dressing, limb salvage patients are at a higher risk for postoperative wound complications, such as infection, dehiscence, and hematoma and seroma formation [5]. Shiroky and colleagues in a review of 44 randomized controlled trials with $N = 5693$

patients reported that patients treated with NPWT) for closed incisions experienced nearly a 40% reduction in the risk of surgical site infections relative to those with standard dry sterile dressings. A statistically significant reduction in wound dehiscence and seroma incidence was also reported [6]. MGUH's limb surgeons began applying NPWT to closed incisions with the introduction of disposable short term use NPWT devices and were among the early identifiers of the same benefits described by Shiroky and colleagues. Now it is a frequent practice for our surgeons to place NPWT at the time they close an incision.

Once a patient is ready for discharge the surgeons will decide if NPWT should be continued. These patients are transitioned from the standard NPWT device that had been placed at the time of closure to a disposable seven or fourteen day unit. The patient will be instructed to leave the device on and operating until clinic follow-up. In cases where the device's preprogrammed life will end before follow-up can be arranged, the patient will either be advised to disconnect the tubing, discard the device, and leave the dressing on and intact until follow-up or remove the NPWT dressing and place a dry dressing on the incision.

A One Page Snapshot of Each Admission Provides an Invaluable Bridge

Once the myriad elements involved in discharging a limb patient come together and the patient is discharged, ensuring appropriate follow-up and capturing and communicating key elements of the admission are the next priority. Given the volume of patients discharged every day and the complicated nature of their care, an immediately available, easy-to-reference resource is necessary in order for the limb outpatient clinic staff to be able to field the barrage of questions they receive. Literally within hours of discharge the clinic receives calls from patients, their families, home health nurses, and rehabilitation or skilled nursing facility staff. As the result of close interaction with the clinic staff, the limb NP team developed a reference document called a discharge white sheet (Fig. 4.3) which they complete for every inpatient seen by the limb service. The document is available to all users of MGUH's electronic medical record EMR (Cerner) and is found in Clinical Documents-Discharge Documents. Information contained in the one page document goes beyond that found in a traditional discharge summary and unlike a discharge summary which may not appear for weeks is available within 24 h of a patient's discharge.

Before the implementation of the white sheet, clinic staff spent a frustratingly long period of time trying to find answers to commonly asked questions such as, "How often should my dressing be changed?" or "Can I bear weight on my incision?" Home health nurses and skilled nursing facilities also bombard the clinic with an assortment of questions. Using the white sheet, clinic staff can quickly answer just about any question regarding a recent admission.

Part of completing a white sheet involves confirming postoperative or follow-up appointments for discharged patients. Before the document was introduced the limb service invariably lost some patients to follow-up. This was most likely to happen with patients who the limb team saw as consults. By maintaining a patient list of all patients both primary and secondary and not removing patients from the list until a discharge white sheet is completed, limb NPs ensure appropriate follow-up is arranged for every patient seen by their team.

In addition to providing a snapshot of an admission, the white sheet can be used to manage post-discharge care. Some patients with less complicated, non-surgical wounds may not need to be seen in clinic immediately after discharge. Instead the NP team will forward the white sheet to the clinic RN pool requesting the patient be called within a certain period of time and asked about the status of his or her wound. Based on the patient's response, the RN can then either advise the patient to continue monitoring their wound or arrange a clinic appointment for them.

White sheets are also forwarded to the outpatient clinic staff of other services such as the mus-

DISCHARGE WHITE SHEET

Discharge Date: 02/11/2021

HPI and Procedures: 65-year-old male with a PMH of DM TYPE2, HTN, CKD Stage 3, seen in clinic since 1/2020 for chronic R heel ulcer. Presents with worsening drainage, odor and pain,
Procedures:
2/1 Debridement R heel, instill VAC placement
2/4 Debridement R heel, instill VAC placement
2/9 Debridement and closure R heel

When to Return to Clinic: 2/21 @ 9:00 with CEA

Discharged to: Home or Facility Name and Phone Number
Cliffwood Health and Rehab 301- 555- 1239

VNA Name and Phone Number:
n/a

Dressing Change Orders:
R Heel: every 3 days
Remove dressing, cleanse w/ normal saline, pat dry
Apply non adherent over incisions
Cover with gauze and wrap with rolled cast padding
Apply light ACE. Reapply shoe wear provided at discharge

Weight bearing status of operative extremity:W
Non-weight bearing R LE

Nascott / DME:
[X] CAM Boot

Antibiotics:
Prescriber, Medication, Dose, Duration:
Davis, Vancomycin 1.5gram IVPB q 12 hr thru 3/16/2021
Labs Required: Include Frequency and Fax Number:
CBC, CMP, ESR and vancomycin trough weekly to 202 555 1234

Anticoagulation:
none

Pain Medication, dosage and quantity prescribed:
Oxycodone 5 mg ,1-2 tabs q 4 prn, qty: 20 tabs

Fig. 4.3 Discharge white sheet

culoskeletal/soft tissue infectious disease. This keeps the service updated regarding patients who were discharged on IV antibiotics and may need follow-up with an ID attending. It also provides the necessary information needed to contact a patient's infusion company should dosing levels or duration of therapy require adjustment.

Skillful Outpatient Clinic Care Furthers the Progress Made During an Inpatient Stay

MGUH's Center for Wound Healing sees over 300 patients a week; there are often ten exam rooms in use at a time. As the limb team's volumes grew to this level, clinic staff learned to maximize efficiency in order to see such a large number of new, follow-up, and postoperative patients. Patients are first taken to an exam room by a medical assistant who obtains vital signs, removes any dressing, and starts the visit entry in the electronic medical record. An RN then sees the patient, documenting HPI and wound dimensions, updating medications, and further updating the visit note. Next the attending sees the patient. At this stage procedures such as debridements or biopsies may be performed and imaging may be obtained. Once the attending has finished with the patient, the RN finalizes the visit, reviews instructions, confirms follow-up plans, and initiates visiting nurse orders or starts surgery coordination packets if necessary. If orthotic or prosthetic needs exist, a specialist is available to be called into the exam room.

In addition to the limb team's attendings, two outpatient NPs see patients in the outpatient clinic. These NPs have their own designated independent clinic days and see a variety of patient types of particular benefit, they often see postoperative appointment patients and patients with chronic wounds such as venous stasis ulcers that do not require surgical intervention. By managing these patients, the NPs free up time for the team's surgeons to spend with more complex and new patients. When not running their own clinics the NPs work alongside the surgeons during patient visits and contribute their clinical expertise to the triaging of patient inquiries. In the District of Columbia NPs have full independent prescriptive privileges which allow clinic staff to turn to them to handle patient medication requests, once again, freeing up the surgeons.

Communication Between the NP Team and the Outpatient Clinic Staff Is Critical

Recognizing their shared responsibility for a limb patient's outcome, the inpatient NPs and outpatient nursing staff regularly communicate with one another. In addition to the exchange of information through discharge white sheets, an inpatient NP will often reach out to the clinic nursing staff with information about a patient's admission or to discuss possible clinic follow-up options. Conversely the clinic nursing staff regularly reaches out to the inpatient NPs to alert them to details regarding a complicated admission such as a patient with poor venous access who will require a central line. In some cases where very close monitoring is warranted, arrangements are made for a patient to have RN appointments in addition to their regular provider appointments.

Day-After-Discharge Calls Flag Problems

The Joint Commission recommends hospitals develop a process that provides for timely post-discharge follow-up with patients. Ideally telephone or in-person follow-up should take place within 24–48 h after discharge [7]. At MGUH, a case management staff member makes this phone call. During the call, patients are asked about their understanding of their medications, home care, and planned follow-up. Regularly information gleaned from these calls is forwarded to the inpatient NPs who then reconnect with patients to clear up any post-discharge confusion. A frequent issue encountered is the failure of home nursing services to see patients as ordered. Prior to this program's implementation, it was not until

the first post-op visit that the limb team became aware of the fact a patient was not receiving wound care that had been ordered. These calls also identify problems regarding the medications prescribed at discharge. Because medication errors are behind many of the adverse events patients experience following hospital discharge [8], these calls are particularly important. In some cases patients are found to be unaware of new medications prescribed for them or to not have received scripts for new medications.

Well Managed Transitions Impact a Hospital's Bottom Line

Beginning in October of 2012 the Patient Protection and Affordable Care Act instituted the Hospital Readmission Reduction Program. As part of the program hospitals were financially penalized if they had excess readmissions among patients with select conditions. The initial round of penalties was for readmissions after admission for heart attack, congestive heart failure, or lung infection [9]. Recently knee arthroplasty was added to the program. It is reasonable to expect that over time, pressure on readmissions will be exerted on most admissions. In this environment, an effective discharge process becomes critical for a hospital's financial health.

Readmissions are not the only discharge related events that can negatively impact a hospital's bottom line. 2013 Care Transition Measures were added to the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS). HCAHPS is the survey tool used by the Centers for Medicare and Medicaid to determine if a facility can collect 100% of its Medicare reimbursements or is docked up to 2% in the event of poor ratings on the survey. The three questions that comprise the Care Transition Measures were:

- Question 1:"The hospital staff took my preferences and those of my family or caregivers into account in deciding what my health care needs would be when I left the hospital" (focus on when the patient was in the hospital).
- Question 2: "When I left the hospital, I had a good understanding of the things I was responsible for in managing my health" (focus on discharge preparedness).
- Question 3: "When I left the hospital, I clearly understood the purpose for taking each of my medications" (focus on medication understanding at time of hospital discharge).

With the addition of these measures, well managed transitions are important not only for patients' health and safety, but also for a hospital's bottom line.

MGUH's limb salvage patients consistently rate their discharge experience very highly as shown in Fig. 4.4 benchmarking the limb salvage team's 2020 performance on the three care transition questions against all hospitals and against academic hospitals. The work that the limb NPs do to manage every patient's discharge is felt to be a significant driver for these results.

	Percentile When Benchmarked Against all Hospitals	Percentile When Benchmarked Against Academic Hospitals
Question 1	94th	96th
Question 2	98th	99th
Question 3	91st	90th

Fig. 4.4 MGUH limb service performance on HCAHPS care transition measures

Conclusion

Effectively bridging inpatient admission and outpatient care is a key element behind MGUH's successful limb salvage program. The process, spearheaded by a team of nurse practitioners includes the fundamental elements for effective care transitions put forth by The Joint Commission in 2014: interdisciplinary coordination and collaboration of patient care in care transitions, shared accountability by all clinicians involved in care transitions, and provision of appropriate support and follow-up after discharge [10]. The process enjoys unilateral support from the team's surgeons and residents and from the outpatient clinic staff. In addition patients and their families often communicate to the providers and staff that they appreciate the continuity of care provided by the inpatient nurse practitioners. The process's linchpins, timely, effective communication, and attention to detail ensure smooth transitions and allow the team to maximize its rate of limb salvage successes.

References

1. Kleinpell RM, Grabenkort WR, Kapu AN, Constantine R, Sicoutris C. Nurse practitioners and physician assistants in acute and critical care: a concise review of the literature and data 2008–2018. Crit Care Med. 2019;47(10):1442–9. https://doi.org/10.1097/CCM.0000000000003925.
2. Kripalani S, Jackson AT, Schnipper JL, Coleman EA. Promoting effective transitions of care at hospital discharge: a review of key issues for hospitalists. J Hosp Med. 2007;2:314–23. https://doi.org/10.1002/jhm.228.
3. Patel H, Yirdaw E, Yu A, Slater L, Perica K, Pierce RG, Amaro C, Jones CD. Improving early discharge using a team-based structure for discharge multidisciplinary rounds. Prof Case Manag. 2019;24(2):83–9. https://doi.org/10.1097/NCM.0000000000000318. PMID: 30688821
4. The Joint Commission. Hot topics in health care, issue #2. Transitions of care: The need for collaboration across entire care continuum. 2013. http://www.jointcommission.org/assets/1/6/TOC_Hot_Topics.pdf. Accessed 12 Jan 2021.
5. Hyldig N, Birke-Sorensen H, Kruse M, Vinter C, Joergensen JS, Sorensen JA, Mogensen O, Lamont RF, Bille C. Meta-analysis of negative-pressure wound therapy for closed surgical incisions. Br J Surg. 2016;103(5):477–86. https://doi.org/10.1002/bjs.10084. PMID: 26994715; PMCID: PMC5069647.
6. Shiroky J, Lillie E, Muaddi H, Sevigny M, Choi WJ, Karanicolas PJ. The impact of negative pressure wound therapy for closed surgical incisions on surgical site infection: a systematic review and meta-analysis. Surgery. 2020;167(6):1001–9. https://doi.org/10.1016/j.surg.2020.01.018. Epub 2020 Mar 3. PMID: 32143842.
7. The Joint Comission. Hot topics in health care: transitions of care: the need for a more effective approach to continuing patient care. 2012. https://www.jointcommission.org/assets/1/18/Hot_Topics_Transitions_of_Care.pdf. Accessed 26 Dec 2020.
8. Moore C, Wisnivesky J, Williams S, McaGinn T. Medical errors related to discontinuity of care from an inpatient to and outpatient sett. J Gen Intern Med. 2003;18:646–51.
9. McIlvennan CK, Eapen ZJ, Allen LA. Hospital readmissions reduction program. Circulation. 2015;131(20):1796–803. https://doi.org/10.1161/CIRCULATIONAHA.114.010270. PMID: 25986448; PMCID: PMC443993.
10. Sheikh F, Garhecha E, Bellantonni M, Christmas C, Lafrenierre J, Arbaje A. A call to bridge across silos during care transitions. Jt Comm J Qual Patient Saf. 2018;44(5):270. https://doi.org/10.1016/j.jcjq.2017.10.006.
11. Wukich DK, Armstrong DG, Attinger CE, Boulton AJ, Burns PR, Frykberg RG, Hellman R, Kim PJ, Lipsky BA, Pile JC, Pinzur MS, Siminerio L. Inpatient management of diabetic foot disorders: a clinical guide. Diabetes Care. 2013 Sep;36(9):2862–71. https://doi.org/10.2337/dc12-2712. PMID: 23970716; PMCID: PMC3747877.

5 Diabetic Foot Ulcers by the Numbers: Epidemiology of Limb Salvage

Romina Deldar, Adaah A. Sayyed, Zoe K. Haffner, and John S. Steinberg

Introduction

According to the International Working Group on the Diabetic Foot (IWGDF), a diabetic foot is an infection, ulceration, or destruction of the foot associated with neuropathy and/or peripheral arterial disease (PAD) in people with diabetes mellitus [1]. Diabetic foot ulcers (DFUs) are a preventable complication of diabetes that can lead to increased disability if left untreated, lower extremity (LE) amputation. DFUs have profound implications for the individual, community, and health system at large. It is estimated that 4.8 million people (7% of the population) in the UK, 30.3 million (9.4%) in the USA, and 366 million (7%) of the world's population carry a diagnosis of diabetes [2, 3]. In 2019, the International Diabetes Federation (IDF) estimated that 463 million people globally live with diabetes and predicted that by 2045, more than 700 million people will be living with the disease [4].

DFUs serve as a major source of global morbidity and mortality due to repeated hospital admissions and increased risk of amputations, which may incur substantial healthcare costs [2, 4]. Approximately 50% of DFUs will become infected, and about 20% will require LE amputation [5]. In fact, diabetic foot wounds are the most common cause of non-traumatic LE amputations worldwide and are responsible for an estimated 67% of LE amputations in the USA [6–8]. Furthermore, patients with diabetic foot complications have a high rate of recurrent foot ulcers [9] and worse survival than that of many common cancers [10]. Recent advances in management have focused on limb salvage modalities and multidisciplinary team collaboration to prevent DFUs and avoid amputations. This chapter provides an overview of the epidemiology of diabetic foot wounds, including the associated healthcare costs and implications associated with major amputations versus limb salvage efforts.

Prevalence and Scope of the Problem

The incidence of DFUs has risen secondary to the increasing worldwide prevalence of diabetes and the prolonged life expectancy of diabetic patients [11]. Among those living with diabetes, the lifetime risk of developing a DFU is approximately 25%, with up to 40% of diabetics having a risk of

R. Deldar (✉) · A. A. Sayyed · Z. K. Haffner
Department of Plastic and Reconstructive Surgery, MedStar, Georgetown University Hospital, Washington, DC, USA
e-mail: romina.deldar@medstar.net; zkh@georgetown.edu

J. S. Steinberg
Department of Plastic Surgery, Georgetown University School of Medicine and MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: John.Steinberg@medstar.net

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_5

undergoing LE amputation [2, 4, 12, 13]. By 2050, the number of people in the USA with diabetes is expected to exceed 48.3 million, which will consequently increase the DFU burden [14, 15]. The prevalence of DFUs is estimated to be 19–34%, whereas the recurrence rate of DFUs is estimated to be 40% within 1 year and 65% within 3 years [1]. Approximately 50% of patients with DFUs will experience infectious complications that necessitate hospitalization [16, 17]. Patients with infected DFUs have a 55.7 times greater risk of hospitalization and a 154 times higher risk of amputation compared to patients with non-infected DFUs [16]. In 2006, it was reported that 1.6 million people underwent amputation in the USA; this number is expected to rise to 3.6 million in 2050 [18].

The annual prevalence of DFUs among Medicare beneficiaries with diabetes is approximately 8% [19]. It has been reported that during foot ulcer episodes-of-care, all-cause inpatient admissions were 2.8 times more likely, and death was 1.5 times more likely compared to periods following healing within the same beneficiaries [20]. Several possible physiological mechanisms for the independent association between foot ulceration and all-cause mortality have been hypothesized, including acute consequences of DFUs, such as severe sepsis and its sequelae (e.g., multiorgan failure), and long-term consequences such as chronic inflammation of the cardiovascular and renal systems associated with DFUs [21].

The provision of comprehensive preventive care to arrest the development of DFUs in high-risk populations may improve healthcare outcomes beyond those associated traditionally with diabetic foot syndrome. Evidence-based preventive care includes routine foot exams by specialist providers, structured education regarding patient self-care, daily self-exams, use of appropriate therapeutic footwear worn by the patient at all times, once-daily foot temperature monitoring to identify inflammation that could precede DFUs, and aggressive and prompt treatment of any pre-ulcerative lesions (e.g., callus or blister) [22]. A study by Isaac et al. [23] incorporated these recommended practices and found significant reductions in all-cause inpatient admissions (RRR = 52%). Another study found that patients receiving preventive foot exams over 1 year had lower odds of hospitalization for any cause within that year (OR = 0.67) [24].

Healthcare Costs of the Diabetic Foot

DFUs place a significant burden on healthcare budgets worldwide due to the complex and lengthy course of treatment from prevention of foot disease to LE amputation. Direct costs include admissions, wound dressings, antibiotics, and surgery, while indirect costs result from the social and psychological impacts of diabetic foot disease [25]. Although the largest direct expenditures are related to hospital admissions, the loss of productivity and decreased quality of life further contribute to additional expenses [25]. Compared to colorectal cancer, the costs derived from diabetic foot care contribute to three-fold higher expenses [26]. Although many studies over the past 20 years have published economic analyses of DFUs, the exact costs related to this complication are difficult to ascertain due to the complexity of the condition and variations in healthcare systems, reimbursement methods, access to care, and research methodologies.

From the time a patient is diagnosed with a DFU, the patient and hospital systems experience exponential increases in expenses; a five-fold increase in costs occurs within the first year following development of the ulcer, with costs rising as the severity of ulcers increases [27]. This necessitates team-based interventions and aggressive treatment strategies at earlier disease stages to try and prevent amputations. Other major sources of expenditure in patients with DFUs are the use of emergency room services and repeated hospitalizations [27]. Compared to diabetic patients without foot ulcers, DFU-related costs are estimated to add approximately 9–13 billion USD to the costs already associated with diabetes [28]. From 2006 to 2010, DFUs further contributed 1.9 billion USD to the US Emergency Department and 8.78 billion USD to inpatient

departments per year [14]. An estimated 10.5% of DFU cases underwent LE amputations, resulting in 115,957 USD cost per major amputation [14].

Few studies address the economic benefits of interventions for prevention and treatment of diabetic foot disease. The most common predictive model used is the Markov model for cost-effectiveness, a mathematical tool utilized to obtain projections of costs and effects for interventions [27]. Use of preventive strategies has led to reductions in 5-year costs related to DFUs, with the Markov model predicting cost-savings of greater than 90% if low-cost preventive measures are implemented to reduce the incidence of DFUs and resultant amputations [26]. Educational interventions, therapeutic footwear coverage, and multidisciplinary team approaches can avoid up to 72%, 53%, and 47% of amputations, respectively. These cost reductions translate into $1,100,000, $850,000, and $750,000 in potential savings within 1 year of use of each intervention, highlighting the significant cost-saving benefits of preventive measures [29].

Guideline-based management of DFUs has been shown to improve survival, reduce diabetic foot complications, and decrease cost when compared to usual care. Clinical and economic outcomes illustrate reduced amputation rates, costs, and length of stay. Emphasis on early recognition and prevention of DFUs alongside early consultation of limb preservation services is of immense importance in order to prevent significant pathologic abnormality and increased risk of amputation.

Amputation Versus Limb Salvage

The incidence of non-traumatic LE amputations is at least 15 times greater in patients with diabetes than with any other concomitant medical illness [12]. Over 85% of major LE amputations in diabetics are preceded by foot ulcers [30, 31]. Previous studies have reported that apart from severity of ulcer, age [32], low socioeconomic status, smoking [33, 34], male sex [35], renal impairment [36], diabetic neuropathy [37], glucose levels [38], and PAD [39] are factors associated with risk of amputation [30]. Among diabetics, approximately 55% of all amputations occur in people over the age of 65 [2].

While our data shows that a well performed LE amputation in a multidisciplinary setting can greatly improve outcomes, the general literature tells us that only two-thirds of diabetic patients who undergo major LE amputation will ambulate with a prosthesis [40]. This likely contributes to why major LE amputees are three times more likely to die within 1 year of surgery compared to patients who have not undergone major LE amputation [40]. A retrospective review by Ducic and Attinger found that by preserving the limb in diabetic patients using advanced soft-tissue reconstructive techniques, the survival at 8 years was 59% [41]. Oh et al. evaluated 121 cases of reconstructed diabetic foot and reported a limb salvage rate of 84.9% and 5-year survival of 86.8% [42]. Aggressive limb salvage attempts are justified in diabetic patients with foot wounds, whenever possible...and especially when the patient has poor prosthetic rehabilitation potential.

Globally, the rate of major LE amputations is decreasing. This is likely secondary to several factors, including improved management of diabetes and its complications, advanced wound healing modalities, and increased pursuit of diabetic limb salvage. Limb salvage is defined as preservation of the ankle joint and avoidance of a major amputation [43]. Partial foot (or minor) amputations up to the level of the transverse tarsal joint (Chopart's joint) and calcanectomies are considered to be successful limb salvage procedures. These surgeries are performed once the diabetic foot wound has been adequately debrided to healthy tissue. It has been shown that wounds heal 30% faster when debrided weekly [44]. Evans et al. [45] reported a 2-year survival rate of 80% (70 of 88 patients) following proximal forefoot and midfoot amputations, compared to 48% (12 of 25) in patients who underwent BKA. A 2014 study of 154 diabetic patients who underwent toe amputations or transmetatarsal amputation (TMA) for forefoot gangrene reported the 5-year survival of the limb salvage group was 81.6% and 36.4% for the failed limb salvage group [46]. A recent study evaluated diabetic

patients with ulcers of the heel, the second most common location of DFUs [47], who underwent a vertical contour calcanectomy [48] and found that nearly one-third of patients had no ulcer recurrence, amputation, or mortality 1 year after the procedure. Limb salvage efforts in diabetic patients should be considered before major LE amputations due to increased morbidity and mortality.

Socioeconomic and Ethnic Disparities in Diabetic Foot Management

Research has shown a correlation between level of education and diabetes prevalence, with an estimated 12.6% of adults with less than a high-school level education having diabetes compared to 7.2% of adults with an education level greater than high school [3]. Furthermore, socioeconomic status and insurance coverage may influence which diabetic patients will have an opportunity for limb salvage. Multiple studies have found that nonwhite, low-income, Medicare, and Medicaid patients were more likely to undergo amputation for leg ischemia and to have less access to limb salvage procedures compared with higher-income patients who had private insurance [49, 50]. A possible explanation for this observed disparity is that economically disadvantaged individuals often present with more advanced ischemia probably due to a lack of access to preventative care.

Amputation rates vary within ethnic populations across the world. Reports have shown a higher incidence of major LE amputation in African-Americans compared to Caucasian people with diabetes [51]. A Kaiser health study found that from 2011 to 2017, doctors in California performed more than 82,000 diabetic amputations; African American and Latino patients were more than twice as likely as Caucasians to undergo amputations secondary to diabetes [52]. Risk factors, such as smoking, low socioeconomic status, and poor access to healthcare, may contribute to these ethnic disparities [53, 54]. Asian diabetic patients have a much lower incidence of LE amputation than Caucasian patients [55]. The lower prevalence of PAD and neuropathy among Asians may serve as protective factors against LE amputation [56, 57].

Mortality and Outcomes

In the USA, diabetes-related mortality has surpassed the number of deaths due to acquired immunodeficiency syndrome (AIDS) and breast cancer combined [2, 3, 58]. In 2016, diabetes was the direct cause of 1.6 million deaths [59]. There is a significant mortality risk associated with development of DFUs. A 2015 study from the UK demonstrated the 5-year mortality risk for patients with DFUs is 2.5 times higher than diabetic patient without a foot ulcer [60]. A similar study in Norway showed the 10-year mortality risk was twice as high for patients with history of DFU compared to diabetic patients without history of foot ulceration when adjusted for age, sex, and various comorbidities [61]. The 1-year mortality rate for DFU patients alone is estimated to be 5% [62]. This mortality rate increases up to 25% if the DFU becomes infected [63]. The mortality rate dramatically increases up to 68% at 5 years, a rate comparable to several types of cancer and congestive heart failure [58, 63, 64]. Furthermore, DFU patients typically present with metabolic syndrome, the constellation of insulin resistance, central obesity, dyslipidemia, and hypertension, placing them at increased risk of cardiovascular events [64].

Even with aggressive management, many DFUs will eventually require LE amputation, often within just 4 years of diagnosis. The risk of amputation in diabetics is 30–40 times higher than non-diabetics [64]. Following major LE amputations, 30-day mortality rates of 5.7% for below-knee amputations and 16.5% for above-knee amputations have been reported [65]. A recent systematic review found that following major LE amputation, mortality is estimated at over 33%, 53%, 64%, and 80% at 1, 3, 5, and 10 years, respectively [66]. A New Zealand study evaluating 300,000 patients who underwent

major LE amputation observed an overall 30-day mortality rate of 11% and 90-day mortality rate of 18% [67]. Infected DFUs that require emergent amputation carry a mortality risk of up to 50% due to severe sepsis and the effects of tissue necrosis [68]. In general, more proximal LE amputations in diabetic patients are associated with higher in-hospital and 30-day mortality [69].

Mortality risk following with LE amputation increases with concurrent PAD and renal disease [70, 71]. One-year survival rate after LE amputation in patients with end-stage renal disease (ESRD) on hemodialysis is estimated to approach 50% [72], which is notably lower than those of patients who are hospitalized for heart failure or myocardial infarction. In comparison, diabetic limb salvage procedures, such as minor LE amputations, portend significantly lower mortality rates compared to major amputations. A meta-analysis found the mortality rates after minor amputation in diabetic patients to be 3.5% at 1 month, 20% at 1 year, 28% at 3 years, 44.1% at 5 years [59]. Therefore, whenever possible, limb salvage should be attempted in diabetic patients who present with foot ulcers to minimize morbidity and mortality.

Financial Disclosure Statement The authors have no financial disclosures, commercial associations, or any other conditions posing a conflict of interest to report.

References

1. International Working Group of the Diabetic Foot - epidemiology, psychosocial, and economic factors. Maastricht: IWGoD; 2019 [cited 2019. https://iwgdf-guidelines.org/wp-content/uploads/2019/05/IWGDF-Guidelines-2019.pdf.
2. Dayya D, O'Neill OJ, Huedo-Medina TB, Habib N, Moore J, Iyer K. Debridement of diabetic foot ulcers. Adv Wound Care. 2021;11:666.
3. 2021 National Diabetes Statistics Report: Centers for Disease Control and Prevention. https://www.cdc.gov/diabetes/data/statistics-report/index.html.
4. Jodheea-Jutton A, Hindocha S, Bhaw-Luximon A. Health economics of diabetic foot ulcer and recent trends to accelerate treatment. Foot. 2022;52:101909.
5. Wu SC, Driver VR, Wrobel JS, Armstrong DG. Foot ulcers in the diabetic patient, prevention and treatment. Vasc Health Risk Manag. 2007;3(1):65–76.
6. Ahmad N, Thomas GN, Gill P, Torella F. The prevalence of major lower limb amputation in the diabetic and non-diabetic population of England 2003-2013. Diab Vasc Dis Res. 2016;13(5):348–53.
7. Wukich DK, Raspovic KM. Assessing health-related quality of life in patients with diabetic foot disease: why is it important and how can we improve? The 2017 Roger E. Pecoraro Award Lecture. Diabetes Care. 2018;41(3):391–7.
8. Morbach S, Furchert H, Gröblinghoff U, Hoffmeier H, Kersten K, Klauke GT, et al. Long-term prognosis of diabetic foot patients and their limbs: amputation and death over the course of a decade. Diabetes Care. 2012;35(10):2021–7.
9. Armstrong DG, Boulton AJM, Bus SA. Diabetic foot ulcers and their recurrence. N Engl J Med. 2017;376(24):2367–75.
10. Armstrong DG, Wrobel J, Robbins JM. Guest Editorial: are diabetes-related wounds and amputations worse than cancer? Int Wound J. 2007;4(4):286–7.
11. Zhang P, Lu J, Jing Y, Tang S, Zhu D, Bi Y. Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis (†). Ann Med. 2017;49(2):106–16.
12. Margolis DJ, Allen-Taylor L, Hoffstad O, Berlin JA. Diabetic neuropathic foot ulcers: the association of wound size, wound duration, and wound grade on healing. Diabetes Care. 2002;25(10):1835–9.
13. Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. JAMA. 2005;293(2):217–28.
14. Skrepnek GH, Mills JL Sr, Armstrong DG. A diabetic emergency one million feet long: disparities and burdens of illness among diabetic foot ulcer cases within Emergency Departments in the United States, 2006-2010. PLoS One. 2015;10(8):e0134914.
15. Deshpande AD, Harris-Hayes M, Schootman M. Epidemiology of diabetes and diabetes-related complications. Phys Ther. 2008;88(11):1254–64.
16. Lavery LA, Armstrong DG, Wunderlich RP, Mohler MJ, Wendel CS, Lipsky BA. Risk factors for foot infections in individuals with diabetes. Diabetes Care. 2006;29(6):1288–93.
17. Lavery LA, Davis KE, Berriman SJ, Braun L, Nichols A, Kim PJ, et al. WHS guidelines update: diabetic foot ulcer treatment guidelines. Wound Repair Regen. 2016;24(1):112–26.
18. Varma P, Stineman MG, Dillingham TR. Epidemiology of limb loss. Phys Med Rehabil Clin N Am. 2014;25(1):1–8.
19. Margolis DJ, Malay DS, Hoffstad OJ, Leonard CE, MaCurdy T, Nava KLD, et al. Prevalence of diabetes, diabetic foot ulcer, and lower extremity amputation among Medicare beneficiaries, 2006 to 2008: Data Points #1. Data Points Publication Series, Agency for Healthcare Research and Quality (US); 2011.
20. Petersen BJ, Linde-Zwirble WT, Tan T-W, Rothenberg GM, Salgado SJ, Bloom JD, et al. Higher rates of all-cause mortality and resource utilization during

episodes-of-care for diabetic foot ulceration. Diabetes Res Clin Pract. 2022;184
21. Brownrigg JR, Griffin M, Hughes CO, Jones KG, Patel N, Thompson MM, et al. Influence of foot ulceration on cause-specific mortality in patients with diabetes mellitus. J Vasc Surg. 2014;60(4):982–6.e3.
22. Bus SA, Lavery LA, Monteiro-Soares M, Rasmussen A, Raspovic A, Sacco ICN, et al. Guidelines on the prevention of foot ulcers in persons with diabetes (IWGDF 2019 update). Diabetes Metab Res Rev. 2020;36(Suppl 1):e3269.
23. Isaac AL, Swartz TD, Miller ML, Short DJ, Wilson EA, Chaffo JL, et al. Lower resource utilization for patients with healed diabetic foot ulcers during participation in a prevention program with foot temperature monitoring. BMJ Open Diabetes Res Care. 2020;8(1):e001440.
24. Albright RH, Fleischer AE. Association of select preventative services and hospitalization in people with diabetes. J Diabetes Complications. 2021;35(5):107903.
25. Jeffcoate WJ, Vileikyte L, Boyko EJ, Armstrong DG, Boulton AJM. Current challenges and opportunities in the prevention and management of diabetic foot ulcers. Diabetes Care. 2018;41(4):645–52.
26. Barshes NR, Saedi S, Wrobel J, Kougias P, Kundakcioglu OE, Armstrong DG. A model to estimate cost-savings in diabetic foot ulcer prevention efforts. J Diabetes Complications. 2017;31(4):700–7.
27. Driver VR, Fabbi M, Lavery LA, Gibbons G. The costs of diabetic foot: the economic case for the limb salvage team. J Vasc Surg. 2010;52(3 Suppl):17s–22s.
28. Rice JB, Desai U, Cummings AK, Birnbaum HG, Skornicki M, Parsons NB. Burden of diabetic foot ulcers for medicare and private insurers. Diabetes Care. 2014;37(3):651–8.
29. Ollendorf DA, Kotsanos JG, Wishner WJ, Friedman M, Cooper T, Bittoni M, et al. Potential economic benefits of lower-extremity amputation prevention strategies in diabetes. Diabetes Care. 1998;21(8):1240–5.
30. Vadiveloo T, Jeffcoate W, Donnan PT, Colhoun HC, McGurnaghan S, Wild S, et al. Amputation-free survival in 17,353 people at high risk for foot ulceration in diabetes: a national observational study. Diabetologia. 2018;61(12):2590–7.
31. Jeffcoate WJ, Harding KG. Diabetic foot ulcers. Lancet. 2003;361(9368):1545–51.
32. Winkley K, Stahl D, Chalder T, Edmonds ME, Ismail K. Risk factors associated with adverse outcomes in a population-based prospective cohort study of people with their first diabetic foot ulcer. J Diabetes Complications. 2007;21(6):341–9.
33. Van Olmen J, Marie KG, Christian D, Clovis KJ, Emery B, Maurits VP, et al. Content, participants and outcomes of three diabetes care programmes in three low and middle income countries. Prim Care Diabetes. 2015;9(3):196–202.
34. Quddus MA, Uddin MJ. Evaluation of foot ulcers in diabetic patients. Mymensingh Med J. 2013;22(3):527–32.
35. Lombardo FL, Maggini M, De Bellis A, Seghieri G, Anichini R. Lower extremity amputations in persons with and without diabetes in Italy: 2001-2010. PLoS One. 2014;9(1):e86405.
36. Markowitz JS, Gutterman EM, Magee G, Margolis DJ. Risk of amputation in patients with diabetic foot ulcers: a claims-based study. Wound Repair Regen. 2006;14(1):11–7.
37. Carlson T, Reed JF 3rd. A case-control study of the risk factors for toe amputation in a diabetic population. Int J Low Extrem Wounds. 2003;2(1):19–21.
38. Chaturvedi N, Stevens LK, Fuller JH, Lee ET, Lu M. Risk factors, ethnic differences and mortality associated with lower-extremity gangrene and amputation in diabetes. The WHO Multinational Study of Vascular Disease in Diabetes. Diabetologia. 2001;44(Suppl 2):S65–71.
39. Won SH, Chung CY, Park MS, Lee T, Sung KH, Lee SY, et al. Risk factors associated with amputation-free survival in patient with diabetic foot ulcers. Yonsei Med J. 2014;55(5):1373–8.
40. Wukich DK, Raspovic KM. What role does function play in deciding on limb salvage versus amputation in patients with diabetes? Plast Reconstr Surg. 2016;138(3 Suppl):188s–95s.
41. Ducic I, Attinger CE. Foot and ankle reconstruction: pedicled muscle flaps versus free flaps and the role of diabetes. Plast Reconstr Surg. 2011;128(1):173–80.
42. Oh TS, Lee HS, Hong JP. Diabetic foot reconstruction using free flaps increases 5-year-survival rate. J Plast Reconstr Aesthet Surg. 2013;66(2):243–50.
43. Wukich DK, Hobizal KB, Brooks MM. Severity of diabetic foot infection and rate of limb salvage. Foot Ankle Int. 2013;34(3):351–8.
44. Wickline S. Wounds heal better when debrided often. MedPage Today; [updated July 26, 2013]. https://www.medpagetoday.com/dermatology/generalderm atology/40692#:~:text=Weekly%20or%20even%20 more%20frequent,in%20Jacksonville%2C%20 Fla.%2C%20and.
45. Evans KK, Attinger CE, Al-Attar A, Salgado C, Chu CK, Mardini S, et al. The importance of limb preservation in the diabetic population. J Diabetes Complications. 2011;25(4):227–31.
46. Choi MSS, Jeon SB, Lee JH. Predictive factors for successful limb salvage surgery in diabetic foot patients. BMC Surg. 2014;14(1):113.
47. Randall DB, Phillips J, Ianiro G. Partial calcanectomy for the treatment of recalcitrant heel ulcerations. J Am Podiatr Med Assoc. 2005;95(4):335–41.
48. Elmarsafi T, Pierre AJ, Wang K, Evans KK, Attinger CE, Kim PJ, et al. The vertical contour calcanectomy: an alternative surgical technique to the conventional partial calcanectomy. J Foot Ankle Surg. 2019;58(2):381–6.
49. Eslami MH, Zayaruzny M, Fitzgerald GA. The adverse effects of race, insurance status, and low income on the rate of amputation in patients presenting with lower extremity ischemia. J Vasc Surg. 2007;45(1):55–9.

50. Hughes K, Mota L, Nunez M, Sehgal N, Ortega G. The effect of income and insurance on the likelihood of major leg amputation. J Vasc Surg. 2019;70(2):580–7.
51. Gregg EW, Li Y, Wang J, Rios Burrows N, Ali MK, Rolka D, et al. Changes in diabetes-related complications in the United States, 1990–2010. N Engl J Med. 2014;370(16):1514–23.
52. Gorman A. Diabetic amputations a 'Shameful Metric' of inadequate care. Kaiser Health Network; 2019. https://khn.org/news/diabetic-amputations-a-shameful-metric-of-inadequate-care/.
53. Moxey PW, Gogalniceanu P, Hinchliffe RJ, Loftus IM, Jones KJ, Thompson MM, et al. Lower extremity amputations--a review of global variability in incidence. Diabet Med. 2011;28(10):1144–53.
54. Narres M, Kvitkina T, Claessen H, Droste S, Schuster B, Morbach S, et al. Incidence of lower extremity amputations in the diabetic compared with the non-diabetic population: a systematic review. PLoS One. 2017;12(8):e0182081.
55. Gujral JS, McNally PG, O'Malley BP, Burden AC. Ethnic differences in the incidence of lower extremity amputation secondary to diabetes mellitus. Diabet Med. 1993;10(3):271–4.
56. Sebastianski M, Makowsky MJ, Dorgan M, Tsuyuki RT. Paradoxically lower prevalence of peripheral arterial disease in South Asians: a systematic review and meta-analysis. Heart. 2014;100(2):100–5.
57. Abbott CA, Chaturvedi N, Malik RA, Salgami E, Yates AP, Pemberton PW, et al. Explanations for the lower rates of diabetic neuropathy in Indian Asians versus Europeans. Diabetes Care. 2010;33(6):1325–30.
58. Hoffmann M, Kujath P, Flemming A, Proß M, Begum N, Zimmermann M, et al. Survival of diabetes patients with major amputation is comparable to malignant disease. Diab Vasc Dis Res. 2015;12(4):265–71.
59. Yammine K, Hayek F, Assi C. A meta-analysis of mortality after minor amputation among patients with diabetes and/or peripheral vascular disease. J Vasc Surg. 2020;72(6):2197–207.
60. Walsh JW, Hoffstad OJ, Sullivan MO, Margolis DJ. Association of diabetic foot ulcer and death in a population-based cohort from the United Kingdom. Diabet Med. 2016;33(11):1493–8.
61. Iversen MM, Tell GS, Riise T, Hanestad BR, Østbye T, Graue M, et al. History of foot ulcer increases mortality among individuals with diabetes: ten-year follow-up of the Nord-Trøndelag Health Study, Norway. Diabetes Care. 2009;32(12):2193–9.
62. Everett E, Mathioudakis N. Update on management of diabetic foot ulcers. Ann N Y Acad Sci. 2018;1411(1):153–65.
63. Chastain CA, Klopfenstein N, Serezani CH, Aronoff DM. A clinical review of diabetic foot infections. Clin Podiatr Med Surg. 2019;36(3):381–95.
64. Dietrich I, Braga GA, de Melo FG, da Costa Silva Silva ACC. The diabetic foot as a proxy for cardiovascular events and mortality review. Curr Atheroscler Rep. 2017;19(11):44.
65. Aulivola B, Hile CN, Hamdan AD, Sheahan MG, Veraldi JR, Skillman JJ, et al. Major lower extremity amputation: outcome of a modern series. Arch Surg. 2004;139(4):395–9; discussion 399.
66. Meshkin D, Anghel E, Fan KL, Evans KK, Steinberg J, Kim PJ, et al. Abstract: a surgical algorithm for sustainable healing in real-world complex wounds. Northeastern Society of Plastic Surgeons. Philadelphia, PA. 2021.
67. Gurney JK, Stanley J, Rumball-Smith J, York S, Sarfati D. Postoperative death after lower-limb amputation in a national prevalent cohort of patients with diabetes. Diabetes Care. 2018;41(6):1204–11.
68. Ruth CE. Surgical treatment of the diabetic foot. Diabetes Metab Res Rev. 2000;16(Suppl 1):S66–9.
69. Lavery LA, van Houtum WH, Armstrong DG, Harkless LB, Ashry HR, Walker SC. Mortality following lower extremity amputation in minorities with diabetes mellitus. Diabetes Res Clin Pract. 1997;37(1):41–7.
70. O'Hare AM, Feinglass J, Reiber GE, Rodriguez RA, Daley J, Khuri S, et al. Postoperative mortality after nontraumatic lower extremity amputation in patients with renal insufficiency. J Am Soc Nephrol. 2004;15(2):427–34.
71. Lavery LA, Hunt NA, Ndip A, Lavery DC, Van Houtum W, Boulton AJM. Impact of chronic kidney disease on survival after amputation in individuals with diabetes. Diabetes Care. 2010;33(11):2365–9.
72. McGrath NM, Curran BA. Recent commencement of dialysis is a risk factor for lower-extremity amputation in a high-risk diabetic population. Diabetes Care. 2000;23(3):432–3.

6 Unlocking the Mystery of Peripheral Neuropathy in Diabetes

Andrew J. M. Boulton

Introduction

Whereas there can be little doubt that peripheral neuropathy in diabetes (DPN) contributes to the many foot problems that require functional limb salvage, I was somewhat intrigued by the title of the chapter that I was asked to write. In a somewhat unconventional way, I will therefore consider why one might think that peripheral neuropathy is indeed a mystery by posing a few questions which I will briefly answer and then the main text will contain the detail to support the answers that I have already given.

Question: Why Should DPN Be a Mystery?

I am posing a few questions which will help understand what I thought was somewhat of a rhetorical question!

(a) Why does DPN result in diabetic foot ulceration (DFU)?

This is not difficult to answer as it is not neuropathy per se, but the results of neuropathy that contribute to foot ulceration. It was Dr Paul Brand working in leprosy who described neuropathy leading to "the loss of the gift of pain" [1]. Indeed, it is neuropathy itself and not the underlying cause such as diabetes or leprosy that puts the patients' limbs at risk of insensitive injury.

(b) Why is the warm but insensitive foot at risk of DFU?

I have already answered the first part of this question, but the second part relates to the diabetic patient who has no significant peripheral arterial disease (PAD). DPN is indeed a peripheral neuropathy but this involves both somatic and autonomic systems. Autonomic neuropathy in the lower limb leads to release of sympathetic tone and in the absence of PAD, there is increased blood flow and functional arterio-venous shunting that results in the neuropathic foot being warm [2, 3].

(c) Why is neuropathy the main contributory factor to Charcot neuroarthropathy (CN)?

The answer is not dissimilar to that given above in that the patient with loss of the gift of pain and disturbances in balance which are so common in DPN [4] is prone to recurrent minor injuries which because of the loss of

A. J. M. Boulton (✉)
Division of Diabetes, Endocrinology and Gastroenterology, University of Manchester, Manchester, UK

Manchester Royal Infirmary, Manchester, UK

University of Miami, Miami, FL, USA
e-mail: ABoulton@med.miami.edu

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_6

the gift of pain go unnoticed. The autonomic neuropathy, again as noted above, leads to increased blood flow including arterio-venous shunting through bone and as noted in the chapter on CN elsewhere in this text, recurrent minor injuries which go unnoticed may lead to sprains and indeed fractures which again remain unrecognized by the subject and this leads to recurrent fractures and new bone formation resulting in marked deformity.

(d) How can a patient with DPN have painful symptoms but at the same time have insensitivity on examination?

It was my mentor, Professor John D Ward, with whom I was working with 40 years ago in Sheffield, UK, that first described the "painful painless foot" in diabetes [5]. This refers to the patient with severe uncomfortable neuropathic symptoms, often disturbing sleep, who is completely insensitive to sensory testing such as pin-prick and vibration on examination. The explanation for this is that there is a spectrum of symptomatology in diabetic neuropathy: at one end of the spectrum one finds patients with severe symptoms and few signs, whereas at the other end of the spectrum patients who have no symptoms whatsoever but very much the at-risk foot with complete loss of sensation on examination. Thus, some patients with painful symptoms may have complete loss of sensation on examination to pain, temperature, and vibration. How can this be—that is, how can a patient experience severe burning pain in the feet and yet be completely insensate on examination? Although DPN is a "dying-back" phenomenon characterized by neural degeneration, there are attempts at regeneration that accompany degeneration: proximal to the foot there may be small-fiber regeneration and such fibers can act like a neuroma giving rise to spontaneous discharges that are interpreted as pain from where that nerve used to supply, i.e., the foot [6–8].

(e) Why are there still no definitive therapies for DPN?

The lack of a complete understanding as to the pathogenesis of diabetic neuropathy has resulted in there being no generally acceptable pathogenetic treatment for the condition. Whereas there are a number of proven symptomatic therapies for pain [9], most drugs are actually treating the symptoms but not the underlying cause: it must be remembered that most of these drugs also have quite marked side effects. The so-called pathogenetic therapies may follow when we have a clearer understanding of the pathogenesis of the condition.

The Diabetic Neuropathies

The neuropathies are among the commonest chronic complications of diabetes mellitus and can be a presenting feature of type 2 diabetes: indeed, in the large United Kingdom Prospective Diabetes Study, 13% of patients at the diagnosis of type 2 diabetes had neuropathy of sufficient severity to put them at risk of foot ulceration [2, 10]. The neuropathies of diabetes may present in many different forms but the commonest is the distal symmetrical polyneuropathy which is referred to in this chapter as DPN. This is a sensorimotor neuropathy involving both sensory and motor fibers. Moreover, as noted above, the DPN involving the lower limbs also has an autonomic component which leads, in the absence of PAD, to increased blood flow, but also to lack of sweating resulting in dry skin in the peripheries [2]. As up to 50% of patients with DPN may be asymptomatic, neuropathy cannot be excluded without a careful clinical examination of both lower limbs.

Much can be learned by considering the history of any condition. It is often said that "nothing is new in medicine—it is simply rediscovered." Interestingly therefore it was Dr RT Williamson, a physician at the Manchester Royal Infirmary where I currently work, who introduced physiological measurements such as measurement of vibration in the lower limb, to the assessment of neuropathy early in the twentieth Century [11]. Coincidentally, I was appointed as a Consultant Physician to the same hospital in 1986 and it was my group that confirmed, in a prospective study,

that loss of vibration sensation was the most reliable predictor of foot ulceration in diabetes [12].

A full classification of the diabetic neuropathies agreed by the American Diabetes Association Position Statement on Neuropathy is provided in Table 6.1 [9]. DPN is classified in this table as a diffuse neuropathy and in relation to the diabetic foot is a mixed small and large-fiber neuropathy also involving autonomic fibers. For full details of the many other varieties of the diabetic neuropathies, the reader is referred to several thorough reviews [2, 9, 13].

Diagnosis of DPN

Up to 50% of all patients with DPN experience symptoms at some time during its natural history. These symptoms are often difficult to describe because they are of a neuropathic nature rather than symptoms with which the patients will be familiar as might be caused, for example, by a bruise, a fall, or a burn. Pain may be described in many ways, but common symptomatology includes burning pain, altered temperature perception (freezing or boiling), electrical shock sensations, stabbing or shooting pain, and many more. As shown in Table 6.2, these are a result of small myelinated nerve fiber disease. Whereas numbness and tingling have been recognized as symptoms caused by large myelinated fibers for many years, more recently, disturbances of balance such as unsteadiness have been recognized as common [14]: patients often put such symptomatology down to aging or arthritis, but careful examination should confirm loss of proprioception.

Table 6.1 Classification of the diabetic neuropathies

Diabetic neuropathies
(a) Diffuse neuropathy DPN
• Primarily small-fiber neuropathy
• Primarily large-fiber neuropathy
• Mixed small- and large-fiber neuropathy (most common)
• Autonomic
• Cardiovascular
• Gastrointestinal
• Urogenital
• Sudomotor dysfunction
• Hypoglycemia unawareness
• Abnormal pupillary function
(b) Mononeuropathy (mononeuritis multiplex) (atypical forms)
• Isolated cranial or peripheral nerve
• Mononeuritis multiplex
(c) Radiculopathy or polyradiculopathy (atypical forms)
• Radiculoplexus neuropathy (also known as diabetic amyotrophy or proximal motor neuropathy)
• Thoracic radiculopathy
Non-diabetic neuropathies common in diabetes
Pressure palsies
Chronic inflammatory demyelinating polyneuropathy
Radiculoplexus neuropathy
Acute painful small-fiber neuropathies (treatment induced)

Adapted from Table 1 in Pop-Busui R, Boulton AJM, Feldman EL et al. [9] with permission from American Diabetes Association

The diagnosis of DPN remains a clinical one in day-to-day practice and no expensive equipment is required to make this diagnosis [9]. Small-fiber function can be checked by assessing pin-prick sensation or the ability to differentiate between hot and cold rods. Large-fiber function can be checked by assessing vibration perception and proprioception or using a 10 g monofilament [15]. Ankle reflexes are also useful in the clinical examination and absent reflexes have been shown to be a predictor of foot ulceration [2].

A simple composite score was developed for a large UK diabetic neuropathy study as shown in Fig. 6.1 [2]. This comprises three sensory signs: vibration, pin-prick, and temperature differentiation together with the ankle reflex. Any normal sensation found during this examination scores a zero, whereas absence of any sensations scores one for each leg. Reflexes are scored as zero = normal, one = present on reinforcement, two = absent. Thus, the total maximum score for the most severe neuropathy would be ten. This modified neuropathy disability score (NDS) has been used in many studies and in the large North-West Diabetes Foot Care Study in the UK, for a study of 15,000 patients, a modified NDS score of ≥6 was a strong predictor of foot ulcer development [16].

Table 6.2 Symptoms and signs of DPN

	Large myelinated nerve fibers	Small myelinated nerve fibers
Function	Pressure, balance	Nociception, protective sensation
Symptoms[a]	Numbness, tingling, poor balance	Pain: burning, electric shocks, stabbing
Examination (clinically diagnostic)[b]	Ankle reflexes: reduced/absent	Thermal (cold/hot) discrimination: reduced/absent[b]
	Vibration perception: reduced/absent	
	10-g monofilament: reduced/absent	Pin-prick sensation: reduced/absent[b]
	Proprioception: reduced/absent	

Reproduced from Pop-Busui R, Boulton AJM, Feldman EL et al. [9] with permission from American Diabetes Association

[a]To document the presence of symptoms for diagnosis

[b]Documented in symmetrical, distal to proximal pattern

Neuropathy and the Pathway to Foot Ulceration

As stated above, a DPN is a contributory factor to foot ulceration in people with diabetes but it must be remembered that the neuropathic foot will not spontaneously ulcerate. It is a combination of neuropathy (the loss of pain) and some form of external injury that results in skin breakdown and eventually ulceration. As Dr Paul Brand described, any peripheral neuropathy can put the patient at risk of foot ulceration. His work was predominantly in leprosy or Hansen's disease in the mid-twentieth Century. Trained as a surgeon, he left London to work at the Christian Medical Center (CMC) in Vellore, Tamil Nadu, South India where he was convinced that the horrific lesions described in biblical times seen in people with leprosy were not due to infection, but due to loss of sensation. Leprosy is caused by the Mycobacterium Leprae

Neuropathy Disability Score (NDS)			
		Right	Left
Vibration Perception Threshold 128 Hz tuning fork; apex of hallux; trial pair = vibrating, non-vibrating (hit the wrong end of the tuning fork); normal = can distinguish vibrating / not vibrating	subject sitting, eyes closed, legs outstretched: demonstrate on clavicle or dorsum of hand; in each case repeat 3 pairs of trials (mix up stimulus order within trial pair, in each case maintain stimulus 2 seconds); in each case ask "do you feel vibration / cold / sharp now or now?"; abnormal is at least 2 of 3 trials wrong or "cannot tell" Normal = 0 Abnormal = 1		
Temperature Perception rest Tip-Therm rod on dorsum of foot, trial pair = plastic end ("not cold"), metal end ("cold"); normal = can distinguish cold / not cold			
Pin-Prick apply Neurotip on proximal big toe just enough to deform skin; trial pair = sharp end, blunt end; normal = can distinguish sharp / not sharp			
Achilles Reflex kneeling on a chair, upright holding back of chair; stretch tendon to ankle neutral first; reinforcement – hook fingers together and pull when asked	Present = 0 Present with reinforcement = 1 Absent = 2		
NDS Total out of 10			

Fig. 6.1 The modified neuropathy disability score (nds)

bacillus and is primarily a granulomatous disease of skin and peripheral nerves. As the leprosy bacillus prefers cold areas, it affects the skin and peripheral nerves in the upper and peripheral nerves in the upper and lower limbs. Despite being an infectious disease, leprosy is not highly contagious but in biblical times, the horrific, trophic lesions of the hands and feet were thought to have formed as a result of the leprosy infection, hence the establishment of "leprosy colonies." When Brand arrived at the CMC, Vellore, he was appalled to see people with extensive ulceration of the hands and feet due to leprosy receiving no specific treatment. However, the medical staff there just reported to him that it was "a curse from God" as people went to bed with intact skin and woke up with new lesions in the morning. He was told "there is nothing that can be done for these patients: it's just leprosy" [17] and that the injury to the feet of people with leprosy was caused by trauma to insensitive skin and not "a curse from God" was proven by Brand when it was observed that patients asleep at night in huts often had their feet traumatized by vermin such as rats which could injure the foot without disturbing the patients because of complete sensory loss.

Similarly, even today in some countries, rat bites and other animal bites remain causes of foot ulceration in patients with severe peripheral neuropathy [18].

A regular diabetic foot exam to identify those with "at-risk neuropathic feet" is recommended by the American Diabetes Association [19]. Simple tools such as those described above are all that is needed to identify the high-risk foot. Patient self-care of the feet by regular inspection, wearing sensible shoes are pivotal in the management of the insensitive foot. The team approach involving diabetes specialist nurses, podiatrists, physician assistants, diabetologists, and many others remains the keystone in the prevention of foot ulceration in the twenty-first century.

Treatment of DPN

The majority of this section will refer to management of those patients with painful or difficult to describe uncomfortable symptoms in the lower limbs. In day-to-day clinical practice, the management normally falls mainly to the diabetes physician (endocrinologist), the primary care physician, and occasionally a neurologist or pain clinic. Most of those agents licensed for the management of neuropathy pain simply treat the symptoms rather than the underlying cause as noted above. A realistic objective would be to achieve around a 50% reduction in the painful symptoms. As DPN has a major impact on quality of life (QOL) [20], a secondary objective should be improving QOL and especially sleep and mood. As studies suggest that whereas those with painful symptoms tend to have predominant anxiety, those with painless symptoms such as poor balance, unsteadiness, etc. are more prone to depression [21].

There is strong evidence to implicate poor glycemic control as one of the most important factors in the etiology of DPN. Unfortunately, there is and never will be evidence from randomized controlled trials of tight glycemic control that this is the case in the treatment of neuropathic pain. However, there is the evidence that increased blood glucose flux might contribute to pain and therefore the general consensus is that good blood glucose control should be the first step in management [7, 9, 22].

Pharmacological Treatment

Although many different agents have been shown to provide symptomatic relief for neuropathic pain, none is without side effects. The first line recommended drugs for neuropathic pain in the ADA Position Statement come under two classes: firstly, anti-epileptics and secondly, anti-depressants [9]. The algorithm developed for the ADA Position Statement is reproduced in Fig. 6.2. Indeed, most recent guidelines on the pharmacological treatment of painful diabetic neuropathy include these two classes of drugs as alternatives to be used as first line agents [9, 23, 24].

Although opioid and opioid-like drugs have been shown in several trials to be efficacious in

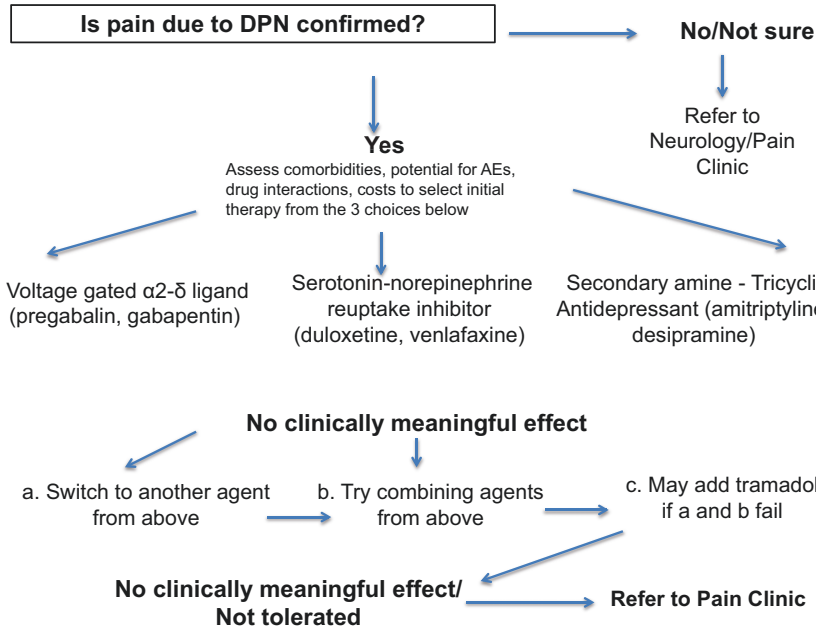


Fig. 6.2 Algorithm for the management of patients with pain secondary to DPN. *AE* adverse effects. Pharmacokinetic profile, spectrum of AEs, drug interactions, co-morbidities, and costs to be considered when selecting agent of choice. (Reproduced from Pop-Busui R, Boulton AJM, Feldman EL et al. [9] with permission from American Diabetes Association)

neuropathic pain, there is a high risk of addiction, abuse, sedation, and other complications with any of these drugs including Tramadol and Oxycodone. For these reasons, opioids are not recommended in the treatment of painful DPN before failure of other agents that do not have such side effects. It is highly recommended that patients who may require opioids should be referred to a specialized pain clinic.

All patients with DPN whether with painful symptoms or not require education on good foot self-care as well as regular visits to the podiatrist.

(a) Anti-epileptic agents

Pregabalin, a drug used in complex partial epilepsy, is licensed for the treatment of neuropathic pain in diabetes in the USA, Europe, and Canada. A number of randomized controlled trials have confirmed the efficacy of this drug with 30–50% improvement in pain [7, 9]. The usual dose range of Pregabalin is 150–600 mg daily, normally given on a b.i.d regimen. As noted above, all these agents have side effects and central side effects and occasional fluid retention are recognized to occur in people treated with Pregabalin [9]. It is therefore recommended that one should start at a low dose perhaps 75 mg daily and gradually increasing to a maximum of 300 mg bd. Drugs used for complex epilepsy including Gabapentin and Pregabalin are both proven in several randomized controlled trials (RCTs). It must be remembered, however, that the mean dose required for Gabapentin in RCTs was approximately 1.5–2 g daily in divided doses such as 600 mg tid. However, as with all agents used in neuropathic pain, one should start with a low dose and gradually increase as required: moreover, it should be noted that Gabapentin is not licensed for use in painful DPN by the FDA. As with all agents, adverse events are common and more common in older patients [9].

(b) Anti-depressants

The most commonly used anti-depressant for neuropathic pain is the selective norepi-

nephrine and serotonin reuptake inhibitor, Duloxetine. Additionally, Amitriptyline may be used although it is not FDA approved. This and other tricyclic anti-depressants have been used for many years, but they have quite marked side effects in up to 50% of patients including a dry mouth, blurred vision, drowsiness, and also a risk of falls. However, some patients can tolerate low dose drugs such as Amitriptyline 10–25 mg at night which can be very helpful in those who can tolerate the agent, and on occasions, the dose may be increased to 75 mg daily or more, given as a single dose in the evening [9].

The selective norepinephrine and serotonin reuptake inhibitor, Duloxetine, is licensed for use in neuropathic pain in diabetes and can be given at 60 or 120 mg daily. As with Pregabalin, Duloxetine has been shown in several randomized controlled trials to be efficacious in the relief of neuropathic pain. Its side effects include somnolence, dizziness, and occasionally gastrointestinal symptoms.

(c) Other agents

Although there is evidence to suggest that opioid and opioid-like agents may be helpful in the relief of neuropathic pain, there is always a high risk of addiction and abuse with such agents and their use cannot be recommended unless agents listed above fail to provide pain relief. In such cases, referral to a specialist clinic or pain clinic is recommended. Evidence has been shown for pain relief with drugs such as controlled relief Oxycodone and Tramadol as well as others [9, 24].

(d) Combination therapy

Combination therapy may occasionally be effective and might include a combination with one of the first line agents and a low dose of an opioid-like drug. Other potential combinations are beyond the scope of this review and the reader is referred to recent literature [9, 24]. A simple algorithm to the approach and management of pain due to DPN can be found in Fig. 6.2 which is adapted from the ADA Position Statement [9].

Conclusions

As will be apparent, the diabetic neuropathies comprise broad spectrum of clinical conditions and only the commonest, DPN, is covered in any detail in this review. It must be remembered that diabetic neuropathy cannot be diagnosed without a careful clinical examination as up to half of all patients may be asymptomatic. The only effective preventative approach to diabetic neuropathy confirmed in the literature is tight glycemic control. All patients with diabetes require an annual review for evidence of complications which are often silent until it is too late. The annual review should include a comprehensive diabetic foot exam [19] and those found to have neuropathy require much more frequent review, preventative foot care, and symptomatic treatment as required.

A reduction in neuropathic foot problems will only be achieved if we remember that patients with insensitive feet have lost their warning signal—pain—that ordinarily brings the patients to their doctor. Thus, the care of the patient with sensory loss is a new challenge for which few of us have received any training. It might be difficult for us to understand, for example, that an intelligent patient might buy a pair of shoes three sizes too small and then come to the clinic with extensive shoe-induced ulceration: the explanation, however, is that with reduced sensation, a very tight fit stimulates the remaining pressure nerve endings and is therefore perceived as a normal fit. Helping the patient to understand that sensory loss puts them at great risk of unnoticed injury is vital in the management of all patients with DPN.

References

1. Boulton AJM. Diabetic foot – what can we learn from leprosy? The legacy of Dr Paul W Brand. Diabetes Metab Res Rev. 2012;28(Suppl 1):3–7.
2. Boulton AJM, Malik RA, Arezzo JC, Sosenko JM. Diabetic somatic neuropathies: a technical review. Diabetes Care. 2004;27:1458–86.
3. Boulton AJM. The Banting Memorial Lecture: the diabetic lower limb – a 40-year journey: from clinical observation to clinical science. Diabet Med. 2019;36:1539–49.

4. Boulton AJM, Whitehouse RW. The diabetic foot. In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext. South Dartmouth: MDText.com, Inc; 2020.
5. Ward JD. The diabetic leg. Diabetologia. 1982;22:141–7.
6. Boulton AJM. Causes of neuropathic pain. Diabet Med. 1993;10(Suppl 2):s87–8.
7. Tesfaye S, Boulton AJM, Dickenson AH. Mechanisms and management of diabetic painful distal polyneuropathy. Diabetes Care. 2013;36:2456–65.
8. Shillo P, Sloan G, Greig M, et al. Painful and painless diabetic neuropathies: what is the difference? Curr Diab Rep. 2019;19:32. https://doi.org/10.10007/S11892-019-1150-5.
9. Pop-Busui R, Boulton AJM, Feldman EL, et al. Diabetic neuropathy: a position statement by the American Diabetes Association. Diabetes Care. 2017;40:136–54.
10. Tesfaye S, Sloan G. Diabetic polyneuropathy – advances in diagnosis and intervention strategies. Eur Endocrinol. 2020;16:15–20.
11. Williamson RT. A clinical lecture on the vibrating sensation in diseases of the nervous system: delivered at the Manchester Royal Infirmary. Br Med J. 1907;2:125–7.
12. Young MJ, Breddy JL, Veves A, Boulton AJM. The prediction of diabetic neuropathic foot ulceration using vibration perception thresholds: a perspective study. Diabetes Care. 1994;17:557–60.
13. Vinik AI, Maser RE, Mitchell RD, Freeman R. Diabetic autonomic neuropathy. Diabetes Care. 2003;26:1553–79.
14. Brown SJ, Handsaker JC, Bowling FL, et al. Diabetic peripheral neuropathy comprises balance during daily activities. Diabetes Care. 2015;38:1116–22.
15. Perkins BA, Olaleye D, Zinman B, Bril V. Simple screening tests for peripheral neuropathy in the diabetes clinic. Diabetes Care. 2001;24:250–6.
16. Abbott CA, Carrington AL, Ashe H, et al. The North-West Diabetes Foot Care Study: incidence of, and risk factors for, new diabetic foot ulceration in a community-based patient cohort. Diabet Med. 2002;19:377–84.
17. Brand PW. The biomechanics of ulceration. In: Third Roger Pecoraro Lecture, American Diabetes Association annual meeting, Atlanta; 1995.
18. Abbas ZG, Lutale JK, Archibald LK, Jeffcoate WJ. Rat bite as a cause of diabetic foot ulcer in Sub-Saharan Africa. Int Wound J. 2020;17:897–9.
19. Boulton AJM, Armstrong DG, Albert SF, et al. Comprehensive foot examination and risk assessment: a report of the Task Force of the Foot Care Interest Group of the American Diabetes Association. Diabetes Care. 2008;31:1679–85.
20. Vileikyte L, Gonzalez JS. Recognition and management of psychosocial issues in diabetic neuropathy. Handb Clin Neurol. 2014;126:195–209.
21. Vileikyte L, Crews RT, Reeves ND. Psychological and biomechanical aspects of patient adaption to diabetic neuropathy and foot ulceration. Curr Diab Rep. 2017;11:109. https://doi.org/10.1007/s11892-017-095-5.
22. Oyibo SO, Prasad YD, Jackson NJ, et al. The relationship between blood glucose excursions and painful diabetic peripheral neuropathy: a pilot study. Diabet Med. 2002;19:870–3.
23. Tesfaye S, Boulton AJM, Dyck PJ, et al. Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity and treatments. Diabetes Care. 2010;33:2285–93.
24. Azmi S, Alam U, Burgess J, Malik RA. State-of-the-Art pharmacotherapy for diabetic neuropathy. Expert Opin Pharmacother. 2021;22:55–68.

7 The Science and Utility of Offloading the Diabetic Foot

Caitlin S. Zarick, Kurtis D. Bertram, and Thomas F. Milisits

Introduction to Offloading and Its Utility

Diabetes mellitus affects over 400 million people around the world and over the next 25 years, it is estimated that more than 700 million people will be living with diabetes globally [1]. With this drastic rise in the prevalence of the disease, diabetic foot problems put an excessive burden on the healthcare system due to repeated hospitalizations, increased risk of amputation, and substantial healthcare costs. For people living with diabetes, the lifetime risk of developing a diabetic foot ulcer (DFU) is 25% and subsequently a 40% risk of lower extremity amputation [2]. Nearly 70% of amputations in the United States are reported to be a result of diabetes and its consequences [2]. The harsh reality is that a large number of ulcerations that lead to amputation can be prevented and treated with proper conservative and surgical offloading techniques.

Offloading, an often underutilized tool in diabetic foot prevention and management, is a term generally used to describe decreasing pressure to a targeted area of the foot. Offloading is a crucial component of the DFU treatment algorithm as it removes and redistributes forces to other areas of the foot to prevent and/or treat ulceration [3]. Understanding the etiology of the ulceration will help determine the best mechanism of offloading. One must take into account all deformities, contractures, prior amputations, and global appearance of the foot when prescribing offloading devices.

It has been shown that as many as 50% of patients suffering from diabetes will lose sensation in their feet secondary to peripheral neuropathy [4]. Neuropathy not only removes protective sensation but also leads to an imbalance of intrinsic musculature leading to deformity. It is the combination of deformity and loss of sensation that leads to tissue breakdown and ultimately ulceration [5]. Understanding the pathological forces and their potential consequences will allow you to properly help choose the best offloading mechanism for your patients. Shear, frictional, compressive, and tensile forces all play a part in the development of ulcerations as well as the treatment (See Table 7.1). The goal of offloading devices is to help counteract the forces at play.

C. S. Zarick (✉) · K. D. Bertram · T. F. Milisits
MedStar Washington Hospital Center, MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: caitlin.s.zarick@medstar.net; kurtis.bertram@medstar.net; thomas.milisits@medstar.net

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_7

Table 7.1 Different forces that act on the diabetic foot and contribute to ulceration [5]

Type of force	Definition
Shear force	When a material moves in one or more directions at the same time
Frictional force	When a force moves along a material while in direct contact with it
Compressive force	When a material is pressed together between two or more loads
Tensile force	When a material is stretched by two or more opposing forces

Biomechanics of the Diabetic Foot

The biomechanics of the diabetic foot are different from that of a nondiabetic foot at both a structural and functional level. On the structural level, there are changes to the soft tissue of the foot, particularly to the plantar aspect (i.e., dryness) as well as loss of the plantar fat pad. On a functional level, a disorganized pattern occurs within diabetic ligaments, capsules, and tendons leading to significant decrease in elasticity and tensile strength. As a result of these changes, there is increased propensity for joint instability, overall stiffness, and contractures of the foot and ankle which leads to inefficiencies in gait, lack of accommodation with weight-bearing, and increased areas of local pressure [6].

The classic example of this in the diabetic patient is Charcot Neuroarthropathy which is defined as a chronic destruction of the bones and joint subluxations in patients with neuropathy [6–8]. The main deforming force is the Achilles tendon which becomes contracted causing an equinus deformity. During propulsion of a patient with Charcot, there is an increased upward force of the Achilles tendon, causing a break or subluxation of different areas of the foot (most commonly the midfoot). Additionally, this increased pull leads to increased pressures on the forefoot. If these issues are not addressed in a timely manner with proper offloading, whether conservative or surgical, this can lead to devastating consequences on the patient's function and quality of life. Increased plantar foot pressure can occur which leads to ulceration, infection, or even amputation.

Thorough radiographic and physical examinations are paramount in diabetic patients, particularly in the uncontrolled diabetic. There are certain areas of the physical exam that are crucial for evaluation as it pertains to offloading.

Key components of the examination in the diabetic patient as it pertains to offloading:

- Radiographic Evaluation: Radiographic analysis should be completed as it can give vital information on areas of subluxation and bony prominences. *Weight-Bearing films* are crucial for an accurate assessment of bony architecture.
- Plantar Callus: Careful examination of the plantar aspect of the foot for any callus formation will help determine areas that require offloading. In a study by Potter et al., they found that there was a 25% decrease in peak plantar pressure after callus removal. However, there was no significant difference between the two groups. Callus removal alone is not sufficient; the area must also be offloaded [9].
- Range of Motion: One should assess the mobility of joints, whether hypermobile or immobile. This can give you predictors of potential future areas of pressure, Charcot breakdown, and ulcer formation.
- Gait Analysis: A gait exam should always be performed in order to understand the mechanics of how a patient ambulates and can give clues to high pressure areas. If one has access to a gait lab this would add even further benefit to the exam [10]. This should be done without shoe gear to assess aspects of gait such as forefoot to rearfoot relationship, collapse of the midfoot, etc. Efficacy of an offloading device can then be evaluated by comparing pedobarometric data before and after application of an offloading mechanism.
- Contractures and deformities: The presence or absence of both ankle and foot deformities must be evaluated. Some of the more common pathologic deformities are equinus, ankle varus/valgus, rocker bottom deformity, pes planus, pes cavus, digital contractures, and

bunions. It is of utmost importance to assess all possible underlying issues.
– Prior amputation: Amputations lead to predictable mechanical imbalances. Prior amputation can help the practitioner prophylactically offload areas that are at high risk for ulceration. When a patient undergoes any kind of amputation, whether it be a digit amputation or a transmetatarsal amputation, there is a loss of tendinous attachments making the mechanics of the foot less optimal. For example, hammertoes often develop after a partial first ray amputation while equinus or even equinovarus can develop after a midfoot amputation.

The importance of understanding the biomechanics in the diabetic patient is so that we can prevent and treat ulcerations with proper offloading, whether it be from conservative or surgical methods.

Conservative ("External") Methods of Offloading the Diabetic Foot

Sound offloading principles are necessary in any wound care plan, regardless of the etiology of the wound. The biomechanics are paramount to choosing a device; however the practitioner cannot forget other key variables such as age, weight, skin integrity, vascular status, neurological status, presence of infection, and purpose of the device (i.e., prophylactic or treatment of an open wound) [11].

In an ideal world, a device that assists with total non-weight-bearing would be used to remove pressure from the plantar surface of the foot. These include crutches, wheel chairs, or knee walkers. However, these are rarely practical because of factors such as obesity, social burdens, and debility [11].

There are several different ways that you can conservatively offload the foot. There is often not a "one size fits all" method in choosing a device. Each patient will have unique factors about them that will sway you to one method over another. The choice also often comes down to provider preference and what they feel works best in their own hands as well as what is readily available in practice. Compliance, or the ability of a patient to adhere to treatment, must also be considered.

Felt Padding

Felt padding is one of the oldest methods of offloading and often overlooked in today's practice. It is extremely inexpensive and an easy way to begin offloading immediately while waiting for custom or permanent devices. The premise of the felt pad is to increase contact area around the ulcer and redistribute pressure to other parts of the foot in order to optimize the ulcer's healing potential.

In the author's opinion, this is most effective for a smaller ulceration (i.e., size of a nickel) on the plantar forefoot, or medial/lateral aspects of the foot. For this padding, you would use either ¼ or ½ inche felt, cut as an aperture pad (donut shape). It would get placed over top of the wound and would ideally redistribute pressure away from the ulceration.

This is a method that can be done right away during the first office visit. It is also a device that patients typically tolerate very well and compliance will not be much of a concern. A downside to felt pad offloading is that it very well may not offload enough pressure or could be placed inaccurately and cause increased pressure to other areas. Additionally it could create an edge effect leading to a larger wound if not monitored closely [12]. This occurs when the healthy epidermis surrounding the wound breaks down due to increased pressure from the pad. It is more likely to occur in completely insensate patients.

Custom Accommodative Orthotics

There are two different types of orthoses: functional and accommodative. In the diabetic population, the authors prefer the use of the accommodative orthotic because they are soft and aid in accommodating and offloading the foot (Fig. 7.1) [13]. There are several different



Fig. 7.1 Custom accommodative orthotics. (**a**) Plastazote top layer; (**b**) Side view of plastazote, EVA, and poron; (**c–e**) Example of patient with hallux amputation fitting a custom accommodative orthotic with toe filler

materials that are used when creating a custom accommodative orthotic; however in the diabetic population, they must offload the foot and prevent further breakdown.

At our institution, we use a layered device when designing an accommodative insert as we believe it provides the most offloading characteristics. The base of the device should be the most dense and each layer above that, or towards the foot, should be less dense, or a decreased durometer. Two durable and easy to work with materials for the base are Ethylene vinyl acetate (EVA) and

Poron. For the top layer, plastazote is a great option because it is modifiable, comes in various densities, and is typically well tolerated by the patients.

Custom accommodative orthotics are typically best utilized to prevent ulceration either from occurring or reoccurring, particularly after a limb salvage surgery with reconstruction or amputation. The premise behind custom orthotics is to control the biomechanics of the foot and to offload certain areas of the foot with different modifications made to the device. They also help to relieve strain on the tendons/muscles of the lower extremity as the biomechanics are controlled. Several studies have examined the effectiveness of custom orthotics with the use of F-Scan systems and found that these devices increase the contact area of the foot and decrease pressure [14]. The goal is to help prevent future ulcers from happening by offloading areas at risk for ulceration.

Another key point when it comes to custom orthotics is that they should be checked for durability every 3–6 months. Once the device becomes thin, they become less effective and are no longer beneficial to the patient. While custom orthotics can be expensive, numerous insurance companies do cover new prescriptions on a yearly basis so it is crucial to check the device during each visit.

Diabetic Shoes

Diabetic shoes should be made an option for high-risk diabetic patients particularly if they have components of neuropathy combined with deformity. Patients with a history of an ulceration or amputation should also be prescribed diabetic shoes with accommodative inserts. Diabetic shoes are made with minimal stitching to avoid irritation and typically come with extra depth to accommodate custom orthotics for added support and protection. Additionally, they come with a large protective toe box to prevent extra pressure of the digits as well as a multi-density diabetic insole that prevents shearing forces [15].

Diabetic shoes provide better motion control, prevent skin breakdown and callus formation, and reduce high pressure areas of the foot. Due to the *Therapeutic Shoe Bill* passed by Congress in 1993, Medicare covers diabetic shoes and should always be in the back of the provider's mind when treating diabetics [16]. Our opinion is that any patient who has decreased sensation, a deformity, or history of an ulceration or amputation should get a prescription for diabetic shoes.

Custom Shoes

Custom shoes are designed for patients who cannot get into an extra depth shoe because of a particular deformity, prior amputation, or large foot size. Patients will typically get a custom shoe after a large limb salvage attempt with reconstruction to accommodate their deformity and provide balance and stability. Custom shoes are fit to each specific patient and molded to a specific foot and ankle shape and size (Fig. 7.2).

Controlled Ankle Movement (CAM) Walker

A controlled ankle movement or "CAM" walker (Fig. 7.3) is an adjustable and removable device which is used for a variety of different clinical



Fig. 7.2 Custom shoe molded specifically to patient's foot and ankle shape, size, and deformity



Fig. 7.3 Controlled Ankle Movement (CAM) Walker. CAM walkers are dispensed in short or long form to accommodate specific deformities

circumstances. Indications for a CAM walker include plantar foot ulcers, Charcot neuroarthropathy, trauma (such as ankle sprain or ankle fracture), and postoperatively from elective surgery (such as a bunion correction or flatfoot/cavus reconstruction). There are also specific CAM walkers made for diabetic patients that come with an accommodative inlay to help offload pressure from the plantar foot even further. Some of the diabetic-specific CAM walkers have softer outer shells to help prevent rubbing or new wounds.

Specifically when it comes to the diabetic foot, the CAM walker is particularly helpful in the patient with a forefoot ulceration. One study found that the CAM walker when compared to a total contact cast had greater reduction in forefoot peak pressure, maximum force, and force-time integral [17, 18].

One of the main advantages of the CAM walker is the ease of wound inspection in a patient with this device due to the fact that it is removable. However, this is also a disadvantage in the noncompliant patient. Some patients will not adhere to your treatment regimen and take the walker off once they leave your office. In a recent study, the authors found that patients using a removable cast walker only used it as prescribed for 34% of their treatment duration [19]. In a patient that is noncompliant, a trick you can use in the office is to use a layer of fiberglass cast around the CAM walker to make it difficult for the patient to take off while at home.

The CAM walker is an excellent device to use for diabetic foot wounds, but the practitioner must always examine the boot and investigate whether the patient is actually wearing it as prescribed.

Total Contact Cast (TCC)

The Total Contact Cast or TCC (Fig. 7.4) is the *gold standard* offloading device for diabetic foot ulcers. The TCC is made of fiberglass and can incorporate different types of offloading pads





Fig. 7.4 Total Contact Cast (TTC); it is important to have the patient dorsiflex ankle and ensure that bony prominences are well padded, particularly medial and lateral malleoli and heel. Patients can weight bear in the TTC while utilizing a special brace

which offer a customized fit for each patient. The cast encases the patient's entire foot including the toes and leg. This allows for maximal offloading and is best suited for forefoot and midfoot ulcerations. There are numerous high powered studies in the literature supporting this claim [20, 21]. One randomized controlled trial comparing a cast shoe, removable cast walker (i.e., CAM boot), and TCC determined that the TCC healed 90% of wounds in half the amount of time compared to the other two groups. Additionally, the TCC group took half the amount of steps as the other two groups [20, 21].

There are several advantages to a TCC. The first is decreased plantar pressure and weight transfer to the tibia. It has been shown that approximately 30% of plantar pressure from the foot is removed when the patient is in a TCC. This is likely due to the conical shape of the tibia which allows this cast to act as an external offloading device redistributing weight [21, 22]. The next advantage is the elimination of ankle joint motion. When properly applied, the ankle should be firmly held in neutral which will decrease the amount of plantarflexion with each step and, as a result, decrease forefoot pressure midstance and propulsion. With the decreased ankle motion comes a shortened stride length which results in less time on the ground and fewer ground reactive forces [21]. TCCs are also a method of "forced compliance" for patients because they are not easy to take off and also tend to be heavy for patients, which keeps them minimally weight-bearing. This should be considered if deciding between a CAM boot and TCC for treatment.

Another great use of the TCC is with patients with Charcot Neuroarthropathy. Patients in the active state of Charcot need proper offloading to minimize collapse and to help begin healing and consolidation. A TCC is an excellent tool for this and often used in diabetic patients to maximize offloading during early phases of Charcot. One must be careful, however, to not place patients in a TCC until acute swelling is also managed.

There are several contraindications to think about when you are deciding if you should use a TCC versus another offloading device. The first is active infection. You always want to eradicate the infection prior to utilizing a TCC. The reason is twofold: one is that the patient will not be able to have daily dressing changes done and second is that they will not be able to tell if the infection is worsening or improving (i.e., increased drainage, redness, or malodor). The next is exposure of deep structures such as tendons. This is a contraindication because you will not be able to adequately keep a close eye on the wound and may make the wound worse if the cast is not applied right. A heavily draining wound would also be challenging to place into a TCC for fear of this leading to an infection. A relative contraindication would be a patient with a large amount of swelling or the ability to easily swell. If patients were to swell into the cast it could cause friction, blistering, or new wounds.

There is a learning curve to applying these casts. The author recommends that proper training or workshops on TCC application be employed for anyone utilizing these in their practice. TCCs are not without their own risks if improperly applied. Below are some key points that the authors use when applying these casts:

1. Apply a dressing to the wound prior to placing any cast padding. This can be a dry sterile dressing, medicated dressing, or synthetic graft on the wound prior to putting on the TCC.
2. Place extra absorbant dressings for any expected exudate.
3. Take extra care to make sure that the entire cast is in contact with the foot/leg because even the smallest amount of movement can lead to another pressure point leading to a new ulceration.
4. Pad bony prominences extremely well and any areas of increased pressure. Pads are applied directly over the anterior tibial crest, medial and lateral malleoli, and the heel. The toes also get protected with felt padding.

TCCs are typically changed weekly but can be left on for 2 weeks at a time if there is no wound present at all or a small, minimally exudative wound. Educating the patients on the risks and benefits of the cast will assist with compliance.

Charcot Restraint Orthotic Walker: "CROW" Boot

The Charcot Restraint Orthotic Walker or CROW (Fig. 7.5) is a long-term custom device that functions as a custom molded removable TCC for



Fig. 7.5 Charcot restraint orthotic walker: "CROW" Boot; custom walker typically used after total contact cast with a rocker bottom insole to help alleviate pressure on the plantar foot and aide in gait

patients with Charcot Neuroarthropathy. It comes in two fiberglass or plastic pieces: one for the front of the foot/leg and one for the back. The CROW is typically utilized after a TCC when swelling has decreased and the patient has proven to be compliant with weight-bearing restrictions. A recent study showed that 25.9% of patients transitioning from a TCC used a life-long CROW as a way to prevent further Charcot breakdown [23]. The walker consists of a fully enclosed custom orthotic, typically with a rocker bottom insole to help alleviate pressure on the plantar aspect of the foot and to help support the ankle joint.

Long-Term Bracing Options

Arizona Brace

The Arizona Brace is a custom-fabricated ankle foot orthosis which was originally designed for posterior tibial tendon dysfunction. However, this can be used to offload the diabetic foot as it stabilizes the ankle, subtalar, and midtarsal joints and provides medial and lateral stability to the foot [24]. In the authors hands, this device is most effectively used postoperatively after a partial calcanectomy as the attachment of the Achilles is lost to give the patient more stabilization through the gait cycle. It is also beneficial after Charcot reconstructive surgery. It increases ankle stability and can help provide support and offloading after ankle or tibiotalocalcaneal arthrodesis procedures. It is also beneficial after midfoot Charcot reconstruction to help stabilize the ankle and potentially prevent breakdown or Charcot from occurring in the ankle joint as well.

Patellar Tendon Bracing

The patellar tendon brace (PTB) was first described in the 1960s for the treatment of tibial fractures as it is said to offload the tibia, fibula, and bones of the foot by transferring weight through lateral uprights [25, 26]. The PTB has been shown to have approximately a 30% reduction in body weight to the foot [27]. They are made either as fixed-ankle or non-fixed ankle. One study showed that plantar pressures were significantly decreased in a fixed-ankle PTB brace [26]. For obvious reasons the PTB can be another great option for continuously offloading pressure to the plantar diabetic foot.

Surgical ("Internal") Methods of Offloading the Diabetic Foot

Surgical intervention is indicated when the patient is getting recurrent calluses or areas of ulceration, despite other offloading measures. Armstrong and Frykberg revised a classification system for diabetic foot surgery mainly based on the presence of an ulcer and acuity. Class I surgeries were considered "elective" and were performed to correct deformity in patients without neuropathy. Class II procedures were classified as "prophylactic" as they were performed in patients with neuropathy to help reduce the risk of ulceration when no wound was present. Class III procedures were considered "curative" and were performed when ulcers were present in order to heal the ulcer. An example of this would be to perform a tendoachilles lengthening procedure in order to cure a plantar forefoot ulceration. The final Class IV procedures were those considered "emergent" and performed when there was presence of severe infection [28].

Soft Tissue Procedures

Percutaneous Flexor Tenotomy

Flexible deformity of the digits can be treated with a percutaneous flexor tenotomy (Fig. 7.6). This will help alleviate pressure at the top or tip of the digit to heal or prevent an ulceration.

This procedure can be done in the office with or without local anesthesia. The authors have found that in the presence of complete neuropathy local anesthesia is not needed. To get maximal effect from the procedure, the provider should maximally dorsiflex the toe while the



Fig. 7.6 Example of flexor tenotomy being performed with an 18 gauge needle for distal toe wound with associated hammertoe deformity

patient flexes the toe to cause a "bowstring" effect of the flexor tendon. Utilizing a beaver blade or 18-gauge needle, puncture the skin midline at the base of the middle phalanx and carefully move medial and lateral until you feel the tendon release. You will notice an immediate difference in the motion of the toe. The puncture site can be dressed with a band aid and the patient is weight-bearing as tolerated. In a patient who needs a partial first ray there should be a low threshold to prophylactically perform this procedure on the lesser digits.

Tendoachilles Lengthening

Normal gait requires 10–15 degrees of ankle dorsiflexion which is determined by the flexibility of the gastroc-soleus complex. Below 10 degrees, there is a significant increase in plantar pressure of the forefoot which poses a problem for diabetics, particularly ones with a forefoot ulcer [29]. While degrees of dorsiflexion is important the surgeon should consider an Achilles tendon lengthening anytime there is a forefoot ulceration. An additional indication is when the biomechanics are

altered in a way that gives advantage to the Achilles, such as a transmetatarsal amputation. The tendoachilles lengthening or TAL is the surgical gold standard in these clinical scenarios. In a study by Mueller et al., they looked at 30 patients with forefoot ulcerations with which a TAL was performed and all patients healed the ulceration [30]. The author's preferred technique is the percutaneous triple hemisection as described by Hoke. The smaller incisions afford less complications in the comorbid patient.

Tendon Transfers

Tendon transfers are utilized to improve motor function when weakness and imbalance exist in the diabetic foot, particularly after an amputation of different parts of the foot. Key tendon insertion sites are amputated and soft tissue imbalance can lead to deforming forces on different areas of the foot.

In the authors opinion, there are key clinical principles that are crucial when deciding to perform a tendon transfer: (1) Tendon transfers cannot overcome a fixed deformity; therefore, these are only of functional use in a flexible deformity, (2) the tendon being harvested should be a minimum strength grade of 4+ as the tendon loses one grade of strength following transfer, (3) the ideal tendon to transfer is one that functions in the same phase of gait, although this is not an absolute contraindication of transplantation, (4) perhaps most importantly, muscle-tendon tension should be adequately fixated to give optimal function postoperatively.

Understanding agonist and antagonist actions of the different muscles of the lower extremity is imperative when deciding when to do a tendon transfer. One of the most common muscle imbalances in the foot is after amputation of the fifth ray and losing the peroneus brevis tendon attachment. The direct antagonist to the peroneus brevis is the posterior tibial tendon, which over time will lead to an equinovarus deformity of the foot. One method to correct this is utilizing a posterior tibial tendon transfer to the lateral aspect of the foot (typically the lateral cuneiform) through the interosseous membrane to create a more plantigrade foot.

Bone Procedures

Modified Keller Resection Arthroplasty for First MPJ Ulcers Under Hallux

The Keller arthroplasty is typically reserved for the elderly population with moderate to severe osteoarthritis for the first metatarsophalangeal joint and associated osteoporotic bone. However, this procedure can be useful in the case of a recurring plantar hallux ulceration. In a study by Tamir et al., the authors looked at 28 keller arthroplasties with a plantar hallux wound. 78% of the ulcerations recovered in a mean of 3.1 weeks and had no recurrence at a mean follow-up of 26 months [31]. The procedure essentially acts to decompress the hallux and allow for more extension of the metatarsophalangeal joint. This acts to decrease the pressure associated with the formation of the wound.

MIS Invasive Floating Metatarsal Osteotomy for Pressure Under Metatarsal Heads

There are several operations that can be utilized for plantar metatarsal head ulcerations such as the Weil osteotomy, plantar condylectomy, or dorsal closing wedge osteotomy. These are great procedures to offload the plantar aspect of the foot; however with these open procedures in the diabetic population, there is an increase in postoperative complications such as wound dehiscence or infection [32].

This procedure is done by making a small 3mm incision over the affected metatarsal. Next, utilize a mosquito or curved hemostat for blunt dissection down to bone. Using a Shannon burr, make a perpendicular or short oblique osteotomy in the metatarsal to dorsally displace the metatarsal head. In a study by Tamir et al., they looked at 20 cases of this osteotomy in patients with plantar metatarsal head ulcerations. In 17 of the 20 cases, the ulcer fully healed at 6 weeks. The

remaining 3 showed clinical improvement but not full healing of the ulcer [32].

As minimally invasive procedures are gaining traction in foot and ankle surgery, this is an attractive procedure for numerous reasons. First, there is no hardware needed which is ideal in a patient with a wound. Additionally, there is a minimal chance of wound complications and these patients are able to be full weight-bearing immediately post-op in a surgical shoe further decreasing post-op recovery.

Utility of External Fixation for Offloading

Surgical offloading via the use of external fixation (Fig. 7.7) is a unique and valuable tool for any foot and ankle surgeon, particularly when conservative offloading methods fail due to excess drainage from the wound or patient compliance issues. It is used for the stabilization, protection, and immobilization of the soft tissue and osseous structures and is particularly helpful with limb salvage plastic surgery techniques [33]. Soft tissue reconstruction can easily be disrupted postoperatively from weight-bearing or premature joint motion. The external fixator helps to avoid these complications as well as gives you access to wounds and/or free flaps.

As we stated earlier, total contact casts are the gold standard for diabetic foot offloading. The only pitfall to this cast is that the patient, physician, or home nurse cannot examine a wound regularly which can lead to advancement of the ulcer, infection, or even new ulcerations.

The benefits of utilizing an external fixator for offloading purposes is that you remove absolutely all weight from the foot and eliminate all tension on the plantar aspect of the foot. Additionally as stated above, wound care can be done at any time and any skin graft or free flap used can be protected from areas of pressure.

On the other hand, there are downsides to the use of external fixation. First, the surgeon must be skilled and confident in applying these frames. Perhaps the largest downside to external fixation is the high possibility of pin tract infection which occurs at the skin-pin interface. One systematic review reported that the cumulative pin tract infection rate throughout the literature was 27% [34] which every surgeon should be aware of and diligent wound care should be done daily.

In the author's opinion the times to use an external fixation for offloading are: ulcerations not responding to total contact cast treatment or other typical methods of offloading, large plantar

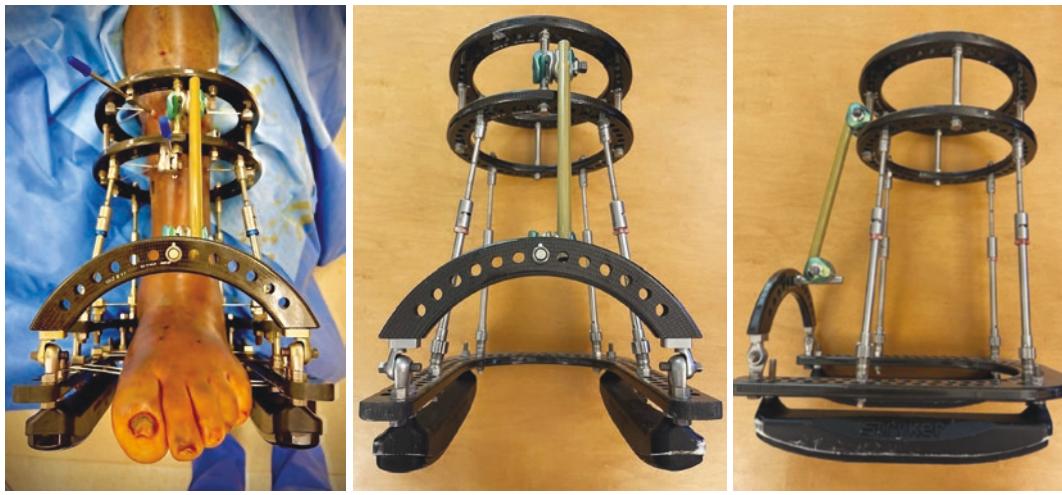


Fig. 7.7 Circular external fixation device

Table 7.2 This table demonstrates different methods for offloading based on wound location

Location	Common pathology	Conservative	Surgical
Hallux	– Hallux limitus/rigidus	– Diabetic shoe/ insert	– Keller arthroplasty
		– Custom orthotics	– Exostectomy
Digits	– Mallet, claw, hammertoe	– Diabetic shoe	– Flexor tenotomy
			– Arthroplasty
Forefoot	– Distal fat pad displacement	– Diabetic shoe/ insert	– Tendoachilles lengthening
	– Transfer pressure from elongated or shorten ray	– Felt metatarsal pad	– Gastroc recession
	– Equinus	– CAM walker	– Tendon transfers
			– Floating metatarsal head osteotomy
Midfoot	– Rigid flatfoot	– Diabetic shoe/ insert	– Exostectomy
	– Charcot neuroarthropathy	– Total contact cast	– External fixator
		– CAM walker	– Surgical reconstruction
		– CROW boot	– Tendon transfers
Hindfoot	– Calcaneal gait	– Diabetic shoe/ insert	– External fixator
	– Charcot neuroarthropathy	– Total contact cast	– Achilles repair
	– Pressure	– CAM walker	– Ankle fusion
		– CROW boot	– Tibio-Talo-Calcaneal arthrodesis

Listed are both conservative and surgical methods of offloading

ulcerations, ulcers in patients that have extreme difficulty being non-weight-bearing perhaps due to obesity, ulcerations that require skin grafting or flaps, and for reconstructive surgeries when internal fixation is contraindicated.

Offloading Options Categorized by Wound Location

Conservative and surgical offloading of the diabetic foot is paramount in both the treatment and the prevention of ulcerations. One must take into account many factors when selecting both short-term and long-term offloading options. Each ulceration and each patient is unique and thus a plan, whether conservative or surgical, must be developed based on each unique situation. Please see Table 7.2 for a summary of different methods of offloading both surgical and conservative based on wound location.

Every diabetic patient should be evaluated periodically for proper offloading mechanisms. If conservative offloading devices are not working and a patient continues to develop an ulceration, then a surgical offloading mechanism may be necessary. The treatment of diabetic foot ulcers begins with prevention and begins with the basic knowledge and understanding of offloading.

References

1. International Diabetes Federation. IDF diabetes atlas. 9th edn. 2019. p. 14–25.
2. Jodheea-Jutton A, Hindocha S, Bhaw-Luximon A. Health economics of diabetic foot ulcer and recent trends to accelerate treatment. Foot. 2022;52:101909. https://doi.org/10.1016/j.foot.2022.101909.
3. Blume P, Stephanie W. Updating the diabetic foot treatment algorithm: recommendations on treatment using advanced medicine and therapies. 2017;30(2):29–35.
4. Cavanagh P, Bus S. Off-loading the diabetic foot for ulcer prevention and healing. 2010;52(3):37–43.
5. Baker N, Osman I. The principles and practicalities of offloading diabetic foot ulcers. 2016;19(4):172–81.
6. Kim P. Biomechanics of the diabetic foot: consideration in limb salvage. 2013;2(3):107–11.
7. Pham H, Armstrong DG, Harvey C, Harkless LB, Giurini JM, Veves A. Screening techniques to identify

people at high risk for diabetic foot ulceration: a prospective multicenter trial. 2000;23:606.
8. Dardari D. An overview of Charcot's neuroarthropathy. J Clin Transl Endocrinol. 2020;22:100239.
9. Potter J, Potter MJ. Effect of callus removal on peak plantar pressures. Foot. 2000;10(1):23–6.
10. Veves A, Murray HJ, Young MJ, Boulton AJ. The risk of foot ulceration in diabetic patients with high foot pressure: a prospective study. Diabetologia. 1992;35:660.
11. Mrdjenovich D. Off-loading practices for the wounded foot: concepts and choices. J Am Col Certif Wound Spec. 2010;2(4):73–8.
12. Armstrong DG, Athanasiou KA. The edge effect: how and why wounds grow in size and depth. Clin Podiatr Med Surg. 1998;15(1):105–8.
13. McCartan BL, Rosenblum BI. Offloading of the diabetic foot: orthotic and pedorthic strategies. Clin Podiatr Med Surg. 2014;31:71–88.
14. Albert S, Rinouie C. Effect of custom orthotics on pressure distribution in the pronated diabetic foot. J Foot Ankle Surg. 1994;33:598–604.
15. Lanez-Sharma R. Diabetic shoes: why you need them. https://www.ankle-footspecialist.com/blog/diabetic-shoes-why-you-need-them. Accessed 21 March 2022.
16. Tejada A. The difference between diabetic shoes and regular shoes. 2019. https://www.orthofeet.com/blogs/news/the-difference-between-diabetic-shoes-and-regular-shoes. Accessed 22 March 2022.
17. Gutekunst DJ, Hastings MK, Bohnert KL, Strube MJ, Sinacore DR. Removable cast walker boots yield greater forefoot off-loading than total contact casts. Clin Biomech. 2011;26(6):649–54.
18. Pollo FE, Brodsky JW, Crenshaw SJ, Kirksey C. Plantar pressures in fiberglass total contact casts vs a new diabetic walking boot. Foot Ankle Int. 2003;24(1):1–5.
19. Ababneh A, Finlayson K, Edwards H, Lazzarini PA. Factors associated with adherence to using removable cast walker treatment among patients with diabetes-related foot ulcers. BMJ Open Diabetes Res Care. 2022;10:e002640.
20. Armstrong DG, Nguyen HC, Lavery LA, van Schie CH, Boulton AJ, Haarkless LB. Off-loading the diabetic foot wound: a randomized clinical trial. Diabetes Care. 2001;24(6):1019–22.
21. Rogers LC, Hanft J. Point-counterpoint: is total contact casting better than the CAM Walker Boot for plantar diabetic wounds? 2019. https://www.hmpgloballearningnetwork.com/site/podiatry/point-counterpoint-total-contact-casting-better-cam-walker-boot-plantar-diabetic-wounds. Accessed 22 March 2022.
22. Messenger G, Masoetsa R, Hussain I. A narrative review of the benefits and risks of total contact casts in the management of diabetic foot ulcers. J Am Coll Clin Wound Spec. 2017;9(1–3):19–23.
23. Griffiths DA, Kaminski MR. Duration of total contact casting for resolution of acute Charcot foot: a retrospective cohort study. J Foot Ankle Res. 2021;14(1):44.
24. Elattar O, Smith T, Ferguson A, Farber D, Wapner K. Uses of braces and orthotics for conservative management of foot and ankle disorders. Foot Ankle Orthop. 2018;3(3).
25. Sarmiento A. A functional below-the-knee cast for tibial fractures. J Bone Joint Surg Am. 1967;49:855–75.
26. Alimerzaloo F, Kashani RV, Saeedi H, Farzi M, Fallahian N. Patellar tendon bearing brace: combined effect of heel clearance and ankle status on foot plantar pressure. Prosthet Orthot Int. 2014;38(1):34–8.
27. Tanaka H, Goto NT, Inoue A. The effect of the patellar tendon-bracing cast on loading. J Bone Joint Surg Br. 2000;82(2):228–32.
28. Armstrong DG, Frykberg RG. Classifying diabetic foot surgery: toward a rational definition. Diabet Med. 2003;20:329–31.
29. Armstrong DG, Stacpoole-Shea S, Nguyen H, Harkless LB. Lengthening of the Achilles tendon in diabetic patients who are at high risk for ulceration of the foot. J Bone Joint Surg Am. 1999;81:535–8.
30. Mueller M, Sinacore DR, Hastings MK, Strube MJ, Johnson JE. Effect of Achilles tendon lengthening on neuropathic plantar ulcers. A randomized clinical trial. J Bone Joint Surg Am. 2003;85(8):1436–45.
31. Tamir E, Tamir J, Beer Y, Kosashvili Y, Finestone AS. Resection arthroplasty for resistant ulcers underlying the Hallux in insensate diabetics. Foot Ankle Int. 2015;36(8):969–75.
32. Tamir E, Finestone AS, Avisar E, Agar G. Mini-invasive floating metatarsal osteotomy for resistant or recurrent neuropathic plantar metatarsal head ulcers. J Orthop Surg Res. 2016;11:78.
33. Ramanujam CL, Facaros Z, Zgonis T. Surgical off-loading external fixation and plastic reconstruction of the foot and ankle. 2016. https://musculoskeletalkey.com/surgical-off-loading-external-fixation-and-plastic-reconstruction-of-the-foot-and-ankle/. Accessed 26 March 2022.
34. Lobst CA, Liu RW. A systematic review of incidence of pin track infections associated with external fixation. J limb lengthening reconstr. 2016;2(1):6–16.

8 Medical Management of the Limb Salvage Inpatient

Marie M. Alternburg, Jennifer M. Haydek, Sara Kiparizoska, Nina K. Weaver, and Margot G. Wheeler

Section 1: Perioperative Management of Cardiac Risk Factors and Disease

Noncardiac surgeries, including limb salvage procedures, are a robust part of a functioning healthcare system, with 1 in every 30–40 adults undertaking such procedures at some point in their lives. In a large-scale WHO-funded inquiry, among the 200 million adults worldwide who undergo noncardiac surgery each year, more than ten million will suffer from a major vascular event—myocardial infarction, cardiac arrest, cardiac death—within 30 days from surgery [1]. Effective, evidence-based perioperative cardiac management can improve mortality, avoid subsequent morbidities, decrease length of hospitalization, and minimize the cost burden on the healthcare system.

M. M. Alternburg · J. M. Haydek · S. Kiparizoska · N. K. Weaver · M. G. Wheeler (✉)
Department of Internal Medicine, Medstar Georgetown University Hospital, Washington, DC, USA
e-mail: Marie.M.Altenburg@medstar.net; Jennifer.M.Haydek@medstar.net; Sara.Kiparizoska@medstar.net; Nina.K.Weaver@medstar.net; Margot.G.Wheeler@gunet.georgetown.edu

Estimate Risk

It is crucial to begin any preoperative management with an assessment of the patient's cardiac risk as well as the risk inherent in the planned surgery. This assessment can and should inform a range of clinical decisions regarding testing, monitoring, and medical management leading up to the surgery as well as perioperatively.

Risk of Procedure

The first step in any perioperative evaluation is to risk stratify the procedure itself. The American guidelines consider noncardiac surgeries with <1% risk of major adverse cardiac event (MACE) low risk, whereas high risk are procedures with higher rates of adverse events including vascular (7.7%), thoracic (6.5%), transplant (6.2%), general surgeries (3.9%) [2]. While most limb salvage procedures fit in the low-risk category, more complex surgeries such as flap procedures are high-risk surgeries due to prolonged surgical time.

Conditions That Confer Risk

It has been established that pre-existing cardiac conditions like CAD, cardiac stents, CHF, arrhythmias including atrial fibrillation and valvular pathologies including aortic stenosis can increase the risk of perioperative morbidity and mortality.

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_8

Tools

The Revised Cardiac Risk Index (RCRI) is the most used risk assessment tool given its relative simplicity, taking into account the risk of the surgery, a history of ischemic heart disease, congestive heart failure, cerebrovascular disease, preoperative insulin dependence, and a preoperative creatinine greater than 2 mg/dL. More recent prospective studies suggest higher risk estimates for major adverse cardiac events than originally established; up to a sixfold increase in events vs. the rate predicted by the RCRI. The NSQIP has been found to have superior ability to discriminate for adverse cardiac events vs. the RCRI [3, 4], though these studies did not routinely monitor perioperative troponins and likely missed a significant number of cardiac events, which are often silent [5]. The major American and Canadian guidelines recommend using the RCRI over the NSQIP. Patients with 0 points on the RCRI score have a 3.9% risk of MACE; 1 point confers a 6.0% risk; 2 points confer a 10.1% risk; 3 or more points convey a 15% risk.

Functional Capacity

The next crucial step in any preoperative evaluation is to assess functional capacity. The inability to perform more than four metabolic equivalents (METS), which is equivalent to walking up two flights of stairs or undertaking heavy housework has been associated with double the perioperative cardiac complications [6].

Myocardial Injury After Noncardiac Surgery (MINS)

The MINS protocol helps identify patients who are at high risk for developing myocardial injury after noncardiac surgery. Patients >age 65 with known coronary artery disease should have troponin measurements on day 1, 2, and 3 after surgery. An elevation in the troponin allows physicians to identify MINS and start secondary measures [7].

Preoperative Cardiac Testing

Based upon the risk of the procedure being undertaken and the patient's risk assessment, various preoperative diagnostic testing might be appropriate.

EKG

American guidelines recommend a preoperative EKG when there is a history of coronary artery disease (CAD), arrhythmia, CVA, or structural cardiac disease *and* prior to a higher risk procedure [8]. Multiple studies have found little benefit to a preoperative EKG in low-risk surgeries, and while bundle blocks were associated with increased risk, no more so than when history identified risk [9–11].

Transthoracic Echocardiography

American guidelines do not support preoperative transthoracic echocardiography (TTE) unless the patient has a history of moderate or severe valvular disease without a TTE in past 12 months or in those with symptoms of severe valvular disease such as syncope, dyspnea, angina, dyspnea, or edema [8]. Overall, routine TTE is not recommended if there are no history of symptoms indicating active heart failure or structural disease. These recommendations are based on studies that have found an increased risk of perioperative cardiac events in patients with congestive heart failure and structural disease. Aortic stenosis with a gradient >40 mmHg, left ventricular hypertrophy, and left ventricular systolic dysfunction associated were associated with increased cardiac events, including myocardial infarction, pulmonary edema, ventricular fibrillation or arrest, and complete heart block [12]. A preoperative TTE w/ any degree of systolic dysfunction, moderate to severe LVH, moderate to severe mitral regurgitation, or AS w/ gradient >20 mmHg was 80% sensitive for perioperative cardiac events w/ negative predictive value of 97% [12]. AS on preoperative TTE was associated with increased risk of perioperative death or MI (14% vs. 2% w/out aortic stenosis) [13]. Left ventricular ejection fraction (LVEF) <30% was associated with greater risk of perioperative death, MI, or heart failure decompensation (53.5% vs. 26% w/ LVEF >30%) [14].

Cardiac Stress Testing

The current American guidelines suggest preoperative stress test only when a patient cannot perform >4 METS ***and*** if the outcome would change perioperative management [8].

These guidelines are based on studies associating poor functional capacity with worse perioperative outcomes. The inability to perform four METS was associated with a twofold increase in perioperative MACE [6]. In an assessment using the Duke Activity Score Index, which is validated to access functional capacity, lower scores were associated with death or MI in 2% of patients within 30 days of surgery [15]. In small, prospective studies myocardial ischemia at low workload (<60% of maximum predicted heart rate) was associated with increased event rates (23% risk of death/MI vs. 5% in those without ischemia) [16]. A negative dobutamine stress echo *and* no wall motion abnormalities had excellent negative predictive value for perioperative MACE [17].

Cardiac Catheterization/CTA

The current American and Canadian guidelines recommend invasive angiography only if a preceding stress test indicates myocardial ischemia *and* when results would change perioperative care. A randomized controlled study assigning 510 patients with CAD about to have vascular surgery to either revascularization or conservative management found that revascularization did not significantly impact long-term outcomes, though the study was not adequately powered to assess differences in short-term outcomes [18].

There is no current guideline for coronary CT scans [19]. It is an area of active inquiry whether noninvasive preoperative coronary CT scans might help predict perioperative MACE and potentially inform management. In a study of 239 patient getting pre-op CT coronary angiography, a higher RCRI, a high CACS (113), the presence of significant coronary artery stenosis (diameter stenosis 50%), and multivessel coronary artery disease were significantly associated with postoperative cardiovascular events. CTCA was more sensitive than RCRI alone in patients with RCRI <2. This suggests CTCA might be a good option for patients who cannot tolerate exercise or chemical stress test [20]. A 2019 meta-analysis found incremental risk of MACE with CAD by coronary CT and that multivessel CAD on coronary CT conferred eightfold increased risk of perioperative MACE [21]. A prospective cohort study of 955 patients found that while pre-op coronary CT can improve estimated risk, it can also overestimate the risk by fivefold in patients who will not have these outcomes [22].

Cardiac Biomarkers

N-terminal-pro-BNP (NT-ProBNP) is a polypeptide released by cardiac cells in response to stretch. It is an area of active investigation to see if serum NT-ProBNP levels might be associated with perioperative cardiac risk. The current AHA/ACC guidelines do not endorse preoperative BNP measurement as there has been no data showing that this practice might reduce cardiovascular risk [8]. The Canadian guidelines, however, recommend checking pro-bnp prior to surgery for patients who have cardiovascular disease and RCRI >1, or for anyone >65 years old [5].

Optimizing Medical Therapies Preoperatively

Beta-Blocker

Beta-blockers are known to decrease myocardial wall stretch, prolong coronary artery diastolic filling time, and reduce myocardial oxygen supply and demand mismatch. As such, they were previously prescribed perioperatively with abandon, including starting new beta-blockers on the day of surgery. Current ACC/AHA guidelines support continuing previously prescribed beta-blockers and starting them for patients with appropriate BB indications if >7 days prior to surgery, but do not support initiating beta-blockers in the immediate pre-op period [19], which is in line with European guidelines. In a retrospective cohort analysis of 136,745 patients exposed to beta-blockers on the day of or following surgery, perioperative beta-blocker exposure was associated with lower rates of 30-day all-cause mortality in patients with 2 or more Revised Cardiac Risk Index factors [23].

A 2014 metanalysis including 16 RCTs showed that while beta-blockers were associated with a trend toward reduced all-cause mortality rate in the DECREASE trials (RR: 0.42; 95% CI:

0.15–1.22), they were associated with increased all-cause mortality rate in other trials (RR: 1.30; 95% CI: 1.03–1.64). Additionally, this study found that while perioperative beta-blockers started within 1 day or less before noncardiac surgery prevents nonfatal MI, these patients had increased risks of stroke, death, hypotension, and bradycardia. As such, putting aside the DECREASE studies, there are insufficient data on beta blockade started 2 or more days prior to surgery [24].

An international, multicenter RCT of 8351 patients with cardiovascular disease or at risk for cardiac disease randomized to receive 100 mg metoprolol succinate on day of surgery and then continued for 30 days found that fewer patients in the metoprolol group than in the placebo group had a myocardial infarction. However, there were more deaths in the metoprolol group than in the placebo group, as well as more strokes [25].

In a 2010 prospective study of 940 vascular surgery patients given beta-blockers 0–1, 1–4, and 4 weeks before surgery, beta-blocker treatment initiated >1 week before surgery is associated with lower preoperative heart rate and improved outcome, compared with treatment initiated <1 week preoperatively [26].

Aspirin

Aspirin is an irreversible cox-1 inhibitor and as such reduces the aggregation of platelets and is associated with increased bleeding risks. The current American guidelines recommend to hold aspirin prior to noncardiac surgery unless the ischemic risks outweigh the chances of bleeding [19]. However, more recent data supports continuing aspirin in patients who have had a history of PCI [27]. In practice, many of the limb salvage patients do have a history of PCI or lower extremity stenting and aspirin is continued throughout the perioperative period.

Statin/Lipid-Lowering

Statin therapy might have a role in minimizing perioperative cardiac risk, as they have been found to have anti-inflammatory and stabilizing effects on cardiac lesions more generally. European guidelines support continuing statins and initiating them at least 2 weeks in advance for patients with indications not currently on statin therapy [28]. Canadian guidelines support continuing but not initiating statin therapy preoperatively. ACC/AHA guidelines support initiating statin therapy prior to a vascular surgery in patients with indications for lipid lowering therapy. While there have been observational studies, there are no major RCT data to support this. In practice, many limb salvage patients have pre-existing coronary artery and peripheral vascular disease and are already on a moderate to high dose statin. If not, the internist should consider the addition of a statin during the hospitalization.

Ace-I/Arb

Angiotensin converting enzyme inhibitors and angiotensin II receptor blockers have a neurohormonal effect by reducing activation of the renin-angiotensin-aldosterone axis, resulting in downstream vasodilation and decreased circulating blood volume. They are part of the backbone of heart failure with reduced ejection fraction treatment. Canadian guidelines suggest stopping ACE-I/ARBs 24 h prior to surgery and restarting on postoperative day 2 [5]; European guidelines suggest a temporary hiatus if they are prescribed for blood pressure control but continuing them if prescribed for heart failure with decreased left ventricular systolic function [28]; American guidelines suggest that continuing Ace/Arb medications “is reasonable” in all cases and suggests restarting them as soon as possible if they are held [8]. Debate about best practices remains as there is yet to be a well-designed RCT comparing administration vs. holding of these medications.

The recommendations are based upon prospective and observational studies. A prospective randomized trial analyzing hemodynamics during anesthesia induction showed an increased incidence of severe hypotension during induction for people who continued their chronic ARB on day of surgery [29]. An international prospective cohort study of 14,687 patients found that when compared to patients who continued their angiotensin-converting enzyme inhibitors/angio-

tensin II receptor blockers, the 1245 (26%) angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker users who withheld their angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers in the 24 h before surgery were less likely to suffer the primary composite outcome of all-cause death, stroke, or myocardial injury and intraoperative hypotension [30].

Summary of Cardiovascular Assessment

The preoperative history and physical examination are used to assess the patient's cardiovascular risk factors and medication management. A risk assessment utilizing the RCRI is performed in order to quantify the patient's risk of cardiac complications. Next, consideration of further cardiac testing is made and only pursued if the results will affect the patient's management. A careful review of medications is performed prior to surgical intervention. The internists' role is to perform a risk assessment, communicate that risk to the patient and surgical team, and to guide further testing and treatment for known or suspected heart disease. A clear analysis of the patient's risk and management options is essential in surgical planning.

Section 2: Diabetes Management

Glucose Management

Inpatient care for limb salvage patients often requires diabetes management. Diabetes mellitus puts patients at greater risk for atherosclerotic disease, including peripheral arterial disease (PAD). A disproportionate share of diabetic patients has PAD, and 20–30% of patients with PAD have diabetes [31]. Diabetic neuropathy, a complication of long-standing diabetes, and PAD put patients at increased risk for limb salvage procedures, as patients with both PAD and diabetes are five times as likely to need amputation [32]. Therefore, inpatient diabetes care—including glucose management, medication management, insulin initiation and titration, and discharge planning—is crucial for many hospitalized limb salvage patients.

A diabetic patient's glucose should be checked regularly while admitted and kept within a goal range, avoiding both hypoglycemia and hyperglycemia.

Hypoglycemia

Hypoglycemia, defined by the American Diabetes Association (ADA) and the Endocrine Society as glucose <70 mg/dL, is a serious adverse event that can complicate antidiabetic therapy in the hospital [33]. In many cases, hypoglycemia is a side effect of the antidiabetic therapy itself. Overtreatment with insulin or the continuation of an insulin secretagogue like a sulfonylurea can result in hypoglycemia, particularly when a patient is hospitalized and might be suffering from a severe illness or not eating their normal diet. Many patients recognize the symptoms of hypoglycemia, but hospitalized patients may have impaired awareness and be unable to detect these symptoms [34]. Hypoglycemia triggers the autonomic nervous system, producing symptoms including tremulousness, anxiety, diaphoresis, and palpitations. Hypoglycemia also deprives neurons of glucose, producing fatigue, weakness, and confusion. When severe or prolonged, acute hypoglycemia can cause seizures, neuronal damage, or even death [35]. Even after symptom resolution, episodes of hypoglycemia have been associated with long-term increased morbidity and mortality.

Hyperglycemia

Hyperglycemia presents a more visible and common conundrum for the inpatient provider. Many patients, diabetic or not, experience hyperglycemia while hospitalized due to glucocorticoid use or acute illness. Hyperglycemia has been associated with increased morbidity and mortality during hospitalizations [36]. In surgical patients specifically, preoperative hyperglycemia has been linked in some studies to elevated infection rates and worse overall outcomes [37, 38].

Goal Glucose Range

Providers should aim to keep a diabetic patient's glucose between 140 and 180 mg/dL, in accordance with the 2020 ADA Standards of Care and Endocrine Society guidelines [39]. Titrating therapy to this goal generally protects against hyper- and hypoglycemia. A patient who is eating should have their blood glucose checked at bedside fasting in the morning and before every meal. A patient who is NPO or on continuous tube feeds should have blood glucose checked every 4–6 h.

The optimal range of 140–180 mg/dL has been studied in perioperative patients. A Cochrane review of perioperative glycemic control in diabetic patients noted that lower targets were associated with no improved outcomes but with more episodes of hypoglycemia [40]. A subsequent meta-analysis of perioperative outcomes noted that a liberal glucose target of >200 mg/dL resulted in higher mortality and stroke than a target of <200 mg/dL. However, a very strict glucose goal of <140 mg/dL showed no additional benefits but higher rates of hypoglycemia [41].

The 2009 NICE-SUGAR trial demonstrated the risk of strict glucose control in critically ill patients. Those patients maintained at a blood glucose of <108 mg/dL had a significantly higher mortality rate than those maintained at <180 mg/dL. Patients receiving tighter control also had more episodes of hypoglycemia and no better outcomes in length of stay or mechanical ventilation [42]. Per the Endocrine Society guidelines, a patient's antidiabetic therapy should be reevaluated and potentially lessened if a patient's glucose falls below 100 mg/dL.

Antidiabetic Medications

Non-insulin Medications

Many patients will be taking oral or injectable antidiabetic medications when admitted to the hospital. In general, these antidiabetic agents should be withheld on admission [43]. An admitted patient may develop acute abnormalities, such as kidney injury or critical illness, which are contraindications to use of these medications. Some medications, like SGLT-2 inhibitors, do not yet have safety data supporting use for hospitalized patients [39]. Oral and injectable medications also tend to act slowly, limiting easy titration. Particularly for patients scheduled for surgery, the Endocrine Society recommends discontinuing oral and non-insulin injectable antidiabetic agents and typically transitioning to insulin [44].

Insulin

In most cases, insulin should be the primary therapy used to manage hyperglycemia during a hospital stay [44]. If a patient is not already on insulin, they should be started when they have a persistent glucose >180 mg/dL. Insulin dosing should be calculated using the patient's weight and diet. If a patient is NPO or has poor oral intake, insulin should be provided as a basal dose with a correctional sliding scale. A patient on continuous tube feeds or TPN should receive subcutaneous rapid-acting insulin every 4–6 h. A patient eating a normal diet should receive basal insulin, prandial insulin, and a mealtime correctional sliding scale [44]. Figure 8.1 shows standard dosing of insulin in patients with diabetes and hyperglycemia depending on type and amount of intake [43].

Some clinicians may be concerned about causing hypoglycemia when starting a patient on a weight-based insulin regimen. A retrospective

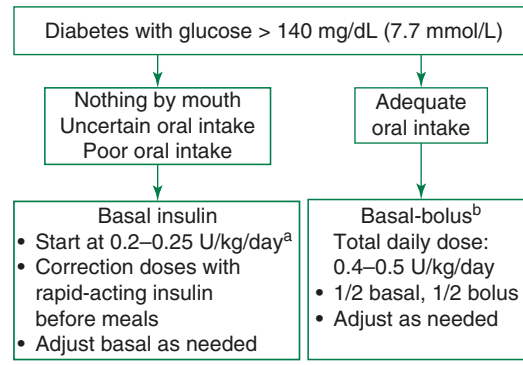


Fig. 8.1 Insulin dosing in a patient with diabetes and hyperglycemia depending on type and amount of intake

study found that hypoglycemia was relatively uncommon at weight-based doses below 0.6 units/kg. Above that threshold, hypoglycemia became much more common [45].

A patient should not be started on sliding scale insulin alone [39]. Sliding scale insulin is not a physiologic therapy. When used in this way, insulin treats hyperglycemia that has already occurred, so the body has already been exposed to the elevated glucose. By contrast, basal-bolus insulin, in which a basal rate of insulin is delivered along with prandial boluses to address postprandial glucose spikes, prevents hyperglycemia in the first place [46]. Sliding scale insulin has been associated with worse glycemic control overall. One study of hospitalized patients found that patients treated with sliding scale insulin had a mean glucose level 20 mg/dL higher than a similar group on basal-bolus insulin [46]. The randomized, controlled RABBIT 2 trial also noted a significant improvement in glycemic control in inpatients treated with basal-bolus insulin. These patients had a daily mean glucose level 27 mg/dL lower than those treated with sliding scale insulin [47].

Perioperative Insulin Management

A patient's insulin regimen needs adjustment prior to surgery. All oral antidiabetic medications should be held in the perioperative period. The ADA recommends giving basal insulin at 60–80% of the full dose the night before the operation. In a 2017 study, patients who received 100% of their previous insulin dose the night before surgery had higher rates of hypoglycemia than patients who received 60–87% of their previous dose. The patients receiving the reduced dose of insulin were more likely to be within the goal range of 100–180 mg/dL during the operation [39]. From a review in *Anesthesiology* on perioperative hyperglycemia, Tables 8.1 and 8.2 recommend the following insulin regimens on the day before and day of surgery [38].

The review recommends that patients with type 1 diabetes receive 80% of their usual basal dose the evening before surgery and 80% again the morning of. In diabetic patients receiving morning doses of insulin, the NPH should be reduced to 50% of the usual dose and longer acting insulins reduced to 60–80%. Prandial insulin should be held at the time the patient becomes NPO [38].

Preparation for Discharge

Education

A patient nearing discharge should be prepared for continued diabetes management at home. The ADA recommends reviewing the patient's outpatient diabetes provider, the patient's understanding of their diagnosis, how to monitor glucose levels, recognition and plan of action for hyperglycemia and hypoglycemia, a healthy nutrition plan or referral to diabetes dietician, and the patient's antidiabetic medications [39]. A recent

Table 8.1 Standard recommendations for day before surgery insulin regimens

Day before surgery insulin regimens based on oral intake status								
	Glargine or detemir		NPH or 70/30 insulin		Lispro, aspart, glulisine, regular		Non-insulin injectables	
Day before surgery insulin regimens	AM dose	PM dose	AM dose	PM dose	AM dose	PM dose	AM dose	PM dose
Normal diet until midnight (includes those permitted clear liquids until 2 h prior to surgery)	Usual dose	80% of usual dose	80% of usual dose	80% of usual dose	Usual dose	Usual dose	Usual dose	Usual dose
Bowel prep (and/or clear liquids only 12–24 h prior to surgery)	Usual dose	80% of usual dose	80% of usual dose	80% of usual dose	Usual dose	Usual dose	Hold when starting clear liquid diet/ bowel prep	Hold when starting clear liquid diet/ bowel prep

Table 8.2 Standard recommendations for day of surgery insulin regimens

Day of surgery insulin regimens			
Glargine or detemir	NPH or 70/30 insulin	Lispro, aspart, glulisine, regular	Non-insulin injectables
80% of usual dose if patient uses twice daily basal therapy	50% of usual dose[a] if BG 120 mg/dL Hold for BG <120 mg/dL	Hold	Hold

BG blood glucose
[a] 6.6 mmol/L

review of inpatient diabetes education notes that although most diabetes education occurs in the outpatient setting, hospitalization is an ideal time to provide this education. There is growing evidence for the benefit of inpatient diabetes education, particularly on reducing readmission rates and improving health outcomes [48].

Home Medication Management

While a patient is admitted, a hemoglobin A1c should be obtained if none is identified within the last 3 months. Based on this value, the Endocrine Society suggests an algorithm for discharge medication management that the ADA subsequently found to be useful. If the patient's hemoglobin A1c is <7%, there should be no change made to the home diabetes regimen. If the patient has a hemoglobin A1c of 7–9%, the patient has suboptimal control. At discharge, the patient should be considered for intensified oral medication or basal insulin. If the hemoglobin A1c is >9%, the patient's diabetes is poorly controlled. These patients should be considered for a basal-bolus insulin regimen. This discharge algorithm was found to be safe and efficacious in a prospective trial. The study started patients with a hemoglobin A1c of 7–9% on home glargine at 50% of the hospital dose and patients with hemoglobin >9% on glargine or basal-bolus at 80% of their hospital dose. The patient should otherwise be restarted on their pre-admission oral antidiabetic medications at discharge [49].

Prevention of Atherosclerotic Disease

A diabetic patient's admission presents an ideal time to ensure that they are on all recommended medications for comorbid conditions. Many limb salvage patients with diabetes also have PAD, a form of atherosclerotic disease. For secondary prevention, diabetic patients of all ages with atherosclerotic disease should be started on a high-intensity statin and aspirin 81 mg daily and should be considered for an ACE inhibitor or angiotensin receptor blocker (ARB) medication [50]. A diabetic patient aged 40–70 even without atherosclerotic disease should be started on a medium-intensity statin for primary prevention. Diabetic patients over 50 without atherosclerotic disease but with other risk factors likely benefit from a high-intensity statin [50].

Goal Hemoglobin A1c Ranges

Providers should also review goal hemoglobin A1c ranges with patients. There is no consensus guideline for goal hemoglobin A1c, so the discussion should be individualized and take into account patient preference, patient characteristics and comorbidities, and pre-existing complications of diabetes. The ADA 2020 Glycemic Control guideline states that a goal hemoglobin A1c of <7% is appropriate for many patients to prevent microvascular and macrovascular complications. However, for patients with a history of severe hypoglycemia, limited life expectancy, advanced macrovascular or microvascular complications, extensive comorbidities, or long-standing diabetes, a goal of <8% may be more reasonable [33]. Many limb salvage patients already have advanced macrovascular and microvascular complications in the forms of PAD and diabetic neuropathy, likely making the <8% goal more appropriate. Similarly, American College of Physician guideline suggests a goal hemoglobin A1c of 7–8% for most patients [51]. Providers should discuss these factors with each patient to set a reasonable, individualized goal.

Follow-Up

Appropriate outpatient follow-up is for diabetic patients. The ADA recommends follow-up with a primary care physician, diabetes educator, or endocrinologist within 1 month of discharge for all patients. If the patient's medications were adjusted while inpatient or on discharge, the

ADA recommends follow-up within 1–2 weeks [39]. Coordination of care does not end with hospital discharge; the internist should ensure that the discharge summary includes any medication changes communicated to the outpatient physician.

Section 3: Anticoagulation and Antiplatelet Management

Background

Many patients requiring limb salvage surgery will be chronically on anticoagulation or antiplatelet agents. Managing these medications perioperatively is a challenging task as interruption increases the risk of thromboembolic events and continuation through a procedure increases the risk of bleeding. Interruption in anticoagulation for invasive procedures confers a risk of an adverse event from a VTE or cardioembolic cerebrovascular accident (CVA). The RE-LY trial (Randomized Evaluation of Long-Term Anticoagulant Therapy) showed that of 4591 people who underwent a procedure there was a 1.2% risk of cardioembolic events defined as CVA, cardiovascular death, and pulmonary embolism (PE) [52]. Care of the surgical patient on chronic anticoagulation presents risks both of thrombosis and bleeding. A methodical assessment of the patient-specific thrombosis risk and the surgery-specific bleeding risk is essential in the care of these patients. We will focus on patients who are anticoagulated for a history of venous thromboembolism (VTE), atrial fibrillation, and prosthetic heart valves and outline decision-making in the surgical setting.

Thrombotic Risk

The first step in decision-making involves an estimation of the patient's thrombotic risk.

Thrombotic risk in a patient with a history of deep venous thrombosis and/or pulmonary embolism is affected by the timeline of thrombotic events, the presence of an underlying hypercoagulable state, and the presence of active malignancy. Patients with a recent DVT/PE within 3 months or who have a known severe thrombophilia including antiphospholipid syndrome or deficiency of protein S, C or antithrombin1 [53] are at highest risk of recurrent thrombosis. Moderate risk patients include those who have had a VTE 3–12 months ago, recurrent VTE, active cancer or presence of non-severe risk factors for thrombophilia including heterozygous factor V Leiden or prothrombin gene mutation1. Patients with a DVT/PE greater than 12 months prior to surgery have a low risk of thromboembolic events.

Thrombotic risk with atrial fibrillation accounts for the largest proportion of patients on anticoagulation. Disruption of systemic anticoagulation increases the risk of a cardioembolic stroke. These patients represent a diverse group which can be further risk stratified based on the prevalence of risk factors including age, sex, hypertension, diabetes, prior CVA, congestive heart failure, and other vascular disease. These variables can be used to calculate a CHA2DS2-VASc score. The score is proportional to stroke risk with a score of 0–3 indicating a low risk for stroke. A score of 4–6 indicating a moderate risk, and a score of 7–9 indicating a high risk for cardioembolic stroke. A CVA or transient ischemic attack (TIA) within the past 3 months or having rheumatic valvular heart disease also makes the patient at high risk for a thromboembolic event [54].

Thrombotic risk also needs to be assessed for patients with mechanical prosthetic heart valves. These patients can be further risk stratified based on which valve has the prosthesis and the presence of additional medical comorbidities. Low-risk patients include those with bileaflet aortic valve prosthesis without atrial fibrillation or additional risk factors for CVA. Moderate risk patients are those with bileaflet aortic valve prosthesis plus one or more comorbidities including atrial fibrillation, prior CVA or TIA, diabetes, hypertension, congestive heart failure, or age greater than 75 years. Patients who are at highest risk for a thromboembolic event include anyone with a CVA/TIA in the past 6 months, any mitral valve prosthesis, and presence of a caged-ball or tilting disc aortic valve prosthesis [54].

Bleeding Risk

The second step in decision-making about anticoagulant therapy involves a review of the surgery-specific bleeding risk.

Having assessed our patients' risk of thrombosis, next we turn our attention to the risk of surgical bleeding. Bleeding risk is determined by the type of procedure being performed. By definition, procedures that have a 2-day major bleeding risk of 2–4% are high-risk bleeding procedures; procedures with a bleeding risk of 0–2% are low-risk bleeding procedures [54]. Limb salvage surgery is typically a low risk of bleeding procedure and therefore discussion here will be limited to low-risk procedures.

Now that we have assessed the patient-specific thrombotic risk and the surgery-specific bleeding risk, the decision on whether to disrupt anticoagulation can be made. For procedures with a very low risk of bleeding, anticoagulation can often be continued throughout the perioperative period. This would apply only to simple and superficial debridement. Limb salvage surgery is often urgent and may be complex; therefore, interruption of anticoagulation is usually necessary. If anticoagulation is held for a procedure, it should be stopped for a time that is sufficient for the anticoagulation effects to resolve. I will review the common anticoagulants including vitamin K antagonists, unfractionated heparin, low molecular weight heparin (LMWH), direct thrombin and direct Xa inhibitors and antiplatelet agents.

Anticoagulants

Warfarin

Warfarin is a vitamin K antagonist that inhibits factors II, VII, IX, and X. It is monitored using prothrombin time (PT) and international normalized ratio (INR). Warfarin should be discontinued 5 days prior to surgery for a goal INR of less than 1.51 [55]. Check INR on the day prior to surgery and if the INR is greater than 1.5, oral vitamin K can be given (1–2 mg). Coumadin should be restarted 12–24 h after the last planned procedure [55]. If the procedure is urgent/emergent, coumadin can be reversed. Oral or IV vitamin K (2.5–5 mg) can be effective in 1–2 days. If the surgery is emergent, fresh frozen plasma (FFP) or four factor prothrombin complex concentrate (4F-PCC) can be given.

Since VKA antagonists must be held for days prior to surgery, patients at high risk of thrombosis will require the interval use of short acting anticoagulants such as low molecular weight heparin or unfractionated IV heparin. This practice is call "bridging anticoagulation." Bridging reduces the amount of time a patient is not anticoagulated and thereby reduces thrombotic and cardioembolic events. Bridging is primarily used for long-acting anticoagulants such as coumadin. Bridging anticoagulation also increases the risk of surgical bleeding. In patients who are at a high risk for a cardioembolic event (recent dvt/pe, atrial fibrillation with a high CHADs2Vasc score, and high-risk mechanical heart valves), bridging with an unfractionated heparin drip or LMWH is indicated. Patients with low risk of thrombosis do not require bridging. Bridging is achieved by dosing LMWH (enoxaparin 1 mg/kg every 12 h or dalteparin 100 units/kg every 12 h) or starting an unfractionated heparin drip either 3 days prior to surgery (2 days after stopping coumadin) or when INR is no longer in the therapeutic range [55]. Discontinue LMWH 24 h prior to the procedure. Discontinue an unfractionated heparin drip 4–5 h prior to the procedure. After the last planned procedure, Warfarin may be resumed that day, and LMWH or an unfractionated heparin drip is typically started 24–48 h after the procedure assuming adequate hemostasis. The short acting heparinoids and coumadin are overlapped and both continued until the INR is in a therapeutic range for at least 24 h [55]. At that point the heparin or LMWH can be stopped as the patient is therapeutic on their warfarin.

Direct Thrombin and Direct Xa Inhibitors

The direct Xa inhibitors include apixaban and rivaroxaban and the direct thrombin inhibitors include dabigatran. These medications are also known as the DOACs. The timing of discontinuing these medications was studied in the perioperative

anticoagulation use for surgery evaluation (PAUSE) trial. This study standardized the time in which DOACs that were being taken for atrial fibrillation were held. It showed the rates of major bleeding as less than 2% and ischemic stroke as less than 0.5%. Based on this data, for low to moderate risk procedures, DOACs should be stopped 1 day prior to a procedure and resumed 1 day after surgery [56]. One exception is that dabigatran should be held 2 days prior to the procedure if the creatinine clearance is 30–505,6. Reversal of these agents is not typically necessary but is available. Dabigatran can be reversed by idarucizumab. Apixaban and rivaroxaban can be reversed by andexanet alfa. Because of the much shorter half-life, DOACs do NOT require bridging anticoagulation with heparin/or LMWH. You simply stop the agent 1–2 days prior to surgery and resume postoperatively once adequate hemostasis is obtained. We are more conservative in resuming NOACs and DOACs postoperatively, and in general prefer waiting 48–72 h after surgery.

Antiplatelet Agents

Antiplatelet agents include aspirin, clopidogrel, prasugrel, and ticagrelor. Aspirin irreversibly inhibits platelet cyclooxygenase. Clopidogrel, prasugrel, and ticagrelor are platelet P2Y12 receptor blockers. Aspirin can be used as a monotherapy or in combination with one of the P2Y12 receptor blockers which is referred to as dual antiplatelet therapy (DAPT).

Aspirin monotherapy is used for both primary and secondary prevention of cardiovascular events including myocardial infarction (MI) and CVA. The POISE-2 trial suggests that discontinuing aspirin for noncardiac surgery reduces bleeding without increasing cardiovascular events. Aspirin should be held 5–7 days prior to surgery and restarted when there is no longer a risk for major bleeding [57].

One of the primary indications for DAPT is following a percutaneous intervention (PCI). These patients are at an increased risk for MI or stent thrombosis, and premature cessation of DAPT is the strongest risk factor for these complications [58]. Per the 2016 ACC/AHA guidelines, surgery would ideally be delayed until 6 months following PCI regardless of the stent type. If a bare metal stent was placed, then DAPT may be discontinued as soon as 30 days after PCI. If a drug-eluting stent was placed, DAPT should be continued for 6 months after PCI, but if the surgery is urgent discontinuation may be considered after 3 months [59]. When DAPT is interrupted, aspirin should be held 5–7 days prior to the procedure. Clopidogrel should be held 5 days prior to the procedure. Prasugrel should be discontinued 7 days prior to surgery. Ticagrelor should be discontinued 3–5 days prior. DAPT can be restarted when there is no longer a risk for major bleeding.

In practice, many of the limb salvage patients have strong indications for antiplatelet therapies. Care coordination with the surgical team is critical in decision-making. Often, DAPT can be continued if surgical bleeding is controlled. Where possible, we recommend at least continuing aspirin in the high-risk patients with a history of cardiac or peripheral arterial stenting.

Venous Thromboembolism (VTE) Prophylaxis

DVT/PE is a common postoperative problem and one of the most preventable types of hospital morbidity/mortality [60]. Limb salvage surgery is typically a lower risk procedure for major bleeding. LMWH can therefore be started 12 h prior to surgery and resumed 2–12 h after a procedure. The most commonly used agents include enoxaparin 40 mg every 24 h and dalteparin 5000 units every 24 h [61]. An alternative is fondaparinux, which is started 6–8 h postoperatively and dosed at 2.5 mg every 24 h [62]. In patients with advanced kidney disease, subcutaneous unfractionated heparin at 5000 q8 h is recommended. VTE prophylaxis should be continued until the patient becomes ambulatory or until hospital discharge.

Summary of Anticoagulation

Management of anticoagulation in the surgical setting is one of the most high-risk areas of medical decision-making. Resuming anticoagulation

after surgery requires careful coordination with the surgical team. In general, full anticoagulation is usually permitted 48 h after surgery. This timeline can be accelerated to 24 h post-procedure in low-risk bleeding situations or extended to 72 h or longer if significant surgical bleeding is encountered. Other factors that will delay the resumption of full anticoagulation include neuroaxial anesthesia with a lumbar epidural catheter and a history of postoperative bleeding. In settings where there is not full confidence that anticoagulation will be tolerated, we recommend beginning a heparin drip as it can be most rapidly stopped and/or reversed. If the heparin drip is tolerated, then the patient can be transitioned back to their outpatient regimen. The reason for the longer wait period for the DOACs is that they are not readily reversible. With the complicated management decisions and potential life-threatening possibilities of DVT/PE, stroke, and postoperative bleeding, regular communication between the surgical and medical teams is essential.

Section 4: Postoperative Complications

Postoperative complications are common in the hospitalized patient and require prompt medical evaluation and treatment. The limb salvage patients are at higher risk of complications due to their underlying age and comorbidities including diabetes, vascular disease, chronic kidney disease. Medical complications increase length of stay, morbidity, and mortality. We will focus on the recognition and treatment of acute kidney injury, delirium, and postoperative gastrointestinal complications. Development of complications can affect a patient's readiness for the operating room and also for safe hospital discharge. The internist must work in careful coordination with the surgical team as delay in surgery may be required.

Acute Kidney Injury

Acute kidney injury (AKI) is a common complication in surgical patients undergoing limb salvage treatment. The limb salvage patients have an increased rate of underlying chronic kidney disease which further increases their risk for AKI. A thorough evaluation to determine the etiology of the decline in kidney function involves an assessment of the patient's volume status, a review of potentially reno-toxic medications and evaluation to rule out obstruction.

Pre-renal AKI can be triggered by volume depletion or hypotension. Limb salvage patients are at increased risk of volume depletion due to NPO status for multiple days due to staged procedures. Poor oral intake is common in the postoperative setting due to postoperative nausea and vomiting (PONV), sedation due to narcotic analgesia and delirium. Hypotension is another known precipitator of pre-renal AKI. Hypotension occurs preoperatively in patients with severe sepsis, intraoperatively due to anesthetic response or surgical blood loss, and postoperatively due to the effects of opioid analgesia.

Intrinsic injury to the kidney occurs from direct nephrotoxicity from medications and contrast agents. Common culprits include intravenous antibiotic, intravenous contrast, and NSAIDs. Contrast induced nephropathy is much less common now that lower osmolality contrast agents are utilized [63]. Renal injury from contrast is possible in patients with an estimated GFR less than 30 and in patients with a recent AKI [64]. Likewise, directed angiography to assess for peripheral vascular disease now can involve smaller amounts of contrast. Antibiotic associated nephropathy is also common. Careful monitoring of dosing and drug levels for vancomycin is recommended to help reduce the incidence of toxicity.

Urinary tract obstruction also occurs in the surgical patient. It can be precipitated by urinary retention due to spinal/epidural anesthesia, postoperative ileus, and medications. Mechanical obstruction more commonly occurs in male patients with underlying BPH. A simple bladder scan to check post void residual will detect both of these obstructive causes of AKI. A renal US is needed to rule out the less common etiologies of obstruction such as ureteral obstruction due to anatomic problems, nephrolithiasis, malignant processes.

Delirium

Delirium is common in the hospitalized patient, affecting up to 50% of hospitalized patients and may be preventable in as much as 30–40% of cases [65]. The development of delirium is associated with increased length of stay, increased risk of discharge to a nursing facility, and increased risk of death. Risk factors for delirium include dementia or cognitive impairment, functional impairment, vision impairment, history of alcohol abuse, age >70, comorbidity burden, polypharmacy, psychoactive medication use, physical restraints, and anormal laboratory values [65].

Initial evaluation of delirium should include ascertaining baseline mental status cognitive function utilizing information obtained from the patient, family, and other caregivers. It is important to determine the patient's pre-morbid cognitive status so that subtle changes will be noticed and identified early. The initial exam should be focused to screen out acute physiologic problems such as hypoxemia, hypoventilation, hypoglycemia, acute cardiac decompensation. Next steps include medication review, assessment of metabolic derangements, ruling out intercurrent or intreated infection, checking an EKG to evaluate for silent ischemia, with consideration of neuroimaging reserved for cases where the exam is focal, head trauma suspected, or a complete evaluation has failed to yield a suspected etiology. While often multifactorial in etiology, identification, and removal of inciting factors along with careful application of delirium protocols can help to minimize the consequences of delirium.

Simple non-medical interventions such as keeping shades up/lights on during daytime, frequent reorientation, therapeutic activities, maintaining hydration and nutrition, and providing vision and hearing aids such as is described in the Hospital Elder Life Program (HELP) and help with prevention [66]. Minimization of psychoactive medications such as narcotic analgesics, muscle relaxants, benzodiazepines will help the patient to clear their delirium. The addition of antihistamines, sedative hypnotics, and anti-psychotic medications should be avoided where possible [65]. Current recommendations do not support the use of anti-psychotic medications [67].

Postoperative GI Complications

Common gastrointestinal complications that will be addressed include postoperative nausea and vomiting (PONV), opioid induced constipation (OIC), postoperative ileus (POI), and antibiotic associated diarrhea. The internist should be prepared to institute preventive therapies, recognize complications, and implement appropriate treatment options.

Postoperative Nausea and Vomiting

Postoperative nausea and vomiting (PONV) is a term used to describe a patient's nausea and vomiting in the immediate 24 h post-procedure. If not managed properly, PONV can lead to prolonged hospitalizations, patient dissatisfaction, and even severe medical complications like aspiration and wound dehiscence. A strategic approach for treatment of PONV includes identifying high-risk patients, using prophylactic antiemetics, and understanding the different treatment options. Table 8.3 is a simplified risk calculator that can be sued to decide if prophylactic PONV treatment is appropriate.

While medical treatment options for PONV can differ based on hospital formularies and a patient's underlying disease, there are several other strategies that can be universally applied. PONV can be reduced when using combination antiemetics from different classes, using localized instead of generalized anesthesia if possible, ensuring patient hydration, and providing ade-

Table 8.3 Simplified risk calculator by Apfel [68] that can be used to decide if prophylactic PONV treatment is appropriate

Risk factors (1 point each)	Points	Prevalence of PONV (%)
Female	0–1	10–20
Non smoker	2–3	40–60
History of PONV	4	80
Post operative opioids		

Table 8.4 List of commonly used antiemetics and their side effects. For maximum efficacy, a rescue treatment should include an antiemetic from a different class than the ones that were used for prophylaxis unless significant time has passed

Drug class	Example	Side effects
Serotonin 5-hydroxytryptamine type 3 (5-HT3) receptor antagonists	Ondansetron	QTc prolongation
Glucocorticoids	Dexamethasone	Slow onset, can interfere with cell counts and glucose metabolism
Anticholinergic	Scopolamine	Slow onset, dry mouth, blurry vision, confusion or agitation in older adults, acute angle closure glaucoma
Antidopaminergic	Droperidol	Sedation, cardiac arrythmias and sudden cardiac deaths
Antihistamine	Diphenhydramine, promethazine	Sedation, dry mouth, dizziness, urinary retention

quate pain control. Common antiemetics and their side effects are listed in Table 8.4.

Opioid Induced Constipation

Opioid induced constipation (OIC) is a common manifestation of chronic or acute opioid use. To diagnose OIC, we use the Rome IV criteria which include new or worsening constipation symptoms when opioids are initiated or increased. Prevention is the recommended treatment strategy for OIC and can include an osmotic laxative like polyethylene glycol or a stimulant laxative like senna. Additional modifications to consider are proper hydration, increased mobility, and adequate dietary fiber intake. It is reasonable to up titrate the frequencies of current management or consider adding another agent for those patients who develop OIC despite a preventative regimen. If a patient is refractory to increase of the current management, if ileus and obstruction have been ruled out, it is important to consider impaction as the source of the constipation. Mineral oil enemas and soap water enemas are useful and safe. Peripherally acting mu-opioid receptor antagonists (PAMORAs) should be reserved for refractory OIC in the absence of bowel obstruction.

Ultimately, we suggest following the regimen that is most effective and best tolerated by the patient. However, there are two important considerations worth mentioning when choosing a bowel regiment including fleet enemas and lactulose. Fleet enemas should be avoided in patients with renal failure as they contain high amounts of phosphate [69]. Lactulose should not be used in lactose intolerant patients as it may cause abdominal discomfort [70].

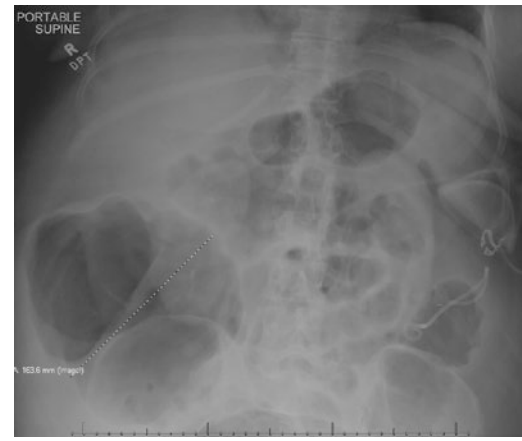


Fig. 8.2 Megacolon measuring 16.3 cm on plain abdominal radiograph (author's own image)

Postoperative Ileus

Postoperative ileus (POI) is a physiologic process that is usually benign and typically resolves by postoperative day 3. The proposed physiology of POI is multimodal and includes gastrointestinal dysmotility secondary to bowel inflammation, inhibitory neural reflexes, and neurohormonal peptides. Logically, the risk of POI is higher with intraabdominal surgeries and perioperative opioid use. Common clinical symptoms of POI include nausea and vomiting, inability to tolerate an oral diet, absence of flatus, abdominal distention, and radiologic confirmation without an alternative mechanical cause. Figure 8.2 shows an impres-

sive abdominal radiograph of a megacolon measuring 16.3 cm.

Initiation of treatment for prolonged POI (greater than 3 postoperative days) is focused on supportive care. Interventions such as management of pain with avoidance of opioid agents, bowel rest and decompression if indicated, electrolyte replacement, and nutritional support are common ways to shorten the course of POI. While fluid replacement is also an important factor of supportive therapy, it is important to mention that studies have shown that overly aggressive fluid resuscitation in the perioperative setting could lead to edema in the gastrointestinal tract and may actually lead to postoperative ileus [71]. The use of prokinetic agents remains controversial as studies have shown limited utility.

Antibiotics Associated Diarrhea

The first step in evaluating the cause of a patient's diarrhea is to look over the patient's existing bowel regimen and eliminate any offending agents as the possible cause of symptoms. Next, the most concerning diagnosis in a patient with antibiotics associated diarrhea is C. difficile colitis and must be properly investigated.

Although any recent antibiotic use can predispose patients to C. Diff. infection, the most common offending agents are fluoroquinolones, clindamycin, cephalosporins, and penicillins [72]. In addition to antibiotic use, suspicion for C. difficile colitis should arise if the patient has any of the following: advanced age, recent hospitalization, >3 loose stools per day, unexplained leukocytosis, and abdominal pain. Once there is a clinical suspicion, the patient should be placed on contact precautions and tested for C. Diff. via a stool test.

If clinical suspicion and testing is positive, initial treatment for uncomplicated C. Diff. without evidence of toxic megacolon includes oral vancomycin or oral fidaxomicin. For recurrent episodes, a prolonged course of vancomycin with a taper is an option. For fulminant episodes that include toxic megacolon and hemodynamic instability, IV metronidazole and oral vancomycin are both recommended along with additional considerations for rectal vancomycin and fecal microbiota transplant.

If there is a low clinical suspicion for C. Diff. colitis or other infectious diarrheal sources, most antibiotic associated diarrhea can be supportively managed with proper hydration, antidiarrheal agents, and consideration of the risk vs. benefit of removing the suspected antibiotic.

Summary of Complications

The internist follows each patient daily during the hospital stay in order to detect and treat complications that may arise. Early recognition of kidney injury, delirium, and gastrointestinal problems will aide in the treatment and recovery of the limb salvage inpatient.

Conclusion: Medical Management of the Limb Salvage Inpatient

Limb salvage inpatients are medically complex and at substantial risk of complications. Preparation for surgery involves coordination between the internal medicine specialist and the surgical team. Careful review of cardiac status and risk factors is essential to quantify the perioperative cardiac risk. This evaluation also provides the opportunity to review a patient's cardiac medication management and to optimize it prior to surgery. Diabetes is present in the vast majority of the limb salvage inpatients. The internist reviews current diabetic medications and control and converts oral medications to insulin. These treatment decisions must be coordinated daily with the surgical team as the patient will frequently be NPO for procedures. Anticoagulation management is critically important in surgical patients due to competing risks of thrombosis and bleeding. The internist works with the surgical team to assess the need for and safety of anticoagulants around the time of surgery. Lastly, the internist works to prevent and identify medical complications. Surgical success is aided by careful control of medical comorbidities. The importance of close coordination between the medical and surgical teams cannot be overemphasized. We have found the best way to achieve this coordination with

daily multidisciplinary rounds in which each inpatient case is discussed with the surgical and medical teams.

References

1. Weiser TG, Regenbogen SE, Thompson KD, Haynes AB, Lipsitz SR, Berry WR, Gawande AA. An estimation of the global volume of surgery: a modelling strategy based on available data. Lancet. 2008;372(9633):139–44.
2. Smilowitz NR, Gupta N, Ramakrishna H, Guo Y, Berger JS, Bangalore S. Perioperative major adverse cardiovascular and cerebrovascular events associated with noncardiac surgery. JAMA Cardiol. 2017;2(2):181–7.
3. Gupta PK, Gupta H, Sundaram A, Kaushik M, Fang X, Miller WJ, Esterbrooks DJ, Hunter CB, Pipinos II, Johanning JM, Lynch TG, Forse RA, Mohiuddin SM, Mooss AN. Development and validation of a risk calculator for prediction of cardiac risk after surgery. Circulation. 2011;124(4):381–7. https://doi.org/10.1161/CIRCULATIONAHA.110.015701. Epub 2011 Jul 5. PMID: 21730309.
4. Bilimoria KY, Liu Y, Paruch JL, Zhou L, Kmiecik TE, Ko CY, Cohen ME. Development and evaluation of the universal ACS NSQIP surgical risk calculator: a decision aid and informed consent tool for patients and surgeons. J Am Coll Surg. 2013;217(5):833–42.
5. Duceppe E, Parlow J, MacDonald P, Lyons K, McMullen M, Srinathan S, Graham M, Tandon V, Styles K, Bessissow A, Sessler DI, Bryson G, Devereaux PJ. Canadian cardiovascular society guidelines on perioperative cardiac risk assessment and management for patients who undergo noncardiac surgery. Can J Cardiol. 2017;33(1):17–32.
6. Reilly DF, McNeely MJ, Doerner D, Greenberg DL, Staiger TO, Geist MJ, Vedovatti PA, Coffey JE, Mora MW, Johnson TR, Guray ED, Van Norman GA, Fihn SD. Self-reported exercise tolerance and the risk of serious perioperative complications. Arch Intern Med. 1999;159(18):2185–92.
7. Devereaux PJ, Szczeklik W. Myocardial injury after non-cardiac surgery: diagnosis and management. Eur Heart J. 2020;41(32):3083–91.
8. Fleisher LA, Fleischmann KE, Auerbach AD, Barnason SA, Beckman JA, Bozkurt B, Davila-Roman VG, Gerhard-Herman MD, Holly TA, Kane GC, Marine JE, Nelson MT, Spencer CC, Thompson A, Ting HH, Uretsky BF, Wijeysundera DN, American College of Cardiology; American Heart Association. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol. 2014;64(22):e77–137.
9. Noordzij PG, Boersma E, Bax JJ, Feringa HH, Schreiner F, Schouten O, Kertai MD, Klein J, van Urk H, Elhendy A, Poldermans D. Prognostic value of routine preoperative electrocardiography in patients undergoing noncardiac surgery. Am J Cardiol. 2006;97(7):1103–6. https://doi.org/10.1016/j.amjcard.2005.10.058. Epub 2006 Feb 28. PMID: 16563926.
10. Gold BS, Young ML, Kinman JL, Kitz DS, Berlin J, Schwartz JS. The utility of preoperative electrocardiograms in the ambulatory surgical patient. Arch Intern Med. 1992;152(2):301–5. PMID: 1739358.
11. van Klei WA, Bryson GL, Yang H, Kalkman CJ, Wells GA, Beattie WS. The value of routine preoperative electrocardiography in predicting myocardial infarction after noncardiac surgery. Ann Surg. 2007;246(2):165–70.
12. Rohde LE, Polanczyk CA, Goldman L, Cook EF, Lee RT, Lee TH. Usefulness of transthoracic echocardiography as a tool for risk stratification of patients undergoing major noncardiac surgery. Am J Cardiol. 2001;87(5):505–9.
13. Kertai MD, Bountioukos M, Boersma E, Bax JJ, Thomson IR, Sozzi F, Klein J, Roelandt JR, Poldermans D. Aortic stenosis: an underestimated risk factor for perioperative complications in patients undergoing noncardiac surgery. Am J Med. 2004;116(1):8–13.
14. Healy KO, Waksmonski CA, Altman RK, Stetson PD, Reyentovich A, Maurer MS. Perioperative outcome and long-term mortality for heart failure patients undergoing intermediate- and high-risk noncardiac surgery: impact of left ventricular ejection fraction. Congest Heart Fail. 2010;16(2):45–9.
15. Wijeysundera DN, Pearse RM, Shulman MA, Abbott TEF, Torres E, Ambosta A, Croal BL, Granton JT, Thorpe KE, Grocott MPW, Farrington C, Myles PS, Cuthbertson BH, METS Study Investigators. Assessment of functional capacity before major noncardiac surgery: an international, prospective cohort study. Lancet. 2018;391(10140):2631–40.
16. Das MK, Pellikka PA, Mahoney DW, Roger VL, Oh JK, McCully RB, Seward JB. Assessment of cardiac risk before nonvascular surgery: dobutamine stress echocardiography in 530 patients. J Am Coll Cardiol. 2000;35(6):1647–53.
17. Labib SB, Goldstein M, Kinnunen PM, Schick EC. Cardiac events in patients with negative maximal versus negative submaximal dobutamine echocardiograms undergoing noncardiac surgery: importance of resting wall motion abnormalities. J Am Coll Cardiol. 2004;44(1):82–7.
18. McFalls EO, Ward HB, Moritz TE, Goldman S, Krupski WC, Littooy F, Pierpont G, Santilli S, Rapp J, Hattler B, Shunk K, Jaenicke C, Thottapurathu L, Ellis N, Reda DJ, Henderson WG. Coronary-artery revascularization before elective major vascular surgery. N Engl J Med. 2004;351(27):2795–804.
19. Smilowitz NR, Berger JS. Perioperative cardiovascular risk assessment and management for non-

cardiac surgery: a review. JAMA. 2020;324(3): 279–90.
20. Ahn JH, Park JR, Min JH, Sohn JT, Hwang SJ, Park Y, Koh JS, Jeong YH, Kwak CH, Hwang JY. Risk stratification using computed tomography coronary angiography in patients undergoing intermediate-risk noncardiac surgery. J Am Coll Cardiol. 2013;61(6):661–8.
21. Koshy AN, Ha FJ, Gow PJ, Han HC, Amirul-Islam FM, Lim HS, Teh AW, Farouque O. Computed tomographic coronary angiography in risk stratification prior to non-cardiac surgery: a systematic review and meta-analysis. Heart. 2019;105(17):1335–42.
22. Sheth T, Chan M, Butler C, Chow B, Tandon V, Nagele P, Mitha A, Mrkobrada M, Szczeklik W, Faridah Y, Biccard B, Stewart LK, Heels-Ansdell D, Devereaux PJ. Coronary Computed Tomographic Angiography and Vascular Events in Noncardiac Surgery Patients Cohort Evaluation Study Investigators. Prognostic capabilities of coronary computed tomographic angiography before non-cardiac surgery: prospective cohort study. BMJ. 2015;350:h1907.
23. London MJ, Hur K, Schwartz GG, Henderson WG. Association of perioperative β-blockade with mortality and cardiovascular morbidity following major noncardiac surgery. JAMA. 2013;309(16):1704–13.
24. Wijeysundera DN, Duncan D, Nkonde-Price C, Virani SS, Washam JB, Fleischmann KE, Fleisher LA. Perioperative beta blockade in noncardiac surgery: a systematic review for the 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol. 2014;64(22):2406–25.
25. POISE Study Group, Devereaux PJ, Yang H, Yusuf S, Guyatt G, Leslie K, Villar JC, Xavier D, Chrolavicius S, Greenspan L, Pogue J, Pais P, Liu L, Xu S, Málaga G, Avezum A, Chan M, Montori VM, Jacka M, Choi P. Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial. Lancet. 2008;371(9627):1839–47.
26. Flu WJ, van Kuijk JP, Chonchol M, Winkel TA, Verhagen HJ, Bax JJ, Poldermans D. Timing of preoperative Beta-blocker treatment in vascular surgery patients: influence on post-operative outcome. J Am Coll Cardiol. 2010;56(23):1922–9.
27. Sessler DI, Conen D, Leslie K, Yusuf S, Popova E, Graham M, Kurz A, Villar JC, Mrkobrada M, Sigamani A, Biccard BM, Meyhoff CS, Parlow JL, Guyatt G, Xavier D, Chan MTV, Kumar PA, Forget P, Malaga G, Fleischmann E, Amir M, Torres D, Wang CY, Paniagua P, Berwanger O, Srinathan S, Landoni G, Manach YL, Whitlock R, Lamy A, Balasubramanian K, Gilron I, Turan A, Pettit S, Devereaux PJ, Perioperative Ischemic Evaluation-2 Trial (POISE-2) Investigators. One-year results of a factorial randomized trial of aspirin versus placebo and clonidine versus placebo in patients having noncardiac surgery. Anesthesiology. 2020;132(4):692–701.
28. Kristensen SD, Knuuti J, Saraste A, Anker S, Bøtker HE, Hert SD, Ford I, Gonzalez-Juanatey JR, Gorenek B, Heyndrickx GR, Hoeft A, Huber K, Iung B, Kjeldsen KP, Longrois D, Lüscher TF, Pierard L, Pocock S, Price S, Roffi M, Sirnes PA, Sousa-Uva M, Voudris V, Funck-Brentano C, Authors/Task Force Members. 2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). Eur Heart J. 2014;35(35):2383–431.
29. Bertrand M, Godet G, Meersschaert K, Brun L, Salcedo E, Coriat P. Should the angiotensin II antagonists be discontinued before surgery? Anesth Analg. 2001;92(1):26–30.
30. Roshanov PS, Rochwerg B, Patel A, Salehian O, Duceppe E, Belley-Côté EP, Guyatt GH, Sessler DI, Le Manach Y, Borges FK, Tandon V, Worster A, Thompson A, Koshy M, Devereaux B, Spencer FA, Sanders RD, Sloan EN, Morley EE, Paul J, Raymer KE, Punthakee Z, Devereaux PJ. Withholding versus continuing angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers before noncardiac surgery: an analysis of the vascular events in noncardiac surgery patients cohort evaluation prospective cohort. Anesthesiology. 2017;126(1):16–27.
31. Marso SP, Hiatt WR. Peripheral arterial disease in patients with diabetes. J Am Coll Cardiol. 2006;47(5):921–9.
32. Criqui MH, Aboyans V. Epidemiology of peripheral artery disease. Circ Res. 2015;116(9):1509–26.
33. American Diabetes Association. 6. Glycemic targets: standards of medical care in diabetes-2020. Diabetes Care. 2020;43(Suppl 1):S66.
34. Umpierrez G, Korytkowski M. Diabetic emergencies—ketoacidosis, hyperglycaemic hyperosmolar state and hypoglycaemia. Nat Rev Endocrinol. 2016;12(4):222.
35. Cryer PE, Davis SN, Shamoon H. Hypoglycemia in diabetes. Diab Care. 2003;26(6):1902–12.
36. Lleva RR, Inzucchi SE. Hospital management of hyperglycemia. Curr Opin Endocrinol Diab Obes. 2011;18(2):110–8.
37. Frisch A, Chandra P, Smiley D, Peng L, Rizzo M, Gatcliffe C, Hudson M, Mendoza J, Johnson R, Lin E, Umpierrez GE. Prevalence and clinical outcome of hyperglycemia in the perioperative period in noncardiac surgery. Diabetes Care. 2010;33(8):1783–8.
38. Duggan EW, Carlson K, Umpierrez GE. Perioperative hyperglycemia management: an update. Anesthesiology. 2017;126(3):547–60.
39. American Diabetes Association. 15. Diabetes care in the hospital: standards of medical care in diabetes—2020. Diabetes Care. 2020;43(Suppl 1): S193–202.

40. Buchleitner AM, Martínez-Alonso M, Hernandez M, Sola I, Mauricio D. Perioperative glycaemic control for diabetic patients undergoing surgery. Cochrane Database Syst Rev. 2012;(9):CD007315.
41. Sathya B, Davis R, Taveira T, Whitlatch H, Wu WC. Intensity of peri-operative glycemic control and postoperative outcomes in patients with diabetes: a meta-analysis. Diabetes Res Clin Pract. 2013;102(1):8–15.
42. Nice-Sugar Study Investigators. Intensive versus conventional glucose control in critically ill patients. N Engl J Med. 2009;360(13):1283–97.
43. Lansang MC, Umpierrez GE. Inpatient hyperglycemia management: a practical review for primary medical and surgical teams. Cleve Clin J Med. 2016;83(Suppl 1):S34–43.
44. Umpierrez GE, Hellman R, Korytkowski MT, Kosiborod M, Maynard GA, Montori VM, Seley JJ, Van den Berghe G. Management of hyperglycemia in hospitalized patients in non-critical care setting: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2012;97(1):16–38.
45. Rubin DJ, Rybin D, Doros G, McDonnell ME. Weight-based, insulin dose–related hypoglycemia in hospitalized patients with diabetes. Diabetes Care. 2011;34(8):1723–8.
46. Badlani S, Ford WT, David JY, Brogan GX, Pollack CV, Volturo GA. Evidence for basal–bolus insulin versus slide scale insulin. Curr Emerg Hosp Med Rep. 2014;2(1):26–34.
47. Umpierrez GE, Smiley D, Zisman A, Prieto LM, Palacio A, Ceron M, Puig A, Mejia R. Randomized study of basal-bolus insulin therapy in the inpatient management of patients with type 2 diabetes (RABBIT 2 trial). Diabetes Care. 2007;30(9):2181–6.
48. Nassar CM, Montero A, Magee MF. Inpatient diabetes education in the real world: an overview of guidelines and delivery models. Curr Diab Rep. 2019;19(10):103.
49. Umpierrez GE, Reyes D, Smiley D, Hermayer K, Khan A, Olson DE, Pasquel F, Jacobs S, Newton C, Peng L, Fonseca V. Hospital discharge algorithm based on admission HbA1c for the management of patients with type 2 diabetes. Diabetes Care. 2014;37(11):2934–9.
50. American Diabetes Association. 10. Cardiovascular disease and risk management: standards of medical care in diabetes—2020. Diabetes Care. 2020;43(Suppl 1):S111–34.
51. Qaseem A, Wilt TJ, Kansagara D, Horwitch C, Barry MJ, Forciea MA. Hemoglobin A1c targets for glycemic control with pharmacologic therapy for nonpregnant adults with type 2 diabetes mellitus: a guidance statement update from the American College of Physicians. Ann Intern Med. 2018;168(8):569–76.
52. Healey JS, et al. Periprocedural bleeding and thromboembolic events with dabigatran compared with warfarin: results from the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) randomized trial. Circulation. 2012;126(3):343–8.
53. Douketis JD, et al. Clinical risk factors and timing of recurrent venous thromboembolism during the initial 3 months of anticoagulant therapy. Arch Intern Med. 2000;160(22):3431–6.
54. Spyropoulos AC, Douketis JD. How I treat anticoagulated patients undergoing an elective procedure or surgery. Blood. 2012;120(15):2954–62.
55. Douketis JD, et al. Perioperative management of antithrombotic therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e326S–50S.
56. Shaw JR, et al. Predictors of preprocedural direct oral anticoagulant levels in patients having an elective surgery or procedure. Blood Adv. 2020;4(15):3520–7.
57. Devereaux PJ, et al. Aspirin in patients undergoing noncardiac surgery. N Engl J Med. 2014;370(16):1494–503.
58. Hawn MT, et al. The incidence and timing of noncardiac surgery after cardiac stent implantation. J Am Coll Surg. 2012;214(4):658–66; discussion 666–7.
59. Levine GN, et al. 2016 ACC/AHA Guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2016;68(10):1082–115.
60. White RH, et al. Incidence of symptomatic venous thromboembolism after different elective or urgent surgical procedures. Thromb Haemost. 2003;90(3):446–55.
61. Gould MK, et al. Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American Coll Chest Physicians. Chest. 2012;141(2):E419S–96S.
62. Kumar A, et al. Fondaparinux sodium compared with low-molecular-weight heparins for perioperative surgical thromboprophylaxis: a systematic review and meta-analysis. J Am Heart Assoc. 2019;8(10):e012184.
63. Luk L, et al. Intravenous contrast induced nephropathy: The rise and fall of a threatening idea. Adv Chronic Kidney Dis. 2017;24(3):169–75.
64. Davenport MS, et al. Use of intravenous iodinated contrast media in patients with kidney disease: Consensus statements from the American College of Radiology and the National Kidney Foundation. Kidney Med. 2020;2(1):85–93.
65. Inouye SK, et al. Delirium in elderly people. Lancet. 2014;383(9920):911–22.
66. Inouye SK, et al. The Hospital Elder Life Program: a model of care to prevent cognitive and functional decline in older hospitalized patients. Hospital Elder Life Program. J Am Geriatr Soc. 2000;48(12):1697–706.
67. Oh ES, et al. Delirium in older persons; Advances in diagnosis and treatment. JAMA. 2017;318(12):1161–74.

68. Apfel CC, Laara E, Kojvuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. Anesthesiology. 1999;91:693.
69. Ori Y, Rozen-Zvi B, Chagnac A, et al. Fatalities and severe metabolic disorders associated with the use of sodium phosphate enemas: a single center's experience. Arch Intern Med. 2012;172(3):263–5.
70. Teuri U, et al. Fructooligosaccharides and lactulose cause more symptoms in lactose maldigesters and subjects with pseudohypolactasia than in control lactose digesters. Am J Clin Nutr. 1999;69(5):973–9.
71. Chowdhury AH, Lobo DN. Fluids and gastrointestinal function. Curr Opin Clin Nutr Metab Care. 2011;14(5):469–76.
72. Deshpande A, Pasupuleti V, Thota P, et al. Community-associated Clostridium difficile infection and antibiotics: a meta-analysis. J Antimicrob Chemother. 2013;68(9):1951–61.

9 Evaluation and Examination of the Diabetic Foot

Michael Edmonds, Rajesh Kesavan, and Arun Bal

Introduction

There have been several consensus documents depicting best practice recommendations for clinical evaluation of the diabetic foot [1–3]. In this chapter, we describe a simple practical approach to the evaluation and examination of the diabetic foot which informs the practitioner how to carry out a comprehensive assessment. From this, a diagnostic classification and staging of the foot can be made which will enable the correct treatment to be performed.

The diabetic foot can be classified into two main clinical groups:

1. The neuropathic foot
2. The ischaemic foot

It is important to differentiate the neuropathic foot from the ischaemic foot as management of each differs in many respects. Usually there will be little doubt as to which category the foot should be placed in. However, if the examiner has any doubt, then the foot should be regarded as ischaemic, because if an ischaemic foot is wrongly classified as neuropathic, there may be resulting failure to do further tests to identify ischaemia and adapt the care plan accordingly. This may lead to preventable catastrophe and loss of the foot.

The neuropathic foot may be further stratified into two clinical scenarios.

1. Foot with neuropathic ulceration (Fig. 9.1)
2. Charcot foot, which may be secondarily complicated by ulceration and infection (Fig. 9.2)

The ischaemic foot may be stratified into three clinical scenarios:

1. Neuroischaemic foot characterised by mild or moderate ischaemia and neuropathy and often complicated by ulcer (Fig. 9.3)
2. Severely ischaemic foot otherwise known as the critically ischaemic foot (Fig. 9.4)
3. Acutely ischaemic foot (Fig. 9.5)

M. Edmonds (✉)
King's College Hospital, London, UK

Diabetic Foot Medicine, King's College, London, UK
e-mail: michael.edmonds@nhs.net

R. Kesavan
Dr. RK Diabetic Foot and Podiatry Institute and Rakesh Jhunjhunwala Amputation Prevention Centre, Chennai, India

SRM Institute of Science and Technology, Chennai, India

A. Bal
Raheja Fortis Hospital, Mumbai, India

Amrita Institute of Medical Sciences, Kochi, India

Diabetic Foot Society of India, Mumbai, India

International Association of Diabetic Foot Surgeons, Frederiksberg, Denmark

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_9



Fig. 9.1 Neuropathic ulcer



Fig. 9.2 Charcot foot with ulcer over lateral malleolus



Fig. 9.3 Neuroischaemic ulcer on medial aspect of first toe



Fig. 9.4 Necrosis of toes in critically ischaemic foot



Fig. 9.5 Necrosis and mottling of the foot secondary to acute ischaemia



Fig. 9.6 Simple Staging System showing natural history of the five scenarios of the diabetic foot

With reference to the ischaemic scenario, the Global Vascular Guidelines have recently proposed the term Chronic Limb Threatening Ischaemia to include a broad group of patients with varying degrees of ischaemia that can often delay wound healing and increase amputation risk [4]. This will include both the neuroischaemic and the critically ischaemic scenarios.

Each of the above five main clinical scenarios (two neuropathic and three ischaemic) are characterised by having specific stages in their natural history. These stages have been described in a Simple Staging System [5] (Fig. 9.6).

Simple Staging System

The Simple Staging System covers the entire spectrum of diabetic foot disease. It describes five stages in the natural history of each of the five clinical scenarios. It also traces the rapid progression of each scenario from the normal foot through the stages to necrosis. In particular, it emphasises the development of the ulcer as a pivotal stage in the natural history of the diabetic foot demanding urgent and aggressive management.

The Simple Staging System is thus based on clinical presentation and clinical assessment and allows all practitioners, whether experienced in diabetic foot care or not, to make an initial assessment of the diabetic foot and establish at what stage the foot may be in its natural history. The stage then determines treatment. The aim is to keep all diabetic feet at as low a stage as possible [5].

The stages are

1. Normal foot
2. High-risk foot
3. Foot with tissue damage (ulceration, Charcot foot, or ischaemic tissue)
4. Threatened foot
5. Necrotic foot

Classifications of the Diabetic Foot

There are various classifications of the diabetic foot which are suited to different circumstances, such as characterising populations, designing clinical trials and assessing comparative effectiveness of treatments. Classifications such as the Wagner, the University of Texas and SINBAD are established classifications of ulcers [6–8]. In a person with diabetes and a foot ulcer, the SINBAD system has been used for communication among health professionals to convey the characteristics of the ulcer, and to allow comparisons between institutions on the outcomes of people with a diabetic foot ulcer in regional/national/international audits [9, 10].

In the Lower Extremity Threatened Limb Classification System of the Society for Vascular Surgery, perfusion of the foot is considered in the context of wound characteristics and infection. It stratifies amputation risk according to wound extent, the degree of ischaemia, and severity of foot infection and thus is known as WIfI [11]. It provides accurate and early risk stratification for patients with threatened lower limbs. It aids clinical management and predicts risk of amputation at 1 year and the need for limb revascularization. It has been correlated with the probability of limb salvage and wound healing following revascularization [12].

In order to classify and stage the diabetic foot, according to the Simple Staging System, a comprehensive assessment, consisting of full history and examination and bedside (or chair side) investigations, should be carried out.

History

The history can be divided into the following sections:

- Presenting complaint
- Past foot history
- Diabetic history
- Past medical history
- Family history
- Drug history

Presenting Complaint (Be Aware That Some Patients May Be Asymptomatic Due to Neuropathy)

The presenting complaint is usually concerning one or more of the following features:

Skin breakdown
Discharge
Swelling
Colour change
Pain

For skin breakdown, discharge, swelling and colour change or any other specific presenting complaints, the following questions may be helpful:

- Where is the problem?
- When did it start?
- How did it start?

Were there any injuries, burns, rat bites (Figs. 9.7 and 9.8), ant bites (Figs. 9.9 and 9.10),



Fig. 9.7 Rat bites over the third and fifth toes



Fig. 9.8 Rat bite with partial amputation of the tip of the left third toe



Fig. 9.9 Ants attracted to the neuropathic foot



Fig. 9.10 Excoriations due to ant bites over the dorsum of the left lateral forefoot

application of native medicines or chemicals, self-surgery, massage, treatment from unauthorised personnel or damage caused by footwear [13].

Assessment of Pain

It is important for personnel who work in a diabetic foot clinic or limb salvage clinic to understand the various causes of pain in the diabetic lower limb.

Pain may be a lone specific complaint or it may accompany the other problems. It may arise locally or be diffuse. Local sources may come from bone, joint or soft tissue including skin and subcutaneous tissue. Generalised burning pain in both feet suggests a diagnosis of painful neuropathy. Diffuse localised pain in a single foot at rest suggests ischaemia, classically known as rest pain which is relieved by dependency such as achieved by hanging the foot over the side of the bed. However, pain in the mild or moderately ischaemic foot should not always be blamed on reduced arterial perfusion. It may be caused by infection. In the neuropathic or ischaemic foot, severe infection can still cause pain, particularly throbbing pain. Pain around an ulcer also suggests infection or ischaemia.

Neuropathy and ischaemia may co-exist in the foot, and it is important to understand the presentation of pain in neuropathy and also in ischaemia. It should be noted that, in general, peripheral neuropathy in diabetes is usually NOT painful and secondly when painful neuropathy does occur, it is not usually associated with tissue loss. Thus caution must be exercised in attributing pain to neuropathy when it is more likely due to infection or ischaemia.

Pain may be unilateral or bilateral and of neuropathic or ischaemic origin. Pain may also be caused by focal pathology such as infection. The following sections will discuss first the assessment of bilateral and then unilateral pain of neuropathic origin and secondly bilateral and then unilateral pain of ischaemic origin.

Bilateral Neuropathic Pain

Bilateral symmetrical neuropathic pain is usually due to painful neuropathy. It is important to ask three questions to aid in the diagnosis of painful neuropathy.

What is the nature of the pain?
When is the pain worse?
Where is the pain?

What Is the Nature of the Pain?

Pain may be spontaneous or be brought on by a specific stimulus. Spontaneous pain may comprise one or several of the following:

- Sharp, shooting, stabbing or burning pain
- Paraesthesiae ('pins and needles')
- Unpleasant tingling (dysaesthesiae)
- Deep muscular aching pain
- Restless legs
- Cramps
- Sensation of cold
- Sensation of tightness (as if a constricting band is around the foot)
- Heaviness

Patients may complain of walking on marbles. The pain may be continuous, varying in intensity or intermittent and episodic and of short duration, like electric shocks. Itching may also be a symptom of painful neuropathy. Pain can vary according to the evolution of the disease. The pain often has an acute early phase which lasts a few months followed by a gradual reduction in pain over the subsequent year.

Patients with painful neuropathy may characteristically have pain which may be described in medical terms as allodynia, hyperalgesia or hyperpathia.

Allodynia is defined as the patient feeling painful sensations from stimuli which are not usually painful to normal individuals such as pain evoked by contact with bedclothes.

Hyperalgesia refers to increased sensation to stimuli which are normally painful.

Hyperpathia is a greatly exaggerated painful sensation to a stimulus after cessation of the stimulus especially a repetitive stimulus.

When Is the Pain Worse?

Painful neuropathy is worse in bed at night, and when the feet and legs are in contact with clothes, including bedclothes. Pain intensity is altered by emotion and fatigue. The pain may vary in relation to the temporal evolution of the condition, being especially painful in the initial stages.

Where Is the Pain?

The distribution of pain is usually in both feet extending into the lower legs in a stocking distribution. Often there is poor localisation and it is usually diffuse. Pain does not generally extend above the knees but one limb may be slightly worse than the other. In severe cases, pain does extend above the knees and it may also be felt in the hands and arms and also on the skull. However, unilateral lower pain with no pain at all on the contralateral limb does not suggest a classical painful neuropathy. It may be due to a focal ischaemic neuropathy or compression of a nerve plexus or root by a prolapsed intervertebral disc.

General Symptoms

Relentless, burning pain and contact discomfort make patients extremely miserable. Patients in severe pain cannot sleep and can become profoundly disturbed, confused and depressed. Pain interferes with the activities of daily living and the quality of life is reduced. There is a negative impact on sleep, ability to work, mood, recreational activity, mobility and enjoyment of life [14, 15].

Patients with painful neuropathy may also present with the following syndromes.

Diabetic Neuropathic Cachexia

The syndrome of diabetic neuropathic cachexia is characterised by profound weight loss and severe pain [16]. The weight loss can be up to 60% of the normal weight and can be so great that patients often appear cachectic. The weight loss is not related to diabetic control. The emotional disturbances are severe and depression, anorexia and often erectile dysfunction may be present. Depression is an inherent part of the syndrome rather than related to the pain.

The sensory loss is mild or absent. There is usually no motor weakness but ankle jerks may be absent. The initial incorrect diagnosis may be metastatic carcinoma or carcinomatous neuropathy. Usually there is spontaneous resolution with weight completely restored and the painful neuropathic symptoms resolved.

Acute Painful Neuropathy of Rapid Glycaemic Control

This is often known as insulin neuritis but the condition is associated with rapid improvement of glycaemic control whether it results from insulin therapy, oral hypoglycaemic agents or diet alone. Symptoms are burning pain and paresthesiae worsening at night. Sensory loss may be minimal or absent. There is usually resolution of symptoms within about 1 year.

Acute Reversible Neuropathy

This has an acute onset and is characterised by distal pain and weakness associated with very high blood glucose levels and often ketosis. There is a sensory neuropathy but usually complete recovery ensues after improvement in diabetic control.

Painful Neuropathy of Impaired Glucose Tolerance

Prediabetic states are associated with neuropathy that typically is predominantly sensory and painful [17]. It is often known as '**impaired glucose tolerance neuropathy'** and may represent the earliest stage of diabetic neuropathy. Patients with impaired glucose tolerance usually have small fibre neuropathy, whereas those with diabetes more often have neuropathy involving both small and large fibres.

Unilateral Neuropathic Pain

Neurological symptoms and signs limited to one leg are indicative of a focal neuropathy. Focal neuropathy may be due to ischaemic damage to the nerve from diabetes itself or due to a compression of the nerve or nerve root by external factors in an entrapment neuropathy. Focal neuropathies due to ischaemic damage with resulting subsequent infarction have an acute onset but they heal spontaneously in 6–8 weeks. They must be distinguished from entrapment syndromes which start slow and progress and persist without treatment.

Pain is a prominent symptom of focal neuropathies. It is present at rest and worse at night. Pain can be felt both proximal and distal to the compression point. Sensory symptoms are sharp burning pain associated with paraesthesiae. Allodynia may also be present. Complex regional pain syndromes which often present with unilateral neuropathic pain must be considered in the differential diagnosis.

Focal Nerves Affected in the Leg

- Lateral cutaneous nerve of thigh
- Common peroneal nerve
- Posterior tibial nerve
- Femoral nerve
- Saphenous nerve

Lateral Cutaneous Femoral Nerve of Thigh-Meralgia Paraesthetica

This is entrapment of the lateral cutaneous femoral nerve of thigh as it exits the pelvis. It is compressed or stretched as it passes through the lateral end of the inguinal ligament next to the anterior superior iliac spine. It causes burning, tingling, itching and numbness over the anterolateral surface of thigh which demonstrates contact sensitivity. Similar symptoms may be caused by a prolapsed disc which is compressing the Lumbar 3 nerve root. The causes are surgical interventions to that area, as well as a tight belt or corset and weight gain underneath inguinal ligament.

Posterior Tibial Nerve: Tarsal Tunnel Syndrome

This is an entrapment neuropathy which develops from compression of the posterior tibial nerve or its associated branches as the nerve passes below the flexor retinaculum at ankle level or more distally [18]. There is tingling and burning pain in the sole and toes which is worse at night. There is also cramping of the intrinsic muscles of the plantar region. Weakness of the small muscles of the foot includes abductor hallucis but not extensor digitorum brevis which is supplied by deep peroneal nerve. Dysaesthesia, paraesthesia and contact sensitivity are present in the distribution of medial and plantar nerves on the sole of the foot.

Common Peroneal Nerve

The nerve is compressed around the head of the fibula. External compression can be caused by squatting, leg crossing or a tight plaster cast in circumstances of diminished consciousness. The common peroneal nerve splits into two branches: the superficial branch supplies the skin of lateral side of lower leg and the lateral calf muscles that evert the foot and the deep peroneal branch, which supplies the toe and ankle dorsiflexors and an area of skin on dorsum between first and second toes. The nerve can further be compressed as it splits and passes through the origin of the peroneus longus muscle 1 inch inferior to the fibular neck.

Injury to the common peroneal nerve leads to a painless foot drop with weakness of tibialis anterior and the evertors and also numbness over the dorsal aspect of the ankle and foot There may be pain over the lateral aspect of the shin and the dorsum of the foot. The sensory impairment over the lateral leg and dorsum of the foot must be distinguished from an Lumbar 5 nerve root lesion.

Femoral Nerve

The femoral nerve arises from Lumbar 2,3,4 roots which pass through the psoas muscle and beneath the inguinal ligament to supply the anterior thigh muscles. It may be compressed by a psoas abscess, retroperitoneal haematoma, particularly in patients on anticoagulants, or by a pelvic tumour. A femoral nerve lesion produces weakness of knee extensors of the quadriceps group, with muscle wasting, a depressed or absent knee jerk and sensory loss in anterior thigh and medial part of knee. Diabetic amyotrophy and upper lumbar radiculopathy (Lumbar 2,3,4) can present in a similar way to entrapment of the femoral nerve.

Diabetic amyotrophy is a focal neuropathy of the lumbosacral radiculoplexus and presents with severe pain in the proximal lower limb, usually involving the thigh, sensory loss, significant weight loss and weakness of thigh muscles. The knee reflex is also absent. There is usually a spontaneous resolution of diabetic amyotrophy by 1 year with return of the knee reflex. It is important to differentiate between diabetic amyotrophy and root compression.

Saphenous Nerve

The saphenous nerve is compressed as it pierces the roof of the subsartorial fascia in the lower third of the thigh. The nerve is commonly damaged during the stripping of the long saphenous vein. There is pain in thigh and lower leg on walking.

Lumbar Spinal Stenosis

This is a common cause of leg pain and results from the narrowing of the spinal canal or neural foramina leading to root ischaemia and neurogenic claudication. Stenosis of the spinal canal is most often caused by loss of disc space, osteophytes and a hypertrophic ligamentum flavum. Lumbar stenosis can be caused by other pathologies that decrease the space of the spinal canal, including tumours and infection.

There is gradual onset of unilateral or bilateral leg pain (with or without back pain), numbness, and weakness which develop after the patient walks a certain distance. Painful sensations shoot down the legs with continued walking and diminish with resting. Standing and bending backwards can exacerbate the symptoms because bending forward increases the space in the spinal canal and vertebral foramen, while bending backward decreases the space. The pain is usually decreased by sitting, leaning forward, putting the foot on a raised cushion or stool. Walking uphill may be easier than downhill. The patient may have leg fatigue, and numbness or paraesthesiae of the leg.

If not treated, there can be increasing weakness and dysfunction of the bladder and bowel leading to a cauda equina syndrome. This results in lower back pain, severe bilateral pain radiating down the legs, weakness of legs and feet, retention of urine, bowel dysfunction and impotence with sensory deficits and reduced or absent reflexes in the legs. The cauda equina syndrome is a surgical emergency.

Complex Regional Pain Syndrome

Another cause of unilateral neuropathic pain is complex regional pain syndrome (CRPS), previously called Reflex Sympathetic Dystrophy (RSD). It is a chronic, painful and progressive

neurological condition that affects the skin, muscles, joints and bones [19, 20]. The syndrome usually develops in an injured limb but often there is only a minor injury or no precipitating event at all. Typically, there is burning pain, excessive sweating, swelling and sensitivity to touch. The presentation of swollen hot foot may be mistaken for an acute Charcot neuroarthropathy. Although CRPS does demonstrate sensory loss, it is characterised by severe neuropathic pain compared with the Charcot foot which is relatively painless [19]. Both conditions demonstrate areas of bone marrow oedema on MRI although in CRPS, it is diffuse, patchy and fluctuating. Pain may begin in one area or limb and then spread to other limbs. In some cases, symptoms of RSD/CRPS diminish for a period and then reappear with a new injury.

Bilateral ischaemic pain.
Ischaemic pain rarely develops in both legs simultaneously but can occur in the following circumstances.

1. Saddle embolus in the lower aorta.
   Patients with acute embolic occlusion of the aortic bifurcation appear marble white or mottled to the waist. They may also present with paraplegia due to ischaemia of the cauda equina, which can be irreversible. Immediate bilateral embolectomy restores lower limb perfusion.
2. Acute aortic dissection extending into the iliac arteries can lead to acute lower extremity ischaemia which can accompany the predominant symptom of chest pain.
3. Rupture of an abdominal aortic aneurysm may also lead to acute lower limb ischaemic pain. Nevertheless, severe pain in the back or abdomen is the dominant symptom.
4. Leriche syndrome is claudication of the gluteal muscles due to severe disease at the aortic bifurcation.

Other Causes of Bilateral Leg Pain

Osteoarthritis of hips, knees and feet
Rheumatoid arthritis
Venous hypertension of the legs
Polymyalgia rheumatica
Polymyositis
Restless legs syndrome

Unilateral Ischaemic Pain

Pain in the lower limb due to ischaemia is known as rest pain and by this stage the ischaemia is severe and has been previously termed critical ischaemia. Rest pain is usually a constant pain, occurring in the toes and the forefoot, often worse at night. It is exacerbated after lying down because of the loss of gravity-assisted flow and is relieved by sitting or standing. Rest pain is eased by hanging the leg down outside the bed.

Although atherosclerosis is usually present in both limbs, marked deterioration of the occlusive disease leading to critical ischaemia often occurs in one leg at any one time leading to the classical presentation of rest pain predominantly in one leg. This is commonly due to a thrombosis on top of existing atherosclerosis. It can lead to the pink painful foot or in cases of sudden complete occlusion a pale mottled foot. Claudication of the calf is another sign of ischaemia but may be absent in people with diabetes because of the very distal site of atherosclerosis in the tibial vessels of the diabetic leg as well as the presence of neuropathy. Thus diabetic patients do not usually go through the classical natural history in peripheral vascular disease of claudication, then rest pain and then tissue loss.

Differentiation of Neuropathic Pain from Ischaemic Pain

Most patients with painful neuropathy have palpable dorsalis pedis and posterior tibial pulses, thus ruling out significant ischaemia. However, when both these pulses are absent, it is necessary to assess how much pain is due to neuropathy and how much may be due to ischaemia. One helpful clinical point is that ischaemic rest pain initially presents unilaterally although background peripheral vascular disease may be present in both legs, whereas painful neuropathy is usually bilateral.

The rest of the history is devoted to gathering important relevant information about the patient to aid diagnosis and management.

Past Foot History

- Previous ulcers and treatment
- Previous surgery to the lower limb
- Amputations Major/Minor
  - Peripheral angioplasties
  - Peripheral arterial bypass

Diabetes History

- Type of diabetes
- Duration of diabetes
- Treatment of diabetes:
  - Insulin
  - Oral hypoglycaemics
  - Diet

Complications of diabetes

Retinopathy
- Background
- Proliferative
- Previous laser therapy
- Vitrectomy
- Cataract

Nephropathy
- Proteinuria
- Renal replacement therapy:
  - Continuous ambulatory peritoneal dialysis (CAPD)
  - Haemodialysis
  - Renal transplant

Cardiovascular
- Angina
- Heart failure
- Myocardial infarction
- Coronary artery angioplasty
- Coronary artery bypass

Cerebrovascular
- Transient ischaemic attack
- Stroke

Past Medical History

- Serious illness
- Accidents
- Injuries
- Hospital admissions
- Operations

Drug History

- Present medication
- Known allergies

Family History

- Diabetes
- Other serious illness
- Cause of death of near relatives

Psychosocial History

- Occupation
- Number of cigarettes smoked per day
  - Number of cigarettes previously smoked per day and for number of years
- Number of units of alcohol per day
- Recreational drugs
- Psychiatric illness
- Home circumstances:
- Type of accommodation
- Lives alone

Examination

This comprises three parts:

- Simple inspection
- Palpation
- Special assessments that can be carried out at the bedside/chairside

In practice, these are often integrated into a comprehensive examination with the aim to look for and assess particular diagnostic features that will enable the practitioner to accurately classify and stage the feet [20, 21]). Examination of the feet should be carried out in a systematic fashion: first the right and then the left, including dorsum, sole, medial border, lateral border, back of the heel, malleoli and interdigital areas. It is useful to compare the feet particularly when assessing colour and temperature. The examination should particularly focus on the following aspects of the foot.

Skin and Skin Breakdown

Skin

In the initial inspection, the general features of the skin including colour and temperature should be examined. The skin under the metatarsal heads should be specifically assessed, looking for any redness as sign of inflammation, particularly in the neuropathic foot in which the skin is dry and fissured. Prominent dilated veins secondary to autonomic neuropathy may be visible. Signs of pruritus may indicate dryness (Fig. 9.11). Hair loss can be a sign of ischaemia or neuropathy.



Fig. 9.11 Scratch marks due to itching secondary to dryness of skin complicated by cellulitis

Colour of the Skin of Foot

It is important to observe the colour of the foot including the toes. Colour changes may be localised or diffuse. Common colour changes are red, blue, pale (white) or black. In dark skins, the red colour may present as a tawny (orange-brown) hue (Fig. 9.12).

Causes of the red foot/toe

- Cellulitis
- Critical ischaemia, especially on dependency (dependent rubor—may be dusky red (Fig. 9.13)
- Charcot foot
- Gout
- Burn or scald
- Chilblain
- Dermatitis/eczema



Fig. 9.12 Cellulitis of right foot, with tawny (orange-brown) hue on the dorsum of the foot and ulcer on dorsum of right great toe with infection of the extensor hallucis longus tendon



Fig. 9.13 Red discolouration of the dependent critically ischaemic foot

Causes of the blue foot/toe
- Peripheral arterial disease
- Severe infection
- Cardiac failure
- Chronic pulmonary disease
- Venous insufficiency (often with brownish pigmentation due to haemosiderosis)

Causes of the pale foot/toe
- Critical ischaemia, especially on elevation.
- Acute ischaemia, the foot is pale, often with purplish mottling.

Causes of the black foot/toe
- Wet necrosis
- Dry necrosis
- Severe chronic ischaemia
- Acute ischaemia
- Emboli
- Bruise
- Blood blister
- Shoe dye
- Application of Henna Black
- Tumour (melanoma)

Temperature of the Skin Foot

Skin temperature is compared between both feet with the back of the examining hand. The temperature gradient is checked by gently moving the back of the hand from the pretibial region of the leg towards the dorsum of the foot and then to the toes while keeping in contact with the patient's skin. An asymmetric gradient may indicate either unilateral ischaemia on the colder side or unilateral inflammatory response such as Charcot's osteoarthropathy or infection on the warmer side.

It is helpful to follow up the clinical assessment of skin temperature by measuring skin temperature using a digital skin thermometer. An infrared thermometer is ideal and skin temperatures can be compared between similar areas on each foot. This is particularly helpful in the management of the Charcot foot. Warm areas or hot spots indicate inflammation which may be due to infection, fracture, Charcot's osteoarthropathy or soft tissue trauma. Unilateral temperature increase in the foot especially in the absence of ulceration is best presumed to be Charcot's osteoarthropathy until proved otherwise. In the neuroischaemic foot, coexisting autonomic neuropathy may keep the foot relatively warm, although an ice-cold foot is indicative of acute ischaemia.

Causes of the hot foot [22]
- Cellulitis
  - Charcot foot
  - Gout
- Venous insufficiency
- Deep vein thrombosis

Causes of the cold foot
- Chronic ischaemia
- Acute ischaemia
- Low output cardiac failure
- Deep vein thrombosis

Skin Breakdown

An active search should be made for breaks in the skin or wounds over the entire surface of the foot and ankle, not forgetting the areas between the toes and at the back of the heel. Toes should be gently held apart for inspection (Fig. 9.14). This may reveal web space fungus infection.

- Abrasions, bullae and fissures also represent breakdown of the skin. Bullae are often the first sign of skin breakdown in the ischaemic foot. They are also a feature of fungal skin infections (tinea pedis), as is web space maceration. Bullae at pressure points may indicate an impending ulcer.
- Dry skin around the heel will form deep fissures (Fig. 9.15) unless an emollient is applied regularly.
- In assessing any wound, it is important to note the size, edge, shape, nature of the base of ulcer, any slough, discharge, exposure of bones and tendons and the characteristics of the surrounding tissue.
- As well as skin lesions specific to the diabetic foot, it is important to recognise inflammatory skin disease such as psoriasis, eczema and dermatitis, which may complicate the diabetic foot and leg.



Fig. 9.14 Toes gently stretched apart to reveal interdigital ulcer

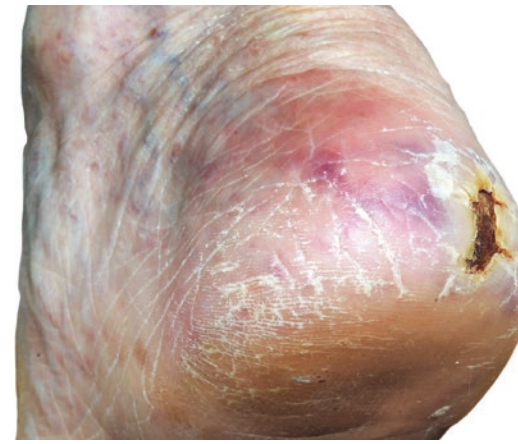


Fig. 9.15 Dry fissured heel in neuroischaemic foot

Infection

When skin breakdown develops, it may act as a portal of entry for infection which develops in 50% of ulcers. A close examination for signs of infection should be made. These include purulent discharge from the lesion and cellulitis as indicated by erythema, swelling and warmth of the toe or foot although in the presence of neuropathy, these classical signs of infection may be diminished. Signs of infection may also be limited in the presence of ischaemia as the inflammatory response to infection needs increased blood supply.

Thus, it is important to look for subtle signs of infection including increased friability of granulation tissue, wound odour, wound breakdown and delayed healing. There may be tracking of the ulcer beneath the surrounding skin and tracking of fluid underneath callus. Deep infection may spread from the site of skin breakdown along tendons and their sheaths (Fig. 9.12). This may not be obvious.

In the presence of infection, it is important to look for signs suggestive of necrotising fasciitis including purpuric rash and blistering. Palpation may reveal crepitus as a fine crackling sensation indicating gas in the tissues.

Osteomyelitis may be suspected by an exposed or visible bone at the base of the ulcer or the appearance of the 'sausage toe' as a red fusiform swelling (Fig. 9.16). It is often associated with an ulcer on the dorsum of the toe which probes to bone.

The probe-to-bone involves inserting a sterile metal probe into the suspected ulceration. A



Fig. 9.16 Sausage-shaped discoloured toe suggesting osteomyelitis

'click' (solid or gritty end point) indicates a positive finding. Osteomyelitis is unlikely after a negative test in the outpatient or low-risk location. However, it is likely after a positive test in a high-risk or inpatient situation [23, 24].

Ischaemia

On inspection the foot has thin atrophic shiny skin without hair. There is atrophy of the subcutaneous tissue. Ulcers may be present on the margin of the foot and the toes and there may be patches of necrosis.

The most important manoeuvre to detect ischaemia is the palpation of foot pulses.

- The dorsalis pedis pulse is felt lateral to the extensor hallucis longus tendon on the dorsum of the foot.
- The posterior tibial pulse is felt below and behind the medial malleolus.

A small handheld Doppler can be used to confirm the presence of pulses and to assess the vascular supply and with a sphygmomanometer, it can be utilised to measure the brachial systolic pressure and ankle systolic pressure. The ankle brachial pressure index (ABI), which is the ratio of ankle systolic pressure to brachial systolic pressure, can then be calculated. In normal subjects, the ABI is usually >0.9 but in the presence of ischaemia is <0.9. Thus, absence of pulses and an ABI of <0.9 confirms ischaemia. Conversely, the presence of pulses and an ABI of >1 essentially rules out ischaemia in the leg but not in the foot in which arterial disease may be located in diabetes. Furthermore, the calf arteries in diabetes typically show diffuse medial calcification which renders the vessel incompressible and can limit the utility of assessing the ABI. If arteries are calcified, the ABI may be artifactually raised but the test is still important as long as one understands its interpretation. Thus, if the ABI is 0.5, then it is low, and indicates severe ischaemia, whether the foot arteries are calcified or not. Indeed, if it is calcified, the true ABI may be lower. Furthermore, absence of foot pulses would be an indication to investigate popliteal and femoral arteries.

Further information about the circulation can be obtained from assessing the Doppler waveform which normally is pulsatile with a positive forward flow in systole followed by a short reverse flow and a further forward flow in diastole. In the presence of arterial narrowing, the waveform shows a reduced forward flow and is described as damped and monophasic.

It is now accepted that ischaemia may occur very peripherally in the foot arteries and may not be detected by ABI. Thus it is advisable to measure either the transcutaneous oxygen pressure on the dorsum of the foot or the toe pressures. Recent studies suggest that toe pressure is more sensitive than ankle pressure in the diagnosis of limb threatening ischaemia and is more predictive of amputation risk [25, 26].

As adjunctive tests, it is possible to perform the capillary filling time (also known as the blanch test). In the capillary refill test, pressure is applied to the pulp of the toe until the digit loses colour. On release of pressure, the refill time should be less than 3 secs if the patient has good

cardiac output and digital perfusion. A capillary refill time of more than 5 secs is abnormal and suggests poor peripheral perfusion.

From the history, examination and investigations it is possible to assess the severity of the ischaemia. However, the ischaemic foot covers a wide spectrum ranging from the neuroischaemic foot with mild or moderate ischaemia to the critically ischaemic foot and the acute ischaemic foot. It is important to recognise these two particular presentations, those of critical ischaemia and acute ischaemia.

Critically Ischaemic Foot

The colour of the skin is bright pink or a dusky red. The foot is cool and the pulses absent. In the foot with such severe ischaemia, Buerger's test is positive. This is performed by elevating the leg with the patient supine and within 30 secs it becomes pale. The foot is then allowed to hang over the side of the couch and the dependent limb becomes red due to the chronic dilatation of the microcirculation distal to the arterial occlusion (Fig. 9.12) A positive Buerger's sign is indicative of severe ischaemia which needs urgent vascular investigations. Another sign of critical ischaemia is the leg being held in the knee flexed position.

Acute Ischaemia

Acute ischaemia results from a sudden occlusion of a major artery, usually popliteal or superficial femoral. Classically there are five features of acute limb ischaemia (5 P's):

1. Pain
2. *Pulse*lessness
3. Pallor
4. *Paresthesiaes*
5. Paralysis

Signs are:

- Pallor of the foot
- White or blueish nail beds
- Blueish-grey discolouration with mottling or 'bruised' appearance (Fig. 9.5)

If a hand is run down the leg, a 'cut-off' point will be found where the temperature of the skin suddenly decreases. Acute ischaemia is a clinical emergency with severe morbidity and mortality. If ischaemia is not treated within 6 hours, then mottling becomes fixed, leading to blistering and then digital necrosis.

Necrosis

Areas of necrosis or gangrene can be identified by the presence of black or brown devitalized tissue. Such tissue may be wet (usually related to infection) or dry. Wet necrosis is usually secondary to a septic vasculitis accompanying severe soft tissue infection and ulceration and is the commonest cause of necrosis in the diabetic foot.

In the neuropathic foot, necrosis is usually wet and is caused by infection complicating a digital, metatarsal or heel ulcer, and leading to a septic vasculitis of the digital and small arteries of the foot (Fig. 9.17). Wet necrosis is also prominent in the infected neuroischaemic foot and has a similar pathology of septic vasculitis. However, in the neuroischaemic foot, reduced arterial perfusion to the foot resulting from occlusive disease of the leg and foot arteries is also an important predisposing factor.

Dry necrosis is hard, blackened, mummified tissue and there is usually a clean demarcation line between necrosis and viable tissue. It may be



Fig. 9.17 Wet necrosis of right third toe secondary to a septic vasculitis of the digital arteries

difficult to diagnose in the patient with a dark skin. Dry necrosis can be seen usually in three situations, in the ischaemic foot namely in critical ischaemia (Fig. 9.4), in acute ischaemia and in emboli to the toes.

Deformity (Including Limited Joint Mobility)

Deformity often leads to bony prominences, which are associated with high mechanical pressures on the overlying skin. This results in ulceration, particularly in the absence of protective pain sensation and when the shoes are unsuitable. When assessing deformity it is important to assess whether it is fixed or mobile.

Common deformities include:

- Pes cavus
- Trigger toe
- Hammer toes
- Claw toes
- Hallux valgus
- Fibrofatty padding depletion (FFPD)
- Charcot foot
- Deformities related to previous trauma and surgery

Pes Cavus

Normally the dorsum of the foot is domed due to the medial longitudinal arch, which extends between the first metatarsal head and the calcaneus. When it is abnormally high, the deformity is called pes cavus and results in a reduction of the area of the foot in contact with the ground during walking and an abnormal distribution of pressure. This leads to excessive callus formation under the metatarsal heads. This deformity is a sign of a motor neuropathy but may be idiopathic. It is often associated with clawing of the lesser toes or a trigger first toe.

Trigger Toe

A trigger toe is a flexion or contraction at the interphalangeal joint of the hallux leading to increased vertical pressure on the first metatarsal head.

Hammer Toe

A hammer toe is a flexible or rigid deformity in which there is buckling of the toe with extension at the metatarsal-phalangeal joint, flexion of the proximal interphalangeal joint and extension of the distal interphalangeal joint. In people with diabetic neuropathy, hammer toes are commonly caused by weakness of the small intrinsic muscles (interossei and lumbricals) of the foot (Fig. 9.18). This deformity results in increased pressure over the metatarsal head, over the prominent interphalangeal joint and at the tip of the toe. There is a risk of the toe rubbing against the uppers of the shoe.

Claw Toes

Claw toes are similar to hammer toes, but with more buckling. There is hyperextension at the metatarsal-phalangeal joint and flexion defor-



Fig. 9.18 Typical neuropathic foot demonstrating hammer toes, wasting of lumbricals, xerosis and crowding of toes

mity at the proximal and distal interphalangeal joints. This results in callus formation and ulceration of the apex and dorsal aspect of the interphalangeal joints. Although claw toes may be associated with neuropathy, they are often unrelated, especially when the clawing is unilateral and associated with trauma or surgery of the forefoot. Claw toes may rarely result from acute rupture of the plantar fascia.

Hallux Valgus

Hallux valgus is a deformity of the first metatarsal-phalangeal joint with lateral deviation of the hallux and a medial prominence on the margin of the foot. This site is particularly vulnerable in the neuroischaemic foot and frequently breaks down under pressure from a tight shoe.

Fibrofatty Padding Depletion (FFPD)

There is reduction of the thickness of the fibrofatty padding over the metatarsal heads (Fig. 9.19). Normal feet contain cushions of fibrofatty padding over the metatarsal heads which absorb plantar pressures. In diabetic neuropathy, the fibrofatty padding may be displaced forward or destroyed by infection or ulceration reducing the foot's capacity to absorb pressure.

Charcot Foot

Bone and joint damage in the tarso-metatarsal joints and mid-tarsal joints leads to two classical deformities: the rocker bottom deformity, in which there is displacement and subluxation/dislocation of the tarsus downwards, and the medial convexity (Fig. 9.20) which results from displacement of the talonavicular joint or from tarsometatarsal dislocation. Both are often associated with a bony prominence which is very prone to ulceration. When the ankle and subtalar joints are involved, instability of the hindfoot can result.

Deformities Related to Previous Trauma and Surgery

Deformities of the hip and fractures of the tibia or fibula lead to shortening of the leg and abnormal gait, which predisposes to foot ulceration. Ray



Fig. 9.19 Distal migration of plantar metatarsal fat pad, callus and prominent metatarsal heads



Fig. 9.20 Medial convexity deformity of Charcot foot

amputations remove the toe together with part of the metatarsal. They are usually very successful but disturb the biomechanics of the foot leading to high pressure under the adjacent metatarsal heads. After amputation of a toe, deformities are often seen in adjoining toes.

Limited Joint Mobility (Including Hallux Rigidus)

Limited joint mobility can affect the feet as well as the hands. The range of motion is diminished at the subtalar and first metatarsophalangeal joints. Limited mobility at the subtalar joint leads to reduced dorsiflexion of the ankle and also plantar flexion of the foot resulting in increased plantar pressures on the foot.

Limited joint mobility of the first metatarsal-phalangeal joint, so-called hallux rigidus, results in loss of dorsiflexion of this joint and excessive forces on the plantar surface of the first toe. This leads to overloading of the plantar aspect of the forefoot in the toe off phase of the gait cycle, causing callus formation and ulceration. It is often seen in barefooted and sandal-wearing populations. Furthermore an unbending toe is exposed to repeated traumas.

Callus and Corns

Callus is a thickened area of epidermis which develops at sites of pressure, shear and friction. It should not be allowed to become excessive as callus is a common precursor of ulceration in the presence of neuropathy. Callus is caused by high pressures and is suggestive of unsuitable footwear or unprotected walking and its most common site is under the metatarsal-phalangeal joints, commonly the first metatarsal-phalangeal joint. Interdigital callus is due to crowding of the toes and friction and injury due to adjoining toenail. Callus is a classical feature of the neuropathic foot, forming diffuse plaques. It can be proliferative and hard with a peculiar smell which attracts insects [13]. When proliferation is excessive it may look like a malignant growth. If the neuropathic foot gets wet or infected, it becomes soft. Callus can also occur in the mild or moderately ischaemic foot, when it is glazed in nature. In contrast to callus, corns are discrete areas, usually not more than 1 cm in diameter and can extend to a depth of several millimetres. Neither should be allowed to become excessive as this can be a forerunner of ulceration (usually in the presence of neuropathy). Haemorrhage within callus is an important precursor of ulceration (Figs. 9.21 and 9.22).



Fig. 9.21 Callus with underlying haemorrhage on medial side of left first toe



Fig. 9.22 Callus under second metatarsal head with underlying haemorrhage

Oedema

Oedema of the tissues of the foot is a major factor predisposing to ulceration, and often exacerbates a tight fit inside poorly fitting shoes. It also impedes healing of established ulcers. Oedema already suspected on inspection can be confirmed by gentle digital pressure applied for a few seconds. Oedema may be unilateral or bilateral.

Unilateral Oedema

This is usually associated with local pathology in the foot or leg.

Causes are:

- Infection, when it is usually associated with erythema and skin breakdown
- Charcot foot (a unilateral hot, red, swollen foot is often the first sign and the oedema can extend to the knee)
- Gout, which may also present as a hot, red, swollen foot
- Trauma, sprain or fracture
- Deep vein thrombosis
- Venous insufficiency
- Lymphoedema caused by lymphatic obstruction secondary to malignancy
- Venous obstruction by a pelvic mass, malignancy or ovarian cyst
- Localised collection of blood or pus which may present as a fluctuant swelling

Bilateral Oedema

This is usually secondary to:

- Cardiac failure
- Hypoalbuminaemia
- Renal failure
- Venous insufficiency (sometimes unilateral)
- Inferior vena caval obstruction
- Lymphoedema
- Neuropathic oedema

Neuropathic oedema secondary to diabetic neuropathy is rare and is related to increased arterial blood flow and arteriovenous shunting. It often responds to the drug, ephedrine.

Nails

It is important to inspect the nails closely as the nail bed and periungual tissues may become the site of ulceration. The following should be assessed:

- Structure of the nails
- Colour of the nail bed
- Abnormalities under the nail
- Signs of nail infections

Structure of the Nails

Thickened nails is a common feature in the general population. If the shoe presses on the nail, it may cause bleeding under the nail. Eventually this may lead to ulceration.

Nails in the neuropathic foot may be hard and brittle. The nails in an ischaemic foot may also be brittle but ivory in appearance [13]. Alternatively, nails may become atrophic in patients with neuropathy and ischaemia.

An ingrowing toenail (onychocryptosis) arises when the nail plate is excessively wide and thin, or develops a convex deformity, putting pressure on the tissues at the nail edge. Callus builds up in response to pressure and inflammation. Eventually, usually after incorrect nail cutting or trauma, the nail penetrates the flesh.

Colour of the Nail Bed

Red, brown or black discolouration of the nails may indicate subungual haematoma. The cause may be acute trauma or chronic trauma such as pressure from ill-fitting shoes.

In acute ischaemia, the nail beds are very pale.

Abnormalities Under the Nail

Discharge of fluid from beneath or around the nail, and any maceration or softness of the nail plate, may indicate the presence of a subungual ulcer or infection.

Nail Infections

Fungal infection of the nail usually invades the nail plate dorsally causing onycholysis. The hallux is the most common nail affected. Infection

starts in one corner and over a period of years it spreads to involve the entire toenail and may affect other nails.

Paronychia is associated with a nail that has a convex nail bed with tendency to incurve in the corners. Recurring pressure in the insensitive foot can cause repetitive microtrauma in the nail groove, causing the nail to act as a foreign body, creating a foreign body inflammatory response with secondary inflammation and localised infection.

Neuropathy

Peripheral neuropathy is the most common complication of diabetes affecting 50% of all diabetic patients. Although neuropathy may present with tingling and a feeling of numbness, it is asymptomatic in the majority of patients and neuropathy will only be detected by clinical examination. An important indication of neuropathy will be a patient who has no pain even when significant foot lesions are present. Painless ulceration is definite evidence of a peripheral neuropathy. In practice, any patient who walks on a foot with ulceration or heavy plantar callus without discomfort has significant neuropathy.

Peripheral neuropathy can involve sensory, motor and autonomic nerves. Simple inspection will usually reveal signs of motor and autonomic neuropathy of the feet but sensory neuropathy must be detected by a simple sensory assessment.

Motor Neuropathy

The classical sign of a motor neuropathy is a high medial longitudinal arch, leading to prominent metatarsal heads and pressure points over the plantar forefoot. In severe cases, pressure points also develop over the apices and dorsal interphalangeal joints of associated claw toes. However, claw toe is a common deformity and may not always be related to a motor neuropathy. It may be caused by wearing unsuitable shoes or trauma or may be congenital.

Complicated assessment of motor power in the lower limb is not usually necessary, but it is advisable to assess dorsiflexion of the foot to detect a foot drop secondary to a common peroneal nerve palsy, which is usually unilateral and will affect the patient's gait. If a painful mononeuropathy is suspected from the history, a more detailed neurological examination is indicated to detect a femoral neuropathy or a diabetic amyotrophy and to rule out compressive lesions of nerve roots supplying the lower limb.

Autonomic Neuropathy

The classical signs of autonomic neuropathy are:

- Dry skin with fissuring secondary to decreased sweating (Figs. 9.11 and 9.15). (The sweating loss normally occurs in a stocking distribution, which can extend up to the knee.)
- Distended veins over the dorsum of the foot and ankle, secondary to arteriovenous shunting.

Sensory Neuropathy

Sensory neuropathy can be simply detected by:

- Clinical examination
- Monofilaments examination
- Neurothesiometry

Clinical Examination

A simple clinical examination detecting sensation to light touch using a cotton wisp and vibration using a 128-Hz tuning fork may suffice, comparing a proximal site with a distal site to confirm a symmetrical stocking-like distribution of the neuropathy. It is preferable to avoid the use of 'pin-prick' to detect sensory loss.

Initially, vibratory sensation should be assessed over the tip of the great toe. An abnormal response is determined when the patient can no longer feel the vibratory sensation but the examiner still perceives it. Absence of ankle reflex even after reinforcement confirms a peripheral neuropathy. Small fibre function may be evaluated using quantitative sensory tests of thermal and pain perception [27] or by measuring the axon reflex-mediated Laser Doppler Imager flare response (LDIflare) [28].

The Ipswich Touch Test (IpTT) is an alternative neurologic test that requires only the physician's index finger. During the IpTT, the physician instructs the patient to close his or her eyes while the physician lightly rests his or her finger on

each of the patient's first, third, and fifth toes for 1–2 secs. Patients are instructed to respond with a 'yes' when they feel the physician's touch. In a head-to-head trial, diagnostic results of the IpTT directly paralleled those of the monofilament in detecting Loss of Protective Sensation (LOPS); IpTT was also equally sensitive and specific [29].

Monofilaments Examination

It is important to detect patients who have sufficient neuropathy to render them susceptible to foot ulceration. This can be carried out using a monofilament which, when applied perpendicular to the foot, buckles at a given force of 10g [30]. Ability to feel that level of pressure provides protective sensation against foot ulceration. It is helpful first to demonstrate the technique on the patient's forearm.

The number of sites used varies according to different protocols. Sites examined include the plantar aspects of the first toe, the first, third and fifth metatarsal heads, the plantar surface of the heel and the dorsum of the foot. The filament should not be applied at any site until callus has been removed. If the patient cannot feel the filament at any of the tested areas, then protective pain sensation is lost, indicating susceptibility to foot ulceration [31]. The 10g monofilament may become inaccurate after use on numerous occasions and should be replaced regularly. There are differences in the performance of commercially available 10g monofilaments. Monofilaments were tested using a calibrated load cell. Each monofilament was subjected to ten mechanical bucklings. The monofilaments were mounted vertically and were compressed in the vertical plane by 10 mm while the load cell detected the maximal buckling force. Longevity testing was performed on the monofilaments by subjecting them to continuous compression until the buckling force was less than 9g. Longevity and recovery testing suggested that each monofilament would be reliable on 10 consecutive patients before needing a recovery time of 24 hours before further usage [32].

Neurothesiometry

Quantitative sensory testing can be used to evaluate vibration perception threshold as well as thermal sensory thresholds. Vibration perception threshold (VPT) is a measure of large fibre function that can be semi-quantified by the use of the neurothesiometer (Fig. 9.23). The stylus of the instrument is placed over the pulp of the hallux. The amplitude of vibration is increased until the patient can detect the vibration. The mean of three readings is taken over the hallux. The vibration threshold increases with age and thus should be corrected for age. Standards for normal subjects, their satisfactory reproducibility and relationship to age have been described. However, a VPT >25 V is regarded as abnormal and has been shown to be highly predictive of subsequent foot ulceration.

Determination of an abnormal VPT is important for two reasons. First, it identifies patients with large fibre dysfunction who are susceptible to foot ulceration and second, it identifies a population with increased cardiovascular risk.

A small number of patients have a small-fibre neuropathy with impaired pain and temperature perception but with intact touch and vibration. They are prone to ulceration and thermal traumas but test normal with filaments, and a clinical assessment of light touch and vibration is normal. As yet, there is no simple inexpensive method of detecting and quantifying small fibre neuropathy. However, a simple temperature assessment of cold sensation can be made by placing a cold tuning fork on the patient's foot and leg.



Fig. 9.23 Neurothesiometer measuring vibration perception threshold

Examination of Painful Neuropathy

On examination, there may be few objective neurological deficits and the feet and legs may be normal, although some patients may show a stocking distribution of loss of sensation of pain and temperature. Autonomic dysfunction is not prominent. Vibratory sensation can be mildly reduced at the toes. Motor strength, tendon reflexes, and proprioception, however, may be preserved because they are functions of large nerve fibres. There may be an increased sensation to a normal stimulus such as light touch confirming allodynia.

Gait

There may be high stamping gait due to loss of proprioception [13].

Patients with distal symmetrical neuropathy may walk with a wide gait.

In the presence of foot drop, the foot scrapes along the floor or there is a high stamping gait.

Footwear Assessment

It is important to examine both shoes and socks.

Examination of Patient's Footwear

The following enquiries should be made:

- Is the shoe long enough?
- Is the toe box broad and deep enough?
- Are the heels too low?
- Does the shoe fasten with a lace or strap (slip-ons are unsuitable for everyday wear).
- If using a velcro strap, is it too tight or loose?
- Is the sole thick enough to provide protection from puncture wounds?
- Is the shoe lining worn, with rough areas that may prove irritating and warrant replacement?
- Are there foreign bodies within the shoes?
- Is there excessive wear under hallux suggesting a hallux rigidus?
- Is there wear across whole of tread suggesting pes cavus?
- Do the insoles show excessive wear and tear?
- Are there exudates/blood stains?

Examination of Patient's Socks

- Are the socks large enough?
- Are the seams too prominent?
- Is there a tight band at the top?
- Are the socks in good repair—no holes or lumpy darns?
- Are the socks made of absorbent material?
- Are the socks very thick, taking up too much space in the shoe?
- Are the socks nonelastic and impede lymphatic and venous drainage causing oedema of feet?

General Examination

- As part of the diabetic foot assessment and indeed the diabetic assessment, all patients should have a physical examination including the following systems:
- Cardiovascular
- Respiratory
- Abdomen
- Eyes:
- Visual acuity
- Fundi (A patient lacking necessary visual acuity to give himself a daily foot examination is a patient at risk, and his family or caregiver should help him.)

Classification and Staging of the Diabetic Foot

Evaluation and examination of the foot will facilitate classification and staging. As previously discussed, the neuropathic foot may be stratified into two clinical groups: the foot with neuropathic ulceration and the Charcot foot, which may be secondarily complicated by ulceration and infection. The ischaemic foot may be stratified into three clinical groups: the neuroisch-

aemic foot characterised by mild or moderate ischaemia and neuropathy and often complicated by ulcer, the severely ischaemic foot otherwise known as the critically ischaemic foot and the acutely ischaemic foot (Fig. 9.6).

Staging

Stage 1

At this stage, the patient does not have the risk factors of neuropathy, ischaemia, deformity, callus and swelling rendering him vulnerable to foot ulcers. The normal foot is characterised by no symptoms, including no pain, and examination is normal.

Stage 2

The patient has developed one or more of the risk factors for foot ulceration including neuropathy, ischaemia, deformity, callus and oedema and the foot may be divided into the neuropathic foot and the ischaemic foot.

Stage 3

The neuropathic and the ischaemic foot have developed tissue damage mainly skin breakdown. This is usually an ulcer, but because some minor injuries such as blisters, splits of skin or grazes have a propensity to become ulcers, they are included in Stage 3. Ulceration is usually on the plantar surface in the neuropathic foot and usually on the margin in the ischaemic foot but can occur on the plantar surface in mild distal ischaemia.

Other forms of tissue damage included in this stage are the bone and joint disruption of Charcot osteoarthropathy and severe tissue ischaemia in the critically ischaemic and acutely ischaemic foot.

Stage 4

The foot has become threatened and is in danger of its tissue being destroyed and losing its function. In the neuropathic foot, infection has developed and is the threat driving the foot to tissue necrosis. In the Charcot foot, it is usually infection that is the threat but in some cases severe mechanical instability threatens the integrity of the foot. In the neuroischaemic foot, the threat is predominantly infection together with mild or moderate ischaemia. In the critically ischaemic foot and the acutely ischaemic foot, severe ischaemia is the threat, driving the foot towards necrosis.

Stage 5

Necrosis has supervened. In the neuropathic foot, infection is usually the cause. In the ischaemic foot, infection is still the most common reason for tissue destruction although ischaemia contributes. In some cases, ischaemia alone can lead to necrosis of a previously intact foot. The foot in Stage 5 is at risk of becoming unsalvageable with overwhelming necrosis, or has intractable pain or gross instability and there is a risk a major amputation.

Conclusion

We have described a practical approach to the evaluation and examination of the diabetic foot. Using this approach, the practitioner should be able to carry out a comprehensive assessment to allow an accurate diagnostic classification and staging of the foot. This should enable the correct treatment to be carried out.

References

1. Boulton AJ, Armstrong DG, Albert SF, et al. Comprehensive foot examination and risk assessment: a report of the task force of the foot care interest group of the American Diabetes Association, with endorsement by the American Association of Clinical Endocrinologists. Diabetes Care. 2008;31(8):1679–85. https://doi.org/10.2337/dc08-9021179.
2. Microvascular complications and foot care: standards of medical care in diabetes 2021. Diabetes Care. 2021;44(Suppl 1):S151–67. https://doi.org/10.2337/dc21-S011.
3. Schaper NC, van Netten JJ, Apelqvist J, Bus SA, Hinchliffe RJ, Lipsky BA, Editorial IWGDF, Board. Practical guidelines on the prevention and management of diabetic foot disease (IWGDF 2019 update). Diabetes Metab Res Rev. 2020;36(Suppl 1):e3266. https://doi.org/10.1002/dmrr.3266. PMID: 32176447.
4. Conte MS, Bradbury AW, Kolh P, White JV, Dick F, Fitridge R, et al.; GVG Writing Group. Global vascular guidelines on the management of

chronic limb-threatening ischemia. J Vasc Surg. 2019;69(6S):3S–125S.e40. https://doi.org/10.1016/j.jvs.2019.02.016. Epub 2019 May 28. Erratum in: J Vasc Surg. 2019 Aug;70(2):662. PMID: 31159978.
5. Foster A, Edmonds M. Simple staging system: a tool for diagnosis and management. Diabet Foot. 2000;3:58–62.
6. Wagner F. A classification and treatment program for diabetic, neuropathic, and dysvascular foot problems. Instr Course Lect. 1979;28(1):143–65.
7. Armstrong DG, Lavery LA, Harkless LB. Validation of a diabetic wound classification system. The contribution of depth, infection, and ischemia to risk of amputation. Diabetes Care. 1998;21(5):855–9. https://doi.org/10.2337/diacare.21.5.855. PMID: 9589255.
8. Ince P, Abbas ZG, Lutale JK, Basit A, Ali SM, Chohan F, et al. Use of the SINBAD classification system and score in comparing outcome of foot ulcer management on three continents. Diabetes Care. 2008;31(5):964–7. https://doi.org/10.2337/dc07-2367. Epub 2008 Feb 25. PMID: 18299441.
9. Jeffcoate W, Gooday C, Harrington A, et al. The National Diabetes Foot Care Audit of England and Wales: achievements and challenges. Diabet Foot J. 2020;23(1):70–3.
10. Monteiro-Soares M, Russell D, Boyko EJ, et al. Guidelines on the classification of diabetic foot ulcers (IWGDF 2019). Diabetes Metab Res Rev. 2020;36(S1):e3273. https://doi.org/10.1002/dmrr.3273.
11. Mills JL Sr, Conte MS, Armstrong DG, Pomposelli FB, Schanzer A, Sidawy AN, et al. The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: risk stratification based on wound, ischemia, and foot infection (WIfI). J Vasc Surg. 2014;59(1):220–234.e1–2.
12. Zhan LX, Branco BC, Armstrong DG, Mills JL Sr. The Society for Vascular Surgery lower extremity threatened limb classification system based on Wound, Ischemia, and foot Infection (WIfI) correlates with risk of major amputation and time to wound healing. J Vasc Surg. 2015;61:939–44.
13. Kelkar S, editor. Handbook of diabetic foot care. Bangalore: Diabetic Foot Society of India; 2005.
14. Girach A, Julian TH, Varrassi G, Paladini A, Vadalouka A, Zis P. Quality of life in painful peripheral neuropathies: a systematic review. Pain Res Manag. 2019;2019:2091960. https://doi.org/10.1155/2019/2091960.
15. Vas PR, Mahdi-Rogers M. Diabetic neuropathy. In: Edmonds M, Sumpio B, editors. Interdisciplinary approach to limb salvage. Cham: Springer; 2019. p. 139–49.
16. Ellenberg M, et al. Diabetes. 1974;23(5):418–23. https://doi.org/10.2337/diab.23.5.418.
17. Sumner CJ, Sheth S, Griffin JW, Cornblath DR, Polydefkis M. The spectrum of neuropathy in diabetes and impaired glucose tolerance. Neurology. 2003;60(1):108–11.
18. Doneddu PE, Coraci D, Loreti C, Piccinini G, Padua L. Tarsal tunnel syndrome: still more opinions than evidence. Status of the art. Neurol Sci. 2017;38(10):1735–9. https://doi.org/10.1007/s10072-017-3039-x. Epub 2017 Jun 29. PMID: 28664501.
19. Poll LW, Weber P, Böhm HJ, Ghassem-Zadeh N, Chantelau EA. Sudeck's disease stage 1, or diabetic Charcot's foot stage 0? Case report and assessment of the diagnostic value of MRI. Diabetol Metab Syndr. 2010;2:60.
20. Edmonds ME, Foster AVM. Managing the diabetic foot. 3rd ed. Oxford: Wiley Blackwell; 2014.
21. Edmonds ME, Sumpio B. Limb salvage of the diabetic foot an interdisciplinary approach: an interdisciplinary approach. Cham: Springer; 2019. https://doi.org/10.1007/978-3-319-17918-6. ISBN: 978-3-319-17917-9.
22. National guidelines for management of diabetic foot. Bangalore: Diabetic Foot Society of India; 2007.
23. Wrobel J, Schmidt B. Probe-to-bone testing for osteomyelitis in the diabetic foot: a literature review. Diabet Foot J. 2016;19:64–8.
24. Lam K, van Asten SA, Nguyen T, La Fontaine J, Lavery LA. Diagnostic accuracy of probe to bone to detect osteomyelitis in the diabetic foot: a systematic review. Clin Infect Dis. 2016;63(7):944–8.
25. Høyer C, Høgh AL, Sandermann J, Zacho HD, Petersen LJ. Risk factors and haemodynamic variables in patients with low Toe-Brachial Index but normal Ankle-Brachial Index. Atherosclerosis. 2019;289:21–6.
26. Manu CA, Freedman B, Rashid H, Winkley K, Edmonds ME. Peripheral arterial disease located in the feet of patients with diabetes and foot ulceration demands a new approach to the assessment of ischemia. Int J Low Extrem Wounds. 2020;17:1534734620947979. https://doi.org/10.1177/1534734620947979.
27. Shy ME, Frohman EM, So YT, Arezzo JC, Cornblath DR, Giuliani MJ, et al. Quantitative sensory testing: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2003;60:898–904.
28. Vas PR, Rayman G. Validation of the modified LDIFlare technique: a simple and quick method to assess C-fiber function. Muscle Nerve. 2013;47:351–6.
29. Sharma S, Kerry C, Atkins H, Rayman G. The Ipswich Touch Test: a simple and novel method to screen patients with diabetes at home for increased risk of foot ulceration. Diabet Med. 2014;31(9):1100–3. https://doi.org/10.1111/dme.12450. Epub 2014 Apr 11. PMID: 24673517.
30. Miller JD, Carter E, Shih J, Giovinco NA, Boulton AJ, Mills JL, Armstrong DG. How to do a 3-minute diabetic foot exam. J Fam Pract. 2014;63(11):646–56. Erratum in: J Fam Pract. 2015;64(8):452. PMID: 25362495.

31. Miranda-Palma B, Sosenko JM, Bowker JH, Mizel MS, Boulton AJM. A comparison of the monofilament with other testing modalities for foot ulcer susceptibility. Diabetes Res Clin Pract. 2005;70(1):8–12.
32. Booth J, Young M. Differences in the performance of commercially available 10g monofilaments. Diabetes Care. 2000;23(7):984–8.
33. Maihöfner C, Seifert F, Markovic K. Complex regional pain syndromes: new pathophysiological concepts and therapies. Eur J Neurol. 2010;17:649–60. https://doi.org/10.1111/j.1468-1331.2010.02947.x.
34. Harden RN, Bruehl S, Perez RSGM, Birklein F, Marinus J, Maihöfner C, et al. Validation of proposed diagnostic criteria (the "Budapest Criteria") for complex regional pain syndrome. Pain. 2010;150:268–74. https://doi.org/10.1016/j.pain.2010.04.030.

10 Frailty and Mobility Degeneration in Diabetes and Diabetic Foot Ulceration

Bijan Najafi and Gu Eon Kang

Aging, Diabetes, and Frailty

More than 700 million people were aged 65 years or over worldwide in 2019, according to a report by the United Nations, and the number of people aged 65 years or over will increase to 1.5 billion by 2050 [1]. One serious concern regarding the rapid increase in aging population is growing challenges in the clinical management of chronic health conditions such as diabetes in the population [2]. For example, in 2017, 123 million people aged 65 years or over had diabetes worldwide, and the number will be doubled by 2045 [3].

Diabetes is a group of metabolic disorders that occurs due to deficits in insulin secretion, insulin action, or both [4]. The World Health Organization estimated 1.5 million people died directly from diabetes in 2019 [5]. Diabetes heightens the risk of cardiovascular disease and strokes two- to threefold and further reduces the life expectancies and quality of life of the affected individuals [6]. Studies also demonstrated diabetes accelerates the aging process such as cognitive decline and functional decline at a younger age compared to those without diabetes [7, 8], which raises concerns about the onset of frailty in older adults with diabetes.

Frailty is a geriatric syndrome, defined as increase in vulnerability in older adults to poor resolution of homeostasis after stressful events [9] (Fig. 10.1). Although a gradual decline in cognitive function and physical function is normal with aging, frailty significantly speeds up the decline and starts to fail the homeostatic reserve mechanism [11]. Frailty is also considered a measure of resilience, and increases adverse health outcomes such as falls, pressure ulcers, and disability even after a small insult such as a minor surgical procedure and a minor infection, and results in dramatic decrease in health state [10, 12, 13].

In this chapter, we will review current knowledge of the pathway to develop frailty in diabetes. We will also summarize strategies on how to screen frailty and its impact on adverse outcomes in people with diabetes and will discuss potential treatments to improve health outcomes among frail older adults.

B. Najafi (✉)
Interdisciplinary Consortium on Advanced Motion Performance (iCAMP), Division of Vascular Surgery and Endovascular Therapy, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX, USA
e-mail: Bijan.Najafi@bcm.edu

G. E. Kang
Neuromuscular and Musculoskeletal Biomechanics Laboratory, Department of Bioengineering, Erik Jonsson School of Engineering and Computer Science, University of Texas at Dallas, Richardson, TX, USA
e-mail: GuEon.Kang2@utdallas.edu

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_10

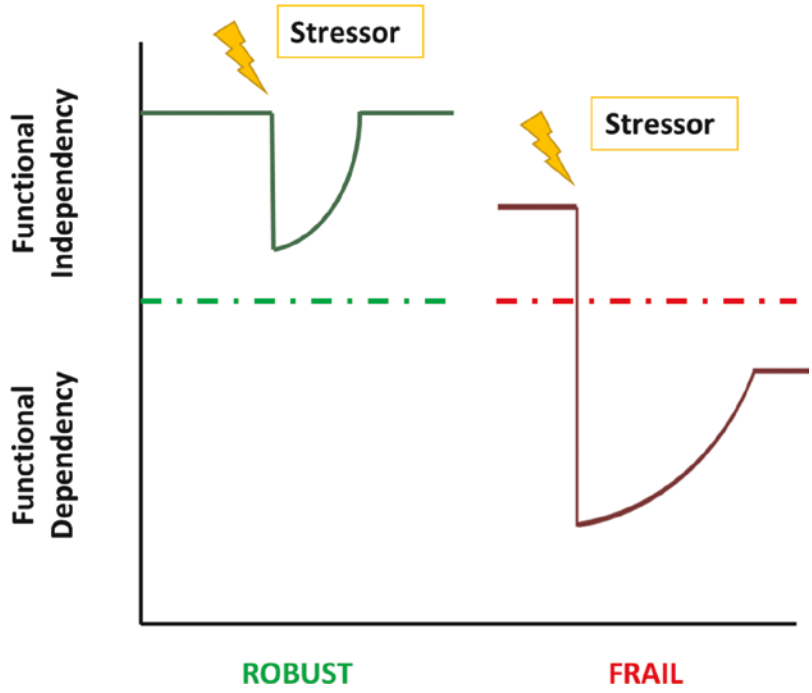


Fig. 10.1 Frailty is a measure of resilient or measures of inability to cope with acute stressors like surgery or an acute illness such as flu or a fall. (This figure is built based on the Figure from [10])

Pathways of Frailty in Diabetes

The two "storms" of aging and diabetes are associated with a greater risk of developing frailty [14]. In people with diabetes, the prevalence of frailty significantly increases by nearly 50% (the prevalence of frailty of 5–10% in non-diabetic individuals) [15]. Although the true pathways from diabetes to frailty are still unclear, one commonly considered pathway is insulin resistance [16] (Fig. 10.2). Insulin resistance might result in muscle loss (i.e., sarcopenia) particularly in people with type 2 diabetes by reducing stimulation of protein synthesis and mitochondrial function and increasing protein degradation [17].

Arteriosclerosis may be another pathway to frailty in diabetic individuals. Diabetes accelerates arteriosclerosis [18]. For example, studies showed peripheral arteriosclerosis, peripheral chronic ischemia with impaired oxygen supply caused by arteriosclerosis can cause muscle atrophy and muscle loss and weakness [19].

Several studies also identified chronic inflammation and increased oxidative stress may be other causes of frailty in diabetes. Chronic inflammation induces anabolic resistance in muscle, which leads to sarcopenia because of reduced production of growth factors and necessary signaling for muscle recovery [20]. Similarly, increased oxidative stress in diabetes can lead to muscle atrophy and sarcopenia by reducing mitochondrial function [21].

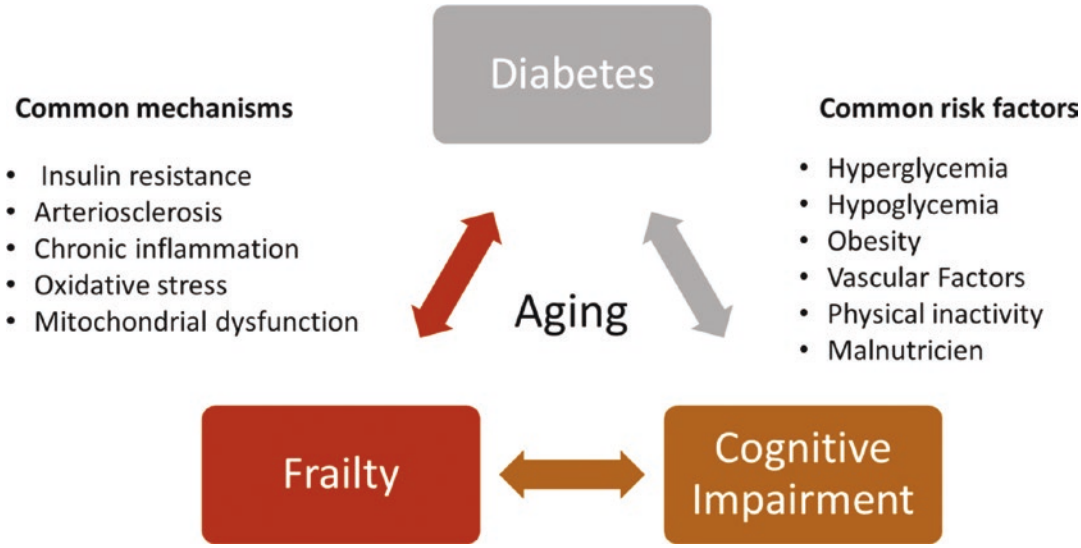


Fig. 10.2 Diabetes, frailty, and cognitive dysfunction are closely related to the mechanisms of aging. It is estimated that between 10% and 25% of older adults with diabetes are frail. Insulin resistance, chronic inflammation, oxidative stress, and mitochondrial dysfunction may be common mechanisms shared by diabetes, frailty, and cognitive impairment. Hyperglycemia, hypoglycemia, obesity, vascular factors, physical inactivity, and malnutrition are important risk factors for frailty in older adults with diabetes. Having one of these clinical syndromes can significantly increase the risk for another one and will significantly impose a substantial personal and public health burden

Frailty and Biomechanics of Lower Extremities

Frailty and aging could alter the biomechanics of lower extremities, which in turn may increase the risk of diabetic foot ulcer (DFU) among older individuals with diabetes. Figure 10.3 is a summary illustration of age-related factors affecting lower extremity biomechanics reported in a systematic review by Neville and colleagues [22]. In summary, aging has been shown to alter the biomechanical properties of the skin and plantar soft tissue of the foot. These soft tissues, which anchor the plantar skin to the underlying bony architecture of the foot, serve as a protection to the underlying neurovascular structures, provide resistance against frictional shear force, and attenuate the pressure and force during collision impact [23]. Because of aging, the dermo-epidermal junction of the skin, which provides resistance against shear stress, becomes flattened, thinner, dehydrated, and loss of elasticity with aging [22]. This in turn could reduce skin reliance against pressure and shear and thus early skin breakdown with a lower magnitude of pressure and shear forces. In addition to the changes in the skin noted above, there are also changes in the tissue properties interfacing with the plantar surface of the foot causing higher tissue stiffness due to aging that in turn could be one of the factors for the high prevalence of foot problems (e.g. foot pain and foot deformity) in frail older adults as reported by Muchna and colleagues [24]. Furthermore, the increase in soft tissue stiffness could be postulated to contribute to the decrease in tactile sensation and limit sensory feedback [25]. Over time this change can reduce the load-bearing capacity of the plantar soft tissues, which might result in reduced shock absorption as well as slower recovery after compression [26]. This

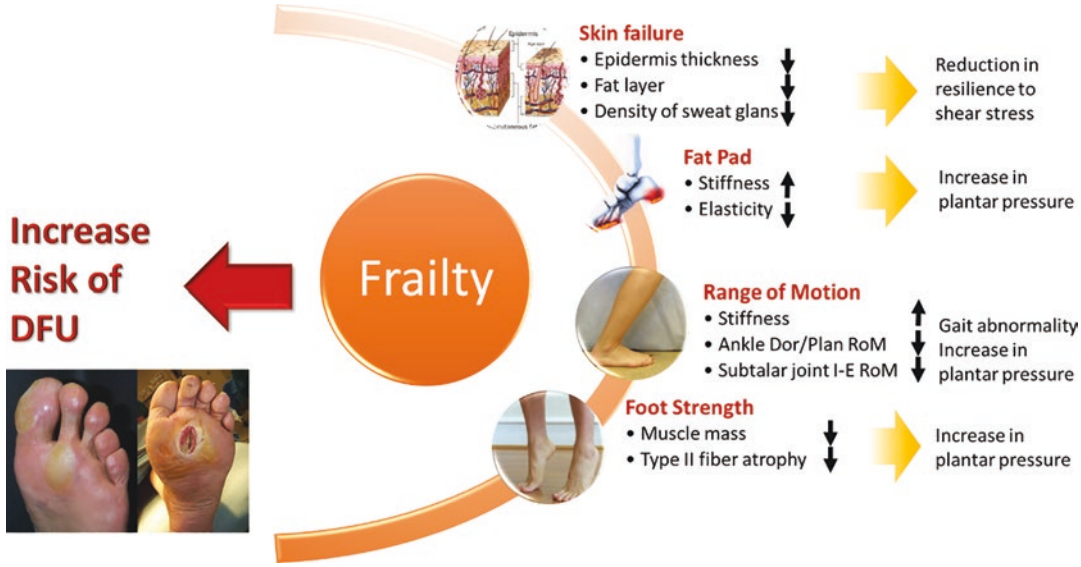


Fig. 10.3 The impact of frailty on lower extremity biomechanics and its association with increased risk of DFU

can increase plantar pressure [27] leading to foot pain and foot deformity [28]. A systematic review by Wrobel and Najafi [25] demonstrated that the changes in the properties of soft tissues led to impaired gait function and adaptation to uneven or irregular surfaces, which may result in falls and increased risk of DFU. In addition, Najafi and colleagues linked poor plantar sensory feedback with poor balance [29].

The impact of aging is not limited to soft tissue and skin properties. Neville and colleagues reported age-related changes in the musculoskeletal properties occurring at specific joints in the foot and ankle negatively impact balance and gait in older adults [22]. Furthermore, loss of muscle mass particularly in type II muscle fibers affects the lower limb strength and results in a decline in force and power production, slower muscle responses, and the reduction in ability developing rapid muscle activation and power [30]. These lower extremity biomechanical changes in the aging population are anticipated to be magnified because of frailty, which in turn may increase the likelihood of joint deformities and joint rigidity, leading to alerted gait, inability to absorb collision shock during walking, higher likelihood of developing callus and lower resilience to pressure and shear, thus increasing likelihood of DFU in response to a lower magnitude of pressure and shear force compared to non-frail and younger populations [22, 24, 25].

Mobility Degeneration in Diabetes and Diabetic Foot Ulceration

Frailty and sarcopenia result in a severe reduction in functional mobility in people with diabetes [31], which can further speed up the progression of frailty [32]. A common manifestation of frailty-related mobility degeneration is impaired gait performance [25]. For example, Petrofsky and colleagues found that people with diabetes walk slower and take shorter and wider steps than people without diabetes [33]. However, interestingly, in terms of walking activity under natural circumstances, often measured by daily step counts, studies have reported mixed results. Tudor-Locke and Bassett reported that daily step counts for people with diabetes (approximately 6660 steps per day) are not necessarily lower than those for healthy adults (between 6000 and 7000 steps per day) [34, 35]. However, Morrato and colleagues reported that approximately 40%

of people with diabetes are engaged in a minimum of 30 min of moderate exercise (3 days/week), but approximately 60% of healthy people are engaged in the same amount of moderate exercise [36].

In people with DFU, in general, mobility impairment worsens compared to those without diabetes and those with diabetes but without foot ulceration. For example, Yavuzer and colleagues reported slower gait speed and cadence in people with diabetic peripheral neuropathy compared to people with diabetes but without peripheral neuropathy and normal controls [37]. Najafi and colleagues demonstrated that 4 weeks' immobilization of the foot after treatment for DFU caused a reduction of daily walking duration by an average of 44% and a reduction of the total number of steps by an average of 23% [38]. A similar observation was reported by Fernando and colleagues: the average daily step counts were reduced from 7762 ± 3590 steps for people with diabetic peripheral neuropathy (DPN) to 3729 ± 2042 steps for people with DFU treated by irremovable offloading devices [39]. This reduction in the level of activity could be due to muscle wasting caused by irremovable offloading, as suggested by de Oliveira and Moore [40]. Interestingly, the level of activity observed in people treated by irremovable offloading devices was similar to activity levels in a frail population as observed in another study performed by Schwenk and colleagues [41]. They reported average daily steps in non-frail, pre-frail, and frail older adults (age 65 years or older) were 6030 ± 3075, 3869 ± 1996, and 3869 ± 1996 steps, respectively. This may suggest that the treatment of DFU by irremovable offloading may lead to frailty, particularly among older patients.

Frailty could significantly impact gait performance, which in turn may increase the risk of DFU in people with diabetes. Rahemi and colleagues analyzed gait performance of 161 older adults (age 65 years and older) using wearable sensors to explore gait parameters among frail and non-frail participants [42]. They used the frailty phenotype criteria developed by Fried and colleagues [43] to determine the frailty status of participants. According to these criteria, 49 individuals were classified as non-frail, 92 as pre-frail, and 20 as frail. The gait parameters associated with propulsion characteristics including propulsion duration and propulsion acceleration had the largest effect size (Cohen's d = 1.28–1.95) to distinguish between frail and non-frail individuals. More specifically, their results suggest that frail individuals have an earlier heel-off phase leading to longer propulsion duration on average by 58% and less efficient propulsion (lower propulsion acceleration) on average by 45% compared to non-frail individuals.

The early heel-off phase in frail individuals could be explained by muscle loss from sarcopenia or fat infiltration and loss of muscle quality and force production capacity in older adults. In a conference paper, Najafi and colleagues reported that treating people with DFU using irremovable offloading for a duration of longer than 4 weeks could lead to reduced propulsion performance with similar characteristics reported in Rahemi and colleagues [44]. Additionally, they found, compared to plantar pressure with an age-matched non-frail individual, peak plantar pressure was 109% higher in people with DFU treated with irremovable offloading probably because of inefficient propulsion, joint rigidity, and reduced area of contact. Thus, irremovable offloading could enhance wound healing outcomes. It may have long-term consequences such as muscle wasting, poor gait, and physical activity reduction, which in turn could increase risk of recurrence of ulcers, increase the risk of falling, and frailty. This speculation however needs to be confirmed by future studies.

Screening Frailty

Frailty is a multidimensional construct including clinical manifestation of cognitive decline or functional decline or both, also referred to as "cognitive frailty" [45]. Although frailty is not routinely screened in primary care settings, due to the impact of frailty on clinical outcomes, it is

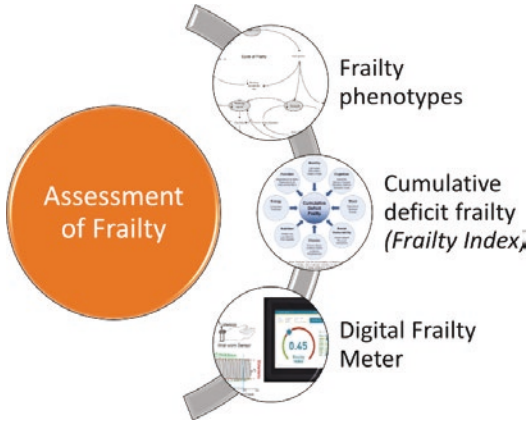


Fig. 10.4 Although more than 20 different methods for frailty assessment have been suggested in literature, two of the most popular methods are frailty phenotype and frailty index. The frailty phenotype, proposed by Fried and colleagues, assesses five physical components: unintentional weight loss, slowness, weakness, exhaustion, and low physical activity. The frailty index, proposed by Rockwood and colleagues, considers health deficits (symptoms, signs, disabilities, diseases, etc.). The frailty index is represented as a ratio between the number of presented deficits and the number of considered deficits. Also, there are several digital health-based technologies that facilitate objective screening of frailty

becoming more critical to properly screen frailty in the primary care setting to early identify when a person starts being frail. Until now, there is no consensus made on how to best measure frailty, but there are several widely used approaches and some recently emerging approaches. Although more than 20 different methods for frailty assessment have been suggested in literature, two of the most popular methods are frailty phenotype and frailty index described in the following. Additionally, recently the use of digital technology facilitates monitoring frailty and its severity based on quick and simple assessment of motor performance (Fig. 10.4).

Frailty Phenotypes and Frailty Index

One approach that is widely used is the frailty phenotype proposed by Fried and colleagues [9]. The frailty phenotype primarily measures functional decline and consists of five criteria of weight loss, weakness (i.e., weak grip strength), exhaustion, slowness (i.e., slow gait speed), and reduced physical activity and classifies people into three categories of robust (those who meet 0 criteria), pre-frail (those who meet 1 or 2 criteria), and frail (those who meet 3 or more criteria). Numerous studies demonstrated frailty assess using the frailty phenotypes is a strong predictor of mortality in a population with specific health condition such as cardiovascular disease and a community-dwelling population [46, 47].

However, administration of frailty using the frailty phenotype can be challenging in patients with limited mobility, or bed-bound patients in the hospital setting. An example is a person with peripheral arterial disease, often with rest pain, foot ulcers, foot gangrene, or previous limb amputations; these issues may make usual assessments of frailty impractical or invalid [48]. Moreover, assessing slowness could be invalid or inaccurate in those with concurrent parental IV therapies, fractures, presence of wounds, need of walking assistance, or on ventilator support. An additional challenge in the hospital setting is allocating space for distance-specific testing. In the absence of complete phenotype assessment, interpretation of frailty results can be narrow, and the predictive power might be reduced [49, 50]. For example, Rockwood et al. [51] showed patients who were missing performance-based measures had a risk of mortality 3 times higher over the span of 5 years than those who were not.

Furthermore, evaluation of frailty using frailty phenotype requires trained personnel to conduct the assessment, especially when evaluating patients with cognitive impairment, limiting their ability to respond to the questionnaires (e.g., inactivity, weight loss, and exhaustion of questionnaires).

Another popular approach is the frailty index proposed by Rockwood and colleagues [52]. The frailty index measures deficits in physical performance, health state, and self- and familial history of diseases including cognitive impairment and is based on cumulative deficits in overall state (total 70 items). The frailty index is calculated as a fraction of the number of existing deficits (e.g., seven deficits out of 70 items = 0.1), which results in a continuous scale between 0 ("no deficit") and 1 ("deficits in all 70 items"). Studies demonstrated the frailty is a strong predictor of mortality across clinical conditions [53]. However, since it consists of a high number of general signs or symptoms, it mainly serves as a "red flag" for potential problems but cannot be used to determine immediate effect of preventive or therapeutic interventions since it is not sensitive to change over short time intervals [54].

Emerging Technologies

The development of wearable technology enhances screening frailty in both clinical and research settings [55]. For example, Toosizadeh and colleagues developed a single wearable sensor worn on the wrist and successfully assessed some of the frailty phenotypes (e.g., slowness, weakness, and exhaustion) as well as other movement characteristics that are associated with frailty (e.g., rigidity) from a 20-s elbow flexion–extension movement (i.e., frailty meter) [56–58].

Wearable technology is also used to measure gait and balance performance under supervised (e.g., lab setting) and unsupervised conditions (e.g., home setting), which is another way of screening frailty. Kang and colleagues examined characteristics of gait initiation in older adults with DPN in comparison with non-diabetic older adults and successfully differentiate the gait initiation phase between the two groups [59]. Kang and colleagues also examined the combining effects of cognitive and functional status on gait and balance performance during single-task gait and dual-task gait in older adults with DPN using wearable sensors and successfully demonstrated cognitive decline exacerbates the risk of physical injury [60].

More recently, with increasing needs of telemedicine in the era of COVID-19, image analysis of human motion is being developed to identify frailty status of older adults during the telemedicine service. Zahiri and colleagues used the 20-s elbow flexion–extension movement and developed an image analysis system to measure frailty state of older adults and successfully identified slowness, weakness, and exhaustion as well as rigidity [61] (Fig. 10.5).

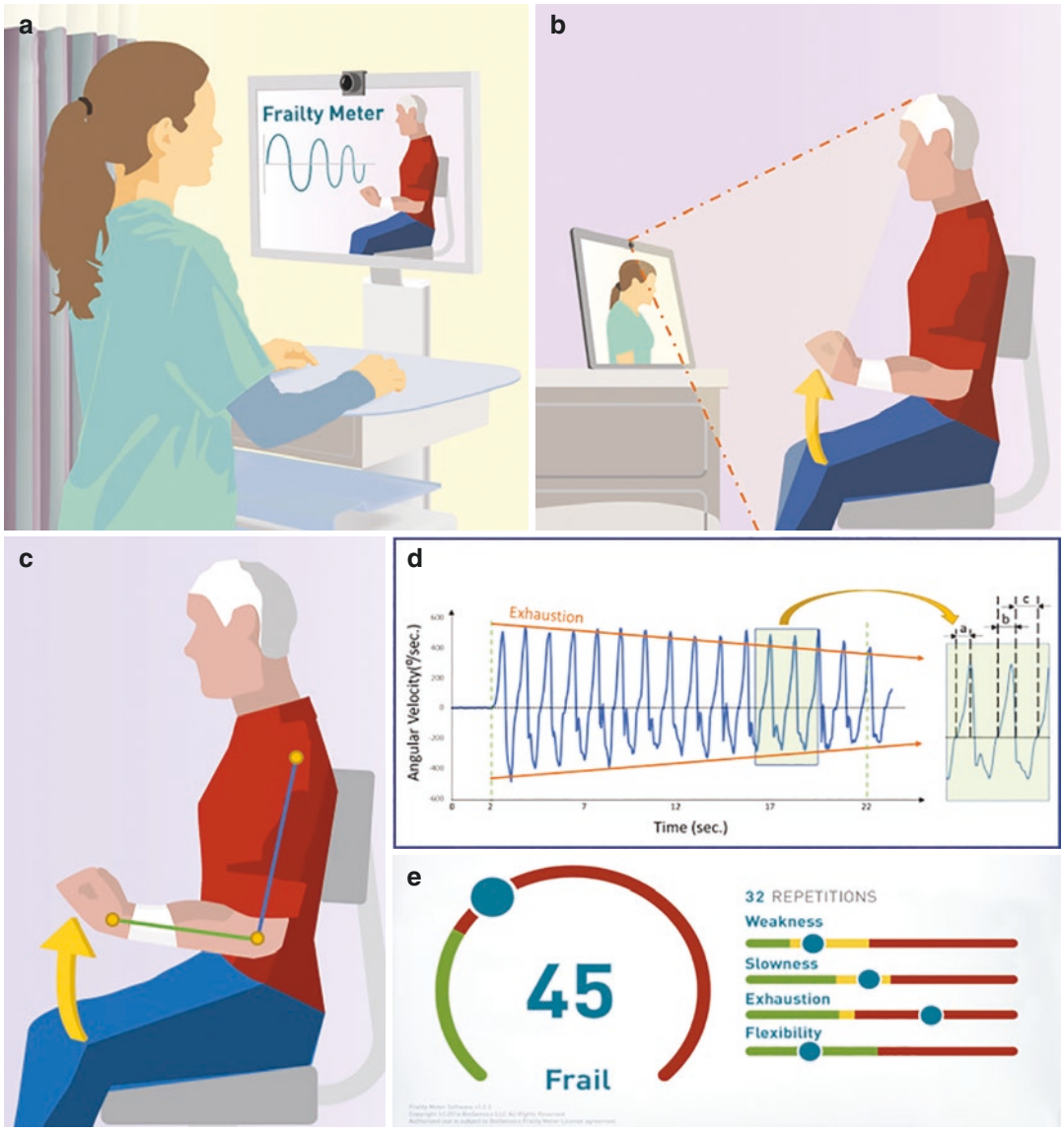


Fig. 10.5 (**a**–**e**) Recent advances in artificial intelligence and image processing allow a new generation of frailty meter over telemedicine. Above is a solution proposed by Zahiri et al. in which frailty and its key phenotypes including weakness, slowness, exhaustion, and flexibility could be measured by a 20-s repetitive elbow flexion–extension test in front of a camera. Using a deep-learning image processing algorithm and a machine learning model, the frailty index and each phenotype are measured from this 20-s test. This method could open an opportunity to remotely assess frailty over telemedicine. (This figure is recreated using one of the figures reported in Zahiri et al. study [60])

The Impact of Frailty in Diabetes

Once an individual starts being frail, it further exacerbates aging process, further deteriorates diabetes itself, and develops diabetic complications, which eventually results in significant reduction in functional abilities, independency, and mortality [62, 63]. To this end, although the association between frailty and diabetes is not fully understood, some studies have reported the impact of frailty state on adverse health outcomes in diabetes and DFU. Examples of the adverse health outcomes include the development of biomechanical risk factors, occurrence of postoperative complications, and delayed wound healing, which will be discussed in the next paragraph (Fig. 10.6).

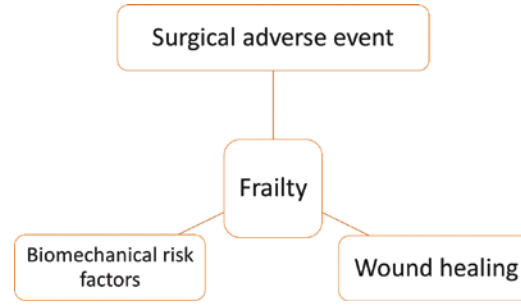


Fig. 10.6 Screening of frailty could be useful to evaluate risk of surgical intervention like revascularization for our patients, it could also help to better determine biomechanical risk factors associated with diabetic foot ulcer; it may be also helpful for predicting chronic and hard to health wounds

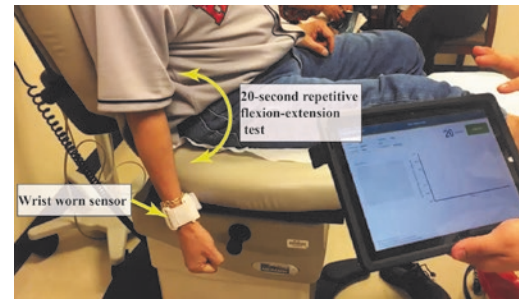


Fig. 10.7 Najafi and colleagues demonstrated that using a sensor-based frailty meter based on a 20-s elbow repetitive flexion–extension test is a practical test to quickly determine physical frailty in a hospital setting and predict adverse events in people with critical limb-threatening ischemia after lower extremity revascularization [13]

Takeji and colleagues investigated the impact of frailty on clinical outcomes (all-cause mortality and major amputation after 2 years) of patients with critical limb ischemia who underwent either endovascular therapy or bypass surgery [64]. In their study, frailty was assessed using the frailty index [52]. They found the frailty index was independently correlated with all-cause mortality and major amputation after 2 years. O'Donovan and colleagues compared psychosocial wellbeing and morality among four groups of people (diabetes and frail, diabetes and non-frail, frail and non-diabetic, and non-diabetic and non-frail) [65]. They found the lowest quality of life for the diabetic and frail group followed by the diabetic and non-frail group, the frail and non-diabetic group, and the non-diabetic and non-frail group. They also found similar mortality rate at 2 year between the diabetic and frail group, and the frail and non-diabetic group (approximately 15%), which was significantly higher than the diabetic and non-frail group (7.3%) and the non-diabetic and non-frail group (2.7%). Bąk and colleagues investigated the impact of frailty on quality of life and depression in older adults with type 2 diabetes [66]. They found frail older adults with type 2 diabetes have significantly higher depression and lower quality of life compared to robust older adults with type 2 diabetes. Najafi and colleagues investigated if preoperative frailty state measured using a single wearable sensor can predict 30-day major adverse events (i.e., myocardial infarction, stroke, all-cause mortality) in people with critical limb-threatening ischemia after lower extremity revascularization [13] (Fig. 10.7). They found the frailty state was able to distinguish the occurrence of 30-day major adverse events. Kang and Najafi used a single wearable sensor to measure biomechanical characteristics during normal daily activities [67]. They found lower level of activity, which is also considered as a domain of frailty, was a strong predictor of the risk of all among older adults with diabetic foot. In another study, Van Epps and colleagues found that frailty is a strong predictor and a better predictor than

age for inflammation and thrombosis in older adults [68]. Although their study was not necessarily on people with diabetes, it provides enough implications on potential impact of frailty in diabetes.

Potential Solutions to Improve Outcomes Among Frail and Pre-frail Diabetic Patients

Then, this question arises: What can we do to prevent (or reverse) frailty or to improve health outcomes in frail or pre-frail diabetic patients? Although frailty has been traditionally considered non-treatable and non-reversible, in 2013, in a consensus conference, it was agreed that frailty state may be reversed with exercise and nutritional solutions [69]. Furthermore, some studies reported possible reverse of frailty in older adults [70, 71]. In this section, we summarize previous methods that researcher has used to improve frailty or a domain of frailty in people with diabetes or diabetic complications, or those at risk of diabetes.

Armstrong and colleagues examined the effect of electrical stimulation on pain level in people with diabetic foot [72]. They reported the electrical stimulation significantly improved pain level after 4 weeks. Najafi and colleagues used plantar electrical stimulation and investigated its effect on postural balance and plantar numbness in people with diabetic foot [73]. They found that daily use of electrical stimulation for 6 weeks significantly improved both postural balance and plantar numbness. Zulbaran-Rojas and colleagues investigated the effect of electrical stimulation on wound healing in people with type 2 diabetes with chronic non-healing wounds [74]. They reported that daily use of electrical stimulation for 4 weeks significantly reduced wound area (22% reduction on average). Another potential solution is mechanical stimulation. For example, Kang and colleagues tested the effect of home-based mechanical stimulation applied to the plantar side of the feet on gait, balance and plantar numbness in people with diabetic foot [75]. They found that daily use of the home-based mechanical stimulation for 4 weeks is effective improving gait speed, balance control, and plantar numbness.

Several studies investigated the effect of exercise on frailty or a domain of frailty in diabetes. Geirsdottir and colleagues investigated the effect of a 12-week resistance exercise intervention on muscle strength and physical function in older adults with prediabetes and type 2 diabetes [76]. They found that the exercise intervention significantly improved muscle strength and physical function. Some recent studies combined the exercise intervention with an interactive computer game, the so-called exergame (Fig. 10.8). Zhou and colleagues investigated the effect of an intradialytic exergame program on psychological distress in people who undergo hemodialysis [77]. They found the exergame program is effective in improving psychological distress. Rahemi and colleagues evaluated the exergame program in improving femoral venous parameters in healthy individuals [78]. They found the exergame program significantly increased the femoral vein mean flow volume and mean velocity and showed its potential in preventing deep venous thrombosis. Grewal and colleagues investigated the effect of exergame on balance control in people with diabetic foot [79]. They reported people with diabetic foot had significant improvement in balance control after the exergame. Despite these studies, we were not able to identify a study that proposed a potential solution that will reverse comprehensive domains of frailty in people with diabetic foot. As such, future research is recommended on this aspect.



Fig. 10.8 Zhou and colleagues have suggested the use of low intensity and gamified non-weight bearing foot and ankle exercise as intradialytic exercise program [62]. These exercises could be tailored for people with limited motilities such as those with plantar ulcer, which in turn may enhance perfusion to lower extremities while reduce lower extremity joint rigidity

Conclusion

Frailty is highly prevalent among people with diabetes and has significant negative impact on health outcomes. Previous research emphasized the importance of appropriate screening of frailty to prevent further deterioration in health state in people with diabetes. Although frailty assessment is not occurring in routine care setting, the development of new technologies may enhance the screening process in the future. Although frailty may be reversed by exercise or other adjunctive treatment, most of the studies in diabetes were limited to report changes in a partial domain of frailty and lack the possibility of reverse in the aspect of comprehensive frailty domain.

References

1. United Nations, Department of Economic and Social Affairs, Population Division. World population ageing 2019 (ST/ESA/SER.A/430). 2019.
2. Fazeli PK, Lee H, Steinhauser ML. Aging is a powerful risk factor for type 2 diabetes mellitus independent of body mass index. Gerontology. 2020;66(2):209.
3. Longo M, Bellastella G, Maiorino MI, Meier JJ, Esposito K, Giugliano D. Diabetes and aging: from treatment goals to pharmacologic therapy. Front Endocrinol. 2019;10:45.
4. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2014;37(Suppl 1):S81–90.
5. World Health Organization. Diabetes fact sheet. Geneva: WHO; 2021. https://www.who.int/news-room/fact-sheets/detail/diabetes.
6. Collaboration ERF. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet. 2010;375(9733):2215–22.
7. McCrimmon RJ, Ryan CM, Frier BM. Diabetes and cognitive dysfunction. Lancet. 2012;379(9833):2291–9.
8. Wong E, Backholer K, Gearon E, Harding J, Freak-Poli R, Stevenson C, et al. Diabetes and risk of physical disability in adults: a systematic review and meta-analysis. Lancet Diab Endocrinol. 2013;1(2):106–14.
9. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol Ser A Biol Med Sci. 2001;56(3):M146–M57.
10. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013;381(9868):752–62.

11. Taffett GE. Physiology of aging. Geriatric medicine. New York, NY: Springer; 2003. p. 27–35.
12. Yen TC, Toosizadeh N, Howe C, Dohm M, Mohler J, Najafi B. Postural balance parameters as objective surgical assessments in low back disorders: a systematic review. J Appl Biomech. 2016;32(3):316–23. https://doi.org/10.1123/jab.2015-0246. PubMed PMID: 26695763; PubMed Central PMCID: PMC6685686.
13. Najafi B, Veranyan N, Zulbaran-Rojas A, Park C, Nguyen H, Nakahara QK, et al. Association between wearable device–based measures of physical frailty and major adverse events following lower extremity revascularization. JAMA Netw Open. 2020;3(11):e2020161.
14. Sinclair AJ, Abdelhafiz AH, Rodriguez-Manas L. Frailty and sarcopenia-newly emerging and high impact complications of diabetes. J Diabetes Complicat. 2017;31(9):1465–73.
15. Perkisas S, Vandewoude M. Where frailty meets diabetes. Diabetes Metab Res Rev. 2016;32:261–7.
16. Barzilay JI, Blaum C, Moore T, Xue QL, Hirsch CH, Walston JD, et al. Insulin resistance and inflammation as precursors of frailty: the Cardiovascular Health Study. Arch Intern Med. 2007;167(7):635–41.
17. Kalyani RR, Corriere M, Ferrucci L. Age-related and disease-related muscle loss: the effect of diabetes, obesity, and other diseases. Lancet Diab Endocrinol. 2014;2(10):819–29.
18. La Sala L, Prattichizzo F, Ceriello A. The link between diabetes and atherosclerosis. Eur J Prev Cardiol. 2019;26(2 Suppl):15–24.
19. Sfyri P, Matsakas A. Crossroads between peripheral atherosclerosis, western-type diet and skeletal muscle pathophysiology: emphasis on apolipoprotein E deficiency and peripheral arterial disease. J Biomed Sci. 2017;24(1):1–25.
20. Tsalamandris S, Antonopoulos AS, Oikonomou E, Papamikroulis G-A, Vogiatzi G, Papaioannou S, et al. The role of inflammation in diabetes: current concepts and future perspectives. Eur Cardiol Rev. 2019;14(1):50.
21. Scicchitano BM, Pelosi L, Sica G, Musarò A. The physiopathologic role of oxidative stress in skeletal muscle. Mech Ageing Dev. 2018;170:37–44.
22. Neville C, Nguyen H, Ross K, Wingood M, Peterson EW, Dewitt JE, et al. Lower-limb factors associated with balance and falls in older adults: a systematic review and clinical synthesis. J Am Podiatr Med Assoc. 2020;110(5):4. https://doi.org/10.7547/19-143. PubMed PMID: 31743051.
23. Menz HB. Biomechanics of the ageing foot and ankle: a mini-review. Gerontology. 2015;61(4):381–8. https://doi.org/10.1159/000368357. Epub 2014/11/18. PubMed PMID: 25402236.
24. Muchna A, Najafi B, Wendel CS, Schwenk M, Armstrong DG, Mohler J. Foot problems in older adults associations with incident falls, frailty syndrome, and sensor-derived gait, balance, and physical activity measures. J Am Podiatr Med Assoc. 2018;108(2):126–39. https://doi.org/10.7547/15-186. PubMed PMID: 28853612; PubMed Central PMCID: PMC6647839.
25. Wrobel JS, Najafi B. Diabetic foot biomechanics and gait dysfunction. J Diabetes Sci Technol. 2010;4(4):833–45. https://doi.org/10.1177/193229681000400411. PubMed PMID: 20663446; PubMed Central PMCID: PMC2909514.
26. Hsu CC, Tsai WC, Chen CP, Shau YW, Wang CL, Chen MJ, et al. Effects of aging on the plantar soft tissue properties under the metatarsal heads at different impact velocities. Ultrasound Med Biol. 2005;31(10):1423–9. https://doi.org/10.1016/j.ultrasmedbio.2005.05.009. Epub 2005/10/15. PubMed PMID: 16223646.
27. Menz HB, Zammit GV, Munteanu SE. Plantar pressures are higher under callused regions of the foot in older people. Clin Exp Dermatol. 2007;32(4):375–80. https://doi.org/10.1111/j.1365-2230.2007.02421.x. Epub 2007/04/12. PubMed PMID: 17425648.
28. Menz HB, Fotoohabadi MR, Munteanu SE, Zammit GV, Gilheany MF. Plantar pressures and relative lesser metatarsal lengths in older people with and without forefoot pain. J Orthop Res. 2013;31(3):427–33. https://doi.org/10.1002/jor.22229. Epub 2012/09/19. PubMed PMID: 22987209.
29. Najafi B, Horn D, Marclay S, Crews RT, Wu S, Wrobel JS. Assessing postural control and postural control strategy in diabetes patients using innovative and wearable technology. J Diabetes Sci Technol. 2010;4(4):780–91. https://doi.org/10.1177/193229681000400403. Epub 2010/07/29. PubMed PMID: 20663438; PubMed Central PMCID: PMC2909506.
30. Orr R. Contribution of muscle weakness to postural instability in the elderly. A systematic review. Eur J Phys Rehabil Med. 2010;46(2):183–220. Epub 2010/05/21. PubMed PMID: 20485224.
31. Davis DH, Rockwood MR, Mitnitski AB, Rockwood K. Impairments in mobility and balance in relation to frailty. Arch Gerontol Geriatr. 2011;53(1):79–83.
32. Schwenk M, Mohler J, Wendel C, Fain M, Taylor-Piliae R, Najafi B. Wearable sensor-based in-home assessment of gait, balance, and physical activity for discrimination of frailty status: baseline results of the Arizona frailty cohort study. Gerontology. 2015;61(3):258–67.
33. Petrofsky J, Lee S, Bweir S. Gait characteristics in people with type 2 diabetes mellitus. Eur J Appl Physiol. 2005;93(5):640–7.
34. Bassett D, Tudor-Locke C. How many steps/day are enough? Preliminary pedometer indices for public health. Sports Med. 2004;34:1–8.
35. Tudor-Locke CE, Bell RC, Myers AM, Harris SB, Lauzon N, Rodger NW. Pedometer-determined ambulatory activity in individuals with type 2 diabetes. Diabetes Res Clin Pract. 2002;55(3):191–9.
36. Morrato EH, Hill JO, Wyatt HR, Ghushchyan V, Sullivan PW. Physical activity in US adults with diabetes and at risk for developing diabetes, 2003. Diabetes Care. 2007;30(2):203–9.

37. Yavuzer G, Yetkin I, Toruner F, Koca N, Bolukbas N. Gait deviations of patients with diabetes mellitus: looking beyond peripheral neuropathy. Eur J Phys Rehabil Med. 2006;42(2):127.
38. Najafi B, Grewal GS, Bharara M, Menzies R, Talal TK, Armstrong DG. Can't stand the pressure: the association between unprotected standing, walking, and wound healing in people with diabetes. J Diabetes Sci Technol. 2017;11(4):657–67. https://doi.org/10.1177/1932296816662959. PubMed PMID: 27510440; PubMed Central PMCID: PMC5588814.
39. Fernando ME, Woelfel SL, Perry D, Najafi B, Khan T, DuBourdieu C, et al. Dosing activity and return to preulcer function in diabetes-related foot ulcer remission: patient recommendations and guidance from the Limb Preservation Consortium at USC and the Rancho Los Amigos National Rehabilitation Center. J Am Podiatr Med Assoc. 2021;111(5):2.
40. de Oliveira AL, Moore Z. Treatment of the diabetic foot by offloading: a systematic review. J Wound Care. 2015;24(12):560. https://doi.org/10.12968/jowc.2015.24.12.560, 2–70. PubMed PMID: 26654736.
41. Schwenk M, Mohler J, Wendel C, D'Huyvetter K, Fain M, Taylor-Piliae R, et al. Wearable sensor-based in-home assessment of gait, balance, and physical activity for discrimination of frailty status: baseline results of the Arizona frailty cohort study. Gerontology. 2015;61(3):258–67. https://doi.org/10.1159/000369095. PubMed PMID: 25547185; PubMed Central PMCID: PMC4452118.
42. Rahemi H, Nguyen H, Lee H, Najafi B. Toward smart footwear to track frailty phenotypes-using propulsion performance to determine frailty. Sensors. 2018;18(6):1763. https://doi.org/10.3390/s18061763. PubMed PMID: 29857571; PubMed Central PMCID: PMC6021791.
43. Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001;56(3):M146–56. https://doi.org/10.1093/gerona/56.3.m146. PubMed PMID: 11253156.
44. Najafi B, Armstrong DG. Gait inefficiency induced by offloading – critically unintended consequences for the diabetic foot in remission. 8th International Symposium on the Diabetic Foot 2019, The Hague, The Netherlands; 2019.
45. Zhou H, Park C, Shahbazi M, York MK, Kunik ME, Naik AD, et al. Digital biomarkers of cognitive frailty: the value of detailed gait assessment beyond gait speed. Gerontology. 2021;68:1–10.
46. Afilalo J, Karunananthan S, Eisenberg MJ, Alexander KP, Bergman H. Role of frailty in patients with cardiovascular disease. Am J Cardiol. 2009;103(11):1616–21.
47. Kulmala J, Nykänen I, Hartikainen S. Frailty as a predictor of all-cause mortality in older men and women. Geriatr Gerontol Int. 2014;14(4):899–905.
48. Lee H, Joseph B, Enriquez A, Najafi B. Toward using a smartwatch to monitor frailty in a hospital setting: using a single wrist-wearable sensor to assess frailty in bedbound inpatients. Gerontology. 2017;64:389. https://doi.org/10.1159/000484241. PubMed PMID: 29176316.
49. Theou O, Cann L, Blodgett J, Wallace LM, Brothers TD, Rockwood K. Modifications to the frailty phenotype criteria: Systematic review of the current literature and investigation of 262 frailty phenotypes in the Survey of Health, Ageing, and Retirement in Europe. Ageing Res Rev. 2015;21:78–94. https://doi.org/10.1016/j.arr.2015.04.001. PubMed PMID: 25846451.
50. Theou O, Brothers TD, Mitnitski A, Rockwood K. Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. J Am Geriatr Soc. 2013;61(9):1537–51. https://doi.org/10.1111/jgs.12420. PubMed PMID: 24028357.
51. Rockwood K, Jones D, Wang Y, Carver D, Mitnitski A. Failure to complete performance-based measures is associated with poor health status and an increased risk of death. Age Ageing. 2007;36(2):225–8. https://doi.org/10.1093/ageing/afl160. PubMed PMID: 17259639.
52. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, et al. A global clinical measure of fitness and frailty in elderly people. CMAJ. 2005;173(5):489–95.
53. Kojima G, Iliffe S, Walters K. Frailty index as a predictor of mortality: a systematic review and meta-analysis. Age Ageing. 2018;47(2):193–200.
54. Cesari M, Gambassi G, van Kan GA, Vellas B. The frailty phenotype and the frailty index: different instruments for different purposes. Age Ageing. 2014;43(1):10–2. https://doi.org/10.1093/ageing/aft160. PubMed PMID: 24132852.
55. Najafi B, Armstrong DG. Smart technology for the diabetic foot in remission. In: Boulton AJM, et al., editors. The foot in diabetes. New York, NY: Wiley; 2020. p. 201–24.
56. Toosizadeh N, Yen TC, Howe C, Dohm M, Mohler J, Najafi B. Gait behaviors as an objective surgical outcome in low back disorders: A systematic review. Clin Biomech. 2015;30(6):528–36. https://doi.org/10.1016/j.clinbiomech.2015.04.005. PubMed PMID: 25921552; PubMed Central PMCID: PMC4714541.
57. Lee H, Joseph B, Enriquez A, Najafi B. Toward using a smartwatch to monitor frailty in a hospital setting: using a single wrist-wearable sensor to assess frailty in bedbound inpatients. Gerontology. 2018;64(4):389–400.
58. Kang GE, Naik AD, Ghanta RK, Rosengart TK, Najafi B. A wrist-worn sensor-derived frailty index based on an upper-extremity functional test in predicting functional mobility in older adults. Gerontology. 2021;67:1–9.
59. Kang GE, Zhou H, Varghese V, Najafi B. Characteristics of the gait initiation phase in older adults with diabetic peripheral neuropathy compared

to control older adults. Clin Biomech. 2020;72:155–60.
60. Kang GE, Yang J, Najafi B. Does the presence of cognitive impairment exacerbate the risk of falls in people with peripheral neuropathy? An application of body-worn inertial sensors to measure gait variability. Sensors. 2020;20(5):1328.
61. Zahiri M, Wang C, Gardea M, Nguyen H, Shahbazi M, Sharafkhaneh A, et al. Remote physical frailty monitoring–the application of deep learning-based image processing in tele-health. IEEE Access. 2020;8:219391–9.
62. Cacciatore F, Testa G, Galizia G, Della-Morte D, Mazzella F, Langellotto A, et al. Clinical frailty and long-term mortality in elderly subjects with diabetes. Acta Diabetol. 2013;50(2):251–60.
63. Chode S, Malmstrom T, Miller D, Morley JE. Frailty, diabetes, and mortality in middle-aged African Americans. J Nutr Health Aging. 2016;20(8):854–9.
64. Takeji Y, Yamaji K, Tomoi Y, Okazaki J, Tanaka K, Nagae A, et al. Impact of frailty on clinical outcomes in patients with critical limb ischemia. Circ Cardiovasc Interven. 2018;11(7):e006778.
65. O'Donovan M, Sezgin D, O'Caoimh R, Liew A. The impact of and interaction between diabetes and frailty on psychosocial wellbeing and mortality in Ireland. Int J Environ Res Public Health. 2020;17(24):9535.
66. Bąk E, Młynarska A, Marcisz C, Bobiński R, Sternal D, Młynarski R. The influence of frailty syndrome on quality of life in elderly patients with type 2 diabetes. Qual Life Res. 2021;30:1–9.
67. Kang GE, Najafi B. Sensor-based daily physical activity: towards prediction of the level of concern about falling in peripheral neuropathy. Sensors. 2020;20(2):505.
68. Van Epps P, Oswald D, Higgins P, Hornick T, Aung H, Banks R, et al. Frailty has a stronger association with inflammation than age in older veterans. Immun Ageing. 2016;13(1):1–9.
69. Morley JE, Vellas B, Van Kan GA, Anker SD, Bauer JM, Bernabei R, et al. Frailty consensus: a call to action. J Am Med Dir Assoc. 2013;14(6):392–7.
70. Kang GE, Sharafkhaneh A, Bryant MS, Nguyen C, Ruiz I, Sharafkhaneh S, et al. Efficacy of telerehabilitation on exercise capacity and frailty in veterans with chronic pulmonary obstructive disease: 1397. Med Sci Sports Exerc. 2021;53(8S):458.
71. McAdams-DeMarco MA, Isaacs K, Darko L, Salter ML, Gupta N, King EA, et al. Changes in frailty after kidney transplantation. J Am Geriatr Soc. 2015;63(10):2152–7.
72. Armstrong DG, Lavery LA, Fleischli JG, Gilham KA. Is electrical stimulation effective in reducing neuropathic pain in patients with diabetes? J Foot Ankle Surg. 1997;36(4):260–3.
73. Najafi B, Talal TK, Grewal GS, Menzies R, Armstrong DG, Lavery LA. Using plantar electrical stimulation to improve postural balance and plantar sensation among patients with diabetic peripheral neuropathy: a randomized double blinded study. J Diabetes Sci Technol. 2017;11(4):693–701.
74. Zulbaran-Rojas A, Park C, El-Refaei N, Lepow B, Najafi B. Home-based electrical stimulation to accelerate wound healing—a double-blinded randomized control trial. J Diabetes Sci Technol. 2021;17:15.
75. Kang GE, Zahiri M, Lepow B, Saleem N, Najafi B. The effect of daily use of plantar mechanical stimulation through micro-mobile foot compression device installed in shoe insoles on vibration perception, gait, and balance in people with diabetic peripheral neuropathy. J Diabetes Sci Technol. 2019;13(5):847–56.
76. Geirsdottir O, Arnarson A, Briem K, Ramel A, Jonsson P, Thorsdottir I. Effect of 12-week resistance exercise program on body composition, muscle strength, physical function, and glucose metabolism in healthy, insulin-resistant, and diabetic elderly Icelanders. J Gerontol A Biomed Sci Med Sci. 2012;67(11):1259–65.
77. Zhou H, Al-Ali F, Kang GE, Hamad AI, Ibrahim RA, Talal TK, et al. Application of wearables to facilitate virtually supervised intradialytic exercise for reducing depression symptoms. Sensors. 2020;20(6):1571.
78. Rahemi H, Chung J, Hinko V, Hoeglinger S, Martinek WA, Montero-Baker M, et al. Pilot study evaluating the efficacy of exergaming for the prevention of deep venous thrombosis. J Vasc Surg Venous Lymph Disord. 2018;6(2):146–53.
79. Grewal GS, Schwenk M, Lee-Eng J, Parvaneh S, Bharara M, Menzies RA, et al. Sensor-based interactive balance training with visual joint movement feedback for improving postural stability in diabetics with peripheral neuropathy: a randomized controlled trial. Gerontology. 2015;61(6):567–74.

11 Anesthesia for the DLS Patient: Minimizing Risk and Maximizing Safety

Kasra Razmjou and Andy Liao

Preoperative Optimization

In an effort to accommodate an aging population with chronic diseases, the American Society of Anesthesiologists (ASA) developed the perioperative surgical home [1]. The PSH aims to optimize patient care through the process of surgery and recovery, beginning in the preoperative stage. During this period, the anesthesiology service will collaborate with the surgeon and primary care physician to evaluate the patient's history, comorbidities, and goals of surgery. They will also make recommendations on additional testing and medical management in preparation for surgery. At this point, the patient's team is focused on optimizing the patient for successful surgery and postoperative recovery. The DLS patient will likely require multiple surgeries and hospitalizations; thus the PSH model is ideal in maintaining anesthesiology's continual presence in the patient's care.

DLS patients tend to have several medical comorbidities including hypertension, coronary artery disease (CAD), arrhythmia, cerebrovascular disease (CVD), obesity, hyperlipidemia, renal disease, elderly age (60+ years of age), chronic lung disease, and history of smoking [2, 3]. These disease processes all negatively impact the cardiovascular system and should be medically optimized in preparation for anesthesia.

In 2014, the American College of Cardiology (ACC) and American Heart Association (AHA) developed guidelines for perioperative cardiovascular evaluation for the management of patients undergoing noncardiac surgery [4]. These guidelines provide a stepwise algorithm stratifying the risk of patients with potential cardiovascular conditions. The first step assesses the urgency of surgery for patients with risk factors or a history of CAD [5]. Risk factors for CAD were first introduced by the Framingham Heart Study [6], but now can be taken from the ACC/AHA Atherosclerotic Cardiovascular Disease (ASCVD) risk calculator [7]. This tool considers age, low-density lipoprotein (LDL), total cholesterol, blood pressure, diabetes, and smoker status. These risk factors and the urgency of surgery should be evaluated in a discussion between the surgeon and anesthesiologist. If surgery can be delayed, the ideal plan of action involves treating the underlying cardiovascular issues prior to surgery. Unfortunately, in the DLS population critical limb ischemia and sepsis are common causes of urgent and emergent surgical interventions [8]. The second step evaluates the patient for acute coronary syndrome (ACS), which requires

K. Razmjou (✉)
Regional Anesthesia and Acute Pain Medicine, MedStar Medical Group Anesthesiology, Baltimore, MD, USA
e-mail: kasra.a.razmjou@medstar.net

A. Liao
North American Partners in Anesthesia, Melville, NY, USA

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_11

referral to the cardiology service for evaluation and management. The third step proceeds if the surgery is deemed non-emergent; the patient does not have ACS, but the patient has risk factors for CAD. At this point, the anesthesiology service will assess the patient's risk for major adverse cardiovascular events (MACE) defined as total death, myocardial infarction (MI), stroke, hospitalization due to heart failure (HF), and ACS requiring revascularization via percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG). This risk can be evaluated by the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) or the Revised Cardiac Risk Index (RCRI). Although there has not been a clear consensus on which calculator is superior [9], the RCRI is easier to remember and simpler to use with only six risk factors. The RCRI risk factors include the type of surgery, ischemic heart disease, congestive heart failure (CHF), CVD, insulin dependence, and preoperative creatinine greater than 2 mg/dL. These risk factors are each assigned one point, cumulatively translating into the risk of MACE. A score of two points indicates a 10% risk of MACE and suggests further evaluation and testing may be necessary.

The common comorbidities of the DLS population will likely fulfill several risk factors for MACE and necessitate further cardiovascular evaluation. In patients with elevated risk for MACE, the next step evaluates functional capacity through the Duke Activity Status Index (DASI). This series of self-reported activities correlate with functional status or assesses metabolic equivalents (METs), which can be objectively tested through cardiopulmonary exercise testing. The ACC/AHA guidelines indicate that moderate functional capacity or about 4 METs (and a DASI score of 10) is the minimum requirement for proceeding to surgery. This can be estimated with the ability to walk up two flights of stairs without chest pain or shortness of breath. Most DLS patients will not be able to answer this question accurately and require further assessment due to unknown functional capacity. Exercise stress testing is typically the next step in objectively assessing functional status. This may not be physically feasible for DLS patients, leaving pharmacologic stress testing as the best alternative. If the stress test results are abnormal, the ACC/AHA guidelines recommend considering coronary angiography and revascularization.

In the DLS population, glucose control is especially important in medically optimizing patients for surgery and recovery. Hospital systems may have their own guidelines for appropriate preoperative serum glucose, and the definition of glucose control may vary across groups. Based on the widely cited NICE-SUGAR study, serum glucose is ideally kept in the 140–180 mg/dL range [10]. Although this is based on patients in the intensive care unit, this can be translated to the realm of anesthesia where surgical stress, medically induced comas, and potentially significant fluid shifts can occur. Glucose control is important for proper wound healing and avoidance of hypoglycemic or hyperglycemic coma [11]. Preoperative glucose control will allow for more optimal control in the intraoperative and postoperative settings.

Intraoperative Risk Mitigation

Surgical interventions will inevitably require the specialty care of anesthesiologists, especially within the DLS patient population. This group typically has several comorbidities affecting the cardiovascular system and requires many anesthetic considerations to maximize patient safety.

Nil per os (NPO) guidelines were developed by the ASA in an effort to prevent aspiration risk associated with sedation and anesthesia [12]. The data was based on gastric pH and volumes relative to the time of fasting, resulting in the recommendation of at least 8 h of fasting prior to surgery. However, these guidelines assume normal gastric motility. In the DLS population, diabetic gastroparesis is a possibility and delayed gastric emptying should be considered when assessing NPO status. Although the incidence of gastroparesis is 4.6% in type 1 diabetics and 1.3% in type 2 diabetics [13], abdominal fullness or bloating are associated with diabetic gastroparesis [14] and should be factored into determining

whether a patient is appropriately NPO. The administration of increasing depths of anesthesia can lead to an inability to protect the airway and the aspiration of gastric contents. In the incidence of an increased risk of aspiration, the anesthetic may be modified to use minimal to no sedation with a regional anesthesia technique to preserve airway reflexes, or general anesthesia with an endotracheal tube to ensure a secure airway.

The intraoperative management of DLS patients can include general or regional anesthesia. General anesthesia is defined as the lack of response to surgical stimulus, allowing the surgeon to safely focus on the procedure. General anesthesia involves administering a mixture of sedatives, hypnotics, and analgesics that invariably lead to hypotension and airway obstruction. This may potentially result in organ damage, brain injury, and death if not managed by an experienced anesthesiologist.

Anesthesiologists are prudent about which patients can safely be anesthetized as there are many considerations to be made prior to proceeding with general anesthesia. Other than cardiovascular catastrophes, the ACC/AHA guidelines do not address other concerns in the perioperative period. Patients with obstructive sleep apnea (OSA) are at risk for many anesthesia-related complications [15]. These same patients are commonly obese and may also have difficult airway placement, which can significantly increase the danger of inducing a general anesthetic [16]. General anesthesia is notorious for having a high incidence of nausea, and prophylactic antiemetics are routinely administered [17]. Due to these risks and adverse effects, the use of regional anesthesia, which includes neuraxial anesthesia and peripheral nerve blockade, may be safer.

Neuraxial anesthesia involves the injection of local anesthetic into the epidural and/or intrathecal space to achieve surgical anesthesia at the spinal cord [18]. When neuraxial anesthesia is utilized, it obviates the need for general anesthesia. These patients generally tolerate surgery with minimal or no sedation, which allows the anesthesiologist to avoid the risks associated with general anesthesia.

Neuraxial anesthesia includes two techniques, spinal and epidural. Spinal anesthesia involves intrathecal injection of local anesthetic with or without an adjuvant, resulting in the abolition of motor and sensory transmission from the level of the injected site. Epidural anesthetics involve injection in the epidural space. Catheters may be used for both techniques, allowing for the continuous infusion of local anesthetic. In addition to providing surgical anesthesia, neuraxial catheters can be used postoperatively for pain control. However, the catheter may be a conduit for potential infection, increasing with the amount of time the catheter remains in place. For this reason, neuraxial catheters are usually used for short-term periods. Contraindications to neuraxial blockade include patient refusal, infection at the injection site, systemic infection, coagulopathy, hemodynamic instability or hypovolemia, preload-dependent states such as hypertrophic obstructive cardiomyopathy (HOCM), severe compressive radiculopathy at the level of insertion, and increased cranial pressure [19]. DLS patients are vasculopathic and are commonly on anticoagulation and/or antiplatelet regimen, especially if recently revascularized. This must be weighed in the decision to pursue neuraxial anesthesia due to the increased risk of epidural hematoma [20].

The use of neuraxial blockade intraoperatively raises concern as neural blockade of sympathetic fibers may lead to hypotension; however, this is usually reversible and can be treated with intravenous hydration and vasopressors. Other intraoperative concerns of neuraxial anesthesia include paresthesia due to trauma to the spinal cord, cardiopulmonary compromise due to high spinal level, nausea and vomiting typically caused by hypotension, postdural puncture headache, urinary retention, and infection [21]. Additionally, neuraxial procedures require a cooperating patient to appropriately position, which may not be feasible for a bedbound, deconditioned DLS patient.

Peripheral nerve (or perineural) blockade extends the concept of neuraxial anesthesia, and entails depositing local anesthetics around nerves distal to the spinal cord. The local anesthetic acts to halt the transmission of pain to the spinal cord.

Since injection around the spinal cord is avoided, peripheral nerve blockade circumvents many of the aforementioned adverse effects related to neuraxial anesthesia, especially autonomic blockade. For upper extremity procedures, common brachial plexus nerve blocks include interscalene, supraclavicular, infraclavicular, and axillary nerve blocks. For lower extremity procedures, common nerve blocks aim to block branches of the lumbar and sacral plexus, including the femoral, obturator, lateral femoral cutaneous, and sciatic nerves. Ankle blocks target the distal branches of the femoral and sciatic nerve and are commonly used for foot procedures. The type of block selected is based on the location of surgery and the associated dermatomes, myotomes, and osteotomes. Like neuraxial procedures, peripheral nerve blocks can be extended with the use of catheters for postoperative pain control.

Peripheral nerve blocks were historically performed based on anatomic landmarks and patient feedback via transient paresthesia. The advent of peripheral nerve stimulators allows the anesthesiologist to assess if the location of the needle is adequate based on the motor response elicited relative to a programmed current. The development of ultrasound technology has allowed providers to achieve successful nerve blockade at a higher rate with a lower amount of local anesthetic, thus reducing the risks of local anesthetic systemic toxicity among other adverse effects [22]. Similar to neuraxial anesthesia, peripheral nerve blockade can be used to obtain surgical anesthesia with minimal to no sedation. Peripheral nerve blocks also avoid many of the risks related to neuraxial anesthesia. Although rare, nerve injury, infection, and local anesthetic systemic toxicity may occur with any regional anesthesia technique. Due to the relative safety of this approach, peripheral nerve blockade is an attractive alternative [23].

Postoperative Recovery Optimization

Up to 40,000 amputations are performed in the United States (US) annually. In 2005, 1.6 million people in the US were living with a limb amputation [24]. Amputation may have sequelae of residual limb pain (RLP), sometimes referred to as stump pain, and phantom limb pain (PLP). Both phenomena can develop into chronic pain after amputation (CPAP) [25]. RLP occurs at the actual site of the amputated limb and is caused by nerve entrapment, neuroma formation, surgical trauma, ischemia, skin breakdown, or infection [26]. PLP is described as chronic, severe pain or unpleasant sensation in a part of the body that no longer exists after amputation. PLP develops as early as 24 h to 1 week after amputation. The prevalence of PLP varies from 40 to 80% depending on the site of amputation, causation leading to amputation, and time since amputation [27]. In differentiating RLP from PLP, a thorough physical exam of the amputation site can rule out RLP, and other pain findings such as the quality and severity of pain, sensation, allodynia, and hyperalgesia should be noted as well. Patients with chronic back pain with radiculopathy can be mistaken for PLP and should be ruled out [28]. The exact cause for the development of PLP is unclear, but has been found to be multifactorial including peripheral, central, and psychological factors. Phantom limb sensation (PLS), RLP, preamputation pain, and diabetes are risk factors for developing PLP [29].

While treatment of RLP involves addressing the underlying cause, treatment for PLP) is more difficult and focuses on symptom management. Poor management of PLP may lead to increased incidence of obesity, cardiovascular disease, sleep disorders, chronic joint pain, and lower back pain [30]. A conservative, interdisciplinary approach to preventing PLP involving physical therapists, prosthetic professionals, mental health professionals, and pain specialists is beneficial in addressing potential RLP and PLP.

Common pharmacotherapies for PLP such as NSAIDs and acetaminophen are starting points for any pain regimen. Opioids are commonly used, but should be used conservatively to avoid tolerance and dependence, and are best used with adjuvants. Adjuvant medications include tricyclic antidepressants (TCAs) such as amitriptyline, and anticonvulsants such as gabapentin and pregabalin. Although both TCAs and anticonvul-

sants have been extensively studied, both show mixed results, and evidence has been inconclusive for recommendation. NMDA antagonists such as ketamine may be helpful, especially in patients with chronic pain syndromes. One review analysis recommends a regimen of intravenous ketamine and intravenous morphine for acute treatment of PLP and oral morphine for intermediate- to long-term treatment (8 weeks to 1 year) [31]. Topical capsaicin can help reduce hypersensitivity, and botulinum toxin type B can improve hyperhidrosis to facilitate prosthetic use. However, a Cochrane review for the current pharmacologic interventions in treating PLP concluded the available studies are not large enough to demonstrate evidence that pharmacologic therapies should be recommended in the treatment of PLP [32]. Pharmacologic therapy will remain a mainstay in patient care due to familiarity with the usage of medications, and the convenience of having a treatment modality that physicians can prescribe in the outpatient setting for patients to self-administer at home.

There is much research without definitive evidence for non-pharmacologic options such as transcutaneous electrical nerve stimulation (TENS), spinal cord simulation (SCS), peripheral nerve stimulation (PNS), sympathetic nerve block, mirror therapy, augmented reality biofeedback, acupuncture, and stump revision. Surgical techniques include peri-neuromal lidocaine injection, targeted nerve implantation, and targeted muscle re-innervation. These techniques have shown some efficacy in preventing PLP.

Peripheral nerve blockade has been studied as a non-opioid, non-systemic, targeted pharmacological therapy for preventing and treating PLP). A pilot study in 1991 found that a catheter inserted in the transected nerve sheath infused with 0.25% bupivacaine at 10 mL/h for 72 h significantly reduced postoperative opioid consumption. The patients did not develop PLP at the 12 month follow-up despite the presence of preoperative limb pain. With the growing body of evidence, perineural analgesia is an essential component of the multimodal approach to postoperative limb amputation and in preventing the development of chronic pain.

Regional anesthesia is also beneficial in managing early postoperative pain. A retrospective study in Turkey found that epidural anesthesia or peripheral nerve blockade can reduce RLP and PLP in the first week after limb amputation compared to general anesthesia and spinal anesthesia, but has no difference across anesthetic techniques at 14–17 months postoperation [33]. Another cross-sectional survey found neuraxial anesthesia led to better pain control in the first postoperative week, but was not different from general anesthesia in the development of RLP or PLP at the 14-month mark [34]. A large retrospective cohort study in South Korea determined that the incidence of PLP after limb amputation was highest when general anesthesia was used, then neuraxial anesthesia, and the least with perineural nerve blockade [35]. Although it appears that anesthetic technique does not impact long-term development of chronic pain, perhaps preoperative pain control helps in preventing postoperative pain. A prospective controlled study in England found that an epidural infusion of bupivacaine, clonidine, and diamorphine started 24–48 h preoperatively and maintained for at least 3 days postoperatively led to a significant reduction in the incidence of PLP) at the 1-year follow-up [36]. A randomized, prospective trial in Greece demonstrated perioperative pain control, whether via neuraxial or intravenous patient-controlled analgesia (PCA), will lead to better pain scores and reduced PLP at 6 months [37]. Despite the numerous studies on perioperative pain and the subsequent development of RLP, PLP, and CPAP, the sample subgroups remain relatively small and difficult to compare [38]. However, studies have shown that perioperative pain control can reduce acute perioperative pain [39] and perineural catheters are recommended as part of the analgesic regimen in all patients undergoing amputation [40]. Despite the promising results of these studies on the benefits of perineural catheters in preventing the onset of RLP, PLP, and CPAP, the evidence remains small and the results are conflicting [41].

Neuraxial and perineural catheters can lead to infection, especially in diabetic patients [42], and the recommendation is to remove and/or replace

both neuraxial and perineural catheters after 4 days [43]; however, the practice varies by hospital. While any infection is a concern in this patient population, infections related to neuraxial catheters can be disastrous since the development of an epidural abscess may necessitate surgical intervention. Perineural catheter infections are generally less significant and rarely require more than short-term antibiotic treatment. There is an ongoing investigation into colonization of catheters and eventual infection [44]. Coagulase-negative staphylococcus is the most commonly found microbe colonizing the catheter, and independent risk factors associated with increased colonization include catheter placement greater than 48 h, diabetes, and use of antibiotics in the month prior to surgery [45]. In this same study, it was noted that the incidence of catheter colonization was mostly from interscalene and femoral catheters. It is imperative to consult the APS for managing these catheters.

The postoperative pain management of DLS patients relies on a robust acute pain service (APS). The APS can help place and manage epidural and perineural catheters, and includes replacing them if dislodged and/or are ineffective, or manipulating the dosage to effect. The APS can also help manage the complex analgesic medications that these patients may be administered.

The PSH model has been in practice for 20 years and is becoming more widespread nationwide. This multidisciplinary approach leads to more usage of Enhanced Recovery after Surgery (ERAS) protocols [46], improved outcomes, more meaningful perioperative measures, and improved costs and efficiency [47]. The optimal care of DLS patients requires early involvement of anesthesia and acute pain services. The anesthesia service is essential to optimize patients prior to surgery and minimize risk intraoperatively. The utilization of an APS employing anesthesia providers with specialized skills for interventional procedures and managing pain syndromes is essential for a successful PSH, especially in the postoperative period [48]. Overall, the PSH model helps improve patient outcomes, improve patient satisfaction, and decrease medical expenditures.

References

1. American Society of Anesthesiologists. https://www.asahq.org/. Accessed 25 Dec 2020.
2. Ciocan R-A, et al. Demographic and comorbidity pattern of patients with critical limb ischemia. Folia Med. 2017;59:14–22. https://doi.org/10.1515/folmed-2017-0014.
3. Abou-Zamzam A, et al. A prospective analysis of critical limb ischemia: factors leading to major primary amputation versus revascularization. Ann Vasc Surg. 2007;21:458–63. https://doi.org/10.1016/j.avsg.2006.12.006.
4. Fleisher LA, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. Circulation. 2014;130(24):e278–333. https://doi.org/10.1161/CIR.0000000000000106.
5. NYSORA. Spinal anesthesia. NYSORA, September 13, 2018. https://www.nysora.com/techniques/neuraxial-and-perineuraxial-techniques/spinal-anesthesia/.
6. Hajar R. Risk factors for coronary artery disease: historical perspectives. Heart Views. 2017;18(3):109–14. https://doi.org/10.4103/HEARTVIEWS.HEARTVIEWS_106_17.
7. Lloyd-Jones DM, et al. Use of risk assessment tools to guide decision-making in the primary prevention of atherosclerotic cardiovascular disease. J Am Coll Cardiol. 2019;73(24):3153–67. https://doi.org/10.1016/j.jacc.2018.11.005.
8. Conte MS, et al. Global vascular guidelines on the management of chronic limb-threatening ischemia. Eur J Vasc Endovasc Surg. 2019;58(1):S1–109.e33. https://doi.org/10.1016/j.ejvs.2019.05.006.
9. Glance LG, et al. Impact of the choice of risk model for identifying low-risk patients using the 2014 American College of Cardiology/American Heart Association perioperative guidelines. Anesthesiology. 2018;129(5):889–900. https://doi.org/10.1097/ALN.0000000000002341.
10. NICE-SUGAR Study Investigators, et al. Intensive versus conventional glucose control in critically ill patients. N Engl J Med. 2009;360(13):1283–97. https://doi.org/10.1056/NEJMoa0810625.
11. Hines RL, Marschall KE, editors. Stoelting's anesthesia and co-existing disease. 7th ed. Philadelphia, PA: Elsevier; 2018.
12. Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Task Force on preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration. Anesthesiology. 2017;126(3):376–93. https://doi.org/10.1097/ALN.0000000000001452.
13. Syed AR, Wolfe MM, Calles-Escandon J. Epidemiology and diagnosis of gastroparesis

in the United States: a population-based study. J Clin Gastroenterol. 2020;54(1):50–4. https://doi.org/10.1097/MCG.0000000000001231.
14. Jones KL, et al. Predictors of delayed gastric emptying in diabetes. Diabetes Care. 2001;24(7):1264–9. https://doi.org/10.2337/diacare.24.7.1264.
15. Chung F, et al. Society of Anesthesia and Sleep Medicine Guidelines on preoperative screening and assessment of adult patients with obstructive sleep apnea. Anesth Analg. 2016;123(2):452–73. https://doi.org/10.1213/ANE.0000000000001416.
16. Adam Law J, et al. The difficult airway with recommendations for management—part 1—difficult tracheal intubation encountered in an unconscious/induced patient. Can J Anaesth. 2013;60(11):1089–118. https://doi.org/10.1007/s12630-013-0019-3.
17. Weibel S, et al. Drugs for preventing postoperative nausea and vomiting in adults after general anaesthesia: a network meta-analysis. Cochrane Database Syst Rev. 2020;10:CD012859. https://doi.org/10.1002/14651858.CD012859.pub2.
18. NYSORA. Spinal anesthesia.
19. Levine WC, Massachusetts General Hospital, editors. Handbook of clinical anesthesia procedures of the Massachusetts General Hospital. 8th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2010.
20. Gogarten W, et al. Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology. Eur J Anaesthesiol. 2010;27(12):999–1015. https://doi.org/10.1097/EJA.0b013e32833f6f6f.
21. Levine and Massachusetts General Hospital. Handbook of clinical anesthesia procedures of the Massachusetts General Hospital. Philadelphia: Wolters Kluwer.
22. Neal JM, et al. The second American Society of Regional Anesthesia and Pain Medicine evidence-based medicine assessment of ultrasound-guided regional anesthesia: executive summary. Reg Anesth Pain Med. 2016;41(2):181–94. https://doi.org/10.1097/AAP.0000000000000331.
23. Malik O, Brovman EY, Urman RD. The use of regional or neuraxial anesthesia for below-knee amputations may reduce the need for perioperative blood transfusions. Reg Anesth Pain Med. 2018;43(1):25–35. https://doi.org/10.1097/AAP.0000000000000687.
24. Hanyu-Deutmeyer AA, Cascella M, Varacallo M. Phantom limb pain. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2020. http://www.ncbi.nlm.nih.gov/books/NBK448188/.
25. Srivastava D. Chronic post-amputation pain: peri-operative management—review. Br J Pain. 2017;11(4):192–202. https://doi.org/10.1177/2049463717736492.
26. Cascella H-D, Varacallo. Phantom limb pain.
27. Luo Y, Anderson TA. Phantom limb pain: a review. Int Anesthesiol Clin. 2016;54(2):121–39. https://doi.org/10.1097/AIA.0000000000000095.
28. Cohen SP, Raja SN. Pathogenesis, diagnosis, and treatment of lumbar zygapophysial (facet) joint pain. Anesthesiology. 2007;106(3):591–614. https://doi.org/10.1097/00000542-200703000-00024.
29. Noguchi S, et al. Factors affecting phantom limb pain in patients undergoing amputation: retrospective study. J Anesth. 2019;33(2):216–20. https://doi.org/10.1007/s00540-018-2599-0.
30. Luo, Anderson. Phantom limb pain.
31. McCormick Z, et al. Phantom limb pain: a systematic neuroanatomical-based review of pharmacologic treatment. Pain Med. 2014;15(2):292–305. https://doi.org/10.1111/pme.12283.
32. Maria JM, Alviar TH, Lim-Dungca M. Pharmacologic interventions for treating phantom limb pain. Cochrane Database Syst Rev. 2016;10:CD006380. https://doi.org/10.1002/14651858.CD006380.pub3.
33. Sahin SH, et al. A retrospective trial comparing the effects of different anesthetic techniques on phantom pain after lower limb amputation. Curr Ther Res Clin Exp. 2011;72(3):127–37. https://doi.org/10.1016/j.curtheres.2011.06.001.
34. Ong BY, Arneja A, Ong EW. Effects of anesthesia on pain after lower-limb amputation. J Clin Anesth. 2006;18(8):600–4. https://doi.org/10.1016/j.jclinane.2006.03.021.
35. Cho H-S, et al. Effects of different anesthetic techniques on the incidence of phantom limb pain after limb amputation: a population-based retrospective cohort study. Korean J Pain. 2020;33(3):267–74. https://doi.org/10.3344/kjp.2020.33.3.267.
36. Jahangiri M, et al. Prevention of phantom pain after major lower limb amputation by epidural infusion of diamorphine, clonidine and bupivacaine. Ann R Coll Surg Engl. 1994;76(5):324–6.
37. Karanikolas M, et al. Optimized perioperative analgesia reduces chronic phantom limb pain intensity, prevalence, and frequency: a prospective, randomized, clinical trial. Anesthesiology. 2011;114(5):1144–54. https://doi.org/10.1097/ALN.0b013e31820fc7d2.
38. Rathmell JP, Kehlet H. Do we have the tools to prevent phantom limb pain? Anesthesiology. 2011;114(5):1021–4. https://doi.org/10.1097/ALN.0b013e31820fc80d.
39. Srivastava. Chronic post-amputation pain.
40. Kent ML, et al. Perioperative pain management strategies for amputation: a topical review. Pain Med. 2017;18(3):504–19. https://doi.org/10.1093/pm/pnw110.
41. Nikolajsen L, et al. Randomised trial of epidural bupivacaine and morphine in prevention of stump and phantom pain in lower-limb amputation. Lancet. 1997;350(9088):1353–7. https://doi.org/10.1016/S0140-6736(97)06315-0.
42. Ata A, et al. Postoperative hyperglycemia and surgical site infection in general surgery patients. Arch Surg. 2010;145(9):858–64. https://doi.org/10.1001/archsurg.2010.179.
43. Bomberg H, et al. Prolonged catheter use and infection in regional anesthesia: a retrospective regis-

try analysis. Anesthesiology. 2018;128(4):764–73. https://doi.org/10.1097/ALN.0000000000002105.
44. Caricato A, Antonelli M. Colonization, contamination, or infection in perineural catheters: how to discriminate? Minerva Anestesiol. 2018;84(3):292–3. https://doi.org/10.23736/S0375-9393.17.12418-1.
45. Aveline C, et al. Perineural ultrasound-guided catheter bacterial colonization: a prospective evaluation in 747 cases. Reg Anesth Pain Med. 2011;36(6):579–84. https://doi.org/10.1097/AAP.0b013e31822e665a.
46. Elhassan A, et al. Perioperative surgical home models and enhanced recovery after surgery. J Anaesthesiol Clin Pharmacol. 2019;35(Suppl 1):S46–50. https://doi.org/10.4103/joacp.JOACP_47_18.
47. Kash BA, et al. The perioperative surgical home (PSH): a comprehensive review of US and non-US studies shows predominantly positive quality and cost outcomes. Milbank Q. 2014;92(4):796–821. https://doi.org/10.1111/1468-0009.12093.
48. Zaccagnino MP, et al. The perioperative surgical home: a new role for the acute pain service. Anesth Analg. 2017;125(4):1394–402. https://doi.org/10.1213/ANE.0000000000002165.

Further Reading

Abou-Zamzam A, Gomez N, Molkara A, Banta J, Teruya T, Killeen J, Bianchi C. A prospective analysis of critical limb ischemia: factors leading to major primary amputation versus revascularization. Ann Vasc Surg. 2007;21:458–63. https://doi.org/10.1016/j.avsg.2006.12.006.

Alviar MJM, Hale T, Lim-Dungca M. Pharmacologic interventions for treating phantom limb pain. Cochrane Database Syst Rev. 2016;10:CD006380. https://doi.org/10.1002/14651858.CD006380.pub3.

American Society of Anesthesiologists (n.d.) https://www.asahq.org/. Accessed 25 Dec 2020

Ata A, Lee J, Bestle SL, Desemone J, Stain SC. Postoperative hyperglycemia and surgical site infection in general surgery patients. Arch Surg. 2010;145(9):858–64. https://doi.org/10.1001/archsurg.2010.179.

Aveline C, Le Hetet H, Le Roux A, Vautier P, Gautier JF, Cognet F, Auger P, Bonnet F. Perineural ultrasound-guided catheter bacterial colonization: a prospective evaluation in 747 cases. Reg Anesth Pain Med. 2011;36(6):579–84. https://doi.org/10.1097/AAP.0b013e31822e665a.

Bell T, O'Grady N. Prevention of central line-associated bloodstream infections. Infect Dis Clin N Am. 2017;31(3):551–9. https://doi.org/10.1016/j.idc.2017.05.007.

Bomberg H, Bayer I, Wagenpfeil S, Kessler P, Wulf H, Standl T, Gottschalk A, et al. Prolonged catheter use and infection in regional anesthesia: a retrospective registry analysis. Anesthesiology. 2018;128(4):764–73. https://doi.org/10.1097/ALN.0000000000002105.

Caricato A, Antonelli M. Colonization, contamination, or infection in perineural catheters: how to discriminate? Minerva Anestesiol. 2018;84(3):292–3. https://doi.org/10.23736/S0375-9393.17.12418-1.

Cho H-S, Kim S, Kim CS, Kim Y-J, Lee J-H, Leem J-G. Effects of different anesthetic techniques on the incidence of phantom limb pain after limb amputation: a population-based retrospective cohort study. Korean J Pain. 2020;33(3):267–74. https://doi.org/10.3344/kjp.2020.33.3.267.

Chung F, Memtsoudis SG, Ramachandran SK, Nagappa M, Opperer M, Cozowicz C, Patrawala S, et al. Society of Anesthesia and Sleep Medicine Guidelines on preoperative screening and assessment of adult patients with obstructive sleep apnea. Anesth Analg. 2016;123(2):452–73. https://doi.org/10.1213/ANE.0000000000001416.

Ciocan R-A, Bolboaca S, Radulescu S, Stancu B, Ciocan A, Gherman C. Demographic and comorbidity pattern of patients with critical limb ischemia. Folia Med. 2017;59:14–22. https://doi.org/10.1515/folmed-2017-0014.

Cohen SP, Raja SN. Pathogenesis, diagnosis, and treatment of lumbar zygapophysial (facet) joint pain. Anesthesiology. 2007;106(3):591–614. https://doi.org/10.1097/00000542-200703000-00024.

Conte MS, Bradbury AW, Kolh P, White JV, Dick F, Fitridge R, Mills JL, et al. Global vascular guidelines on the management of chronic limb-threatening ischemia. Eur J Vasc Endovasc Surg. 2019;58(1):S1–109.e33. https://doi.org/10.1016/j.ejvs.2019.05.006.

Elhassan A, Elhassan I, Elhassan A, Sekar KD, Cornett EM, Urman RD, Kaye AD. Perioperative surgical home models and enhanced recovery after surgery. J Anaesthesiol Clin Pharmacol. 2019;35(Suppl 1):S46–50. https://doi.org/10.4103/joacp.JOACP_47_18.

Fleisher LA, Fleischmann KE, Auerbach AD, Barnason SA, Beckman JA, Biykem B, Davila-Roman VG, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. Circulation. 2014;130(24):e278–333. https://doi.org/10.1161/CIR.0000000000000106.

Glance LG, Faden E, Dutton RP, Lustik SJ, Li Y, Eaton MP, Dick AW. Impact of the choice of risk model for identifying low-risk patients using the 2014 American College of Cardiology/American Heart Association perioperative guidelines. Anesthesiology. 2018;129(5):889–900. https://doi.org/10.1097/ALN.0000000000002341.

Gogarten W, Vandermeulen E, Van Aken H, Kozek S, Llau JV, Samama CM, European Society of Anaesthesiology. Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology. Eur J Anaesthesiol. 2010;27(12):999–1015. https://doi.org/10.1097/EJA.0b013e32833f6f6f.

Hajar R. Risk factors for coronary artery disease: historical perspectives. Heart Views. 2017;18(3):109–

14. https://doi.org/10.4103/HEARTVIEWS.HEARTVIEWS_106_17.

Hanyu-Deutmeyer AA, Cascella M, Varacallo M. Phantom limb pain. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2020. http://www.ncbi.nlm.nih.gov/books/NBK448188/.

Hines RL, Marschall KE, editors. Stoelting's anesthesia and co-existing disease. 7th ed. Philadelphia, PA: Elsevier; 2018.

Jahangiri M, Jayatunga AP, Bradley JW, Dark CH. Prevention of phantom pain after major lower limb amputation by epidural infusion of diamorphine, clonidine and bupivacaine. Ann R Coll Surg Engl. 1994;76(5):324–6.

Jones KL, Russo A, Stevens JE, Wishart JM, Berry MK, Horowitz M. Predictors of delayed gastric emptying in diabetes. Diabetes Care. 2001;24(7):1264–9. https://doi.org/10.2337/diacare.24.7.1264.

Karanikolas M, Aretha D, Tsolakis I, Monantera G, Kiekkas P, Papadoulas S, Swarm RA, Filos KS. Optimized perioperative analgesia reduces chronic phantom limb pain intensity, prevalence, and frequency: a prospective, randomized, clinical trial. Anesthesiology. 2011;114(5):1144–54. https://doi.org/10.1097/ALN.0b013e31820fc7d2.

Kash BA, Zhang Y, Cline KM, Menser T, Miller TR. The perioperative surgical home (PSH): a comprehensive review of US and non-US studies shows predominantly positive quality and cost outcomes. Milbank Q. 2014;92(4):796–821. https://doi.org/10.1111/1468-0009.12093.

Kent ML, Hsia H-LJ, Van de Ven TJ, Buchheit TE. Perioperative pain management strategies for amputation: a topical review. Pain Med. 2017;18(3):504–19. https://doi.org/10.1093/pm/pnw110.

Lambert A, Dashfield A, Cosgrove C, Wilkins D, Walker A, Ashley S. Randomized prospective study comparing preoperative epidural and intraoperative perineural analgesia for the prevention of postoperative stump and phantom limb pain following major amputation. Reg Anesth Pain Med. 2001;26(4):316–21. https://doi.org/10.1053/rapm.2001.23934.

Law JA, Broemling N, Cooper RM, Drolet P, Duggan LV, Griesdale DE, Hung OR, et al. The difficult airway with recommendations for management—part 1—difficult tracheal intubation encountered in an unconscious/induced patient. Can J Anaesth. 2013;60(11):1089–118. https://doi.org/10.1007/s12630-013-0019-3.

Levine WC, Hospital MG, editors. Handbook of clinical anesthesia procedures of the Massachusetts General Hospital. 8th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2010.

Lloyd-Jones DM, Braun LT, Ndumele CE, Smith SC, Sperling LS, Virani SS, Blumenthal RS. Use of risk assessment tools to guide decision-making in the primary prevention of atherosclerotic cardiovascular disease. J Am Coll Cardiol. 2019;73(24):3153–67. https://doi.org/10.1016/j.jacc.2018.11.005.

Luo Y, Anderson TA. Phantom limb pain: a review. Int Anesthesiol Clin. 2016;54(2):121–39. https://doi.org/10.1097/AIA.0000000000000095.

Malik O, Brovman EY, Urman RD. The use of regional or neuraxial anesthesia for below-knee amputations may reduce the need for perioperative blood transfusions. Reg Anesth Pain Med. 2018;43(1):25–35. https://doi.org/10.1097/AAP.0000000000000687.

McCormick Z, Chang-Chien G, Marshall B, Huang M, Norman Harden R. Phantom limb pain: a systematic neuroanatomical-based review of pharmacologic treatment. Pain Med. 2014;15(2):292–305. https://doi.org/10.1111/pme.12283.

Neal JM, Brull R, Horn J-L, Liu SS, McCartney CJL, Perlas A, Salinas FV, Tsui BC-H. The second American Society of Regional Anesthesia and Pain Medicine evidence-based medicine assessment of ultrasound-guided regional anesthesia: executive summary. Reg Anesth Pain Med. 2016;41(2):181–94. https://doi.org/10.1097/AAP.0000000000000331.

NICE-SUGAR Study Investigators, Finfer S, Chittock DR, Su SY-S, Blair D, Foster D, Dhingra V, et al. Intensive versus conventional glucose control in critically ill patients. N Engl J Med. 2009;360(13):1283–97. https://doi.org/10.1056/NEJMoa0810625.

Nikolajsen L, Ilkjaer S, Christensen JH, Krøner K, Jensen TS. Randomised trial of epidural bupivacaine and morphine in prevention of stump and phantom pain in lower-limb amputation. Lancet. 1997;350(9088):1353–7. https://doi.org/10.1016/S0140-6736(97)06315-0.

Noguchi S, Saito J, Nakai K, Kitayama M, Hirota K. Factors affecting phantom limb pain in patients undergoing amputation: retrospective study. J Anesth. 2019;33(2):216–20. https://doi.org/10.1007/s00540-018-2599-0.

NYSORA. Spinal anesthesia. NYSORA, September 13, 2018. https://www.nysora.com/techniques/neuraxial-and-perineuraxial-techniques/spinal-anesthesia/.

Ong BY, Arneja A, Ong EW. Effects of anesthesia on pain after lower-limb amputation. J Clin Anesth. 2006;18(8):600–4. https://doi.org/10.1016/j.jclinane.2006.03.021.

Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration: application to healthy patients undergoing elective procedures: an updated report by the American Society of Anesthesiologists Task Force on preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration. Anesthesiology. 2017;126(3):376–93. https://doi.org/10.1097/ALN.0000000000001452.

Rathmell JP, Kehlet H. Do we have the tools to prevent phantom limb pain? Anesthesiology. 2011;114(5):1021–4. https://doi.org/10.1097/ALN.0b013e31820fc80d.

Sahin SH, Colak A, Arar C, Tutunculer E, Sut N, Yılmaz B, Birtane M. A retrospective trial comparing the effects of different anesthetic techniques on phantom

pain after lower limb amputation. Curr Ther Res Clin Exp. 2011;72(3):127–37. https://doi.org/10.1016/j.curtheres.2011.06.001.

Srivastava D. Chronic post-amputation pain: peri-operative management—review. Br J Pain. 2017;11(4):192–202. https://doi.org/10.1177/2049463717736492.

Syed AR, Wolfe MM, Calles-Escandon J. Epidemiology and diagnosis of gastroparesis in the United States: a population-based study. J Clin Gastroenterol. 2020;54(1):50–4. https://doi.org/10.1097/MCG.0000000000001231.

Weibel S, Rücker G, Eberhart LH, Pace NL, Hartl HM, Jordan OL, Mayer D, et al. Drugs for preventing postoperative nausea and vomiting in adults after general anaesthesia: a network meta-analysis. Cochrane Database Syst Rev. 2020;10:CD012859. https://doi.org/10.1002/14651858.CD012859.pub2.

Yin Y, Zhang L, Xiao H, Wen C-B, Dai Y-E, Yang G, Zuo Y-X, Liu J. The pre-amputation pain and the postoperative deafferentation are the risk factors of phantom limb pain: a clinical survey in a sample of Chinese population. BMC Anesthesiol. 2017;17:69. https://doi.org/10.1186/s12871-017-0359-6.

Zaccagnino MP, Bader AM, Sang CN, Correll DJ. The perioperative surgical home: a new role for the acute pain service. Anesth Analg. 2017;125(4):1394–402. https://doi.org/10.1213/ANE.0000000000002165.

Debridement of the Diabetic Foot and Leg

12

Christopher E. Attinger and Jayson N. Atves

Introduction

The word "debridement" derives from the French *débridement*, which translates into "to remove a constraint." This term was first used by Henri LeDran (1685–1770) (Fig. 12.1) in the context of an incision of skin and fascia to release swelling associated with injury [1]. However, during eighteenth and nineteenth century wartime this definition was greatly refined to include "removal of all materials incompatible with healing in order to prevent gangrene" and it is this definition that still guides clinicians today [2]. Debridement is the excision of foreign, dead, dying, damaged, or infected tissues in order to optimize the healing potential of the remaining healthy and viable tissues. It is performed in a myriad of ways and settings in preparation for soft tissue closure within the steps of the plastics and reconstructive ladder ranging from simple primary closure to the use of complex flaps [3, 4].

Debridement is merely one albeit vital factor in modern wound bed preparation. The fundamental tenets in the management of most lower extremity wounds include the eradication of infection, optimization of local and systemic healing factors, adequate offloading, and/or immobilization with achievement of a biome-



Fig. 12.1 Henry LeDran (1685–1770) first published on *debridement* in the context of an incision of skin and fascia to release swelling associated with injury

C. E. Attinger · J. N. Atves (✉)
Department of Plastic Surgery, Georgetown University School of Medicine and MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: Christopher.Attinger@medstar.net; jayson.atves@medstar.net

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_12

chanically stable and well-aligned extremity through biomechanical correction or accommodation. Diabetic foot and leg wounds in particular require adherence to a multifactorial treatment algorithm that affords the greatest potential for healing while also mitigating costs and minimizing the possibility for recurrence.

Although outside the scope of this chapter, there are numerous factors which may contribute to an acute wound's stagnation into the chronic state and consideration of these factors in addition to sufficient debridement is essential to obtaining and preserving a healthy wound bed. Factors may include a patient's comorbidities, nutrition, glycemic control, smoking status, ambulatory status, wound etiology, biomechanical aberrations, tissue perfusion, access to resources, adherence to prescribed rehabilitation, and perhaps most importantly, wound location and topography. Once the patient and wound have been optimized, several options exist on the plastics reconstructive ladder for definitive wound closure, including primary intention, secondary intention, skin grafting, local tissue transfer, and free tissue transfer [4].

Determining the etiology of a patient's wound, though, is of the utmost importance in order to guide decision making regarding the most appropriate course of wound optimization, including the type of debridement performed. However, it is imperative to understand that debridement type, just as the wound character, may evolve over time, especially in the comorbid population, including individuals with diabetes. Consequently, a thoughtful understanding and careful consideration of the patient, the wound, and feasible methods of debridement are vital to a successful outcome [5].

The achievement of an infection-free, well-aligned and structurally stable lower extremity combined with an appropriately selected mode for soft tissue closure, with optimization of local and systemic healing factors and appropriate offloading and immobilization where warranted, will provide for the best opportunity of a successful outcome both in the acute phases of healing and in the long-term durability and function of the patient. Ultimately, the primary goal in this cascade is the achievement or restoration of maximal ambulatory function within each patient's physical and medical capacity. Debridement though, in its varied forms, is truly the foundation and perhaps the single most important component of this limb salvage cascade (Fig. 12.2).

In this chapter we review the guiding tenets of debridement and offer an assortment of strategies and techniques aimed at appropriate method selection, successful performance, and ultimately a prosperous wound bed preparation. The goals of this chapter will be to gain an understanding and appreciation for the exceptional potential of adequate tissue debridement and its place as a powerful tool in the surgeon's arsenal.

Wound Healing

A review of the normal wound healing cascade is necessary to more clearly understand the complex wound state. Wound healing is a natural physiological reaction to tissue injury. An acute wound is defined as a recent wound that has yet to progress through the sequential stages of wound healing. However, this is not a simple phenomenon but rather involves a complex interplay between numerous cell types, cytokines, mediators, and the vascular system. The traditional cascade of wound healing is described as the sequential and overlapping progression through three phases: inflammation, proliferation, and remodeling [6]. The initial vasoconstriction of blood vessels and platelet aggregation is designed to stop bleeding. This is followed by an influx of a variety of inflammatory cells, starting with the neutrophils. These inflammatory cells, in turn, release a variety of mediators to promote angiogenesis, thrombosis, and reepithelialization. The fibroblasts, in turn, lay down extracellular components which will serve as scaffolding for ultimate wound healing and closure.

The inflammatory phase begins with hemostasis at the initial insult after platelets have collected and adhered at the site of injury to form a hemostatic plug. In this phase, the body activates the clotting cascade and forms a clot to stop continued bleeding. During this process, platelets which have traveled to the site of injury come into contact with collagen, resulting in their acti-



Fig. 12.2 Clinical representation of a sequentially "primed" wound bed (**a**, **b**). In this patient, surgical debridement and local wound care were utilized to eradicate infection and stimulate healing potential (**a**) which led to the formation of a "primed" wound bed (**b**) and ultimately definitive closure via split-thickness skin graft

vation and aggregation. Thrombin initiates the formation of a fibrin plug, which strengthens the platelet clumps into a stable clot. Additionally, platelets contain intracellular structures including alpha-granules that contain growth factors, clotting factors, and other proteins involved in wound healing. Transforming growth factor (TGF-beta) and platelet-derived angiogenesis factor (PDAF) play roles in wound matrix production by promoting collagen production and new capillary formation. Platelet-derived growth factor (PDGF) is one of the key components of wound healing which recruits and activates proinflammatory cells such as fibroblasts, macrophages, monocytes, and neutrophils. These cells, in turn, secrete growth factors such as TGF-beta, fibroblast growth factor (FGF), endothelial growth factor (EGF), and vascular endothelial growth factor (VEGF). These cellular interactions and communications are critical elements in the wound healing cascade. This phase normally lasts a matter of days after the initial insult.

The proliferation or epithelialization phase begins with the proliferation and migration of epidermal cells. Epidermal cells will form linkages with one another and initiate deposition of basement membrane components and degrade the extracellular matrix. Neovascularization occurs at the wound bed causing the formation of granulation tissues, which infiltrates the temporary matrix. Fibroblasts play a crucial role in orchestrating the reorganization of the extracellular matrix into a collagenous matrix through the use of proteases and other enzymes. Growth

factors such as VEGF contribute to the stimulation of angiogenesis to support wound healing. This phase of wound healing can normally last days to weeks in duration.

The remodeling or maturation phase involves slow advances in new tissue strength and flexibility with wound contraction facilitated by fibroblasts that have converted to myofibroblasts stimulated by growth factors. Collagen is continually remodeled through enzymatic degradation by matrix metalloproteinases (MMPs) until final collagen deposition and wound reepithelialization have occurred. This phase's duration can vary greatly lasting from weeks to years.

Wound Bed Preparation

Adequate preparation of a wound bed is the principal aspect of wound management and eventual closure. Functionally speaking the overarching goals of wound bed preparation include effectively removing any and all tissues which would otherwise allow bacterial burden to proliferate, decreasing the overall demand of the local wound site and systemic physiological stress, and stimulating the underlying health of the remaining tissues in order to produce a wound bed which is "primed" for closure (Fig. 12.3). Debridement is the predominant means of achieving these goals of wound bed preparation and should be thought of as not just the gold standard but a necessary treatment modality for nearly every wound type in nearly every patient. Various modes of debridement exist and although most are readily available regardless of clinical setting, individual choice of the particular method of debridement to undertake may depend on clinician and patient access to resources and the logistical feasibility of its implementation (Fig. 12.4).

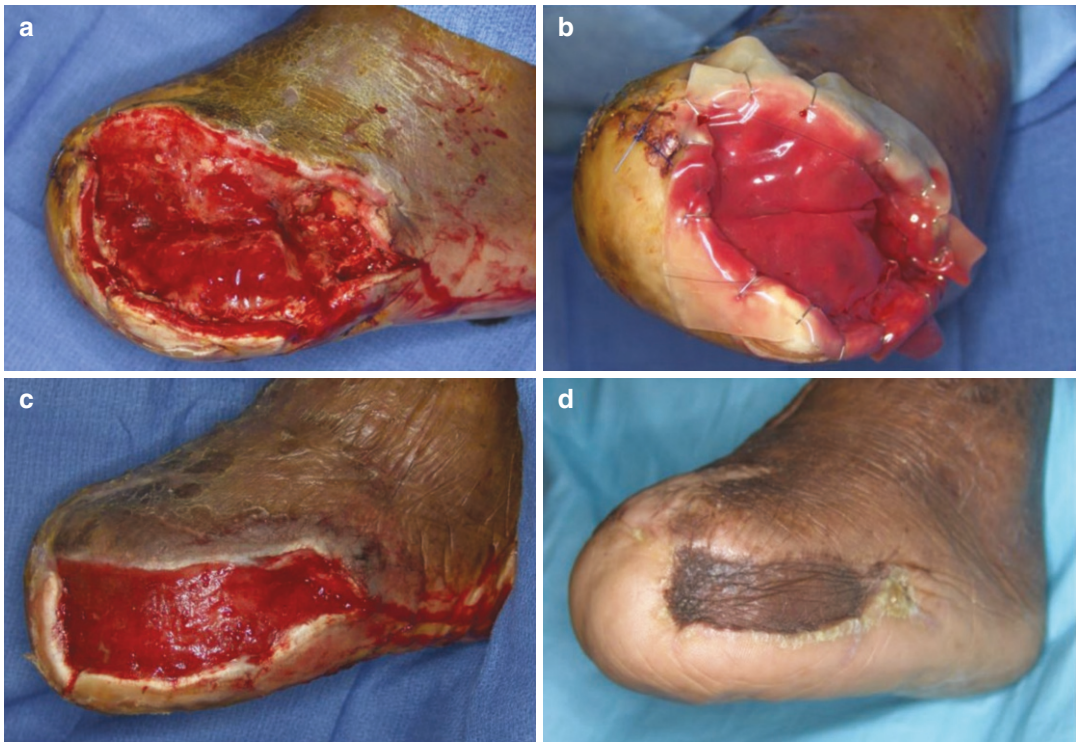


Fig. 12.3 Clinical representation of a sequentially "primed" and ultimately closed wound bed (**a**–**d**) in a patient with a transmetatarsal partial foot amputation. In this patient, surgical debridement and local wound care (**a**) with supplementation via skin substitute grafting (**b**) were utilized to produce a "primed" wound bed (**c**) with subsequent definitive closure via split-thickness skin graft (**d**)

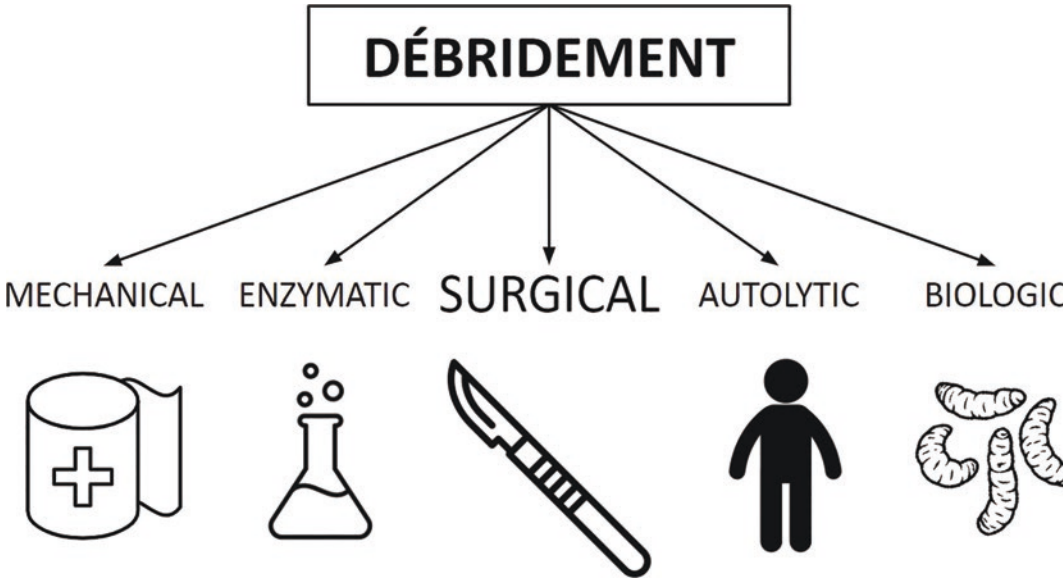


Fig. 12.4 Five modes of debridement exist, including mechanical, enzymatic, autolytic, biologic, and finally surgical. Overwhelmingly, surgical debridement is the most common and varied form of debridement; however, depending on a variety of factors an understanding of the assorted options for debridement is essential

Types of Debridement

Mechanical

Mechanical debridement is perhaps the oldest form of debridement and involves the use of moist or wet flushes or dressings, which are subsequently removed from contact with the wound bed. The removal and physical wound base disruption causes nonselective debridement of loose tissues and slough. Examples include direct wound irrigation with saline, wet-to-dry dressings, and hydrotherapy, including bath and whirlpool. Dressing changes are quite simple and can be performed independently by the patients in many cases. However, because mechanical debridement is considered nonselective in nature, it may remove or damage healthy tissues if not performed judiciously (Fig. 12.5).

Enzymatic

Enzymatic debridement involves using chemical agents to slough necrotic wound tissue. Collectively, these enzymes are derived from microorganisms such as *Clostridium histolyticum* or from plants, including collagenase, varidase, papain, and bromelain. This method is most useful for debridement of wounds with a large amount of necrotic tissue and poses little risk to healthy tissues. This mode of debridement is considered selective in nature; however, judicious use of these products must be implemented so as not to create an environment nonconducive to overall tissue healing.

Autolytic

Autolytic debridement uses the body's own enzymatic processes to debride necrotic tissues and slough. This process interrupts dead and devitalized tissue over time by allowing wound fluids to maintain contact in the wound bed to hydrate, soften, and liquefy necrotic tissue and eschar. This method is achieved with the use of occlusive or semi-occlusive dressings with or without the supplementation of hydrocolloids, hydrogels, and transparent films and is suitable for cases in which the amount of dead tissue is not extensive and there is no infection.



Fig. 12.5 Mechanical debridement in a sequential manner is appreciated spanning approximately 6 months (**a**–**h**). This specific patient utilized mainly mechanical debridement secondary to limitations with pain and inability to safely undergo anesthesia for operative debridement

Autolytic debridement is selective for necrotic tissues, is easy to perform, and is virtually painless to the patient. However, it is by far the slowest type of debridement, and the wound must be rigorously monitored for signs of infection. For these reasons, this method is often reserved for patients with poor access to resources and those contraindicated for the other debridement methods, such as those with intractable pain to the wound during other debridement modes (Fig. 12.6).

Biologic

Biologic debridement employs the use of medical maggots that have been raised in a sterile environment [7]. Several young larvae of the green bottle fly (*Lucilia sericata*) are introduced into a wound bed and secured with a permeable dressing which allows for larvae respiration [8]. The maggots feed selectively on the necrotic tissue of the "host" without injuring living tissue and can quite effectively debride a wound in a



Fig. 12.6 Autolytic debridement in a sequential manner is appreciated spanning approximately 4 months (**a**–**e**). This specific patient utilized mainly autolytic debridement secondary to limitations with access to and resources and contraindications for operative debridement



Fig. 12.7 Use of medical maggots for biologic debridement is a useful and underutilized modality of debridement. An appropriate maggot "house" dressing will permit biologic respiration in order to prevent occlusion, anoxia, and ultimately death of the medical maggots

matter of just a few days. The larvae derive nutrients by secreting a broad spectrum of enzymes that liquefy necrotic tissue for consumption. In an optimum environment, maggots molt twice, increasing in overall size and leaving a clean wound free of necrotic tissue once they are removed. This method has gained popularity over time, but some patients find the method painful, and a patient's aversion to maggots being placed onto the body may impede its use. However, this method has the advantage of being non-surgical in nature and performs quite expediently compared to autolytic or enzymatic debridement with minimal risk to healthy tissues (Fig. 12.7).

Surgical

Surgical debridement is arguably the most common and varied type of debridement. A myriad of instrumentation and adjuncts are used to physically excise dead, dying, or infected tissue from the wound bed, either at the bedside, in the clinic, or in an operating room (Fig. 12.8). The surgeon will debride tissue to viability, as determined by tissue character and the presence of vascularity in healthy tissues, using any combination of instrumentation.



Fig. 12.8 Surgical debridement of severely necrotic tissues of the leg is appreciated both pre-debridement (**a**) and post-debridement (**b**)

Surgical Debridement

Indications

Surgical debridement is best suited for progressive or recalcitrant wounds; larger sized wounds and/or those in atypical or precarious locations; grossly infected wounds; and wounds considered to be of an unknown etiology, which necessitate surgical biopsy or resection. Surgical debridement is considered the most expedient method of debridement because it is very selective and limited only by the skill, experience, and judgement of the surgeon. Overall, surgical debridement affords superior control over which and how much tissue is removed, is the fastest manner to achieve a clean wound bed, and can expedite the healing process in most patients with diabetic foot and leg wounds.

Instrumentation

The surgeon will debride to the level of viable tissue, as determined by tissue character and the presence of vascularity in healthy tissues, using any combination of instruments, such as rongeur, curette, scissors, and scalpel blade (Fig. 12.9). The onus of determining the most appropriate instrumentation should be based on the surgeon's individual preference, availability of instrumentation, and specific wound character, location, and topography. Wounds with overt infection will require arguably more aggressive debridement to reach the level of healthy and living tissues, whereas wounds with no acute signs or symptoms of infection or bioburden may require relatively less overall aggressive debridement. Regardless, surgical debridement should always be performed with the most appropriate instrumentation as deemed by the surgeon and in a manner which is considerate of the surrounding tissue integrity. Perhaps the most deleterious potential complication of surgical debridement is the possibility of injury to the surrounding healthy tissues.

Adjunctive instrumentation for surgical debridement such as the micro water jet device has been developed for an even more meticulous and selective debridement (Fig. 12.10). This device produces a pressurized stream of saline which is dispelled at high speed from its tip and immediately suctioned into the handpiece where the jet action of the saline effectively pulverizes the tissues placed between the outflow and inflow portion of the tip. The authors find this of particularly advantageous use in large surface area wounds where controlled debridement is required. However, it should be noted that the water jet device, although quite beneficial from a practicality standpoint and which provides for precise and controlled debridement, has significant limitations in its ability to debride certain tissue type (i.e., tendon and ligament) and variable tissue topographies and thus should only be used as a supplement to the standard manual instrumentation for traditional surgical debridement. Furthermore, the depth at which the water jet is able to debride in a single pass is fairly shallow and this level of control should not lull the surgeon into believing that use of the water jet alone is a sufficient debridement technique. Again, manual instrumentation is the gold standard for surgical debridement and the water jet should only be utilized as an adjunct, not a replacement.



Fig. 12.9 Surgical debridement instrumentation is appreciated. The time-honored instruments utilized for surgical debridement include, but are not limited to, rounguers, curettes, scissors, and scalpel blades



Fig. 12.10 The micro water jet device is a useful adjunctive instrument utilized for meticulous debridement of tissues of the foot and leg. Despite its obvious benefits, its use should be judiciously implemented as a supplement to the normal manual instrumentation for traditional surgical debridement

Technique

Atraumatic Technique

Regardless of the precise location, topography, or etiology of a wound, proper tissue handling is paramount and may quite literally "make or break" an attempted wound closure, especially in the comorbid population. Sterling Bunnell, M.D. (1882–1957) (Fig. 12.11), first coined the term "atraumatic technique" to describe how tissues ought to be handled during surgery [9]. Although written a century ago, his tenets of tissue handling have remarkably withstood the test of time and are quite pertinent to all surgical specialties today. In the debridement of foot and leg wounds an atraumatic technique should be implemented at all times in order to preserve vascularity to the existing and surrounding tissues and maximize the potential for healing. This is perhaps no more pertinent than in the diabetic and comorbid population, where the risk for complication is exponentially increased. One should minimize excessive traction and manipulation of the tissues. This is best accomplished with strictly intent motions and manipulations and blunt retraction only when necessary for appropriate visualization. Proper instrumentation selection is key to preserving an atraumatic technique. A thorough understanding and knowledge of the available instrumentation and more importantly how well a particular surgical task can be performed in one's own hands is crucial. For example, the authors often prefer to forgo the use of forceps for tissue handling unless



Fig. 12.11 Dr. Sterling Bunnell (1882–1957) first coined the term "atraumatic technique" to describe how tissues ought to be handled during surgery. His tenets remain pertinent to all surgical specialties today, especially in the debridement of the foot and leg

absolutely necessary, especially during suturing as this will cause repeated trauma to the microvasculature of the remaining tissue periphery. Rather, the use of strategically positioned and oriented sutures are best utilized for transposition, rotation, and overall manipulation of tissues during a definitive wound closure attempt. Ideally, when utilizing suture material one should use a nonabsorbable monofilament. The authors prefer a vertical mattress technique when reapproximating most skin layer closures directly for its superior mechanical hold of tensioned stresses. Absorbable monofilament sutures are used when affixing split thickness skin grafts or skin substitute grafts with staple supplementation where warranted; however, this is largely driven by surgeon preference.

Debridement of Skin

Debriding skin consists of removing nonviable and/or nonbleeding skin. Anecdotally, if the injured skin does not blanch, is insensate, and has blistered, it is unlikely that it will survive. This is the equivalent of a third-degree burn. No advantage can be gained by waiting in the hopes that this skin suddenly revitalizes. At the edges and under the dead skin, there is a high concentration of harmful proteases with or without bacteria to inhibit subsequent healing. The protracted course necessary for the dead skin to separate itself from the underlying tissue may lead to functional loss, poor scarring, deeper tissue damage, and disseminated infection. Therefore, the approach to nonviable skin should be to remove it as soon as possible. If the border between live and dead tissue is demarcated clearly, then the skin should be excised along that border. If the border demarcation is unclear, then one should start at the center and remove concentric circles of skin until the level of viable tissue is appreciated. When excising skin, one should seek bleeding at the normal skin edge. Thrombosed venules at the skin edge reflect a complete interruption in the local microcirculation and are an excellent indicator that further skin excision is needed. Only when there is normal arterial bleeding at the edge of the wound can one be satisfied that the cutaneous debridement has been adequate.

When removing the skin, it is important to examine the subcutaneous tissue. If the tissue appears viable but is infected, then a topical antibiotic should be placed on the wound [10–12]. For Pseudomonas infections, 0.25% acetic acid or gentamicin ointment may be more appropriate. For MRSA infections, mupirocin (Bactroban) is an appropriate initial topical antibiotic; however, one should keep in mind that resistance can develop quickly [13].

Debridement of Subcutaneous Tissue

Subcutaneous tissue consists of subcutaneous adipose tissue, cutaneous vessels, and cutaneous nerves. However, due to the decreased concentration of blood vessels in the subcutaneous fat, bleeding at the tissue's edge is not always a reliable indicator of tissue viability. Healthy fat has a shiny yellow color and is soft and resilient. Dead fat has a grey pallor to it, is hard, and is nonpliable. Fat should be debrided until soft yellow normal-appearing fat is attained. Undermining

should be avoided as it threatens the viability of the overlying skin. To prevent desiccation, it is important to keep the fat in a moist environment after debridement. Small blood vessels should be coagulated with bipolar cautery to minimize damage to the surrounding tissues. If the vessels are larger than 2–3 mm, then they should be ligated. Liga-clips are the least reactive foreign body material to accomplish this task. If a suture is to be used, then a small diameter monofilament suture should be used to minimize the risk of facilitating further infection. For example, silk acts like a foreign body and stimulates a vigorous foreign-body reaction, and bacteriostatic, polyglycolic-woven suture has multiple recesses within which bacteria can survive in a semi-protected state.

Nerves, when viable, have a shiny, white, glistening appearance to them. In the subcutaneous tissue, the cutaneous nerves are sensory in function. Intact exposed sensory nerves in a sensate patient can be painful. The decision must be made whether to remove or preserve them. If the nerve is to be preserved, then it has to be kept moist until it can be covered with adequate tissue. A skin graft alone does not provide an adequate tissue interface to prevent pain on contact to the nerve and thus consideration should be given to burying the nerve underneath other tissue or a flap. If the nerve is to be sacrificed, then longitudinal traction should be utilized to allow the nerve to retract within normal tissue when it is cut at the edge of the wound. Taking the epineurium and sewing it over the nerve fascicles with 8-0 or 9-0 suture can minimize the possibility of stump neuroma formation.

Debridement of Deep Tissues

Healthy fascia has a distinct white, glistening, and hard appearance and should be preserved if it appears viable. When devitalized or dead, the appearance is dull, soft, and stringy and is in the process of liquefactive necrosis. All necrotic fasciae should be debrided until solid normal-appearing fascia is reached. Since neurovascular bundles can be close to the overlying fascia, debridement should proceed with caution. The viable fascia must be kept moist in the post-debridement period to avoid desiccation and ultimately necrosis. The underlying muscle must be examined as well. Healthy muscle has a bright red, shiny, and resilient appearance to it and contracts when grasped with forceps or touched with electrocautery. In neuropathic patients, the muscle may have a pale, perhaps yellowish, color and may appear nonviable. It will, however, have some tone and bleed when cut. Frankly dead muscle will be swollen, dull, and grainy when palpated and falls apart when pinched. If viability of the muscle is questionable, it is best to err on the side of caution and remove only what is not bleeding and appears nonviable. Subsequently, the wound should be serially debrided until only viable muscle remains. There is always a question of whether to remove the entire muscle when part of it is dead. Generally, one should remove only what is dead because removing the viable portion of the muscle involves further dissection that may very well compromise blood flow to the surrounding tissues. Tendon debridement is always complex because sacrifice of most tendons may lead to a significant loss of function. All attempts should be made to preserve viable paratenon surrounding the tendon. The tendon must be kept moist after debridement, and this requirement becomes all the more important when the paratenon is removed. The tendon should be covered with viable tissue as soon as the wound is stabilized. Otherwise, the tendon will desiccate, necrose, or become infected. Infected tendon looks dull, soft, and grainy with parts fraying, liquefying, or both. The treatment is to shave the tendon to viable, hard, and shiny texture and appearance and then ensure that it stays moist until it granulates sufficiently to be skin grafted or is clean enough to be covered with other tissue. If the tendon is small or infected, all of the exposed portions should be removed. It is important to make a proximal and distal incision above and below the exposed tendon to ensure that any hidden necrotic tendon is removed also. When the extensor tendons on the dorsum of the foot become exposed, it is hard to preserve them unless they quickly are covered with healthy tissue. If the tendons remain in place while the wound progresses to the point at which it is ready

to be closed, they usually become infected and impede further wound healing until they are removed. When the tendon is larger (i.e., Achilles tendon, anterior tibial tendon, etc.), only that portion of the tendon that is necrotic or infected should be debrided. The hard, shiny tendon underneath should be left intact. Great care should be taken to keep the remaining tendon moist. The Achilles tendon deserves special mention since it is the largest tendon in the body and receives excellent blood supply from the posterior tibial and the peroneal arteries. If exposed and healthy, it should be covered with a local, pedicled or free flap as soon as the wound is stable. If part of the tendon is necrotic, it should be debrided to a hard, shiny tendon. It should be kept moist with an occlusive dressing while granulation tissue forms. Once surrounded by granular tissue the tendon can be skin grafted atop. Granulation tissue formation can be accelerated with the vacuum assisted closure (V.A.C.) device (first covering the tendon with a Vaseline mesh gauze) or with the combined usage of hyperbaric oxygen treatments and a topical growth factor product or skin substitute "graft" [14].

Debridement of Bone

Debridement of necrotic or dead osseous tissue is relatively straightforward. Any soft, nonbleeding bone should be removed. Useful manual instruments include rongeurs, curettes, and rasps. Power instrumentation such as the sagittal saw and the rotary cutting burr is also quite useful, if not necessary. The key in debriding bone is to remove only what is dead and infected, leaving bleeding bone behind. Care should be taken not to significantly disrupt viable bone. In this regard, power instruments are safer to use than rongeurs, chisels, or osteotomes. The best way to debride the osteomyelitic smaller long bones (phalanx, metacarpals, or metatarsals) is to cut slices of bone serially until healthy bone is reached. For larger bones (tibia, fibula, calcaneus, talus, etc.) a rotary cutting burr should be used to remove layer-by-layer of the osteomyelitic bone until healthy bleeding bone is encountered. Copious irrigation should be used to ensure that the heat generated by the burr does not damage the healthy bone. When burring the cortical bone, the process is continued until punctate bleeding is visualized emanating from the cortical bone (Paprika sign). This signifies that healthy bone has been reached. When debriding cancellous bone, bleeding and a normal-appearing marrow is ideal. Biomechanical considerations should not deter the surgeon from debriding enough bone to ensure that all osteomyelitis has been eradicated. Correction of the resultant biomechanical aberration can be made once the wound has been stabilized or healed. Current orthopedic techniques, including bone grafting, antibiotic spacers, and the use of external fixators allow repair of many bone defects with a preservation of alignment and stability. It is important to obtain cultures of what is considered a normal bone margin proximal to the area of debridement and of the debrided osteomyelitic bone. Once the infected bone has been removed and only bleeding healthy bone is left behind, then the wound is "primed" to close, assuming the surrounding soft tissue is also healthy. When healthy uninfected bone remains, only 2–5 days of appropriate antibiotics may be necessary after wound closure [15]. The exception to a 1-week course of antibiotics post closure is when the surgeon suspects that the bone left behind may still harbor osteomyelitis. In this instance, a longer course of antibiotics may be indicated.

Staged Approach

Much has been recognized on the use of a staged approach to lower extremity pathology especially in instances of large soft tissue loss or bony deficit. In truth, surgical wound management is perhaps the prototypical procedure type for a staged approach due to the precarious and potentially catastrophic stakes associated with improper wound management, especially in the diabetic and comorbid population. The successful eradication of infection with minimization of bacterial bioburden should be considered the primary goal of surgical debridement. In this light, it is imperative to accurately and confidently determine the successful acquisition of an infection-free wound bed. This goal may seem simple to the untrained or inexperienced clinician. However, a staged approach is the only manner in which to guaran-

tee the appropriate preparation of a wound bed. Especially in the comorbid population, the eradication of infection and bacterial burden can prove to be a burdensome and exhaustive struggle necessitating numerous returns to the operative theater for continued surgical debridement [16]. Ideally, prior to definitive closure the wound will yield negative microbiology cultures and a healthy progressive character which has not stagnated nor digressed in character with continued infection, bacterial harborization, or tissue necrosis. Rather, tissues will display a progressive improvement in overall character with perhaps improvement in overall wound size. Only once a wound has successfully completed the primary goal of eradication of infection and minimization of bacterial bioburden has it reached candidacy for soft tissue closure. For these reasons we advocate for a staged approach to surgical wound management in order to maximize the potential for a confident closure while minimizing the likelihood for recurrence.

Additionally, we routinely utilize and lobby for the universal use of a two-table or "dual" operative setup for each surgical debridement (Fig. 12.12). In this operative setup the first "dirty" table is utilized for the bulk of surgical debridement and infective source control. Following sufficient debridement and copious lavage of the wound site the second or "clean" table setup is utilized. Between chronological use of the dual tables both outer gloves, draping, and light handles are changed to a new sterile setup. This tact alone provides for significant control of possible cross-contamination of the pre-debridement wound tissues and flora with the post-debridement wound state [17].

Save as Much Tissue as Possible Prior to Closure

An indispensable tact for permitting the greatest potential for soft tissue envelope closure options, regardless of the exact location or topography of the wound, is to save as much of the healthy and viable tissues prior to the definitive closure as possible. This discretion provides several distinct advantages when it comes to the potential closure of a wound site. Namely, by saving as much tissue as is possible during earlier surgical debridements, one does not commit to a specific surgical plan which may very well evolve or change as the wound and the patient react to staged surgical

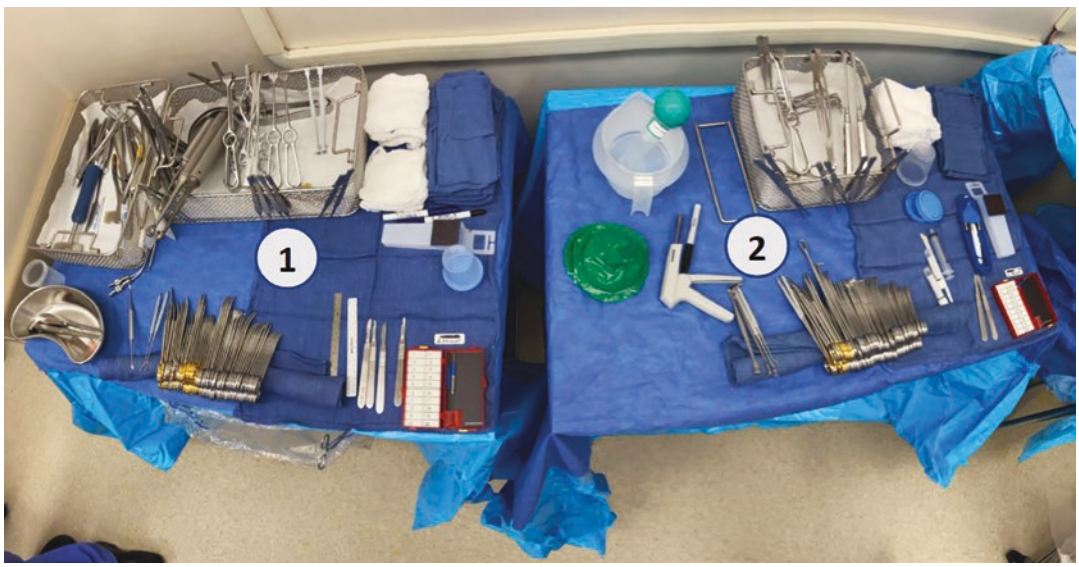


Fig. 12.12 The two-table setup during surgical debridement is a mainstay in our institutions "dirty" operative cases. The judicious prevention of cross-contamination between the "dirty" (1) and "clean" (2) tables is of the utmost importance in order to prevent the spread of bacteria and to avoid the falsification of tissue cultures

debridements. All too often, a surgeon will amputate all toes or rays as part of a drainage amputation to a localized area of infection of the forefoot. While this often ensures the zone of infection has been eradicated, it needlessly disposes of healthy and viable portions of tissue of the toes and forefoot which may have otherwise been utilized during an attempted closure and allows a general contracture of the remaining soft tissues, which can severely limit or even ruin the possibility of a future closure attempt. Saving healthy and viable tissues permits the maintenance of length of tissues, as in the case of a partial foot amputation, which can provide for the much-needed tissues used during a closure attempt.

Methylene Blue

A method employed by the authors to ensure a more accurate evaluation and thus more efficacious debridement, especially those pending soft tissue closure, is to topically "paint" the wound with methylthioninium chloride (methylene blue) immediately prior to surgical debridement (Fig. 12.13). Sharp debridement, sufficient to remove all of the blue-stained tissue, provides a clear delineation between more superficial

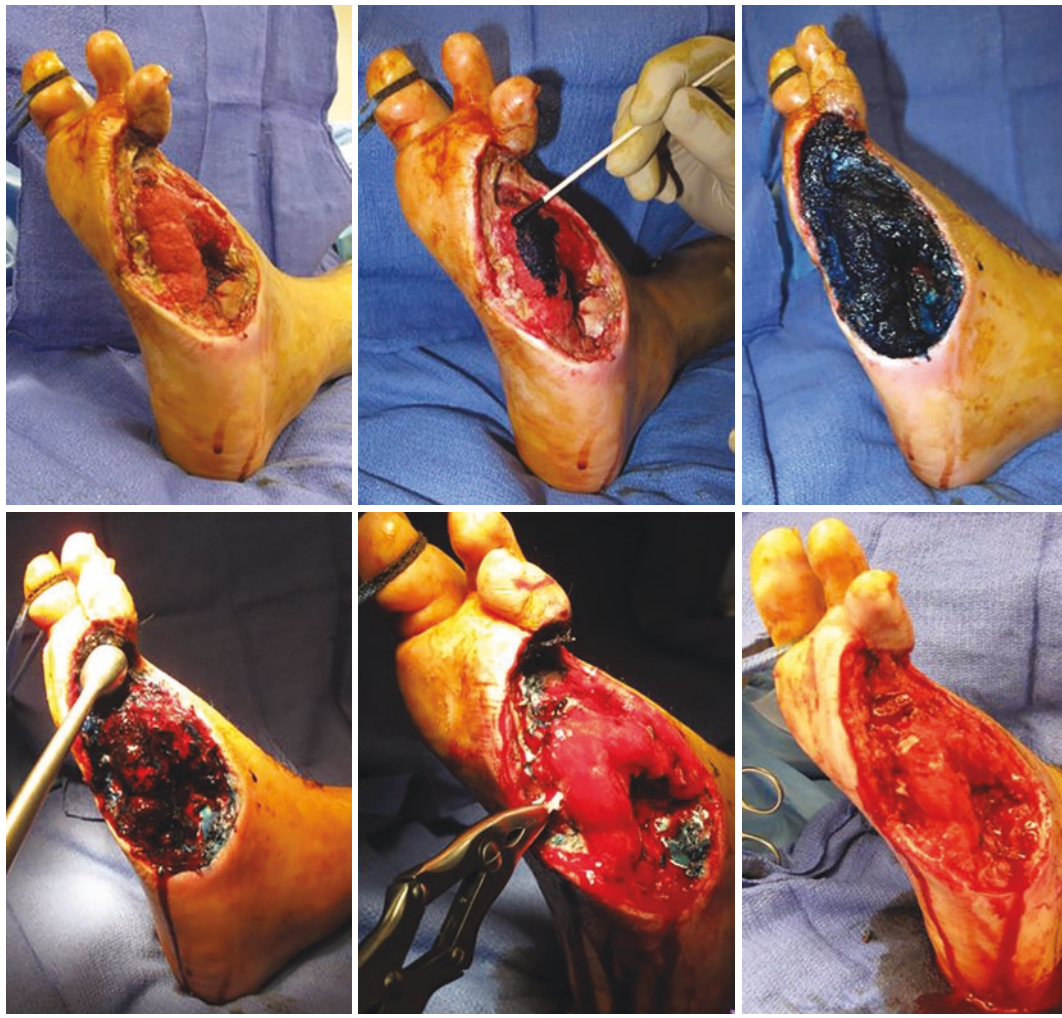


Fig. 12.13 The sequential use of methylthioninium chloride (methylene blue) is a novel method employed at our institution. Sharp debridement, sufficient to remove all of the blue-stained tissue, provides a clear delineation between tissues that harbor bacteria and underlying healthy tissues

exposed tissues that harbor bacterial burden and the healthy tissues below with no deleterious effects to the viable tissues themselves [18].

Assessing Tissue Viability

A vital consideration for the processes of debridement, especially for surgical debridement, is the assessment and ultimately the determination of tissue viability. Those tissues which are foreign, dead, dying, or infected must be removed from the wound bed and failure to do so will mean assured failure of healing. While those tissues that are overtly infected or dead are quite easy to delineate from the frankly healthy and uninjured tissues, it becomes increasingly difficult to make an accurate declaration of tissue viability for those tissues which are merely injured or altered from the wound progression or surgical interventions and lie somewhere between the two ends of the spectrum of tissue health. Additionally, tissues of all varieties and depths may endorse an altered character depending on the overall health of the patient. For these reasons the determination of tissue viability becomes a matter of subjective or qualitative judgement rather than objective or quantitative calculation. Fortunately, through the meticulous process of tissue evaluation one can reliably predict the viability of most tissues based on a thorough clinical and microbiological assessment.

Clinical Determination

A meticulous clinical evaluation of the tissue character is paramount in determining tissue viability. The character of the tissues encountered during surgical debridement may be quite varied and a sufficient evaluation for their viability can be difficult. One should aim to determine the viability of tissues as they relate to the tissue's inherent character. Tissues which deviate more widely from normal quality may be considered nonviable and should be excised. Again, this determination may be easier said than done. However, in this light, we suggest the utilization of several clinical determinants in order to gauge tissue viability. Namely, the color and consistency of tissues are incredibly helpful determinants of tissue viability, or nonviability.

The "color flag" of tissue viability is a useful diagnostic determinate of tissue quality based merely on the color of tissues upon their observation (Fig. 12.14). Healthy and viable tissues will appear red, white, and/or yellow in color. Care should be taken to preserve these tissues during the debridement process. Unhealthy and nonviable tissues will have a black, blue (except for veins), purple, green, brown, and/or orange color to them. These tissues should be clearly and definitively excised in order to properly eradicate their burden within a wound.

Additionally, the consistency of tissues upon palpation and manipulation is a useful determinant of overall viability. Those tissues, especially when seen on the periphery of a wound, which are severely indurated, hardened, and immobile are to be considered nonviable tissues which should be excised. Truthfully, the excision of pathologically altered tissue consistency often permits the mobilization of the remaining tissues for use in primary or delayed primary closure. Alternatively, the removal of indurated and effectively nonviable tissues will account for the removal of stalled tissues which would otherwise impede the healing process of a wound.

Microbiological Determination

Routinely, we perform operative tissue cultures both prior to and immediately following the performance of surgical debridement. These "pre-debridement" and "post-debridement" cultures are an important and guiding diagnostic aspect of wound management. In truth, the culture data can determine the presence of latent infection or chronic bacterial harborization of a wound and are especially useful when the clinical determinants of tissue viability are misleading, as when the wound appears clinically viable and healthy but is actually not yet sufficiently "primed" for closure techniques due to subclinical bacterial harborization. Additionally, culture data are an indispensable adjunct for catering antibiotic choice and duration and when combined with clinical and medical determinants of tissue infection and health can significantly aid in

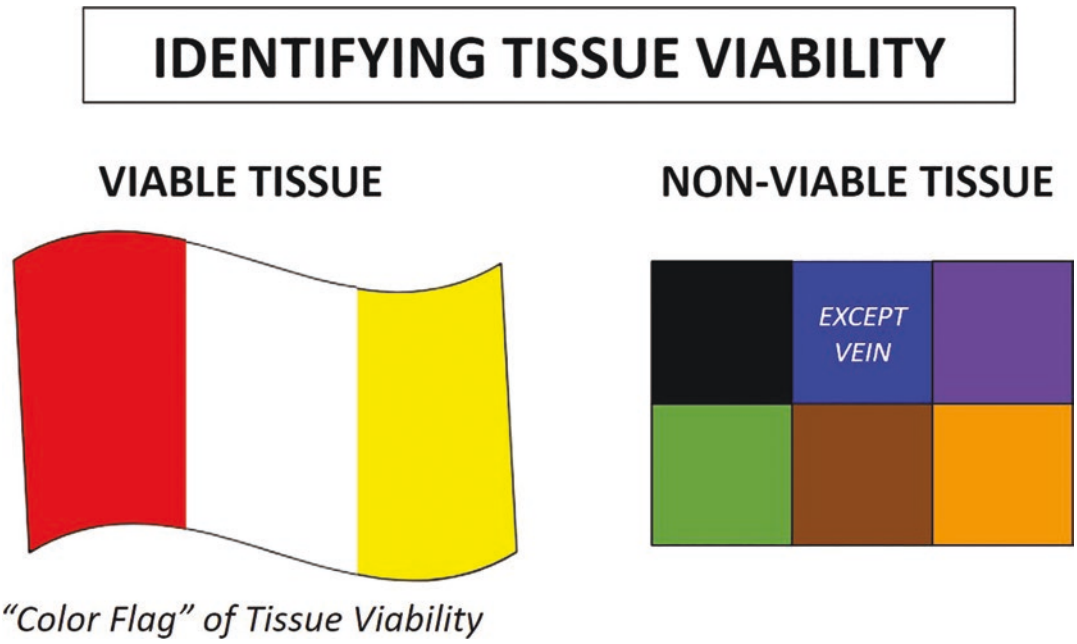


Fig. 12.14 Viable tissues will appear red, white, and/or yellow in color ("Color Flag" of Tissue Viability). Nonviable tissues will appear black, blue (except for veins), purple, green, brown, and/or orange color to them

the clearance of infection and progression of healing. It is important to obtain aerobic and anaerobic cultures of the wound as soon as possible by obtaining a piece of deep, initially unexposed tissue. A swab culture of superficial tissue is of limited utility as it merely reflects the presence of superficial skin flora as opposed to the actual underlying bacteria responsible for the infection. If there is access to a quantitative bacterial culture laboratory, then a minimum of 0.3 cm^3 of tissue specimen is necessary for the culture to be processed. A concentration of greater than 10^5 bacteria per gram of tissue reflects a significant infection that will inhibit healing [19, 20].

Conclusion

With the myriad of local and systemic complications seen in the diabetic and comorbid patient population, treating the complex foot and leg wound environment can be a monumental undertaking for both the patient and physician alike. In chronic wounds, healing is more protracted due to the etiology of the wound being more difficult to determine, and the measures to reverse the medical abnormalities are often much more complex. Even when the wound etiology has been identified and addressed, debridement still plays the prominent role. Debridement converts the chronic wound into an acute state so that it may progress through the normal sequential stages of healing. The key is for clinicians to be aggressive and not allow reservations about the residual tissue defect to limit an appropriate tissue debridement.

Multiple factors and considerations are at play in the diabetic and comorbid populations and must be given attention, respect, and careful consideration in both their assessment and management. A fundamental understanding and working knowledge of the complex interactions between the numerous and varying physiologic components involved in wound healing is paramount. Advances and innovations in research and technology will likely continue to evolve our understanding and ability to efficaciously treat this pathology. To this day, debridement remains the primary means of wound treatment

and is necessary in order to anticipate a successful outcome. However, the surgeon must adapt to the wound as it presents and evolves and cater their treatment modalities to the patient and the environment in which they are treated. Regardless of the exact setting, the multidisciplinary approach should be pursued and utilized. This consortium of disciplines and patient-specific treatment modalities is paramount in order to prevent, heal, and suppress nonhealing wounds in order to ultimately provide patients with the most expedient and functional outcome possible.

Acknowledgments No acknowledgements are made.

References

1. Kamolz LP, Wild T. Wound bed preparation: the impact of debridement and wound cleansing. Wound Med. 2013;1:44–50.
2. Cornell RS, Meyr AJ, Steinberg JS, Attinger CE. Debridement of the noninfected wound. J Vasc Surg. 2010;52:31S–6S.
3. Guthrie HC, Clasper JC. Historical origins and current concepts of wound debridement. J R Army Med Corps. 2011;157:130–2.
4. Attinger CE, Clemens MW, Ducic I, Levin MM, Zelen C. The use of local muscle flaps in foot and ankle reconstruction. In: Dockery GD, editor. Lower extremity soft tissue & cutaneous plastic surgery. 2nd ed. Kidlington: Elsevier Science; 2011. p. 269–88.
5. Attinger CE, Janis JE, Steinberg JS, Schwartz J, Al-Attar A, Couch K. Clinical approach to wounds: debridement and wound bed preparation including the use of dressings and wound-healing adjuvants. Plast Reconstr Surg. 2006;111(Suppl 7):72S–109S.
6. Broughton G, Janis JE, Attinger CE. The basic science of wound healing. Plast Reconstr Surg. 2006;117(7 Suppl):12S–34S.
7. Shi E, Shofler D. Maggot debridement therapy: a systematic review. Br J Commun Nurs. 2014;Suppl Wound Care:S6–13. https://doi.org/10.12968/bjcn.2014.19.Sup12.S6.
8. DeFazio MV, Felder JM III, Economides JM, Attinger CE. Home improvement in Maggot therapy: designing a simple, cost-effective, closed-system habitat to facilitate biodébridement of complex distal lower extremity wounds. Plast Reconstr Surg. 2015;136(5):722e–3e.
9. Bunnell S. An essential in reconstructive surgery: atraumatic technique. Calif State J Med. 1921;19:204.
10. Kucan JO, Robson MC, Heggers JP, Ko F. Comparison of silver sulfadiazine, povidone-iodine and physiologic saline in the treatment of chronic pressure ulcers. J Am Geriatr Soc. 1981;29:232–5.
11. Tredget EE, Shankowsky HA, Groeneveld A, et al. A matched-pair, randomized study evaluating the efficacy and safety of Acticoat silver coated dressing for treatment of burn wounds. J Burn Care Rehabil. 1998;19:531–7.
12. Yin HQ, Langford R, Burrell RE. Comparative evaluation of the antimicrobial activity of Acticort antimicrobial dressing. J Burn Care Rehabil. 1999;20:195–200.
13. Vasquez JE, Walker ES, Franzus BW, et al. The epidemiology of mupirocin resistance among methicillin-resistant Staphylococcus aureus at a Veterans' Affairs hospital. Infect Control Hosp Epidemiol. 2000;21:459–64.
14. Andros G, Armstrong DG, Attinger CE, Boulton AJ, Frykberg RG, Joseph WS, Lavery LA, Morbach S, Niezgoda JA, Toursarkissian B, Tucson Expert Consensus Conference. Consensus statement on negative pressure wound therapy (V.A.C. Therapy) for the management of diabetic foot wounds. Ostomy Wound Manage. 2006 Jun;Suppl:1–32.
15. Lipsky BA, Berendt AR, Cornea PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2012;54(12):e132–73.
16. Elmarsafi T, Garwood CS, Steinberg JS, Evans KK, Attinger CE, Kim PJ. Effect of semiquantitative culture results from complex host surgical wounds on dehiscence rates. Wound Repair Regen. 2017;25:210–6.
17. Carroll AM, Kim KG, Walters ET, Phillips BK, Singh B, Dekker PK, Steinberg JS, Attinger CE, Kim PJ, Evans KK. Glove and instrument changing to prevent bacterial contamination in infected wound debridement and closure procedures: a prospective observational study. Int Wound J. 2021;18:664.
18. Dorafshar AH, Gitman M, Henry G, Agarwal S, Gottlieb LJ. Guided surgical debridement: staining tissues with methylene blue. J Burn Care Res. 2010;31(5):791–4.
19. Krizek TJ, Robson MC. The evolution of quantitative bacteriology in wound management. Am J Surg. 1975;130:579–84.
20. Robson MC, Heggers JP. Delayed wound closure based on bacterial counts. J Surg Oncol. 1970;2:379–83.

13 An Evidence-Based Approach to Treating Osteomyelitis

Benjamin A. Lipsky and Suzanne A. V. van Asten

Introduction

Infections of the foot are a common, complex, and costly complication of diabetes mellitus [1]. They are associated with considerable morbidity, cause substantial discomfort, require extensive medical care (in both outpatient and hospital settings), and frequently lead to serious complications [2, 3]. Among persons with diabetes, about a quarter will develop a foot wound, just over half of which will be infected; the rate of osteomyelitis in these diabetic foot infections (DFIs) ranges from <20% in mild infections to up to 80% in severe infections (Fig. 13.1). Perhaps the most frequent major complication of diabetic DFI is lower extremity amputation. This outcome is associated with 5-year mortality rates of about 50% [4], which exceeds that those of most cancers. Most of the DFIs that lead to hospitalization or amputation are those that progress to involve underlying bone. Thus, diabetic foot osteomyelitis (DFO) has become one of the leading, and fastest growing, causes of bone infection. One study from the USA found that while the rate of osteomyelitis in children and young adults were steady between the years 2000 and 2009, the rate almost tripled among individuals older than 60 years, partly driven by a significant increase in DFO [5]. Furthermore, in this study, despite treatment in a renowned referral medical center (the Mayo Clinic), 68% of those with DFO underwent an amputation.

It is clear that DFIs that involve underlying bone, compared to just skin and soft tissue, are more difficult to successfully treat and are associated with worse clinical outcomes. A study from Pittsburgh found that among patients hospitalized for a DFI, those with bone involvement, compared to those with just soft tissue infection, had a significantly higher: number of operative procedures (an extra 0.5); mean hospital length of stay (by 1 day); and rate of lower extremity amputation (OR 5.6) [6]. Studies from Dallas [7] and Istanbul [8] have shown similar findings, and also significantly longer durations of both antibiotic therapy and time to wound healing for the DFO cases. Similarly, a meta-analysis of 12 studies of DFO found that the likelihood of isolating a multidrug-resistant pathogen was threefold higher than in soft tissue DFI [9]. Thus, optimizing management of DFO is crucial in limiting a variety of associated complications, but especially lower extremity amputations.

B. A. Lipsky (✉)
Department of Medicine, University of Washington, Seattle, WA, USA
e-mail: balipsky@uw.edu

S. A. V. van Asten
Department of Medical Microbiology, Leiden University, Leiden, The Netherlands
e-mail: s.a.v.van_asten@lumc.nl

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_13

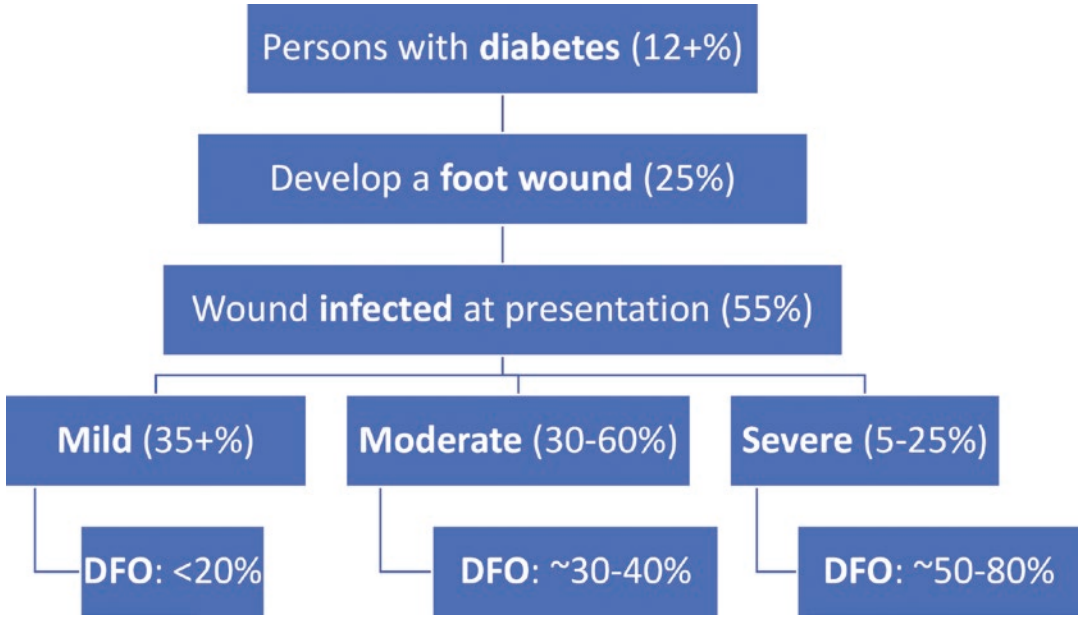


Fig. 13.1 The epidemiology of diabetic foot infections [3]

Pathophysiology

Most cases of DFO represent contiguous spread of infection from adjacent soft tissues to bone [1]. These infections typically begin with a break in the skin envelope, most often related to a diabetic foot ulcer. The main predisposing factors for these ulcers are the long-term presence of peripheral neuropathy, usually accompanied by peripheral arterial disease. Similarly, limited joint mobility or structural deformities (either spontaneous, traumatic, or postoperative) may lead to abnormal weight bearing, thus ulceration. Microorganisms, almost always bacteria, from either contiguous skin flora or an exogenous inoculation, will colonize any open wound. As diabetes of long duration is often accompanied by various humoral and cellular immunological perturbations [10], colonizing organisms can reach critical levels, usually defined as $\geq 10^5$ colony forming units/gram of tissue. At this point signs and symptoms of inflammation, classically redness, warmth, swelling, pain or tenderness, or purulent secretions, may appear. The presence of two or more of these findings classifies the wound as infected. Unchecked, this superficial infection can spread horizontally and vertically, following the path of least resistance along the tendons to involve progressively deeper soft tissues. At some point the infection can involve the cortex of underlying bone (osteitis), and then make its way into the bone medulla or marrow (osteomyelitis). Only in rare instances is DFO specifically a consequence of vascular insufficiency, hematogenous spread, or direct inoculation of microorganisms.

Microbiology

Any microorganism that infects the skin can spread to involve bone. The etiologic agents causing DFI depend on many factors, including the geographic location of the patient (e.g., climate and socio-economic issues), the chronicity of the wound (which can evolve over time), where the infection was acquired (e.g., home versus a health-care institution), specific exposures (e.g., waterborne pathogens like *Pseudomonas*), and any recent antimicrobial treatment (often leading to antibiotic-resistant pathogens). Most DFIs in North American and European countries

are caused by aerobic gram-positive cocci, especially *Staphylococcus aureus*, and to a lesser extent streptococci, enterococci, and coagulase-negative staphylococci [11]. Cultures of specimens from chronic wounds often grow multiple isolates on wound cultures, particularly if they were from a swab rather than tissue. Wound cultures from a patient presenting in a warm climate, with a chronic infection, or who has been recently treated with antimicrobials are more likely to grow aerobic gram-negative organisms, including Enterobacteriaceae and *P. aeruginosa*. Obligately anaerobic bacteria are likely present in many infections, but relatively infrequently isolated because: (1) anaerobic cultures are not specifically ordered or available; (2) appropriate specimens for growing anaerobes (tissue) are not collected; (3) microbiology laboratories often do not process specimens optimally for anaerobes; and (4) reports of the presence of anaerobes are often provided separately and later, and thus do not influence treatment. When anaerobic organisms are reported, they are most often isolated from necrotic or ischemic wounds; they are also more often detected by molecular (genotypic) than standard (phenotypic) microbiologic techniques [12].

As with other DFI, bacteria causing DFO may be resistant to commonly used antibiotics, especially if the patient has recently been treated with antibiotics (topical or systemic). The most common drug-resistant pathogen in DFO is methicillin-resistant *S. aureus* (MRSA) [13]. The incidence of MRSA in DFI, after rising in the late twentieth and early twenty-first century, has decreased more recently. A preliminary study from Rome (likely conducted in the early 2000s) reported that of 765 episodes of DFI among 482 patients, 59.4% of *S. aureus* isolates were MRSA [13]. More recently, a case series of 302 patients with osteomyelitis of the foot and ankle (84% of whom had diabetes) from northern California found that MRSA was isolated in 28.3% of selected patients in 2005, but only 10.6% of selected patients in 2010 ($p = 0.03$) [11].

Several studies have shown that in cases of DFO, cultures of specimens from bone are more accurate than those from soft tissues, even deep tissue specimens near the bone [14, 15]. In general, specimens of bone, compared to those of soft tissue, grow fewer isolates, and most often the predominant pathogen is *S. aureus*. Optimally, a specimen of bone should be obtained by aseptic sampling, either at the time of open surgery or by percutaneous puncture though closed and uninfected skin. Bone specimens taken through an open wound are likely to grow organisms that are contaminants [16]. As with all bacterial cultures, recent or current antibiotic therapy may result in false-negative results. In this case, conducting a histopathologic examination of the specimen may help detect evidence of infection, and even show the Gram-stain morphology of the infecting organism(s). Only a few studies have examined the results of employing molecular microbiological techniques on bone specimens from DFO. In one study of 20 patients in Sydney, DNA sequencing found that 70% of the bone samples had polymicrobial flora, with the most commonly isolated species being *Corynebacterium*, followed by *Finegoldia*, *Staphylococcus*, *Streptococcus*, *Porphyromonas*, and *Anaerococcus* [17]. Another study found that molecular, compared to standard culture, techniques for DFO bone specimens more often revealed anaerobic and fastidious organisms [12]. These results are similar to those from molecular microbiologic studies of soft tissue infections. It remains unclear, however, how to use these data clinically—specifically, which of the several isolated organisms are pathogens that must be specifically targeted with antibiotic therapy.

While sampling a bone specimen provides the most accurate microbiological information for both diagnosing osteomyelitis and selecting pathogen-specific antibiotic therapy, it is not required in every case [18]. Certainly, obtaining a bone specimen is easy if the plan is to operate on the foot. If not, percutaneous bone biopsy is safe, but it requires a skilled clinician, adds expense (for both obtaining and processing the specimen), and takes extra time both to obtain the specimen and for processing (especially for histopathology) [14]. While not always needed, sampling bone is particularly useful when the diagnosis of osteomyelitis remains uncertain based on other

diagnostic studies, or in cases where predicting the pathogen (or its antibiotic susceptibility) is difficult.

Treatment

Osteomyelitis is a difficult infection to treat [19]. Reasons for this include: the infection is usually chronic (characterized by necrotic bone) by the time it is diagnosed; bone has a limited blood flow (and therefore relatively few leukocytes); and the most common pathogens are virulent (e.g., *S. aureus*) and usually biofilm producers [9, 20]. Biofilm infections are characterized by bacteria with a low multiplication rates and reduced susceptibility to antibiotics [21].

Before the 1940s, surgical resection was the only proven successful method of eradicating bone infection. Amputations (most often above-the-knee) were the main treatment for DFO because of concern, in the absence of antibiotic therapy, for infection spreading proximally if all infected bone and soft tissue were not removed. In the early 1940s oral sulfonamide therapy was tried, but with what degree of success is unclear. It was the arrival of penicillin antibiotics in the mid-1940s that led to dramatically improved success rates in treating DFO [19]. While surgical resection was still frequently employed, along with antibiotics, they were more often bone-sparing and any required amputations could usually be performed at a more distal level.

Starting in the mid-1980s reports of outcomes for DFO patients who either refused or could not tolerate surgery demonstrated that antibiotic therapy without bone resection could cure some cases. There are now many published cases series [22, 23], and at least one randomized controlled trial [24], demonstrating that antibiotic therapy without surgery for properly selected patients with DFO can offer similar results to those with surgery. A review of 10 studies of DFO managed with nonsurgical antibiotic treatment found remission rates of 64–83% (Fig. 13.2) [25]. Even with combined antibiotic and surgical therapy, however, failure rates of treatment for DFO can be high. One study that followed 184 cases of foot osteomyelitis (89% of which were in patients known to have diabetes) for a mean of 9 months after they underwent surgical resection found that an unplanned resection of bone or major amputation occurred in 34% of the patients at 1 year, and in 41% by 2 years [26]. Significant risk factors for failure by multivariate analysis included infection with *P. aeruginosa* or *E. coli* and inadequately addressed peripheral arterial disease. Perhaps the most recent and comprehensive guidance for treating DFO is found in the recently updated guidelines on infection from the International Working Group on the Diabetic Foot (IWGDF) [3]. The IWGDF recommendations specific to managing DFO are summarized in Table 13.1.

Surgical Treatment

Surgical resection of infected and necrotic bone was the first, and perhaps remains the principal, approach to treating chronic osteomyelitis. It allows rapid and effective reduction of the bacterial load at the infected site, removes necrotic tissues, and may allow reconstruction that will avoid future foot ulcerations [27]. Surgery may be required in several situations, as when: bone protrudes through the ulcer; imaging reveals extensive bone destruction or progressive bone damage in a patient undergoing antibiotic treatment; the soft tissue envelope is destroyed; or there is gangrene or spreading soft tissue infection [28]. The presence of either limb ischemia or soft tissue infection (especially both) in a case of DFO is associated with a worse prognosis. One study reported that when neither of these complicated DFO, conservative surgery achieved 100% success, while in the cases with ischemia and spreading soft tissue infection 78% required some type of amputation and the mortality rate was 13% [29]. The planned surgical approach to DFO should balance removing as much infected bone as possible against preserving foot function [28]. In the hands of experienced surgeons, "conservative" (foot sparing) surgery, based on preop-

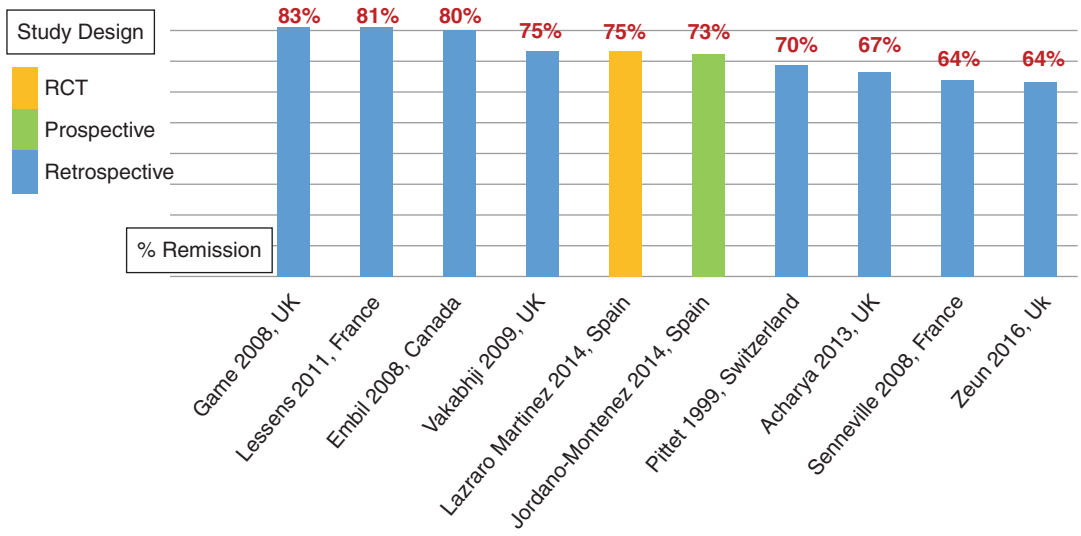


Fig. 13.2 Reported rates of remission of diabetic foot osteomyelitis treated with antibiotic therapy but without surgical resection. (Modified from [25], with permission). *RCT* randomized controlled trial

Table 13.1 Recommendations from the International Working Group on the Diabetic Foot (IWGDF) 2019 guidelines specific to treatment of diabetic foot osteomyelitis (DFO) [3]

Number of the recommendation	Brief description of recommendation	Strength of recommendation; level of evidence
Recommendation 21	(A) In uncomplicated forefoot DFO with no other indication for surgery, consider antibiotic therapy without surgical resection of bone	Strong; moderate
	(B) With probable DFO and concomitant soft tissue infection, urgently evaluate the need for surgery and intensive postoperative medical and surgical follow-up	Strong; moderate
Recommendation 22	Select antibiotic agents for DFO from among those that have demonstrated efficacy for osteomyelitis in clinical studies	Strong; moderate
Recommendation 23	(A) Treat DFO with antibiotic therapy for ≤6 weeks. If infection is not improving within 2–4 weeks: reconsider the need for bone culture; undertake surgical resection; or select an alternative antibiotic regimen	Strong; moderate
	(B) Treat DFO with antibiotic therapy for just a few days if there is no soft tissue infection and all the infected bone has been surgically removed	Weak; low
Recommendation 24	For DFO initially requiring intravenous therapy, consider switching to an oral regimen with high bioavailability after ~5 to 7 days, if the likely or proven pathogens are susceptible to an available oral agent and there is no clinical condition precluding oral therapy	Weak; moderate

erative imaging and intraoperative evaluation with attention to conserving bones and the soft tissue envelope, has produced good long-term outcomes. One prospective study reported a rate of recurrence of infection after conservative surgery for DFO of only 4.6% [30].

Systemic Antibiotic Therapy

Patients who undergo surgical resection for DFO should almost always also receive systemic antibiotic therapy. Exceptions may include cases in which it is clear that all infected bone and soft

tissue have been removed. Treating patients with DFO exclusively with antibiotics may offer the potential to avoid: hospitalization; the expense and risk involved with surgical procedures; and biomechanical problems (e.g., transfer or recurrent ulcers) that may be induced by surgical resection of all or part of the foot [20]. Appropriate cases for nonsurgical treatment are generally those: (1) with infection limited to the forefoot; (2) that do not require extensive soft tissue resection; and (3) in which the causative pathogen is susceptible to highly bioavailable oral antibiotic agents.

After the introduction of penicillin, several other newly developed antibiotic agents were found to be useful for treating bone infections. Starting in the 1970s, studies conducted mainly in the laboratories of Carl Norden (Pittsburgh) and John T. Mader (Galveston) with experimental animal models provided information on characteristics of antibiotics that were associated with better outcomes [22]. In addition to covering the most frequently isolated pathogens, agents that penetrated bone (i.e., had a high bone/serum concentration) appeared to be most clinically useful (Table 13.2). These included penicillins, aminoglycosides, clindamycin, vancomycin, cephalosporins, co-trimoxazole, fluroquinolones, linezolid, and especially rifampi(ci)n. Some believe that bactericidal antibiotics provide better outcomes than bacteriostatic agents for treating osteomyelitis, but there is little published evidence to support this assertion.

Route of Administration

To ensure achieving adequate bone levels of antibiotics, clinicians assumed that high serum concentrations were needed [31]. Achieving these high serum levels to treat osteomyelitis was thought to require parenteral (generally intravenous) therapy. For almost 40 years, however, evidence from case reports and case series suggested that therapy with orally administered antibiotics that had high bioavailability could successfully treat DFO (Table 13.2). The recently published OVIVA study, a randomized controlled multicenter trial in the UK of 1054 evaluable patients treated for complex bone and joint infections (including DFO), demonstrated that predominantly oral antibiotic therapy was noninferior to intravenous antibiotic therapy when used during the first 6 weeks, and was associated with few catheter-related complications and lower financial costs [32]. A retrospective cohort analysis from Switzerland assessing the role of oral amoxicillin/clavulanate in treating DFI reported on the results of 794 cases, including 339 with DFO [33]. They found that the rate of clinical remission with this oral agent was 74%, similar to that with other antibiotic regimens and specifically similar for cases with DFO.

Specific Agents

Recent studies have addressed the value of antibiotics that have been available for decades, but for

Table 13.2 Bioavailability, bone to serum concentration, and activity against biofilm of oral antibiotics for diabetic foot osteomyelitis [27, 31]

Antibiotic agent	Oral bioavailability (%)	Bone/serum concentration (%) activity	Biofilm activity
Fluoroquinolones	65–85	65	Yes
Co-trimoxazole	50	70–90	Yes
Tetracyclines	>90	>70	Yes
Clindamycin	>90	40–67	Yes
Linezolid	>90	>70	Yes
Rifampi(ci)n	>90	40–>90	Yes
Fusidic acid	80–90	44	Yes
Amoxicillin/clavulanate	<80	–	No
Flucloxacillin	5–20	40–75	No
Cefuroxime-axetil	<80	–	No
Clarithromycin	<80	–	?
Metronidazole	>90	100	?

which there have been few studies in DFO (Table 13.3) [34]. A narrative review of the literature from Switzerland found that, in contrast to prevailing opinions and the few descriptive studies available, treatment of osteomyelitis with oral flucloxacillin (a narrow spectrum, safe, low-cost agent) does not appear to be associated with more clinical failures than other oral antibiotic agents

Table 13.3 Systemic (intravenous and/or oral) antibiotic agents to consider for treating diabetic foot osteomyelitis based on bioavailability and bone concentration [34]

Infection severity	Pathogens	Possible antibiotics	Comments
Mild	*Staphylococcus aureus (MSSA)*	Levofloxacin	QD dosing; substandard for *S. aureus*
	(MSSA)	Amoxicillin-clavulanate Cephalexin	Relatively broad spectrum and anti-anaerobic Requires QID dosing; inexpensive
	Streptococcus spp.	Dicloxacillin/ flucloxacillin	Narrow spectrum; QID dosing; inexpensive
		Clindamycin	Covers (most macrolide sensitive) MRSA and anaerobes
	Methicillin-resistant	Doxycycline	MRSA, some gram negatives; QD dosing
	S. aureus (MRSA)	Trimethoprim/ sulfamethoxazole	MRSA, some gram negatives; undefined against *Streptococcus* species
Moderate/ severe	MSSA*; Streptococcus* spp.; *Enterobacteriaceae;* obligate anaerobes	Ertapenem[a]	QD dosing. Broad-spectrum anti-anaerobic; poor against *Pseudomonas aeruginosa*
		Ampicillin-sulbactam	Relatively broad spectrum but not for *P. aeruginosa* or other resistant gram negatives
		Imipenem-cilastatin (other carbapenems)	Broad spectrum; not active for MRSA; consider for proven/suspected ESBL producing pathogens
		Levofloxacin or ciprofloxacin with clindamycin	Both oral and parenteral dosage forms suitable. Limited studies of clindamycin for severe *S. aureus* infections; possible anti-toxin effect
		Moxifloxacin	QD dosing. Broad spectrum, including anaerobes
		Ceftriaxone	QD dosing (IV or IM); 3rd gen. cephalosporin
	MRSA	Linezolid[a]	Oral and IV; adverse effects, drug interactions
		Tigecycline	Broad spectrum including MRSA; frequent gastrointestinal upset; less effective than others
		Vancomycin	Narrow spectrum; rising MICs in MRSA isolates
		Daptomycin	QD dosing; monitor CPK levels
	Pseudomonas aeruginosa	Piperacillin-tazobactam[a]	TID or QID dosing
	MRSA, Enterobacteriaceae, P. aeruginosa, anaerobes	Vancomycin plus:	Very broad spectrum for empiric therapy in severe infections; narrow spectrum when culture and sensitivity results become available
		– Piperacillin-tazobactam, or	
		– Ceftazidime vs. cefepime, or	
		– A carbapenem	

MRSA methicillin-resistant *Staphylococcus aureus, MSSA* methicillin-sensitive *Staphylococcus aureus*
[a] US FDA-approved for diabetic foot infection indication

[35]. The authors concluded that the few published studies demonstrate that after any required debridement, treatment with flucloxacillin by a short intravenous course followed by oral administration is a safe and effective option for treating osteomyelitis, perhaps including DFO.

Rifampi(ci)n is an antibiotic agent that has high bioavailability when taken orally, good penetration into bone, and activity against biofilm organisms, including *S. aureus*. It has been used (always in conjunction with another agent active against *S. aureus* to avoid development of resistance) for decades (especially in Europe) to treat osteoarticular infections, but many clinicians avoid using it because of concerns about resistance and frequent interactions with many other drugs [22]. Recent interest in the potential value for adding rifampi(ci)n to combination therapy for DFO led to an observational cohort study using the database of the US Veterans Health Administration [36]. They found that among 6174 patients treated for DFO with antibiotics (and no amputation), only 130 (2.1%) received rifampin. But, these patients had a significantly lower rate of mortality and amputation within 2 years of diagnosis than those treated without rifampin (odds ratio by logistic regression 0.65, $p = 0.04$). Spurred by these findings, this group is currently conducting a randomized controlled trial of 6 weeks of rifampin therapy (versus placebo) added to conventional treatment (without rifampin) to see the effect on reducing pedal amputations (VA INTREPID) [37].

Some newly marketed antibiotic agents have been approved for treating acute bacterial skin and soft tissue infections (ABSSI), but none have been specifically investigated for DFIs [38]. These include delafloxacin (available in IV and oral formulations), which differs from older fluoroquinolones in having an expanded spectrum of activity that includes MRSA, *P. aeruginosa*, and common obligate anaerobes. Another new agent is omadacycline (available in oral formulation), a tetracycline derivative that is approved for ABSSI that has a very broad spectrum, which even includes vancomycin-resistant enterococci, extended spectrum beta-lactamase producing gram-negative bacilli, and *Acinetobacter baumannii*. These agents, if shown to be effective for DFIs (and specifically DFO), might be useful for treating those that are more serious, polymicrobial, and particularly caused by drug-resistant infections.

Duration of Therapy

Antibiotic therapy is generally given for a considerably longer duration for osteomyelitis than for soft tissue infections—typically 4–6 weeks. Many clinicians, however, treat even longer if all necrotic and infected bone has not been resected [2]. This longer duration of therapy is based more on the theoretical problems associated with treating infected bone, as discussed above, than on data from trials comparing different durations of therapy [22]. Certainly, prolonged treatment of DFO is associated with adverse effects. For example, a study from Dallas of 143 patients with bone biopsy proven osteomyelitis found that 47 (33%) developed acute kidney injury [39]. If there were evidence that prolonged therapy is associated with better clinical outcomes, this benefit might well outweigh the potential risks of higher rates of drug-related adverse events, increased chances of antibiotic resistance developing, or greater financial costs of therapy. The limited available published evidence has not, however, demonstrated any benefit for prolonged therapy.

One open-label, multicenter, controlled randomized study from France compared nonsurgical treatment of DFO with 6 weeks versus 12 weeks of antibiotic therapy [40]. Among the 40 evaluable patients, the remission rate was 65%, with no significant differences between the treatment groups, but with significantly fewer gastrointestinal adverse events in the shorter (6 week) treatment group [40]. Similarly, a retrospective cohort analysis study from Switzerland employing a cluster-controlled Cox regression model assessed factors related to remission of DFIs, including DFO [41]. They found that DFO episodes treated with <3 weeks of antibiotic therapy had similar outcomes to those receiving >3 weeks. They also noted that outcomes were

not significantly different between episodes treated with more than 1 week of intravenous therapy (including the intravenous route throughout the entire course) than for shorter durations of intravenous therapy.

Based on these observations, a recent randomized, non-inferiority pilot trial in Switzerland compared clinical remission and adverse event rates in patients with DFO who underwent surgical debridement, and were then randomized to either 3 weeks or 6 weeks of antibiotic therapy [42]. Among 93 enrolled patients, remission of infection was noted in 84% of patients in the 3-week arm compared to 73% in the 6-week arm, and the rates of adverse events were similar. The same group of investigators is currently conducting a larger trial (with a planned enrollment of 400 diabetic patients with soft tissue or bone infection of the foot) designed to see if they can confirm the results of this pilot study [43]. A group from the UK is also currently undertaking a randomized controlled open-label non-inferiority trial on duration of systemic antibiotic therapy for orthopedic infections treated operatively with local antibiotic therapy [44]. They plan to enroll 500 patients (including those with DFO) who will be treated with either a short course (≤7 days) or long course (≥4 weeks) of systemic antibiotic therapy. The primary endpoint will be definite treatment failure within 12 months of surgery, while secondary outcomes will include treatment side effects, quality of life scores, and cost analysis. For now, it seems unnecessary to treat DFO for more than 6 weeks, and even shorter durations may soon be proven to be sufficient.

Several authorities have reviewed various issues concerning the treatment of DFO in the past few years. A narrative review from France noted that most of the antibiotics that exhibit both satisfactory bone diffusion and oral bioavailability, especially rifampi(ci)n, fusidic acid, and fluoroquinolones, have a substantial propensity to select for resistant mutants; thus, they should be prescribed in combination with agents active against the causative pathogen [31]. A systematic review of interventions for management of DFI identified 11 studies conducted in patients with DFO [45]. The authors deemed that the quality of most of the studies was good, and found no significant differences in the outcomes between the various treatment arms, except for poorer outcomes with tigecycline compared to ertapenem. An evidence-based narrative review of treatment of DFO that particularly focused on the role of surgical as well as antimicrobial therapy included 65 articles [27]. The authors concluded that the main advantage to treating DFO "medically" is that it avoids the biomechanical changes that may occur after surgical procedures, and that it may be more cost effective. They noted that the medical approach is limited by the need for prolonged administration of antibiotics, which is associated with drug-related side effects (including *Clostridioides difficile* disease and the emergence of antibiotic-resistant organisms), risk of relapsing infections (from failing to adequately sterilize bone tissue), and the persistence of any existing bone deformity at the site of the inciting foot ulcer. They point out that antibiotics that achieve the preferred bone to serum concentration ratios of >0.3 (i.e., fluoroquinolones, sulfonamides, tetracyclines, macrolides, rifampi(ci)n, fusidic acid, and oxazolidinones) are also those with the highest oral bioavailability, making them potentially good candidates for prolonged treatment of outpatients with DFO.

Intra-osseus or Topical Antimicrobials

For decades clinicians have treated DFO with a variety of antimicrobial agents (particularly gentamicin, tobramycin, or vancomycin) delivered directly into infected bone in one of several different ways, including in the form of beads (usually polymethylmethacrylate, and more recently calcium sulfate/hydroxyapatite), spacers, or cement [46]. These agents have been used not only to deliver antibiotics to treat bone infection, but to fill dead space, and in some cases to try to prevent infection [47]. Ideal delivery agents should: be biocompatible; have minimal toxicity; allow for osteointegration; and yield prolonged drug release. Although local antibiotic treatments are widely used, there is little high-quality evi-

dence on the appropriate indications, techniques, dosages, types of antibiotics, elution properties, or pharmacokinetics [48, 49].

Outcome of Treatment

Determining the outcome of treatment of osteomyelitis requires having an agreed upon definition of clinical resolution of infection. Clinically, healing of any overlying soft tissue infection or wounds suggests likely clearing of the underlying bone infection. Bone imaging can be helpful in demonstrating probable resolution of infection but, just as evidence of the presence of infection lags the clinical course, resolution of bony changes can lag as well. A fall in previously elevated serum inflammatory markers, especially the erythrocyte sedimentation rate and to a lesser degree C-reactive protein and procalcitonin, may also suggest resolution of infection [14, 15]. In one study of 24 cases of bone biopsy proven DFO prospectively followed during 1 year, 17% had re-infection based on bone biopsy, while 10–20% had failed wound healing, re-ulceration, re-hospitalization, or amputation [50]. Most recurrences of DFO that occur after treatment are diagnosed within a few months, but some present later. Thus, many consider stable and apparently resolved DFO after treatment to be in "remission," and should not be considered cured until the patient has been followed for at least a year.

Key New Trends in Treating DFO

The basic principles of treating DFO were established almost 50 years ago, but in the past few years studies have provided some useful new evidence on optimizing treatment. On the surgical side, it appears that employing more "conservative" (bone sparing) operative procedures is clinically effective and may also reduce postoperative biomechanical problems for patients requiring surgery. On the antibiotic side there are new data supporting some changes in therapy. First, evidence from available studies on the supposed bone penetration of antibiotics is not sufficiently reliable to confidently use this information in selecting an antibiotic regimen. Clinicians should select agents that have demonstrated their effectiveness in clinical trials. Second, antibiotic agents that are active against biofilm organisms may be more effective in treating bone infection. Third, treating osteomyelitis for more than 6 weeks is usually unnecessary, and even shorter durations (perhaps 3 weeks) may be sufficient. Fourth, antibiotic therapy administered predominantly by the oral route appears to be as effective (with lower rates of adverse effects and cost) compared with intravenous therapy. Finally, in appropriately selected cases, antibiotic therapy without surgical resection can resolve DFO. As noted, there are several ongoing trials that should soon further inform our approach to managing this common and difficult infection.

References

1. Lipsky BA. Osteomyelitis of the foot in diabetic patients. Clin Infect Dis. 1997;25:1318–26.
2. Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG, et al. Infectious Diseases Society of America. 2012 Infectious Diseases Society of America clinical practice guideline for diagnosis and treatment of diabetic foot infections guidelines. Clin Infect Dis. 2012;54:e132–73.
3. Lipsky BA, Senneville E, Abbas ZG, Aragón-Sánchez J, Diggle M, Embil JM, et al. International Working Group on the Diabetic Foot (IWGDF). Guidelines on the diagnosis and treatment of foot infection in persons with diabetes (IWGDF 2019 update). Diabetes Metab Res Rev. 2020;36(Suppl 1):e3280.
4. Yammine K, Hayek F, Assi C. A meta-analysis of mortality after minor amputation among patients with diabetes and/or peripheral vascular disease. J Vasc Surg. 2020;72:2197–207.
5. Kremers HM, Nwojo ME, Ransom JF, Wood-Wentz CM, Melton LJ, Huddleston PM. Trends in the epidemiology of osteomyelitis. A population-based study, 1969-2009. J Bone Joint Surg Am. 2015;97:837–45.
6. Wukich DK, Hobizal KB, Sambenedetto TL, Kirby K, Rosario BL. Outcomes of osteomyelitis in patients hospitalized with diabetic foot infections. Foot Ankle Int. 2016;37:1285–91.
7. Lavery LA, Peters EJG, Armstrong DG, Wendel CS, Murdoch DP, Lipsky BA. Risk factors for developing osteomyelitis in patients with diabetic foot wounds. Diabetes Res Clin Pract. 2009;83:347–52.
8. Mutluoglu M, Sivrioglu AK, Eroglu M, Uzun G, Turhan V, Ay H, et al. The implications of the presence

of osteomyelitis on outcomes of infected diabetic foot wounds. Scand J Infect Dis. 2013;45:497–503.
9. Chen Y, Ding H, Wu H, Chen H. The relationship between osteomyelitis complication and drug-resistant infection risk in diabetic foot ulcer: a meta-analysis. Int J Low Extrem Wounds. 2017;16:183–90.
10. Berbudi A, Rahmadika N, Tjahjadi AI, Ruslami R. Type 2 diabetes and its impact on the immune system. Curr Diabetes Rev. 2020;16:442–9.
11. King CM, Castellucci-Garza F, Lyon L, Doyle MD, Nimick C, Williams ML. Microorganisms associated with osteomyelitis of the foot and ankle. J Foot Ankle Surg. 2020;59:491–4.
12. van Asten SA, La Fontaine J, Peters EJ, Bhavan K, Kim PJ, Lavery LA. The microbiome of diabetic foot osteomyelitis. Eur J Clin Microbiol Infect Dis. 2016;35:293–8.
13. Pitocco D, Spanu T, Di Leo M, Vitiello R, Rizzi A, et al. Diabetic foot infections: a comprehensive overview. Eur Rev Med Pharmacol Sci. 2019;23(Suppl 2):26–37.
14. Senneville E, Lipsky BA, van Asten SAV, Peters EJ. Diagnosing diabetic foot osteomyelitis. Diabetes Metab Res Rev. 2020;36(Suppl 1):e3250.
15. Senneville E, Joulie D, Blondiaux N, Robineau O. Surgical techniques for bone biopsy in diabetic foot infection, and association between results and treatment duration. J Bone Jt Infect. 2020;5:198–204.
16. Couturier A, Chabaud A, Desbiez F, Descamps S, Petrosyan E, Letertre-Gilbert P, et al. Comparison of microbiological results obtained from per-wound bone biopsies versus transcutaneous bone biopsies in diabetic foot osteomyelitis: a prospective cohort study. Eur J Clin Microbiol Infect Dis. 2019;38:1287–91.
17. Johani K, Fritz BG, Bjarnsholt T, Lipsky BA, Jensen SO, Yang M, et al. Understanding the microbiome of diabetic foot osteomyelitis: insights from molecular and microscopic approaches. Clin Microbiol Infect. 2019;25:332–9.
18. Heidari N, Kwok I, Vris A, Charalambous A. Should treatment of diabetic foot osteomyelitis be based on bone biopsies? Foot Ankle Int. 2019;40(Suppl 1):73S–4S.
19. Cortés-Penfield NW, Kulkarni PA. The history of antibiotic treatment of osteomyelitis. Open Forum Infect Dis. 2019;6:ofz181.
20. Aragon-Sanchez J, Lipsky BA. Modern management of diabetic foot osteomyelitis. The when, how and why of conservative approaches. Expert Rev Anti Infect Ther. 2018;16:35–50.
21. Lavigne JP, Sotto A. Microbial management of diabetic foot osteomyelitis. Future Microbiol. 2017;12:1243–6.
22. Spellberg B, Lipsky BA. Systemic antibiotic therapy for chronic osteomyelitis in adults. Clin Infect Dis. 2012;54:393–407.
23. Jeffcoate WJ, Lipsky BA. Controversies in diagnosing and managing osteomyelitis of the foot in diabetes. Clin Infect Dis. 2004;39(Suppl 2):S115–22.
24. Lázaro-Martínez JL, Aragón-Sánchez J, García-Morales E. Antibiotics versus conservative surgery for treating diabetic foot osteomyelitis: a randomized comparative trial. Diabetes Care. 2014;37:789–95.
25. Lázaro-Martínez JL. Optimal management of diabetic foot osteomyelitis: challenges and solutions. Diabetes Metab Syndr Obes. 2019;12:947–59.
26. Barshes N, Mindru C, Ashong C, Rodriguez-Barradas M, Trautner BW. Treatment failure and leg amputation among patients with foot osteomyelitis. Int J Low Extrem Wounds. 2016;15:303–12.
27. Aicale R, Cipollaro L, Esposito S, Maffulli N. An evidence based narrative review on treatment of diabetic foot osteomyelitis. Surgeon. 2020;18:311–20.
28. Aragón-Sánchez J, Lázaro-Martínez J, Alvaro-Afonso FJ, et al. Conservative surgery of diabetic forefoot osteomyelitis: how can I operate on this patient without amputation? Int J Low Extrem Wounds. 2015;14:108–31.
29. Aragon-Sanchez J. Clinical-pathological characterization of diabetic foot infections: grading the severity of osteomyelitis. Int J Low Extrem Wounds. 2012;11:107–12.
30. Aragon-Sanchez J, Lazaro-Martinez JL, Hernandez-Herrero C, et al. Does osteomyelitis in the feet of patients with diabetes really recur after surgical treatment? Natural history of a surgical series. Diabet Med. 2012;29:813–8.
31. Senneville E, Robineau O. Treatment options for diabetic foot osteomyelitis. Expert Opin Pharmacother. 2017;18:759–65.
32. Li H-K, Rombach I, Zambellas R, Walker SA, McNally MA, Atkins BL, et al. Oral versus intravenous antibiotics for bone and joint infection. N Engl J Med. 2019;380(5):425–36.
33. Gariani K, Lebowitz D, Kressmann B, von Dach E, Sendi P, Waibel F, et al. Oral amoxicillin-clavulanate for treating diabetic foot infections. Diabetes Obes Metab. 2019;21:1483–6.
34. Bharati SP, Sukumaran SK. A review on the current principles of antibiotic therapy for diabetic foot infection. Infect Disord Drug Targets. 2021;21(5):e270421188440.
35. Preiss H, Kriechling P, Montrasio G, Huber T, Janssen I, Moldovan A, et al. Oral flucloxacillin for treating osteomyelitis: a narrative review of clinical practice. J Bone Jt Infect. 2020;5:16–24.
36. Wilson BM, Bessesen MT, Doros G, Brown ST, Saade E, Hermos J, et al. Adjunctive rifampin therapy for diabetic foot osteomyelitis in the Veterans Health Administration. JAMA Netw Open. 2019;2:e1916003.
37. Bessesen MT, Doros G, Henrie AM, Harrington KM, Hermos JA, Bonomo RA, et al. A multicenter randomized placebo controlled trial of rifampin to reduce pedal amputations for osteomyelitis in veterans with diabetes (VA INTREPID). BMC Infect Dis. 2020;20:23.
38. Polk C, Sampson MM, Roshdy D, Davidson LE. Skin and soft tissue infections in patients with diabetes

mellitus. Infect Dis Clin N Am. 2020;35(1):183–97. S0891-5520(20)30086-6.
39. van Asten SAV, Mithani M, Peters EJG, La Fontaine J, Kim PJ, Lavery LA. Complications during treatment of diabetic foot osteomyelitis. Diabetes Res Clin Pract. 2018;135:58–64.
40. Tone A, Nguyen S, Devemy F, Topolinski H, Valette M, Cazaubiel M, et al. Six-week versus twelve-week antibiotic therapy for nonsurgically treated diabetic toot osteomyelitis: a multicenter open-label controlled randomized study. Diabetes Care. 2015;38:302–7.
41. Gariani K, Lebowitz D, von Dach E, Kressmann B, Lipsky BA, Uçkay I. Remission in diabetic foot infections: duration of antibiotic therapy and other possible associated factors. Diabetes Obes Metab. 2019;21:244–51.
42. Gariani K, Pham R-R, Kressmann B, et al. Three versus six weeks of antibiotic therapy for diabetic foot osteomyelitis: a prospective, randomized, non-inferiority pilot trial. Clin Infect Dis. 2021;73(7):e1539–45.
43. Waibel F, Berli M, Cantanzaro S, Sairanen K, Schöni M, Boni T, et al. Optimization of the antibiotic management of diabetic foot infections: protocol for two randomized controlled trials. Trials. 2020;21:54.
44. Dudareva M, Kumin M, Vach W, Kaier K, Ferguson J, McNally M, et al. Short or Long Antibiotic Regimes in Orthopaedics (SOLARIO): a randomized controlled open-label non inferiority trial of duration of systemic antibiotics in adults with orthopaedic infection treated operatively with local antibiotic therapy. Trials. 2019;20:693.
45. Peters EJ, Lipsky BA, Senneville E, Abbas ZG, Aragón-Sánchez J, Diggle M, et al. Interventions in the management of infection in the foot in diabetes: a systematic review. Diabetes Metab Res Rev. 2020;36(Suppl 1):e3282.
46. Panagopoulos P, Drosos G, Maltezos E, Papanas N. Local antibiotic delivery systems in diabetic foot osteomyelitis: time for one step beyond? Int J Low Extrem Wounds. 2015;14:87–91.
47. van Vugt TAG, Arts JJ, Geurts JAP. Antibiotic-loaded polymethylmethacrylate beads and spacers in treatment of orthopedic infections and the role of biofilm formation. Front Microbiol. 2019;10:1626.
48. Gallarate M, Chirio D, Chindamo G, Peira E, Sapino S. Osteomyelitis: focus on conventional treatments and innovative drug delivery systems. Curr Drug Deliv. 2021;18:532.
49. Hake ME, Young H, Hak DJ, Stahel PF, Hammerberg EM, Mauffrey C. Local antibiotic therapy strategies in orthopaedic trauma: practical tips and tricks and review of the literature. Injury. 2015;46:1447–56.
50. Crisologo PA, Malone M, La Fontaine J, Oz O, Bhavan K, Nichols A, et al. Are surrogate markers for diabetic foot osteomyelitis remission reliable? J Am Podiatr Med Assoc. 2021:111(5).

14 Practical Lessons Learned in Managing Diabetic Foot Infections

Andrew I. Abadeer, Mark R. Abbruzzese, and William Davis

Introduction

The infectious implications in the diabetic foot cannot be overstated. While it is well known that diabetics have an increased propensity to develop both systemic and localized infections, the diabetic foot offers a self-perpetuating cycle for infection that has been well studied as the most common precipitating event leading to lower extremity amputation [1–3]. As such, a firm understanding of the pathophysiology and the medical, surgical, and vascular modalities available to the clinician charged with the care of the infected diabetic foot must inform the allocation of multimodal therapy that is requisite in good outcomes in this population.

Approximately 85% of lower extremity amputations are preceded by a non-healing foot ulcer [4]. Complicating this picture, the presence of infection increases the risk of lower extremity amputation by 50% [5]. In focusing on the diabetic foot, current research has demonstrated that the unique demands in addition to the homeostatic insult of the disease process inherent to the diabetic make the diabetic foot uniquely sensitive to clinically devastating infection [6]. While an exhaustive review of the mechanisms that propagate the susceptibility of the diabetic foot to infection is beyond the scope of this chapter, a brief review must frame the clinical management. The disruption of the homeostatic mechanisms of blood glucose in the diabetic results in a chronic state of hyperglycemia. This, in turn, is the cause of upregulation of multiple metabolic pathways which ultimately results in vascular insufficiency. Nerve damage and subsequent paresthesia impair the natural protective sensation of the foot. The immune system is similarly impaired with studies demonstrating a stunted immune response to infection with decreased TNF-alpha and interleukin-6 release from macrophages, demonstrated in animal models [7], impaired polymorphonuclear leukocyte migration, and decreased efficacy of intracellular killing [5]. Chronic hyperglycemia (beginning as low as serum glucose levels >150 mL/dL [8]) also impairs opsonophagocytosis, the expression of MHC-I expression on myeloid cells [9, 10], as well as myriad other mechanisms that continue to be elucidated. As such, any physical insult to the diabetic foot becomes immediately compounded by a lack of sensation, lack of perfusion, and a dysregulated and inefficient immune system.

Given the "perfect storm" of such disparate factors that balance the diabetic foot into a precarious homeostasis, it is important that the clinician approach the infected diabetic foot armed with an informed understanding of the severity of the patient's presentation, the utility of investigatory studies and imaging, and the indications,

A. I. Abadeer (✉) · M. R. Abbruzzese · W. Davis
Medstar Georgetown University Hospital, Washington, DC, USA
e-mail: Andrew.I.Abadeer@medstar.net; Mark.Abbruzzese@medstar.net; William.Davis@gunet.georgetown.edu

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_14

efficacy, and appropriateness of a prescribed antibiotic regimen.

The Initial Presentation

The infected diabetic foot can present along a broad spectrum ranging from clean ulcers, to a mild cellulitis, to a life-threatening necrotizing fasciitis. As such, in an attempt to objectively grade the severity of the diabetic foot infection, many classification criteria have been set forth. The IWGDF has defined a system ranging from a Classification of 1 (uninfected) to 4 (severe infection) based on a combination of physical examination findings as well as objective laboratory data. Confirmation of infection in this grading system includes physical findings such as local swelling/induration, peri-wound erythema, local pain/tenderness, or purulent discharge. The distinction in the IWGDF classification between moderate and severe infection is defined as the presence or absence of two or more of systemic inflammatory response syndrome symptoms (SIRS, criteria of which include body temperature, heart rate, respiratory rate, and white blood cell count) [2]. The Infectious Diseases Society of America (IDSA) also has a similar grading system based on similar criteria with classifications ranging from "Uninfected" to "Severe Infection" [11, 12]. It is important to note, however, that these classification systems do not then correlate to a prescribed clinical course of action.

The first clinical decision point to be made by the clinician in the ambulatory or emergency setting is a determination of the setting of care including but not limited to ICU admission, floor admission, or clinic follow-up. Given the systemic derangements mentioned previously it is often difficult to efficiently characterize a patient's wound and the need for admission. In recognition of this, we recommend a systematic and organized approach to the initial evaluation of the infected diabetic foot with emphasis on a thorough and focused history and physical exam informed by the judicious use of labs and imaging. The clinician must elicit the relevant course of the diabetic foot with particular emphasis on the temporal changes in symptomatology, inciting events, and antecedent trauma. The patient's baseline ambulatory status before and after the current presentation must also be elucidated. Similarly, glycemic control in the weeks leading up to presentation should be interrogated informed by a current Hemoglobin A1C.

Upon clarification of the presenting history, the physical exam in the infected diabetic foot must first begin with a localization of the area of interest and its character. Often, providers will find that patients have kept a photographic account of their wound which can greatly assist the clinician in establishing the progression or regression of a wound. Infection without a corresponding wound should be delimited, circumscribed, and dated, with a marking pen to assess for attrition. In open wounds, the size of the wound should be measured and compared to historic values. Specific attention should be sequentially given to the base of the wound and the surrounding tissues. The base of the wound should be qualified according to the substrate (bone vs. soft tissue) as well as the presence or absence of granulation tissue, fibrous exudate, and purulence. Should there be suspicion of bone at the base of the wound, the probe-to-bone test should be employed out of concern for osteomyelitis [13]. This test consists of the use of sterile metal probe to assess if bone comprises the base of the diabetic ulcer. In the context of cortical irregularities on X-ray, and laboratory values suggestive of infection, this triad of findings is sufficient to diagnose osteomyelitis without further imaging [2]. The surrounding tissues should also be inspected closely for fluctuance or induration, lymphangitis, or proximal lymphadenopathy.

Laboratory values such as the white blood cell count (WBC), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) have an important role in supplementing and informing the findings of the history and physical exam. The white blood cell is an aggregate marker of lymphoid and myeloid cells in the bloodstream. Leukocytosis is generally accepted as suggesting a pro-inflammatory state with differential diagnoses including infection, autoimmune disorders,

or hematologic neoplastic proliferation. While a markedly elevated or depressed white blood cell count may indeed point to underlying infection, the white blood cell count in diabetics should be used with caution, particularly when normal. Often, given the immunologic derangements described previously, the WBC of a patient with a diabetic foot infection does not correlate to the severity of the infection with some studies demonstrating more than half of patients admitted with diabetic foot infections having a normal WBC [14]. As such, a normal WBC should not deter the clinician from escalating care when confronted with clinical exam findings concerning for severe infection.

Due to the limitations of the WBC in determining the presence or absence of infection, a number of adjunctive laboratory measures have been investigated to supplement the information gleaned from the WBC including ESR and CRP. In the author's experience, these values have little utility in isolation, but act as an additional datapoint with either an equivocal physical exam or in the monitoring of treatment efficacy. In the infected diabetic foot ulcer, a markedly elevated ESR may also hint at the presence of osteomyelitis in addition to soft tissue infection. Importantly, in comparison to ESR, CRP levels are more responsive to the progression and resolution of infection, making it of higher clinical utility in tracking treatment efficacy [15, 16].

The decision to hospitalize or manage a patient as an outpatient depends heavily on each of these factors. Additional reasons to manage a patient in an inpatient manner include the need for advanced diagnostic or interventional procedures, parenteral antibiotics, surgical consultation, the failure of outpatient antibiotics, or the management of preexisting or exacerbated medical conditions including congestive heart failure, coronary artery disease, chronic obstructive pulmonary disease, or acute/chronic kidney disease [2, 17]. Still, while the clinical and laboratory data that define the severity of infection must be a core axis upon which to make the decision for inpatient admission, this cannot be the only factor informing the care setting. Social support, wound stability, patient reliability, complexity of care, and interval of follow-up must also be thoughtfully considered when evaluating the infected diabetic foot patient for potential outpatient management. In fact, many a patient's wound has deteriorated due to a failure to optimize one or more of these factors when the wound was clinically stable upon initial presentation.

Management of the Diabetic Foot Infection

The management of diabetic foot infections is naturally a multidisciplinary endeavor. Due to the generally complex medical and social comorbidities of this population, a coordinated approach between infectious disease, medicine, and surgery must be undertaken to optimize patient care. The mainstay of the clinical approach to the infected diabetic foot ulcer must be comprised of surgical debridement and antibiosis. Both the surgical team and the infectious disease team should adopt a microbiology-driven approach based on the available microbiological testing of their specific institution. Ideally, sterile tissue cultures would be obtained and sent prior to the initiation of any antimicrobial therapy (the "sentinel" culture). Still, this is often not possible in the septic or systemically ill patient in whom antimicrobial therapy should be initiated immediately. Upon presentation to the operating room, it has become our practice to obtain a culture prior to any debridement if it is the first formal debridement the patient has undergone. After appropriate debridement (discussed at length in Chap. 13) and irrigation, a sterile tissue culture is again taken and sent for microbiological assessment. The type of culture will depend largely on the capability of the individual institution though the sensitivity and specificity of tissue specimens are generally higher than those of swabs [18–21]. We do not routinely obtain blood cultures on any patient that is not demonstrating signs of systemic infection.

The duration and type of antimicrobial therapy is made upon the basis of the extent of infection, the involvement of bone, and the type of

pathogen. Osteomyelitis demonstrates a unique challenge in the treatment of the infected diabetic foot ulcer. With a positive probe-to-bone test, and consistent X-ray and clinical findings, the treatment of osteomyelitis is based upon surgical and infectious disease consultation. A sterile bone biopsy obtained after debridement of an infected ulcer remains the gold standard for diagnosis of osteomyelitis as these cultures will assist in the determination of duration and scope of antibiotic therapy. In consultation with infectious disease, it is our general practice to treat osteomyelitis with antibiotics at the higher end of the recommended range and for a longer duration than patients who have a soft tissue infection alone [22]. Discussion with the surgical team after completion of debridement is paramount. Should the surgical team be confident in a comprehensive osseous debridement back to clinically normal bone supported with a negative sterile bone culture supporting these findings, it is reasonable to then reduce the duration of antibiotic therapy.

Whether by swab, or tissue specimen, a culture-based approach to antimicrobial therapy is critical both for antibiotic stewardship, and to appropriately target and comprehensively treat a patient's specific infection. Should empiric coverage be required, this is done based on institutional statistics for most likely pathogens. Coverage for gram-positive cocci should nearly always be included in initial empiric coverage, particularly in MRSA susceptible individuals. After initial identification of the most likely pathogen with the sentinel culture, antibiotic treatment is narrowed according to the institutions antibiogram for local susceptibilities in the context of a patient's drug allergies and comorbidities [2]. Still, due to the chronicity of many diabetic foot ulcers, polymicrobial growth is not uncommon, and these results should be stratified according to relative virulence when planning antibiotic therapy. In infections of the skin and soft tissues, generally treatment duration need not exceed 1–2 weeks. Wounds with associated osteomyelitis are generally treated for 6 weeks or less, with frequent reevaluation for regression or improvement.

Special populations in the infected diabetic foot ulcer include those with recent or threatened skin grafts, free flaps, and underlying hardware. Given the high-risk nature of these circumstances, close consultation with the surgical team is necessary to determine the scope and duration of antimicrobial therapy in a case-by-case manner.

Conclusion

Diabetic foot infections are a devastating, multifaceted, and self-perpetuating consequence of the diabetic insult to homeostasis. Inadequacy of diagnosis, treatment, or follow-up can lead to adverse outcomes including amputation. A thoughtful and thorough history and physical examination, buttressed by judicious use of imaging and laboratory values, will empower the clinician to appropriately triage these patients into an appropriate treatment plan. Close consultation with surgery as well as an objective, culture-based approach is critical in determining the duration, scope, and intensity of treatment. Finally, close surveillance is key to allow for early detection of failure to improve or worsening infection that may warrant a further workup or an alternative treatment regimen.

References

1. Ndosi M, Wright-Hughes A, Brown S, Backhouse M, Lipsky BA, Bhogal M, et al. Prognosis of the infected diabetic foot ulcer: a 12-month prospective observational study. Diabet Med. 2018;35(1):78–88.
2. Lipsky BA, Senneville É, Abbas ZG, Aragón-Sánchez J, Diggle M, Embil JM, et al. Guidelines on the diagnosis and treatment of foot infection in persons with diabetes (IWGDF 2019 update). Diabetes Metab Res Rev. 2020;36(Suppl 1):1–24.
3. Tan T-W, Shih C-D, Concha-Moore KC, Diri MM, Hu B, Marrero D, et al. Disparities in outcomes of patients admitted with diabetic foot infections. PLoS One. 2019;14(2):e0211481.
4. Pecoraro RE, Reiber GE, Burgess EM. Pathways to diabetic limb amputation basis for prevention: an identifiable and potentially preventable pivotal event, in most cases an episode involving minor. Diabetes Care. 1990;13:513–21.

5. Hobizal KB, Wukich DK. Diabetic foot infections: current concept review. Diabet Foot Ankle. 2012:1–8.
6. Boulton AJM. Foot debridement: anatomic knowledge is mandatory. Diabetes Metab Res Rev. 2000;16(Suppl 1):23–6.
7. Zykova SN, Jenssen TG, Berdal M, Olsen R, Myklebust R, Seljelid R. Altered cytokine and nitric oxide secretion in vitro by macrophages from diabetic type II-like db/db mice. Diabetes. 2000;49(9):1451–8.
8. Inzucchi SE. Management of hyperglycemia in the hospital setting. N Engl J Med. 2006;355(18):1903–11.
9. Mazade MA, Edwards MS. Impairment of type III group B streptococcus-stimulated superoxide production and opsonophagocytosis by neutrophils in diabetes. Mol Genet Metab. 2001;73(3):259–67.
10. Price CL, Hassi HOSA, English NR, Blakemore AIF, Stagg AJ, Knight SC. Methylglyoxal modulates immune responses: relevance to diabetes. J Cell Mol Med. 2009;14(6b):1806–15.
11. Ince P, Abbas ZG, Lutale JK, Basit A, Ali SM, Chohan F, et al. Use of the SINBAD classification system and score in comparing outcome of foot ulcer management on three continents. Diabetes Care. 2008;31(5):964–7.
12. Zhan LX, Branco BC, Armstrong DG, Mills JL Sr. The society for vascular surgery lower extremity threatened limb classification system based on wound, ischemia, and foot infection (WIfI) correlates with risk of major amputation and time to wound healing. J Vasc Surg. 2015;61(4):939–44.
13. Grayson ML, Gibbons GW, Balogh K, Levin E, Karchmer AW. Probing to bone in infected pedal ulcers: a clinical sign of underlying osteomyelitis in diabetic patients. JAMA. 1995;273(9):721–3.
14. Armstrong DG, Perales TA, Murff RT, Edelson GW, Welchon JG. Value of white blood cell count with differential in the acute diabetic foot infection. J Am Podiatr Med Assoc. 1996;86(5):224–7.
15. Xu J, Cheng F, Li Y, Zhang J, Feng S, Wang P. Erythrocyte sedimentation rate combined with the probe-to-bone test for fast and early diagnosis of diabetic foot osteomyelitis. Int J Low Extrem Wounds. 2020;20:1534734620923278.
16. Crisologo PA, Davis KE, Ahn J, Farrar D, Van Asten S, La Fontaine J, et al. The infected diabetic foot: can serum biomarkers predict osteomyelitis after hospital discharge for diabetic foot infections? Wound Repair Regen. 2020;28(5):617–22.
17. Wukich DK, Hobizal KB, Brooks MM. Severity of diabetic foot infection and rate of limb salvage. Foot Ankle Int. 2013;34(3):351–8.
18. Nelson A, Wright-Hughes A, Backhouse MR, Lipsky BA, Nixon J, Bhogal MS, et al. CODIFI (concordance in diabetic foot ulcer infection): a cross-sectional study of wound swab versus tissue sampling in infected diabetic foot ulcers in England. BMJ Open. 2018;8(1):e019437.
19. Huang Y, Cao Y, Zou M, Luo X, Jiang Y, Xue Y, et al. A comparison of tissue versus swab culturing of infected diabetic foot wounds. Int J Endocrinol. 2016;2016:8198714.
20. Nelson EA, O'Meara S, Craig D, Iglesias C, Golder S, Dalton J, et al. A series of systematic reviews to inform a decision analysis for sampling and treating infected diabetic foot ulcers. Health Technol Assess 2006;10(12):iii–iv, ix-x, 1–221.
21. O'Meara S, Nelson EA, Golder S, Dalton JE, Craig D, Iglesias C, et al. Systematic review of methods to diagnose infection in foot ulcers in diabetes. Diabet Med. 2006;23(4):341–7.
22. Spellberg B, Lipsky BA. Systemic antibiotic therapy for chronic osteomyelitis in adults. Clin Infect Dis. 2012;54(3):393–407.

15 Managing Soft Tissue Infection in the Diabetic Foot: Cultures, Drugs, and Source Control

Eric Senneville and Romina Deldar

Soft Tissue Infection of the Diabetic Foot

Diabetic foot infection (DFI) is classically defined by the multiplication of microorganisms and invasion of the tissues surrounding a wound located under the malleoli. Although the microorganisms that invade the skin and soft tissues (SSTs) around and/or beneath a wound ulcer cannot be seen on physical examination, they are consistently present on the ulcer surface [1]. The consequences of these postulates are (a) infection of a diabetic foot ulcer cannot be established by means of microbiological assessment and (b) the best way to diagnose infection is to assess the SSTs around the ulcer for the presence of clinical signs of infection [2].

DFIs usually are due to a neuro/vasculopathic ulcer but other causes include a simple puncture, a wound in the interdigital space, or from the nail plate. The colonization of the wound by pathogenic microorganisms such as *Staphylococcus aureus* or beta-hemolytic streptococci (e.g., *Streptococcus agalactiae*) may lead to an acute infection. Non-healing ulcers seen in patients living with diabetes mellitus (DM) are mainly a consequence of peripheral neuropathy which permits the patient to keep walking on the wound because of the loss of pain sensation and/or peripheral arterial disease (PAD) both of which can delay ulcer healing and, as result, favor the occurrence of a DFI. Although not fully understood, the immunological dysfunction associated with diabetes increases the risk of infection [3]. Pathogenic bacteria and commensals (e.g., *S. epidermidis*, *Corynebacterium* spp.) coexist in non-healing foot ulcers and interact with each other as they do in other wounds [1]. Recent advances in knowledge about the microbiota of DFUs have promoted the concept of pathogenicity of bacteria in DFUs as bacterial communities rather than independent specific bacteria [4]. The bacterial population present in a DFU is therefore now considered a functional unit that organizes itself as functionally pathogroups secondary to the interactions between commensals and virulent bacteria. For instance, the commensal bacterium *Helcococcus kunzii* can reduce the virulence expression in *S. aureus* [5].

E. Senneville
Infectious Diseases Department, Gustave Dron Hospital, Tourcoing, France
e-mail: esenneville@ch-tourcoing.fr

R. Deldar (✉)
Department of Plastic and Reconstructive Surgery, MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: Romina.Deldar@medstar.net

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_15

Microbiology of the Diabetic Foot

Numerous distinct microorganisms including bacteria and fungi can be identified in DFUs [6]. Studies have principally addressed bacteria that are consistently identified in DFUs. *S. aureus* is by far the most prevalent microorganism identified in temperate regions, while Gram-negative bacilli especially *Pseudomonas* spp. are most commonly identified in warm climate countries [7, 8].

The duration of a DFU is a major reason it can become infected. *S. aureus* strains present in non-healing DFUs are likely to harbor antibiotic resistance and encode staphylococcal enterotoxin genes resulting in nonspecific stimulation of a wide population of T cells responsible for persistent inflammation which delays the healing process [5]. The expression of bacterial virulence influences the evolution of a DFU towards infection; this has been observed in *S. aureus* in which several virulent genes have been significantly associated with the evolution to infection [6]. Enterobacterales (e.g., *Proteus mirabilis*, *Escherichia coli*, *Klebsiella* sp., or *Enterobacter* sp.) and strict anaerobes (e.g., *Finegoldia* sp., *Bacteroides* sp.) are usually encountered during chronic wound infections [9–12]. Fungal agents, in particular *Candida* sp., are not uncommon [13]. More than half of infected DFUs are polymicrobial [9–12]. Recent data suggest that the expression of virulence can be attenuated by antibiotics and also stress conditions in the ulcer environment (e.g., oxygen pressure, low temperature, elevated glucose concentration, nutrient limitation) [14]. These elements lead to the emergence of quasi-dormant subpopulations of bacteria, including small-colony variants likely to exhibit antibiotic resistance and biofilm formation that are inaccessible to most antibiotic agents [15]. Polymicrobial biofilms, in which bacterial strains organized in pathogroups can escape the host immune responses, are involved in 60–80% of non-healing DFUs compared to 6% in acute DFUs [16].

Diagnosis of Soft Tissue Infections of the Diabetic Foot

The diagnosis of a DFU infection is a major step that allows for the implementation of all therapeutic measures, but also importantly can help reduce the unjustified use of broad-spectrum antibiotics since no clinical studies have demonstrated any benefit of systemic antibiotic therapy on the evolution of an uninfected diabetic foot wound [17]. According to the definition of DFI proposed by the International Working Group on the Diabetic Foot (IWGDF), the clinical elements suggestive of a DFU infection include at least two of the following: local swelling or induration, erythema >0.5 cm around the wound limits, sensibility, or local pain (rare), increased local heat, and the presence of pus located under the malleoli [2]. The IWGDF proposes to grade the severity of the infection according to the surface and depth extension (moderate infection), presence of systemic signs (severe infection), and involvement of underlying osteoarticular structures (see Chap. 17) [2].

Microbiological Assessment of Soft Tissue Infections of the Diabetic Foot

Once a clinical suspicion of DFI is established, a microbiologic assessment is recommended to best target antimicrobial therapy [18]. Overall, tissue samples (curettage-biopsy, true-cut biopsy, needle aspiration, especially in the case of a subcutaneous abscess) have a sensitivity and specificity higher than those of simple swabs which are not recommended as they do not allow for the distinction between pathogens and colonizers [19]. One technique using swabs (Levine's technique) has been validated for microbiological assessment of a DFU. It consists of rotating the wound swab over a 1-cm^2 area of the wound [20]. The quality of the sample is very important since the detection of live bacteria in a tissue sample

taken appropriately to avoid contamination is a strong argument for the pathogenicity of the microorganism(s) identified. However, it may not always be practical or feasible to obtain the most sophisticated samples, thus it is preferable to at least obtain a sample even if it is not of optimal quality than to not do it at all. In cases when obtaining a culture is not feasible, any microbiological information, such as Gram stain [21], can help tailor antibiotic treatment, especially in cases of poor evolution after first-line antibiotic treatment. The concordance between Gram stain and culture results established in diabetic patients with SST infection of the foot is likely to augment the pathogenic role of the identified bacteria and may help providers choose the most appropriate antibiotic regimens [2].

New molecular techniques can now identify most of the microorganisms present in a DFU. These techniques cannot, however, differentiate living from dead microorganisms, and they do not provide data about the antibiotic sensitivities of identified bacteria. At best, they can determine the presence of certain resistance genes. Moreover, there are no criteria to ascertain that isolated bacteria are responsible for an infection diagnosed clinically. As a result, although these new techniques are essential to understand the pathophysiology of wound infection and the relations between microbes and wound healing, they do not yet have a place in the daily care of patients with DFIs [2]. One exception is the detection by direct polymerase chain reaction (PCR) of methicillin-resistant *S. aureus* (MRSA) nasal carriage, which has been significantly associated with MRSA DFI and can aid in the choice of antibiotics in patients with DFIs and screening for MRSA colonization in DFU patients [22, 23].

Biomarkers of Infection

Serum biomarkers of inflammation, such as C-Reactive Protein (CRP) and procalcitonin, may be useful in situations where the clinical diagnosis of DFI is uncertain [24]. They can also be used to assess the evolution of infection as it increases rapidly at the beginning of an infection and then decreases when the infection improves. The level of leukocytes and/or neutrophils is not helpful to diagnose infection as they can be normal in more than half of cases [25]. However, leukocyte counts may be useful since it is part of the criteria for defining a severe infection (grade 4 in the IWGDF classification; see Chap. 15).

Management of the Diabetic Foot Infection

Surgical Part of the Treatment of Infection

The surgical management of DFIs and osteomyelitis is detailed in Chap. 14. It is important to consider surgical intervention as a major, even indispensable in some cases, mode of infection source control. Surgical debridement is a radical weapon against infection to remove any necrotic material and drain purulent collections, which are not accessible to the activity of most antibiotics. Neglecting this essential therapeutic step can lead to the spread of infection and treatment failure. In addition, exposing high bacterial loads to inappropriate antibiotic concentrations because of the necrotic nature of infected tissue will likely favor the emergence of multidrug-resistant bacteria.

Antimicrobial Therapy

General Aspects

Antimicrobial therapy of DFIs is almost always empiric since it is recommended to start treatment as soon as the infection is diagnosed as the outcome of the infection is not predictable in this setting [2]. Knowledge of which microorganisms are likely to be involved in DFIs can aid in choosing empirical antimicrobial treatment. Therefore, to tailor empiric antibiotic therapy, it is important to consider epidemiological data on bacterial

ecology, if available, and to involve microbiologists/infectious disease consultants in complex cases [26]. The goal of empiric initial antibiotic therapy is to cover the likely pathogens and to avoid the use of unnecessary broad-spectrum antibiotics, as antimicrobial resistance is more likely to emerge with broad versus narrow antibiotics.

The choice of an antibiotic regimen to treat a DFI should be based on the likely microorganism(s) and its(their) antibiotic susceptibilities. Patients with infected non-necrotic acute wounds who have not recently been treated with antibiotics are likely to be infected with *S. aureus* and/or beta-hemolytic streptococci [2]. In warm climate countries, the higher prevalence of Gram-negative bacilli may justify the use of broader-spectrum antibiotics. Strict anaerobes involved in DFIs are generally susceptible to most antibiotics, except *Bacteroides* species. Other important criteria include infection severity, existing data on the efficacy of the agent in treating DFIs, its tolerance profile, including the risk of drug-drug interactions, mode of administration, and cost.

Parenteral antibiotic therapy is indicated initially in some moderate and all severe DFIs. A switch to oral form should be considered once the patient is clinically improving, as long as he/she has no contraindications to oral therapy and an oral regimen is available. In other cases, patients with DFIs can be treated with oral agents providing the oral bioavailability is correct (i.e., oral oxacillin should be avoided, but cephalexin is a good option).

The duration of antibiotic therapy for DFI is a matter of debate. The recommendations have evolved in the past few decades to include duration of 1–2 weeks for SST DFIs. Prolonging treatment for up to 3–4 weeks is proposed by IWGDF in cases of extensive infection that is improving slower than expected or if the patient has severe peripheral artery disease [2]. It is important to specify a treatment end date when prescribing an antibiotic regimen to avoid unnecessary prolonged treatments and to discourage prolongation of treatment until the wound has healed [17].

Antibiotics Useful for the Treatment of SST DFIs

As only one randomized study has established the superiority of ertapenem over tigecycline [27], the current recommendations for empiric antibiotic therapy for DFIs are mainly based on expert opinions [2].

Intravenous vancomycin can be used empirically to cover Gram-positive cocci (i.e., methicillin-resistant staphylococci) in conjunction with antibiotics against Gram-negative bacilli (GNB) and strict anaerobes, such as piperacillin-tazobactam or carbapenems, in moderate to severe cases due to the narrow-spectrum of vancomycin. The IDSA recommends a dose of 15–20 mg/kg every 8–12 h for *S. aureus* to achieve a minimal inhibitory concentration (MIC) $\leq$1 mg/L [28]. The use of vancomycin in patients who are age 65 years or older with renal disease and/or take other nephrotoxic medications exposes those patients to the risk of renal toxicity. Daptomycin, a cyclic lipopeptide, has the same antibacterial spectrum as vancomycin, with a higher and faster bactericidal effect and almost no renal toxicity.

The combination of the group A penicillin agent, amoxicillin, with the beta-lactamase inhibitor (BLI) clavulanic acid confers a broad-spectrum oral antibiotic against beta-hemolytic streptococci, methicillin-susceptible staphylococci, some GBN (e.g., *Proteus mirabilis* and some strains of *E. coli*), and almost all strict anaerobes. This combination is recommended for the treatment of mild to moderate SST DFIs especially chronic ulcers in which polymicrobial communities may be involved, DFIs, and localized cellulitis. The drug does not provide any coverage against bone infections.

Among the anti-Gram-negative antibiotics, both ceftazidime and cefepime have the advantage to cover *Pseudomonas aeruginosa,* although the direct pathogenicity of this bacterium has been questioned, as it was for *Enterococcus faecalis*, in the setting of SST DFIs. Cefepime exhibits some activity against AmpC (depressed chromosomic cephalosporinases)-producing GNB, particularly *Enterobacter* sp. Both ceftazidime and cefepime can result in serious adverse nervous system

effects; thus plasma concentrations must be monitored, especially in patients with renal impairment and/or previous history of seizure disorders. The combination of piperacillin and the BLI tazobactam can cover *P. aeruginosa*, *E. faecalis,* and strict anaerobes, as well. This broad-spectrum antibiotic should be limited to the moderate and severe DFIs in conjunction with amikacin in cases of septic shock to both enhance the bactericidal activity and augment the antibacterial coverage to extended-spectrum beta-lactamases (ESBL)-producing GNB. The Food and Drug Administration (FDA) has approved piperacillin-tazobactam for the treatment of complicated SST DFIs but not for diabetic foot osteomyelitis. Among the carbapenems, ertapenem has broad-spectrum bactericidal activity directed against a wide spectrum of Gram-positive cocci, GNB, and anaerobes, except enterococci and *Pseudomonas* sp. (which differs from imipenem and meropenem), and its use is approved by the FDA for treating DFIs [29]. It is effective against ESBL and AmpC-producing bacteria. Confusion and/or seizures may occur especially in elderly patients with renal insufficiency. The main advantage of ertapenem is its long half-life which allows for once-daily dosing via intravenous/intramuscular/subcutaneous administration. Prolonged infusions, including continuous infusion of beta-lactam agents, are likely to maximize the time that serum concentrations remain above the MIC of the bacteria within the infected sites about the time-dependent activity of beta-lactam agents.

Doxycycline is a bacteriostatic tetracycline antibiotic with broad coverage against Gram-positive bacteria including most MRSA strains, GNB including *Klebsiella* sp., *E. coli*, some *Enterobacter* strains, and *Clostridium* sp. The overall tolerance of doxycycline is good with only a few cases of pruritus, photosensitization, few cases of diarrhea, and exceptional lupus-induced reactions reported. The drug is contraindicated in patients with esophageal lesions, liver cirrhosis, and portal hypertension due to the risk of hemorrhage. Doxycycline does not need renal or body weight dosing.

Clindamycin is a member of the macrolide family with a bacteriostatic effect directed against both Gram-positive (streptococci and staphylococci) and anaerobic bacteria but no activity against GNB. The activity of clindamycin against some strict anaerobes such as *Bacteroides* spp. has decreased these last years, making it no longer appropriate as empiric antibiotic treatment in cases where anaerobes may potentially be involved. The D-test should be available for detecting inducible resistance to clindamycin, especially in the case of MRSA-related DFIs. Clindamycin may modify taste (bitter or metallic) and is frequently associated with diarrhea, including *Clostridium difficile* infections, especially in fragile and elderly patients. Clindamycin does not require adaptation to renal function.

Metronidazole has a very broad anti-anaerobic spectrum of activity except for *Cutibacterium acnes*, complete oral bioavailability, and excellent tissue diffusion. The use of this antibiotic may however result in peripheral neuropathy and toxic encephalopathy, especially with a treatment duration longer than 2 weeks. In addition, patients should be cautioned not to drink alcohol while taking metronidazole due to the risk of tachycardia, palpitations, nausea, and vomiting (disulfiram effect).

Fluoroquinolones are concentration-dependent bactericidal antibiotics with good coverage against GNB and Gram-positive bacteria, including *Streptococcus* spp. and *E. faecalis,* for levofloxacin, moxifloxacin, and even some fluoroquinolone-resistant staphylococci for the new agent delafloxacin. These agents achieve excellent tissue diffusion and high oral bioavailability (levofloxacin) but are limited in the treatment of SST DFIs given the risk of selection of resistant mutants, especially with staphylococci, and should probably be reserved for the treatment of diabetic foot osteomyelitis (DFO).

Choice and Adaptation of the Antimicrobial Therapy

Some propositions inspired by the 2019 updated IWGDF guidelines for the empiric antibiotic regimens are presented in Table 15.1.

The use of microbiological results is another important step in the management of DFIs. These results are usually available within 3 days of sam-

Table 15.1 Empiric antibiotic regimens for non-osteomyelitic soft tissue diabetic foot infections

Additional factors	Usual pathogen(s)	Potential empirical regimens
Mild (grade 1) infections		
No complicating features	GPC	S-S pen; 1st-gen. cephalosporin
β-lactam allergy or intolerance	GPC	Clindamycin; FQ; TMP-SMX; doxycycline
Recent antibiotic exposure	GPC + GNB	βL-βLaseI-1; TMP-SMX; FQ
High risk for MRSA	MRSA	Linezolid; TMP-SMX; doxycycline; macrolide
Moderate to severe (grade 2 and 3) infections		
No complicating features	GPC ± GNB	βL-βLaseI-1; 1st, 2nd, 3rd-gen. cephalosporin
Recent antibiotics	GPC ± GNB	βL-βLaseI-1, 2nd, 3rd gen. cephalosporin; group 1 carbapenem (depends on prior therapy; seek advice)
Macerated ulcer or warm climate	GNB, including *P. aeruginosa*	βL-βLaseI-2; S-S pen + ceftazidime or cefepime; ciprofloxacin; group 2 carbapenem
Ischemic limb/ necrosis/gas forming	GPC ± GNB ± strict anaerobes	βL-βLaseI-1 or 2; group 2 carbapenem; 2nd/3rd gen. cephalosporin + clindamycin or metronidazole
MRSA and multi-resistant GNB		
MRSA risk factors	MRSA	Consider adding, or substituting with, glycopeptides; linezolid; daptomycin; fusidic acid; TMP-SMX
MDR GNR risk factors	ESBL	Carbapenems; FQ; aminoglycoside and colistin
Highly resistant GNB risk factors	GNB, carbapenemases-producing rods	New βL-βLaseI (ceftazidime-avibactam); cefiderocol

Inspired by 2019 IWGDF guidelines
"Usual pathogens" refers to isolates from an infected foot ulcer, not just colonization at another site
Antibiotics should be at the usual recommended doses for serious infections. Where more than one agent is listed, only one of them should be prescribed, unless otherwise indicated
Consider modifying doses of agents selected for patients with comorbidities such as azotemia, liver dysfunction, and obesity when required according to the recommendations for each molecule
Oral antibiotic agents should generally not be used for severe infections, except as follow-on (switch) after initial parenteral therapy
Fluoroquinolones (FQ) and Rifampin may ease the emergence of resistant mutants and should be restricted to osteomyelitis complicating DFIs (authors' personal opinion)
βL-βLaseI: β-lactam, β-lactamase inhibitor; βL-βLaseI 1: amoxicillin/clavulanate, ampicillin/sulbactam; βL-βLaseI 2: ticarcillin/clavulanate, piperacillin/tazobactam; doxy: doxycycline; ESBL: extended-spectrum β-lactamase-producing organism; FQ: fluoroquinolone with good activity against aerobic gram-positive cocci (e.g., levofloxacin, moxifloxacin or delafloxacin); gen: generation; GNB: Gram-negative bacilli; GPC: Gram-positive cocci (*Staphylococcus aureus* and β-hemolytic streptococci); group 1 carbapenem: ertapenem; group 2 carbapenem: imipenem, meropenem; ceph: cephalosporin; MRSA: methicillin-resistant *S. aureus*; S-S pen: semisynthetic penicillinase-resistant penicillin; cipro: antipseudomonal fluoroquinolone, e.g., ciprofloxacin: TMP-SMX, trimethoprim/sulfamethoxazole

pling and the patient's situation should be assessed at that time. If signs of infection have decreased, treatment should be maintained unless the spectrum of the initial antibiotic regimen is too broad and, therefore, should be reduced (de-escalation). On the contrary, in the event of a favorable outcome but resistant bacteria have been identified, the treatment should not be modified given the limited accuracy of most ulcer sampling techniques. In cases of an unfavorable outcome and before broadening the antibacterial spectrum of treatment, a non-microbiological cause of failure should be sought such as poor adherence to treatment, presence of deep collection, improper or no off-loading of the foot ulcer, etc. Alternatively, when the infection resolves under an antibiotic regimen that does not cover the microorganisms identified from the ulcer, the treatment should not be modified unless the infection worsens.

Biofilm and Soft Tissue Infections of the Diabetic Foot

While acute DFIs due to metabolically active planktonic bacteria involve a direct host-controlled response to virulence expression, chronic episodes mostly related to polymicrobial biofilms involve an inefficient inflammatory response [30]. Biofilm formation is a complex process that involves different communities of microorganisms that are embedded in an extracellular matrix made of glycoproteins, polysaccharides, proteins, and deoxyribonucleic acids [31]. The biofilm structure differs from one DFU to another, given the multiple different microorganisms potentially involved. The consequences of biofilm formation are globally deleterious for the wound healing process and the response to antibiotic therapy by impairing antibiotic contact with bacteria and their antibacterial activity given the reduced metabolism of the microorganisms present in the biofilm environment. The production of degradative enzymes results in an inflammatory response which is depicted by some experts as a biofilm-related infection [32]. The *frustrated* host immune response results in chronic inflammation (depicted by some authors as "chronic biofilm infection") which delays ulcer healing and creates tissue damage [30, 33].

Given the limitation of this phenomenon in a wound, topical administration of various agents with antimicrobial activity and antibiofilm effect has been assessed. Overall, randomized controlled data on the effectiveness and safety of topical antimicrobial for DFI is limited and has not proven convincing efficacy. The IWGDF suggests against using any currently available topical antimicrobial agent for treating a mild DFI [2, 34]. Topical antimicrobial agents can impact the microbial load and composition of non-healing DFUs but are unlikely to significantly improve the healing process [35]. On the contrary, both chemical biofilm disruptors and wound debridement have shown efficacy in improving non-healing DFUs [35, 36]. The high prevalence of genes carrying resistance to most antibiotics (e.g., beta-lactams, macrolides, aminoglycosides, and tetracyclines) in DFUs may explain the absence of significant effect of antibiotic agents on the microbial diversity in healed versus non-healed wounds, especially when used topically [37, 38]. Topical antibiotic treatment of infected DFUs with gentamicin-laden sponges showed no beneficial effects [39, 40]. Topical cadexomer iodine, which combines a broad-spectrum antimicrobial and antibiofilm effect, is efficacious in a recent meta-analysis on the treatment of chronic wounds, including DFUs [41].

Resolution of Infection

While the definition of successful management of SSTs can easily be based on the resolution of clinical signs of inflammation, including inflammatory biomarkers, and not on microbiological cure, the issue is much more challenging for DFO. Given the high rate of recurrence of DFO, it is generally recommended to evaluate the results of DFO at least 1 year after the end of treatment.

The origin of DFIs being a foot wound in almost all cases and the prevention of a recurrent foot ulcer are of utmost importance (see Chap. 8).

References

1. Jneid J, Cassir N, Schuldiner S, Jourdan N, Sotto A, Lavigne JP, La Scola B. Exploring the microbiota of diabetic foot infections with culturomics. Front Cell Infect Microbiol. 2018;8:282.
2. Lipsky BA, Senneville E, Abbas ZG, Aragón-Sánchez J, Diggle M, Embil JM, et al. Guidelines on the diagnosis and treatment of foot infection in persons with diabetes (IWGDF 2019 update). Diabetes Metab Res Rev. 2020;36:1–24.
3. Hobizal KB, Wukich DK. Diabetic foot infections: current concept review. Diabet Foot Ankle. 2012;3:3.
4. Dowd SE, Wolcott RD, Sun Y, McKeehan T, Smith E, Rhoads D. Polymicrobial nature of chronic diabetic foot ulcer biofilm infections determined using bacterial tag encoded FLX amplicon pyrosequencing (bTEFAP). PLoS One. 2008;3:e33.
5. Ngba Essebe C, Visvikis O, Fines-Guyon M, Vergne A, Cattoir V, Lecoustumier A, Lemichez E, Sotto A, Lavigne JP, Dunyach-Remy C. Decrease of *Staphylococcus aureus* virulence by *Helcococcus kunzii* in a *Caenorhabditis elegans* model. Front Cell Infect Microbiol. 2017;7:77.

6. Lavigne JP, Sotto A, Dunyach-Remy C, Lipsky BA. New molecular techniques to study the skin microbiota of diabetic foot ulcers. Adv Wound Care. 2015;4:38–49.
7. Lipsky BA, Armstrong DG, Citron DM, Tice AD, Morgenstern DE, Abramson MA. Ertapenem versus piperacillin/tazobactam for diabetic foot infections (SIDESTEP): a prospective, randomized, controlled, double-blinded, multicenter trial. Lancet. 2005;366(9498):1695–703.
8. Hatipoglu M, Mutluoglu M, Turhan V, Uzun G, Lipsky BA, Turk-Day Study Group, Sevim E, Demiraslan H, Eryilmaz E, Ozuguz C, Memis A, Ay H, Arda B, Uysal S, Motor VK, Kader C, Erturk A, Coskun O, Duygu F, Guler S, Altay FA, Ogutlu A, Bolukcu S, Yildiz S, Kandemir O, Aslaner H, Polat A, Karahocagil MK, Yasar KK, Sehmen E, Kilic S, Sunbul M, Gencer S, Bozkurt F, Yanik T, Oztoprak N, Batirel A, Sozen H, Kilic I, Celik I, Ay B, Tosun S, Kadanali A, Çomoglu S, Denk A, Hosoglu S, Aydin O, Elaldi N, Akalin S, Kandemir B, Akbulut A, Demirdal T, Balik R, Azak E, Sengoz G. Causative pathogens and antibiotic resistance in diabetic foot infections: a prospective multi-center study. J Diabetes Complicat. 2016;30(5):910–6.
9. Noor S, Zubair M, Ahmad J. Diabetic foot ulcer—a review on pathophysiology, classification and microbial etiology. Diabetes Metab Syndr. 2015;9:192–9.
10. Rahim K, Saleha S, Zhu X, Huo L, Basit A, Franco OL. Bacterial contribution in chronicity of wounds. Microb Ecol. 2017;73:710–21.
11. Liu C, Ponsero AJ, Armstrong DG, Lipsky BA, Hurwitz BL. The dynamic wound microbiome. BMC Med. 2020;18(1):358.
12. Radzieta M, Sadeghpour-Heravi F, Peters TJ, Hu H, Vickery K, Jeffries T, Dickson HG, Schwarzer S, Jensen SO, Malone M. A multiomics approach to identify host-microbe alterations associated with infection severity in diabetic foot infections: a pilot study. NPJ Biofilms Microbiomes. 2021;7(1):29.
13. Kumar D, Banerjee T, Chakravarty J, Singh SK, Dwivedi A, Tilak R. Identification, antifungal resistance profile, in vitro biofilm formation and ultrastructural characteristics of *Candida* species isolated from diabetic foot patients in Northern India. Indian J Med Microbiol. 2016;34:308–14.
14. Pouget C, Gustave CA, Ngba-Essebe C, Laurent F, Lemichez E, Tristan A, Sotto A, Dunyach-Rémy C, Lavigne JP. Adaptation of *Staphylococcus aureus* in a medium mimicking a diabetic foot environment. Toxins (Basel). 2021;13(3):230.
15. Guilhen C, Forestier C, Balestrino D. Biofilm dispersal: multiple elaborate strategies for dissemination of bacteria with unique properties. Mol Microbiol. 2017;105:188–210.
16. James GA, Swogger E, Wolcott R, Pulcini ED, Secor P, Sestrich J, Costerton JW, Stewart P. Biofilms in chronic wounds. Wound Repair Regen. 2008;16:37–44.
17. Abbas M, Uçkay I, Lipsky BA. In diabetic foot infections, antibiotics are to treat infection, not to heal wounds. Expert Opin Pharmacother. 2015;16(6):821–32.
18. Gardner SE, Haleem A, Jao YL, Hillis SL, Femino JE, Phisitkul P, Heilmann KP, Lehman SM, Franciscus CL. Cultures of diabetic foot ulcers without clinical signs of infection do not predict outcomes. Diabetes Care. 2014;37(10):2693–701.
19. Nelson A, Wright-Hughes A, Backhouse MR, et al. CODIFI (Concordance in Diabetic Foot Ulcer Infection): a cross-sectional study of wound swab versus tissue sampling in infected diabetic foot ulcers in England. BMJ Open. 2018;8:e019437.
20. Levine N, Robert B, Lindberg R, Mason A, Basil A, Pruitt B, Colonel MC. The quantitative swab culture and smear: a quick, simple method for determining the number of viable aerobic bacteria on open wounds. J Trauma. 1976;16(2):89–94.
21. Abbas ZG, Lutale JK, Alonso MM, Archibald LK. The utility of Gram stains and culture in the management of limb ulcers in persons with diabetes. Int Wound J. 2012;9(6):677–82.
22. Lin SY, Lin NY, Huang YY, Hsieh CC, Huang YC. Methicillin-resistant Staphylococcus aureus nasal carriage and infection among patients with a diabetic foot ulcer. J Microbiol Immunol Infect. 2020;53(2):292–9.
23. Dunyach-Remy C, Courtais-Coulon C, DeMattei C, Jourdan N, Schuldiner S, Sultan A, Carrière C, Alonso S, Sotto A, Lavigne JP. The link between nasal carriage of Staphylococcus aureus and infected diabetic foot ulcers. Diabetes Metab. 2017;43(2):167–71.
24. Zakariah NA, Bajuri MY, Hassan R, Ismail Z, Md Mansor M, Othman H, Nasruddin DN. Is Procalcitonin more superior to hs-CRP in the diagnosis of infection in diabetic foot ulcers? Malays J Pathol. 2020;42(1):77–84.
25. Armstrong DG, Perales TA, Murff RT, Edelson GW, Welchon JG. Value of white blood cell count with differential in the acute diabetic foot infection. J Am Podiatr Med Assoc. 1996;86(5):224–7.
26. Uçkay I, Aragon-Sanchez J, Lew D, Lipsky BA. Diabetic foot infections: what have we learned in the last 30 years? Int J Infect Dis. 2015;40:81–91.
27. Lauf L, Ozsvar Z, Mitha I, Regöly-Mérei J, Embil JM, Cooper A, et al. Phase 3 study comparing tigecycline and ertapenem in patients with diabetic foot infections with and without osteomyelitis. Diagn Microbiol Infect Dis. 2014;78:469–80.
28. Rybak MJ, Le J, Lodise T, Levine D, Bradley J, Liu C, Mueller B, Pai M, Wong-Beringer A, Rotschafer JC, Rodvold K, Maples HD, Lomaestro BM. Executive summary: therapeutic monitoring of vancomycin for serious methicillin-resistant Staphylococcus aureus infections: a revised consensus guideline and review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society,

and the Society of Infectious Diseases Pharmacists. J Pediatr Infect Dis Soc. 2020;9(3):281–4.
29. Edmonds M. The treatment of diabetic foot infections: focus on ertapenem. Vasc Health Risk Manag. 2009;5:949–63.
30. Moser C, Pedersen HT, Lerche CJ, Kolpen M, Line L, Thomsen K, Høiby N, Jensen PØ. Biofilms and host response—helpful or harmful. APMIS. 2017;125(4):320–38.
31. Percival SL, McCarty SM, Lipsky B. Biofilms and wounds: an overview of the evidence. Adv Wound Care. 2015;4:373–81.
32. Rodríguez-Rodríguez N, Martínez-Jiménez I, García-Ojalvo A, Mendoza-Mari Y, Guillén-Nieto G, Armstrong DG, Berlanga-Acosta J. Wound chronicity, impaired immunity and infection in diabetic patients. MEDICC Rev. 2021;24(1):44–58.
33. Wolcott RD, Rhoads DD, Dowd SE. Biofilms and chronic wound inflammation. J Wound Care. 2008;17(8):333–41.
34. Dumville JC, Lipsky BA, Hoey C, Cruciani M, Fiscon M, Xia J. Topical antimicrobial agents for treating foot ulcers in people with diabetes. Cochrane Database Syst Rev. 2017;6(6):CD011038.
35. Malone M, Radzieta M, Schwarzer S, Jensen SO, Lavery LA. Efficacy of a topical concentrated surfactant gel on microbial communities in non-healing diabetic foot ulcers with chronic biofilm infections: a proof-of-concept study. Int Wound J. 2021;18(4):457–66.
36. Kim D, Namen Ii W, Moore J, Buchanan M, Hayes V, Myntti MF, Hakaim A. Clinical assessment of a biofilm-disrupting agent for the management of chronic wounds compared with standard of care: a therapeutic approach. Wounds. 2018;30(5):120–30.
37. Wang G, Sweren E, Liu H, Wier E, Alphonse MP, Chen R, Islam N, Li A, Xue Y, Chen J, Park S, Chen Y, Lee S, Wang Y, Wang S, Archer NK, Andrews W, Kane MA, Dare E, Reddy SK, Hu Z, Grice EA, Miller LS, Garza LA. Bacteria induce skin regeneration via IL-1β signaling. Cell Host Microbe. 2021;29(5):777–91.
38. Kalan LR, Meisel JS, Loesche MA, Horwinski J, Soaita I, Chen X, Uberoi A, Gardner SE, Grice EA. Strain- and species-level variation in the microbiome of diabetic wounds is associated with clinical outcomes and therapeutic efficacy. Cell Host Microbe. 2019;25(5):641–55.
39. Uçkay I, Kressmann B, Malacarne S, Toumanova A, Jaafar J, Lew D, Lipsky BA. A randomized, controlled study to investigate the efficacy and safety of a topical gentamicin-collagen sponge in combination with systemic antibiotic therapy in diabetic patients with a moderate or severe foot ulcer infection. BMC Infect Dis. 2018;18(1):361.
40. Uçkay I, Kressmann B, Di Tommaso S, Portela M, Alwan H, Vuagnat H, Maître S, Paoli C, Lipsky BA. A randomized controlled trial of the safety and efficacy of a topical gentamicin-collagen sponge in diabetic patients with a mild foot ulcer infection. SAGE Open Med. 2018;6:2050312118773950.
41. Woo K, Dowsett C, Costa B, Ebohon S, Woodmansey EJ, Malone M. Efficacy of topical cadexomer iodine treatment in chronic wounds: systematic review and meta-analysis of comparative clinical trials. Int Wound J. 2021;18(5):586–97.

Surgical Management of Diabetic Foot Infection and Osteomyelitis

16

Venu Kavarthapu and Javier Aragón Sánchez

Introduction

Foot infection in people with diabetes is a dramatic complication. The most common point of entry of the infection to the foot is an ulcer that often is due to associated neuropathy, peripheral arterial disease, or both complications of diabetes. It is estimated that 40–80% of diabetic foot ulcers (DFUs) become infected at any moment during their clinical course [1]. The epidemiology of foot complications showed an increased trend of diabetic foot infections (DFI), including osteomyelitis (OM) and necrotising fasciitis despite an 8-year decrease in the trend of DFUs [2]. Infection is known to increase the costs associated with the treatment, often due to the need for patients' admission [3]. Factors related to infection, such as depth, OM, and severity, will condition the short-term outcomes in terms of mortality and amputations [4]. Severe infections carry a high rate of limb loss at 29.6% [5]. DFIs also carry a readmission rate of about 10% [6, 7] to 24% [8], due to recurrence of infection. Finally, long-term mortality is high in this group of presentations; one study reported a figure of 51.7% of mortality in a 6.5-year follow-up study [9].

Clinical Assessment and Classifications

A detailed and systematic clinical *assessment of a patient with diabetes and foot infection by the surgeon is* crucial for successful management. In the presence of diabetic peripheral neuropathy, the local and systemic clinical signs are often subtle, and it is critical that the clinical assessment is performed in a structured manner that included appropriate history and clinical examination and supplemented with relevant investigations. This allows the surgeon and the multidisciplinary team decide if the patient requires an emergency procedure or delayed surgery after a period of conservative management with antibiotics. Surgery should not be delayed in rapidly spreading and deep infections because these are not well tolerated by patients with diabetes and the risk of progression to diabetic foot attack is high. That is especially true in cases of severe infections which are associated with an inflammatory systemic response [10].

Some diabetic foot infections are not only limb, but life threatening, and such presentations are often best managed in a multidisciplinary setup. Sometimes, a timely minor amputation needs to be considered for prevention of a major

V. Kavarthapu (✉)
King's College Hospital, London, UK
e-mail: venu.kavarthapu@nhs.net

J. A. Sánchez
Department of Surgery and Diabetic Foot Unit,
Hospital La Paloma,
Las Palmas de Gran Canaria, Spain

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_16

amputation, and a major amputation for saving the patient's life. Limb salvage can sometimes be difficult when surgery is inadvertently delayed because it allows the infection to proliferate and destroy tissues beyond recovery and a timely surgical intervention is the key [11–13]. That is especially true in cases of deep tissue infections, defined as those below the fascia [14]. Prompt surgical treatment including extensive use of revascularisation may reduce the need for above-ankle amputations [13, 15–17]. Such presentations are best managed by a multidisciplinary diabetic foot team (MDFT) that has access to specialist diabetic foot surgeons that can perform surgery in a timely manner and offer functional limb salvage. The maxim 'time is tissue' is totally true in cases of DFIs with associated significant ischemia. Another key point is deciding if the patients require admission or can be treated in an ambulatory basis. For these reasons, it is important to perform a detailed clinical assessment, determine the grade, and classify the type of infection in patients with diabetes.

DFIs are classified according to their severity, by International Working Group on the Diabetic Foot (IWGDF) as mild, moderate, and severe [18] and this classification has later been validated [5]. IWGDF classifies DFI presentations that have associated systemic manifestations (of the systemic inflammatory response syndrome) as severe infections [10] and recommends considering hospitalisation for severe DFIs, and those with a moderate infections that are complex or associated with key relevant morbidities [10]. Admission is also necessary in cases of failure of outpatient management, when the patient is unable or unwilling to comply with outpatient-based treatment, there is a need for more complex dressing changes than patient/caregivers can provide or when a careful, continuous observation is needed [10]. However, the current evidence on the protocol recommended for the need for hospitalisation is low [19].

From a pathological point of view, DFIs can be classified into two main groups: soft tissue and bone infections although it is very usual to find both types together [20–22]. Soft tissue infections are then classified as cellulitis, abscesses, tenosynovitis, and necrotising soft tissue infections (necrotising cellulitis, necrotising fasciitis, necrotising tenosynovitis, and myonecrosis), including diabetic foot attack (DFA) [23, 24]. Deep abscesses and deep necrotising soft tissue infections always require surgery and admission. The infection committee of the International Working Group on Diabetic Foot (IWGDF) has recently suggested modifying the classification of the severity of the infection. They proposed adding '(O)' to moderate and severe infections groups that have an associated diagnosis of diabetic foot osteomyelitis (DFO) [10].

Another DFI classification commonly used is from Infectious Diseases Society of America (IDSA). This classifies the DFIs as group 1 with no infection, group 2 as mild soft tissue infection (STI), group 3 as moderate or severe STI, and group 4 is moderate or severe bone infection [25]. Studies have shown that patients with DFO had worse outcomes, more surgeries including amputations, longer hospitalisations, higher rates of recurrent infection and readmission than patients with moderate and severe STI [25]. DFO has frequently been reported as a risk factor for amputation and poor outcomes [4, 8, 26] and for that reason suspecting osteomyelitis is critical at the initial clinical evaluation. However, it has recently been reported that in cases of surgical diabetic foot infections, the presence of bone infection was not associated with worse prognosis [27].

The management of DFO may be different from those infections involving exclusively soft tissues. Osteomyelitis should be suspected in wounds that extended to a bone or joint and in cases in which the patient has previous history of a wound and recurrent ulcers [28]. Checking the depth of the infection after removing infected callus and tissue slough is important. However, it has been reported that nearly 90% of the wounds in one series were not evaluated for involvement of underlying structures [29]. Instrumental evaluation is very useful for determining depth and detecting fistulous tracks, cavities, and bone involvement. A blunt, 14.0-cm, 5F, stainless steel eye probe [30] or a metal forceps (Halsted-mosquito) [31, 32] is gently introduced through

the wound and the probe-to-bone (PTB) is considered 'positive' if bone (a hard or gritty surface) is palpable. PTB test had a sensitivity of 0.95, a specificity of 0.93, positive predictive value of 0.97, and a negative predictive value of 0.83 in advanced cases of infections in one study [33]. A systematic review reported a pooled sensitivity of the PTB test of 87% (95% CI, 75–93%), specificity of 83% (CI, 65–93%), positive predictive value (PPV) of 98%, and negative predictive value (NPV) of 70% [34]. We can summarise that a positive PTB test in advance cases reinforces the suspicion of DFO.

The location of the point of entry of the infection in the foot is very important to predict the infection spread in deep tissue planes and compartments. Suppuration through the ulcer while palpating at a location distant from the ulcer is consistent with a spreading infection. In some presentations, the index ulcer is located on the plantar aspect and there is cellulitis and fluctuation on the dorsum of the foot. In such cases, it is frequent that the infection had involved the bone migrating from a high-pressure plantar area to the low-pressure dorsal area. For this reason, it is uncommon that infections arising on the dorsal aspect of the foot spread to the plantar area. Presence of tissue necrosis is a worrying sign in such infections, especially when the patient has a good distal blood supply. In such cases, the surgeon should suspect the existence of a necrotising soft tissue infection [23, 24] that often resulting in raised pressure inside the foot's compartments.

The initial imaging study to evaluate a DFI infection is weightbearing plain radiographs of the foot in two standard views. It permits to detect any foreign body, free gas in soft tissues, and bone involvement. The reported sensitivity of plain radiography in the diagnosis of osteomyelitis is usually low, especially in early stages of infection [35, 36]. In cases of high suspicion of DFO and an X-ray without pathological findings, a sequential X-ray studies may be useful. That is due to the fact that bone abnormalities can only be detected at least 2–4 weeks after the onset of bone infection when significant bone resorption is evident [37]. Advanced imaging studies are needed not only for diagnosing DFO, but also detecting the soft tissue involvement and spread of the infection in deep tissue planes. Magnetic resonance imaging (MRI) has been suggested as the most useful imaging study to evaluate both deep soft tissue infections and osteomyelitis [38]. However, the exact role of advanced imaging studies to plan the surgery and determine the level of bone resection has still not been clarified. Some studies on DFO reported that the extent of infection could have been overestimated on an MRI [39]. Furthermore, preoperative MRI in cases of DFO in ischaemic feet may be less effective for distinguishing osteomyelitis from reactive bone marrow oedema in cases of neuropathic ulcers [40].

Applied Anatomy of Diabetic Foot Infection

It is essential that the treating surgeon has a good understanding of the compartmental anatomy of the foot. The foot is divided into rigid compartments and when an infection penetrates into a compartment, this can lead to raised compartment pressures resulting in a compartmental syndrome. When the compartmental pressure exceeds the capillary pressure, necrosis of deep tissues including muscle and tendons appears. Bacterial growth, toxins, and leucocyte response may also induce necrosis by direct tissular damage and producing a neutrophilic vasculitis leading to secondary thrombosis and local ischemic changes. These factors increase the extension of tissular death. Another consequence is that antibiotics cannot penetrate to the infection site due to capillary blockage.

The floor of the compartments is formed by plantar aponeurosis, which is attached to the calcaneus and spread distally to the toes. There are three plantar compartments: medial, lateral, and central. The medial and lateral compartments are separated from the central compartments by the medial and lateral intermuscular septum. The interosseus compartment is located between the metatarsal bones and contains the interossei muscles. Finally, the dorsal compartment located on

the dorsal aspect of the foot that contains a thin layer of subcutaneous tissue and the extensor tendons. Infections of the first toe spread along the medial compartment, those involving second to fourth toes spread along the central compartment, and of the fifth toe spread along the lateral compartment. Sometimes, in cases of infections without appropriate treatment the infection breaks the septum and may involve the adjacent compartment. Furthermore, the infection may migrate from the plantar to dorsal compartment through the interosseous compartment. Increasing pressure into the interosseous compartment results in thrombosis of the blood vessels leading to toe necrosis even in well vascularised feet.

The forefoot, involving the phalanxes and metatarsal heads, is the most frequent location of diabetic foot osteomyelitis [23, 41]. A surgical series demonstrated that osteomyelitis was located at the forefoot in 90% of the cases, at the midfoot in 5%, and at the rear foot in another 5% of the cases [23]. Others have reported higher figures of mid- and rear foot osteomyelitis [42]. In the case that a joint is involved, the infection produces a septic arthritis. If the infection progresses, then infection spreads to the cartilage and adjacent bone. The tip of the toes has neither joint nor tendon attachments and ulcers located in this area can easily reach the bone because only subcutaneous tissue lies between the skin and periosteum. Bone prominences from lateral deformities such as the medial eminence from bunions are also high-risk locations for ulceration and osteomyelitis.

Principles of Surgical Debridement of Diabetic Foot Infections

The aim of surgical management of infected diabetic foot is to achieve complete infection eradication while retaining all healthy and non-infected tissue. This is accomplished by attaining infection clearance through surgical removal of all infected tissues, followed by eradication of retained pathogens in the surrounding normal looking tissues by providing targeted antibiotic therapy. It is critical that the technique of surgical debridement is methodical and provides consistent and complete resection of the infected and necrotic tissue to achieve infection clearance. Red–amber–green (RAG) model of surgical debridement provides a structured model for the performing surgeon to achieve this [43]. The RAG model highlights the importance of understanding different zones of infection spread and promotes the surgeon achieve full infection clearance. The infected diabetic foot has a central zone of active infection with tissue necrosis that is recognised as the ‘red zone’. This is surrounded by an area of reactive tissue—a relatively avascular and fibrous tissue that potentially harbours small pockets of infections within it, considered as the ‘amber zone’. Outside this area is the ‘green zone’ that contains normal and healthy tissue that has a full healing potential. The RAG model recommends removal of all tissue in the red and amber zones, until the green zone is reached circumferentially. This principle is applicable to bone debridement as well.

The internal spread of diabetic foot infection is often along the tissue planes, from the zones/compartments of high pressure to low pressure. This is frequently seen along the tendon sheaths and this route is recognised as the ‘superhighway’ for the spread. It is critical that these tissue planes and tendon sheaths are probed, explored, and laid open during debridement so that all areas of necrotic and reactive tissue are excised. Such infections with extensive tissue spread often require repeat surgical debridement as some of the tissue in the amber and green zones and the edge if resection die back.

Clean Margins in Surgical Treatment of DFO

It is critical that during exostectomy and amputation procedures for DFO presentations, all of the infected bone is excised. Residual infection in the proximal bone margins after undergoing amputation for osteomyelitis may be associated with a worse prognosis after surgical treatment of DFO. Usually, the surgeon decides the location at which osteotomy is carried out based on

the intraoperative inspection of the bone. Bone appearance, its consistency, the presence of vascular thrombosis, fracture pus, and discolouration are considered by the surgeon to choose the location of osteotomy and the extent of bone resection. Bone biopsy is taken from the edges of bone resection for microbiological and histological studies. It has recently been suggested a standardised surgical dictation regarding bone appearance based on density, anatomic structure, vascular thrombosis, colour, and draining sinus [44]. However, some reports highlight that those findings may be inaccurate. One group of authors reported that 35.1% of patients had positive margins (defined by histopathology) in a retrospective cohort. Residual osteomyelitis at the proximal margin was associated with a higher rate of treatment failure, despite the longer duration of antibiotic therapy. A retrospective observational study involving 27 patients with DFO showed that the overall rate of residual osteomyelitis (based on intraoperative bone culture) was 40.7%. Nine out of 11 patients (81.8%) with positive margins had poor outcomes [45]. Other authors found that patients in which proximal bone specimens had a positive culture were more likely to undergo repeat surgical intervention. However, the authors stated that the reason for, and benefit of, this additional surgery was unclear [46]. Guidelines suggest that it could be useful obtaining a specimen of bone for culture (and, if possible, histopathology) at the stump of the resected bone to administer post-resection antibiotic therapy if positive [10]. However, the evidence is weak for the moment and the definitive role of proximal culture, histopathology, or both to guide a reintervention is not well stated. Regarding postoperative antibiotic therapy, a retrospective series reported that immediate postoperative stopping of antibiotics after amputation in the absence of residual infection was not a risk factor of failure of the treatment [47]. In cases in which residual infections are apparent after surgery of DFO, a period of 3 weeks was non-inferior to 6 weeks of postoperative antibiotic therapy in a recent randomised clinical trial [48].

Surgical Management of Forefoot Osteomyelitis

The forefoot is the most frequent location of osteomyelitis in the diabetic foot. Forefoot includes toes, metatarsal bones, interphalangeal and metatarsophalangeals joints. Forefoot osteomyelitis that does not respond to local debridement and targeted antibiotic administration is usually treated by means of some type of amputations [42]. The most common amputations performed to remove infected bone and soft tissues in diabetic patients with forefoot osteomyelitis are toe, ray, and transmetatarsal resections [49]. Conservative surgery in which the infected bone and non-viable soft tissue are removed without performing any type of amputation is an accepted alternative to amputation in some presentations [23, 50, 51]. However, the impact of this type of surgery on the quality of life and long-term recurrences when comparing with minor amputations has not been addressed. Some conservative surgeries, as an alternative to toe amputation, have been described. Osteomyelitis of the tip of the minor toes can easily be removed through the ulcer. This procedure can be carried out combined with percutaneous flexor tenotomy to reduce the deformity of the toe [52, 53]. When the interphalangeal joint of lesser toes is involved by the infection, a resection arthroplasty can be considered [23, 54–56]. In a series of 72 toes, a group of authors reported successful outcome of excision arthroplasty for infected IPJs by performing extensive debridement of bone and soft tissues, thorough irrigation of the wound, and stabilisation of IPJ using a Kirschner wire. Just three cases in this series underwent toe amputations and no proximal spreading of the infection was observed in any other cases during the follow-up period. Open arthroplasties leaving the postoperative wound to heal by secondary intention has also been described in cases of diabetic foot osteomyelitis [55, 57, 58].

Neuropathic plantar ulcers under the metatarsal head may become complicated by osteomyelitis. In such cases, amputation of the toe

and partial ray amputation including the metatarsal head are the available surgical options. Plantar or dorsal approach can be used for removing the metatarsal head or the metatarsal phalangeal joint [52]. Conservative surgery consisting of resection of metatarsal head is also widely used [23, 58–64]. A group of authors retrospectively compared the outcomes of both approaches and reported that there were no differences regarding time to healing but patients operated by dorsal approach experienced a higher rate of postoperative complications [65]. Transfer ulcers due to biomechanical changes in the foot are very common when a metatarsal head is removed either as part of ray amputation or in isolation. That is especially true in cases in which the first metatarsal head is removed [66]. First ray amputation is associated with severe biomechanical disturbances of the foot, subsequent amputations [67–71], and even the development of Charcot Neuroarthropathy [72]. It has been suggested that a more proximal level amputation, such as a balanced transmetatarsal, might provide a better functional and reliable residual weight-bearing foot [71]. Conservative approaches leading to save the hallux could be an alternative but there is no long-term follow-up of these procedures. One-stage resection and pin stabilisation [73] or the use of external fixation after removing the infected bone [74] has been described in a short series. Another group reported a cohort including 28 patients with osteomyelitis of the first ray treated by a technique requiring a one-stage surgical approach [75]. After surgical debridement with removal of the infected bone, the authors placed antibiotic-loaded bone cement and stabilised the treated area with an external fixator [75]. Four patients (14.2%) developed a relapse of the ulceration after the procedure. No ulceration recurrences, transfer ulcerations, shoe fit problems, or gait abnormalities were detected in the other 24 patients (85.8%) [75]. Bone debridement and antibiotic-impregnated cement spacer may be another option [58]. However, it is necessary to highlight that additional controlled trials are required to evaluate this further.

Surgical Treatment of Infected Heel Ulcers

Infected plantar heel ulcers in people with diabetic peripheral neuropathy carry a high risk of major amputation as these not only result in osteomyelitis of calcaneal body, but also lead to destruction of plantar heel pad. Heel is the second most common anatomical location for pressure ulcers [76]. The reported outcomes of surgical management of heel ulcers are variable, as the earlier studies showed healing rates ranging from 35% to 74% [77], but the most recent ones revealed better outcomes with 97–100% limb salvage reported from treating centres [78–80].

Various surgical techniques have been reported on the surgical management of calcaneal osteomyelitis to achieve limb salvage. These include partial or total calcanectomy. Cook et al., in 2007, reported a 71.4% healing rate during the first year in their series of 50 partial calcanectomies for chronic non-healing ulcers. However, they found a high rate of ulcer recurrence after 1 year, with higher negative outcomes in the presence of MRSA infection, vascular compromise, low albumin levels, and higher grade of preoperative ulcer [77]. Paola et al. reported a 100% ulcer healing rate, within their follow-up period of 12 months, in their cohort of 18 patients treated with open partial calcanectomy and application of circular external fixator [78]. Ngwe et al., more recently, reported the outcomes of surgical management of 30 diabetic neuropathic heel ulcers with no critical limb ischemia, managed with ulcer debridement without partial calcanectomy when COM was present [80]. At a mean follow-up period of 28 months (12–83), 50% achieved full ulcer healing and 97% had limb salvage. A mortality rate of 38% was observed in this cohort. Only 9 out of 24 ulcers with calcaneal osteomyelitis (p value 0.044) achieved full ulcer healing. Local antibiotic delivery as an adjunct during partial calcanectomy can help eradicate any residual infection and promote complete infection eradication. Antibiotic-loaded injectable bone substitute is injected in multiple channels created by making drill holes in the residual

calcaneal body to achieve this [80]. This provides high tissue concentration of antibiotic for several weeks that eradicates any residual pathogens [81, 82]. Dramploas et al. reported 100% infection eradication and healing rate using similar technique in their series of 12 patients with infected heel ulcers and calcaneal osteomyelitis [79].

Principles of Exostectomy

An infected plantar ulcer, as a result of peak plantar pressures due to underlying bone prominence, requires exostectomy in addition to ulcer debridement, to achieve eradication of infection and ulcer healing. The ulcer first is excised and thoroughly debrided down to the floor, exposing full area of exostosis. The bone prominence is marked by careful palpation, cross checking under fluoroscopy. The edge of the bone prominence is scored with an oscillating saw by about 5 mm depth. A curved osteotome is used to excise the exostosis completely within the marked zone. The bone surface of the excised area is examined for any areas of necrosis, discolouration, and altered consistency, which may represent residual area of infection and if present, this is thoroughly explored and excised. The surface and the edge of the excised area are carefully inspected and palpated for any residual bone prominence and excised if present. Local antibiotic eluting calcium preparation can be applied around the bone or injected into bone channels drilled in the exostectomy area to eradicate any residual infection [79, 80]. The choice of the antibiotic is based on microbiological sensitivities of deep tissue or bone biopsy specimen culture results. The open wound is managed with either a local transposition flap or negative pressure wound therapy (NPWT).

Surgical Management of Diabetic Foot Attack

Diabetic foot infection presentations can occasionally spread rapidly along the tissue planes resulting in necrosis and systemic inflammatory response. This is often triggered by a blister or skin break from minor trauma that leads to local spreading of infection in different tissue planes resulting in development of ulceration and spreading cellulitis. Such presentation is labelled as diabetic foot attack (DFA) and without a timely and emergent intervention, it can be limb and life threatening [83]. Vainieri et al. reported the outcomes of 106 patients presented with diabetic foot attack, with a mean follow-up of 18.4 ± 3.6 months [84]. They noted a major amputation free survival in 71% of patients during the first 12 months from admission that reduced to 55.4% by the end of the follow-up.

DFA presentation is best managed by a multidisciplinary diabetic foot team for optimal outcomes. It is critical that the diagnosis is reached rapidly by performing appropriate clinical assessment and urgent investigations. The investigations should focus on assessing the extent of infection and obtaining microbiological sensitivities. Plain radiographs often show soft tissue changes, including the presence of gas shadow. Deep tissue specimens are obtained for microbiological culture and sensitivities, before commencing empirical intravenous antibiotic therapy [85]. In the absence of an open ulcer or wound, ultrasound examination can be performed for assessment of deep collection and aspiration for microbiological studies. MRI is the most useful imaging investigation as it provides the diagnosis and information on the extent of infection spread that can be useful for surgical planning. However, it is critical that the appropriate investigations are performed in a timely manner so that the surgery is not delayed.

DFA often needs emergent surgical intervention. Aggressive surgical debridement, using the principles described above, is performed soon after diagnosis as delay can cause further tissue necrosis and potential limb loss. Repeat surgical debridement is often required if the systemic inflammatory response does not improve or any further tissue necrosis is identified. Targeted intravenous antibiotic therapy, based on microbiological sensitivities, is continued until the infection is completely cleared, as noted by the improvement in the clinical findings and normali-

sation of serological markers. The open surgical wound is managed with NPWT followed by skin grafting or a local tissue flap. Due to the degree of soft tissue and bone loss from the spread of infection and surgical debridement, the affected feet often require expert treatment after the resolution of DFA presentation, including deformity corrective procedures.

Conclusion

Diabetic foot infections, including osteomyelitis, range from simple presentations to complex limb and life threatening DFA. These require thorough clinical assessment, often in a multidisciplinary setup, and address the sequala of such infections, including revascularisation and deformity correction, to provide optimal outcomes [86, 87]. Surgery is a critical component of treatment and should be considered in the presence of tissue necrosis.

References

1. Geraghty T, LaPorta G. Current health and economic burden of chronic diabetic osteomyelitis. Expert Rev Pharmacoecon Outcomes Res. 2019;19:279–86.
2. Lin CW, Armstrong DG, Lin CH, Liu PH, Hung SY, Lee SR, et al. Nationwide trends in the epidemiology of diabetic foot complications and lower-extremity amputation over an 8-year period. BMJ Open Diabetes Res Care. 2019;7:e000795.
3. Hicks CW, Selvarajah S, Mathioudakis N, Sherman RE, Hines KF, Black JH III, et al. Burden of infected diabetic foot ulcers on hospital admissions and costs. Ann Vasc Surg. 2016;33:149–58.
4. Sen P, Demirdal T, Emir B. Meta-analysis of risk factors for amputation in diabetic foot infections. Diabetes Metab Res Rev. 2019;35:e3165.
5. Lavery LA, Armstrong DG, Murdoch DP, Peters EJ, Lipsky BA. Validation of the Infectious Diseases Society of America's diabetic foot infection classification system. Clin Infect Dis. 2007;44:562–5.
6. Hartemann-Heurtier A, Ha Van G, Danan JP, Koskas F, Jacqueminet S, Golmard JL, et al. Outcome of severe diabetic foot ulcers after standardised management in a specialised unit. Diabetes Metab. 2002;28:477–84.
7. Saltoglu N, Ergonul O, Tulek N, Yemisen M, Kadanali A, Karagoz G, et al. Influence of multidrug resistant organisms on the outcome of diabetic foot infection. Int J Infect Dis. 2018;70:10–4.
8. Arias M, Hassan-Reshat S, Newsholme W. Retrospective analysis of diabetic foot osteomyelitis management and outcome at a tertiary care hospital in the UK. PLoS One. 2019;14:e0216701.
9. Ghanassia E, Villon L, Thuan Dit Dieudonne JF, Boegner C, Avignon A, Sultan A. Long-term outcome and disability of diabetic patients hospitalized for diabetic foot ulcers: a 6.5-year follow-up study. Diabetes Care. 2008;31:1288–92.
10. Lipsky BA, Senneville E, Abbas ZG, Aragon-Sanchez J, Diggle M, Embil JM, et al. Guidelines on the diagnosis and treatment of foot infection in persons with diabetes (IWGDF 2019 update). Diabetes Metab Res Rev. 2020;36(Suppl 1):e3280.
11. van Baal JG. Surgical treatment of the infected diabetic foot. Clin Infect Dis. 2004;39(Suppl 2):S123–8.
12. Faglia E, Clerici G, Caminiti M, Quarantiello A, Gino M, Morabito A. The role of early surgical debridement and revascularization in patients with diabetes and deep foot space abscess: retrospective review of 106 patients with diabetes. J Foot Ankle Surg. 2006;45:220–6.
13. Tan JS, Friedman NM, Hazelton-Miller C, Flanagan JP, File TM Jr. Can aggressive treatment of diabetic foot infections reduce the need for above-ankle amputation? Clin Infect Dis. 1996;23:286–91.
14. Armstrong DG, Lipsky BA. Diabetic foot infections: stepwise medical and surgical management. Int Wound J. 2004;1:123–32.
15. Gibbons GW. The diabetic foot: amputations and drainage of infection. J Vasc Surg. 1987;5:791–3.
16. Taylor LM Jr, Porter JM. The clinical course of diabetics who require emergent foot surgery because of infection or ischemia. J Vasc Surg. 1987;6:454–9.
17. Chang BB, Darling RC III, Paty PS, Lloyd WE, Shah DM, Leather RP. Expeditious management of ischemic invasive foot infections. Cardiovasc Surg. 1996;4:792–5.
18. Lipsky BA, Berendt AR, Deery HG, Embil JM, Joseph WS, Karchmer AW, et al. Diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2004;39:885–910.
19. Peters EJG, Lipsky BA, Senneville E, Abbas ZG, Aragon-Sanchez J, Diggle M, et al. Interventions in the management of infection in the foot in diabetes: a systematic review. Diabetes Metab Res Rev. 2020;36(Suppl 1):e3282.
20. Eneroth M, Apelqvist J, Stenstrom A. Clinical characteristics and outcome in 223 diabetic patients with deep foot infections. Foot Ankle Int. 1997;18:716–22.
21. Aragon-Sanchez J. Clinical-pathological characterization of diabetic foot infections: grading the severity of osteomyelitis. Int J Low Extrem Wounds. 2012;11:107–12.
22. Aragon-Sanchez J. Seminar review: a review of the basis of surgical treatment of diabetic foot infections. Int J Low Extrem Wounds. 2011;10:33–65.
23. Aragon-Sanchez FJ, Cabrera-Galvan JJ, Quintana-Marrero Y, Hernandez-Herrero MJ, Lazaro-Martinez JL, Garcia-Morales E, et al. Outcomes of surgical

treatment of diabetic foot osteomyelitis: a series of 185 patients with histopathological confirmation of bone involvement. Diabetologia. 2008;51:1962–70.
24. Aragon-Sanchez J, Quintana-Marrero Y, Lazaro-Martinez JL, Hernandez-Herrero MJ, Garcia-Morales E, Beneit-Montesinos JV, et al. Necrotizing soft-tissue infections in the feet of patients with diabetes: outcome of surgical treatment and factors associated with limb loss and mortality. Int J Low Extrem Wounds. 2009;8:141–6.
25. Lavery LA, Ryan EC, Ahn J, Crisologo PA, Oz OK, La Fontaine J, et al. The infected diabetic foot: re-evaluating the Infectious Diseases Society of America diabetic foot infection classification. Clin Infect Dis. 2020;70:1573–9.
26. Wukich DK, Hobizal KB, Sambenedetto TL, Kirby K, Rosario BL. Outcomes of osteomyelitis in patients hospitalized with diabetic foot infections. Foot Ankle Int. 2016;37:1285–91.
27. Aragon-Sanchez J, Viquez-Molina G, Lopez-Valverde ME, Rojas-Bonilla JM, Murillo-Vargas C. Surgical diabetic foot infections: is osteomyelitis associated with a worse prognosis? Int J Low Extrem Wounds. 2023;22(1):36–43.
28. Lavery LA, Peters EJ, Armstrong DG, Wendel CS, Murdoch DP, Lipsky BA. Risk factors for developing osteomyelitis in patients with diabetic foot wounds. Diabetes Res Clin Pract. 2009;83:347–52.
29. Edelson GW, Armstrong DG, Lavery LA, Caicco G. The acutely infected diabetic foot is not adequately evaluated in an inpatient setting. J Am Podiatr Med Assoc. 1997;87:260–5.
30. Grayson ML, Gibbons GW, Balogh K, Levin E, Karchmer AW. Probing to bone in infected pedal ulcers. A clinical sign of underlying osteomyelitis in diabetic patients. JAMA. 1995;273:721–3.
31. Alvaro-Afonso FJ, Lazaro-Martinez JL, Aragon-Sanchez J, Garcia-Morales E, Garcia-Alvarez Y, Molines-Barroso RJ. Inter-observer reproducibility of diagnosis of diabetic foot osteomyelitis based on a combination of probe-to-bone test and simple radiography. Diabetes Res Clin Pract. 2014;105:e3–5.
32. Aragon-Sanchez J, Lipsky BA, Lazaro-Martinez JL. Diagnosing diabetic foot osteomyelitis: is the combination of probe-to-bone test and plain radiography sufficient for high-risk inpatients? Diabet Med. 2011;28:191–4.
33. Aragón-Sánchez J, Lipsky BA, Lázaro-Martínez JL. Diagnosing diabetic foot osteomyelitis: is the combination of probe-to-bone and plain radiography sufficient for high risk inpatients? Diabet Med. 2011;28(2):191–4. https://doi.org/10.1111/j.1464-5491.2010.03150.x.
34. Lam K, van Asten SA, Nguyen T, La Fontaine J, Lavery LA. Diagnostic accuracy of probe to bone to detect osteomyelitis in the diabetic foot: a systematic review. Clin Infect Dis. 2016;63:944–8.
35. Dinh MT, Abad CL, Safdar N. Diagnostic accuracy of the physical examination and imaging tests for osteomyelitis underlying diabetic foot ulcers: meta-analysis. Clin Infect Dis. 2008;47:519–27.
36. Butalia S, Palda VA, Sargeant RJ, Detsky AS, Mourad O. Does this patient with diabetes have osteomyelitis of the lower extremity? JAMA. 2008;299:806–13.
37. Senneville EM, Lipsky BA, van Asten SAV, Peters EJ. Diagnosing diabetic foot osteomyelitis. Diabetes Metab Res Rev. 2020;36(Suppl 1):e3250.
38. Dinh T, Snyder G, Veves A. Current techniques to detect foot infection in the diabetic patient. Int J Low Extrem Wounds. 2010;9:24–30.
39. Morrison WB, Schweitzer ME, Wapner KL, Hecht PJ, Gannon FH, Behm WR. Osteomyelitis in feet of diabetics: clinical accuracy, surgical utility, and cost-effectiveness of MR imaging. Radiology. 1995;196:557–64.
40. Fujii M, Armsrong DG, Terashi H. Efficacy of magnetic resonance imaging in diagnosing diabetic foot osteomyelitis in the presence of ischemia. J Foot Ankle Surg. 2013;52:717–23.
41. Valabhji J, Oliver N, Samarasinghe D, Mali T, Gibbs RG, Gedroyc WM. Conservative management of diabetic forefoot ulceration complicated by underlying osteomyelitis: the benefits of magnetic resonance imaging. Diabet Med. 2009;26:1127–34.
42. Karchmer AW, Gibbons GW. Foot infections in diabetes: evaluation and management. Curr Clin Top Infect Dis. 1994;14:1–22.
43. Ahluwalia R, Vainieri E, Tam J, Sait S, Sinha A, Manu CA, Reichert I, Kavarthapu V, Edmonds M, Vas P. Surgical diabetic foot debridement: improving training and practice utilizing the traffic light principle. Int J Low Extrem Wounds. 2019;18(3):279–86. https://doi.org/10.1177/1534734619853657. Epub 2019 Jun 25. PMID: 31237147.
44. Schmidt BM, Jarocki C. Making the equivocal unequivocal: standardization of clean margins in diabetic foot osteomyelitis. Clin Diabetes Endocrinol. 2020;6:8.
45. Atway S, Nerone VS, Springer KD, Woodruff DM. Rate of residual osteomyelitis after partial foot amputation in diabetic patients: a standardized method for evaluating bone margins with intraoperative culture. J Foot Ankle Surg. 2012;51:749–52.
46. Shiraev TP, Lipsky BA, Kwok TMY, Robinson DA. Utility of culturing marginal bone in patients undergoing lower limb amputation for infection. J Foot Ankle Surg. 2019;58:847–51.
47. Rossel A, Lebowitz D, Gariani K, Abbas M, Kressmann B, Assal M, et al. Stopping antibiotics after surgical amputation in diabetic foot and ankle infections—a daily practice cohort. Endocrinol Diabetes Metab. 2019;2:e00059.
48. Gariani K, Pham TT, Kressmann B, Jornayvaz FR, Gastaldi G, Stafylakis D, et al. Three versus six weeks of antibiotic therapy for diabetic foot osteomyelitis: a prospective, randomized, non-inferiority pilot trial. Clin Infect Dis. 2020;73:e1539.
49. Cuttica DJ, Philbin TM. Surgery for diabetic foot infections. Foot Ankle Clin. 2010;15:465–76.

50. Faglia E, Clerici G, Caminiti M, Curci V, Somalvico F. Feasibility and effectiveness of internal pedal amputation of phalanx or metatarsal head in diabetic patients with forefoot osteomyelitis. J Foot Ankle Surg. 2012;51:593.
51. Ha Van G, Siney H, Danan JP, Sachon C, Grimaldi A. Treatment of osteomyelitis in the diabetic foot. Contribution of conservative surgery. Diabetes Care. 1996;19:1257–60.
52. Aragon-Sanchez J, Lazaro-Martinez JL, Alvaro-Afonso FJ, Molines-Barroso R. Conservative surgery of diabetic forefoot osteomyelitis: how can I operate on this patient without amputation? Int J Low Extrem Wounds. 2015;14:108–31.
53. Sanz-Corbalan I, Lazaro-Martinez JL, Garcia-Alvarez Y, Garcia-Morales E, Alvaro-Afonso F, Molines-Barroso R. Digital deformity assessment prior to percutaneous flexor tenotomy for managing diabetic foot ulcers on the toes. J Foot Ankle Surg. 2019;58:453–7.
54. Kim JY, Kim TW, Park YE, Lee YJ. Modified resection arthroplasty for infected non-healing ulcers with toe deformity in diabetic patients. Foot Ankle Int. 2008;29:493–7.
55. Melamed EA, Peled E. Antibiotic impregnated cement spacer for salvage of diabetic osteomyelitis. Foot Ankle Int. 2012;33:213–9.
56. Aragon-Sanchez J. Treatment of diabetic foot osteomyelitis: a surgical critique. Int J Low Extrem Wounds. 2010;9:37–59.
57. Aragon-Sanchez J, Lazaro-Martinez JL, Quintana-Marrero Y, Sanz-Corbalan I, Hernandez-Herrero MJ, Cabrera-Galvan JJ. Super-oxidized solution (Dermacyn Wound Care) as adjuvant treatment in the postoperative management of complicated diabetic foot osteomyelitis: preliminary experience in a specialized department. Int J Low Extrem Wounds. 2013;12:130–7.
58. Aragon-Sanchez J, Lazaro-Martinez JL, Hernandez-Herrero C, Campillo-Vilorio N, Quintana-Marrero Y, Garcia-Morales E, et al. Does osteomyelitis in the feet of patients with diabetes really recur after surgical treatment? Natural history of a surgical series. Diabet Med. 2012;29:813–8.
59. Frykberg R, Wukich D, Kavarthapu V, Zgonis T, Dalla Paola L. Surgery for the diabetic foot: a key component of care. Diabetes Metab Res Rev. 2020;36(Suppl 1):e3251.
60. Wieman TJ, Mercke YK, Cerrito PB, Taber SW. Resection of the metatarsal head for diabetic foot ulcers. Am J Surg. 1998;176:436–41.
61. Freeman GJ, Mackie KM, Sare J, Walsh AK, Pherwani AD. A novel approach to the management of the diabetic foot: metatarsal excision in the treatment of osteomyelitis. Eur J Vasc Endovasc Surg. 2007;33:217–9.
62. Armstrong DG, Rosales MA, Gashi A. Efficacy of fifth metatarsal head resection for treatment of chronic diabetic foot ulceration. J Am Podiatr Med Assoc. 2005;95:353–6.
63. Rosenblum BI, Pomposelli FB Jr, Giurini JM, Gibbons GW, Freeman DV, Chrzan JS, et al. Maximizing foot salvage by a combined approach to foot ischemia and neuropathic ulceration in patients with diabetes. A 5-year experience. Diabetes Care. 1994;17:983–7.
64. Piaggesi A, Schipani E, Campi F, Romanelli M, Baccetti F, Arvia C, et al. Conservative surgical approach versus non-surgical management for diabetic neuropathic foot ulcers: a randomized trial. Diabet Med. 1998;15:412–7.
65. Tardaguila-Garcia A, Sanz-Corbalan I, Molines-Barroso RJ, Alvaro-Afonso FJ, Garcia-Alvarez Y, Lazaro-Martinez JL. Complications associated with the approach to metatarsal head resection in diabetic foot osteomyelitis. Int Wound J. 2019;16:467–72.
66. Molines-Barroso RJ, Lazaro-Martinez JL, Aragon-Sanchez J, Garcia-Morales E, Beneit-Montesinos JV, Alvaro-Afonso FJ. Analysis of transfer lesions in patients who underwent surgery for diabetic foot ulcers located on the plantar aspect of the metatarsal heads. Diabet Med. 2013;30:973–6.
67. Aprile I, Galli M, Pitocco D, Di Sipio E, Simbolotti C, Germanotta M, et al. Does first ray amputation in diabetic patients influence gait and quality of life? J Foot Ankle Surg. 2018;57:44–51.
68. Borg I, Mizzi S, Formosa C. Plantar pressure distribution in patients with diabetic peripheral neuropathy and a first-ray amputation. J Am Podiatr Med Assoc. 2018;108:225–30.
69. Murdoch DP, Armstrong DG, Dacus JB, Laughlin TJ, Morgan CB, Lavery LA. The natural history of great toe amputations. J Foot Ankle Surg. 1997;36:204–8; discussion 256.
70. Dalla Paola L, Faglia E, Caminiti M, Clerici G, Ninkovic S, Deanesi V. Ulcer recurrence following first ray amputation in diabetic patients: a cohort prospective study. Diabetes Care. 2003;26:1874–8.
71. Borkosky SL, Roukis TS. Incidence of repeat amputation after partial first ray amputation associated with diabetes mellitus and peripheral neuropathy: an 11-year review. J Foot Ankle Surg. 2013;52:335–8.
72. Fontalis A, Doorgakant A, Zahra W, Blundell C. Midfoot Charcot neuro-arthropathy precipitated by first or fifth ray amputation. Foot Ankle Surg. 2020;27:673.
73. Johnson JE, Anderson SA. One stage resection and pin stabilization of first metatarsophalangeal joint for chronic plantar ulcer with osteomyelitis. Foot Ankle Int. 2010;31:973–9.
74. Schweinberger MH, Roukis TS. Salvage of the first ray with external fixation in the high-risk patient. Foot Ankle Spec. 2008;1:210–3.
75. Dalla Paola L, Carone A, Morisi C, Cardillo S, Pattavina M. Conservative surgical treatment of infected ulceration of the first metatarsophalangeal joint with osteomyelitis in diabetic patients. J Foot Ankle Surg. 2015;54:536–40.
76. Fowler E, Scott-Williams S, McGuire JB. Practice recommendations for preventing heel pressure ulcers. Ostomy Wound Manag. 2008;54(10):42–8.

77. Cook J, et al. A retrospective assessment of partial calcanectomies and factors influencing postoperative course. J Foot Ankle Surg. 2007;46(4):248–55.
78. Dalla Paola L, Carone A, Boscarino G, Scavone G, Vasilache L. Combination of open subtotal calcanectomy and stabilization with external fixation as limb salvage procedure in hindfoot-infected diabetic foot ulcers. Int J Low Extrem Wounds. 2016;15(4):332–7.
79. Drampalos E, Mohammad HR, Kosmidis C, Balal M, Wong J, Pillai A. Single stage treatment of diabetic calcaneal osteomyelitis with an absorbable gentamicin-loaded calcium sulphate/hydroxyapatite biocomposite: the Silo technique. Foot. 2018;34:40–4.
80. Phyo N, Tang W, Kavarthapu V. Medium-term outcomes of multi-disciplinary surgical management of non-ischemic diabetic heel ulcers. J Clin Orthop Trauma. 2021;17:30–6. https://doi.org/10.1016/j.jcot.2021.01.012.
81. Stravinskas M, Horstmann P, Ferguson J, Hettwer W, Nilsson M, Tarasevicius S, Petersen MM, McNally MA, Lidgren L. Pharmacokinetics of gentamicin eluted from a regenerating bone graft substitute: in vitro and clinical release studies. Bone Jt Res. 2016;5:427–35.
82. Colding-Rasmussen T, Horstmann P, Petersen MM, Hettwer W. Antibiotic elution characteristics and pharmacokinetics of gentamicin and vancomycin from a mineral antibiotic carrier: an in vivo evaluation of 32 clinical cases. J Bone Jt Infect. 2018;3:234–40.
83. Vas PRJ, Edmonds M, Kavarthapu V, et al. The diabetic foot attack: "tis too late to retreat!". Int J Low Extrem Wounds. 2018;17(1):7–13.
84. Vainieri E, Ahluwalia R, Slim H, et al. Outcomes after emergency admission with a diabetic foot attack indicate a high rate of healing and limb salvage but increased mortality: 18-month follow-up study. Exp Clin Endocrinol Diabetes. 2020;130:165. https://doi.org/10.1055/a-1322-4811.
85. Bateman AH, Bradford S, Hester TW, et al. Modern orthopedic inpatient care of the orthopedic patient with diabetic foot disease. Int J Low Extrem Wounds. 2015;14(4):384–92.
86. Frykberg RG, Attinger C, Smeets L, Koller A, Bal A, Kavarthapu V. Surgical strategies for prevention of amputation of the diabetic foot. J Clin Orthop Trauma. 2021;17:99–105. https://doi.org/10.1016/j.jcot.2021.02.019.
87. Kavarthapu V, Budair B. Two-stage reconstruction of infected Charcot foot using internal fixation. Bone Jt J. 2021;103-B:10:1611–8.

Charcot Foot Syndrome: Aetiology and Diagnosis

17

William Jeffcoate and Fran Game

The Bottom Line

Although the Charcot foot is not rare, it is thought to be rare by many clinicians and few are aware that any delay in diagnosis may lead to irreversible, and potentially life-threatening, damage. In a recent survey of medical staff in a very large teaching hospital in Michigan, some 68% respondents admitted that their knowledge of the condition was either rudimentary or non-existent [1]. A similar survey in any other hospital—or in non-specialist practice—in any country of the world would confirm that such ignorance is common. And while most doctors would be mortified if they missed a common cancer in its early stages and failed to arrange for early expert assessment, few realise that the same approach is needed for the best management of the Charcot foot. There are observational data to suggest that delay in diagnosis of active Charcot syndrome is associated with a far worse outcome [2–4]. It is for these reasons that this review starts with its bottom line.

The 1, 2, 3 of Diagnosis of the Charcot Foot: The Bottom Line

Every clinician who is approached for advice by a person with an inflamed foot which has no obvious cause should remember three simple points:

1. Has this person got diabetes?
2. Has this person got peripheral neuropathy?
3. If yes to either of these, it should be assumed that they have an active Charcot foot until proved otherwise. They should be advised to minimise weight-bearing and should be referred for urgent expert assessment.

Introduction

The condition is known variously as the Charcot foot, Charcot neuropathic osteoarthropathy or neuro-inflammatory osteoarthropathy and is a complex disorder which occurs in people with some form of peripheral neuropathy. It is characterised by inflammation and varying degrees of structural damage to the bones and joints of the foot. In some cases the damage is severe, disabling and potentially limb-threatening but in other cases the changes are relatively minor.

W. Jeffcoate
Nottingham University Hospitals NHS Trust, Nottingham, UK

F. Game (✉)
University Hospitals of Derby and Burton NHS Foundation Trust, Derby, UK
e-mail: frances.game@nhs.net

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_17

The Charcot Foot Is a Syndrome: Not a Disease

The Charcot foot should be considered as a syndrome rather than a disease. It can be recognised but has no definition and no current defined diagnostic criteria.

History

The condition was first described by Jean-Martin Charcot (1825–1893) in the spine and upper part of the leg in 1868 and by Herbert William Page (1845–1926) in the foot in 1881 [5]. In these reports, as well as in Charcot's five case series of 1883, the underlying cause was tertiary syphilis with tabes dorsalis and 'progressive locomotor ataxia'. Charcot suggested that the problem was in part the result of reduced pain sensation and in part the result of inflammation with increased blood flow. Non-syphilitic Charcot disease was first described in people with diabetes in 1936. It can also complicate leprosy [6], alcohol abuse, chemotherapy and other causes of neuropathy. There have been a number of major reviews in recent years [7–9].

The Clinical Presentation of the Charcot Syndrome

The condition is most often seen in the foot but it may occur further up the lower limb and even in the spine. In this chapter, however, attention is focused on the foot in diabetes—not least because it is by far the most common site affected and diabetes is by far the most common cause in most parts of the world.

Active Phase

The active phase has been traditionally referred to as 'acute Charcot' but the word 'acute' can be misleading in that the active phase of the disease can be anything but 'acute' and can last for days, weeks or for up to 18 months. The term 'acute Charcot' is a misnomer and should be abandoned in favour of 'active Charcot' [10].

The hallmark/principal feature of the active phase is local inflammation. If there is any associated deformity (from dislocation, fracture), it may be apparent clinically and/or on imaging. There may or may not be associated discomfort. Any discomfort or pain is, however, rarely, if ever, as severe as would be expected from any changes seen on imaging. When the affected foot is fully rested by immobilisation in a below knee cast, the inflammation reduces but it does not settle completely until the underlying process goes into remission.

Active disease is most commonly triggered by minor trauma. Such trauma was recalled by 36% of 288 cases managed in 76 centres in the UK and Ireland between 2005 and 2007. Other triggers were preceding foot ulceration (35%), local surgery (12%) and osteomyelitis (7%) [11]. The observation that 7% cases in this series were triggered by osteomyelitis has also been reported by Ndip et al. [12] and is of great importance—not so much in the diagnosis of Charcot syndrome but in the assessment of apparent lack of resolution in cases of treated osteomyelitis. When a case of pedal osteomyelitis shows signs of deterioration (either on clinical grounds or on imaging) despite appropriate treatment, it might be assumed that the infection was still active. This may not, however, be the case if the original infection has triggered the onset of an active Charcot syndrome. The possibility needs to be considered because it has clear implications for management. A bone biopsy for microbiological sampling could be considered, although more discriminatory radiological imaging may also be considered such as radiolabelled white blood cell (WBC) scans [13].

The activity of the Charcot foot syndrome will eventually prove self-limiting in many and the foot will stabilise once the inflammation settles—even though any skeletal damage or deformity will be permanent. Expert teams manage the condition by minimising trauma by ensuring effective off-loading [11] as well as the management of complications (including secondary deformity, ulceration and infection). Currently, there is no effective systemic therapy to either prevent or

reduce the causative processes [14]. The condition is associated with high levels of anxiety and depression [3, 15].

Inactive Phase and Recurrence

The majority will eventually enter remission but this may not be for a number of months. There is some variation in the reported time to inactivity following conservative management with mean times varying from less than 6 months in Denmark [16], to a median of 51.5 weeks in one centre in UK [17], and 10–12 months in the 76 UK centres in one large study from UK and Ireland [11]. Some of these differences will relate to some people having their off-loading discontinued inappropriately early and hence will be accompanied by a correspondingly high relapse rate [18]. Some of the difference between reported times to resolution will relate also to inclusion of the time which elapses between a decision being made that the condition has entered remission and the availability of the required footwear needed for full ambulation. However, one of the main causes is that there is no agreed definition for resolution of the active stage as demonstrated in a recent systematic review [19].

Once, however, the disease is truly inactive, it is extremely rare for the disease to recur in the same position in the index foot even though occasional cases have been described [20]. Some 20% of affected people will, however, have disease affecting the contralateral foot—either at the same time or usually a short time later.

Aetiology of the Charcot Syndrome

The Charcot syndrome can be regarded as a distortion of the normal complex responses of the body to injury or insult with these responses being normally reliant on close intercellular signalling. The factors contributing to its occurrence are considered under the following subheadings: predisposition, permissive factors, precipitation, presentation, perpetuation and resolution.

Aetiology: Predisposition

The Charcot syndrome results from the variable interaction of three principal factors: neuropathy, fragility of bones and joint capsules and retention of the capacity to mount a local inflammatory response to injury. Additional factors may contribute when the neuropathy is the result of diabetes.

Neuropathy

Neuropathy affects up to 50% people with diabetes [21, 22]. The type and extent of nerve damage varies from person to person but it is typically symmetrical and affects one or more of many aspects of peripheral nerve function including sensory, motor, cardiac and non-cardiac autonomic, neurovascular and skeletal (variously involving bone, joints and bone marrow) innervation. In the people presenting with an active Charcot foot, however, the manifestation of neuropathy which is most obvious clinically is loss of protective sensation and this means that even gross distortion of the foot is relatively pain-free. The loss of significant pain is common to cases which complicate diabetes as well as to those which complicate other conditions, such as the tertiary syphilis in which the syndrome was first described. This is despite the neurological defects being different in different diseases: loss of deep pain sensation in tabes dorsalis is from dorsal column disease of the spine, for example, whereas in diabetes it is mainly from dysfunction of peripheral sensory fibres.

Effect of Neuropathy on Bone

The RANK/RANKL-NFkappaB and Wnt/β--catenin Pathways

One key pathway in bone modelling is the RANKL/RANK signalling pathway. RANKL is derived from monocyte derivatives and is the polypeptide ligand for the RANK receptor, so-called because it is the receptor for the activation of the nuclear transcription factor, NFkappaB. NFkappaB has a number of functions but one of these is the activation of osteoclasts, with resultant bone breakdown. Osteoprotegerin

(OPG) acts as a decoy receptor for RANKL and thereby helps to limit its action. RANKL and OPG are both released at the same time, even though their actions are essentially opposite. The ratio of the two at any one time could, however, be of importance in the relative effects of RANKL vs. OPG on bone quality.

Another pathway which also affects both bone quality is the Wnt/β-catenin pathway. High levels of Wnt ligand prevent the breakdown of β-catenin, which in turn promotes osteoblast maturation and therefore bone formation. Low levels, therefore, would be consistent with bone breakdown. Sclerostin and Dickkopf-1 are inhibitors of Wnt and have been found to be significantly higher in a small series of post-menopausal women with type-2 diabetes than in sex and age-matched controls [23].

Neuropathy is associated with osteolysis and increased bone fragility. The integrity of bones is normally maintained by a variety of nerve-derived neurotransmitters which encourage the synthesis of OPG in preference to activation of RANK receptor and NFkappaB. These are derived from both autonomic and somatic neurones and include calcitonin gene related peptide (CGRP), substance P (SP), vasoactive intestinal polypeptide (VIP), tyrosine hydroxylase (TH), norepinephrine (NE), neuropeptide Y (NPY), glutamate and leptin [24, 25]. All are associated with the release of anti-inflammatory factors, including IL-4 and Il-10 [26]. In contrast, a further nerve-derived transmitter nitric oxide (NO) favours the proliferation of osteoclasts.

In one very small study of bone samples from eight people with diabetes, four samples from those with neuropathy were found to have lower levels of NO compared with the four non-neuropathic diabetic control samples, as well as a trend towards an increase in CGRP [27], although the findings were not conclusive due to the small size of the study.

Effect of Neuropathy on the Joint Capsule

Dislocation is a common feature of the active Charcot foot and may occur even in joints which are not otherwise prone to dislocation, including the tarso-metatarsal (Lisfranc) and talonavicular (Chopart) joints. Such dislocation may be caused by partial avulsion of the joint capsule as a result of weakened attachment or, potentially from changes to the integrity of the capsule and other soft tissues which are normally richly innervated with nerves secreting SP, CRGP and NPY [28]. While the loss of innervation is known to have major effects on bone structure and fragility, it is also possible that it may compromise the integrity of the capsule in people with Charcot foot.

Effect of Neuropathy on the Vasculature

It is well established that there is an association between calcification of the cells of the arterial walls and osteoporosis, including osteopenia associated with neuropathies and it is thought to result from the contrasting effects of the RANKL/OPG signalling system in the two tissues [29, 30]. Both are also associated with neuropathy. Neuropathy is particularly closely associated with calcification of the *tunica media* of the medium to small arteries of the periphery (medial arterial sclerosis, MAC; Mönckeberg's sclerosis) [31, 32] where it has been shown to have the histological features of bone [33].

Additional Predisposing Factors Associated with Diabetes

Effects of Neuropathy on the Vasculature

There is a very extensive literature on the relationships between low grade, metabolic inflammation and disease of the heart and larger arteries in diabetes. In this context, the 'inflammation' is not clinically apparent but refers to the effects which result from the pro-inflammatory effects of glucose, oxidised lipids and advanced glycation end-products (AGEs) linked to reduced expression of the AGE receptor (RAGE) [34]. The broad subject has been well-reviewed elsewhere [35].

In the Charcot foot syndrome, however, it is the distal vasculature which is just as important and any predisposition in a person with diabetes will include the combined effects of both. Indeed, the findings of one controlled observational study suggested that overt clinical signs of more proxi-

mal artery disease were associated with decreased likelihood of the Charcot syndrome [36].

It is recognised that there are changes in distal limb blood flow associated with diabetic neuropathy [37, 38] and these are associated with alterations of distal capillary function [39]. The distribution of blood to the periphery—and the integrity of its normal regulation—is thus dependent on multiple processes in people with diabetes including cardiac function (including the effect of any medications on pulse and blood pressure), patency of larger arteries, changes in peripheral vascular resistance, effective constriction and relaxation of smaller vessels and changes in capillary and extravascular structure and function.

Other Predisposing Factors in Diabetes

While the clinical presentation of the Charcot syndrome may be broadly similar in all underlying pathologies, there are particular features of diabetes that may make it more likely.

Skeletal Fragility in Diabetes

It is known that both type 1 and type 2 diabetes are associated with increased risk of fracture [40].

Chronic Renal Failure

Chronic renal failure may predispose to the development of the syndrome because of the osteopenia it causes.

Simultaneous Pancreas-Kidney Transplant (SPKT) in Type 1 Diabetes

The incidence of active Charcot syndrome is very high in the months following transplantation: affecting between 5% and 15% within a year or two in recent published series [41–44]. The cause is likely to be multifactorial. Both neuropathy and renal osteodystrophy are very likely in the treated population, while those with overt macrovascular disease will have been excluded prior to transplantation. It is also possible that post-transplant Charcot syndrome was particularly common when higher doses of glucocorticoid immunosuppression were used and that the incidence is now falling—even though it remains far higher than in any other at risk group. Of interest is the observation by Valabhji [45] that the use of immunosuppressants may modify the clinical presentation.

Obesity

It is commonly thought that increased body mass index (BMI) predisposes to the onset of the syndrome in diabetes [9] but the evidence is not strong and it is possible that it is the difficulties posed by obesity in the management of particular individuals that encourages the belief in clinical practice. There is one small study that which found no difference in BMI between matched groups with and without Charcot syndrome [46].

Genetic Predisposition

A small number of groups have reported associations with differing candidate genes but the evidence is not currently strong [47–49].

Aetiology: Permissive Factors

The frequency with which neuropathy complicates diabetes contrasts with the relative rarity of the Charcot syndrome, with available data suggesting it might affect between 0.1 and 1.0 people per thousand with diabetes [50]. This indicates that while the presence of one or more components of nerve dysfunction is essential, the syndrome will not occur without one or more key permissive factors.

Of these, it is likely that the most important factor required for the expression of the syndrome is the capacity to mount an adequate inflammatory response by increasing blood flow to the affected area. One piece of evidence in tangential support is provided by the occasional reports of the syndrome being triggered by revascularisation of a major proximal artery [51]. More important evidence is provided by the observations made by two groups that people who have had an episode of active Charcot foot can be distinguished from other people with neuropathy by the fact that they have been shown to retain patterns of pedal blood flow and they retain the capacity for it to increase [52, 53].

Aetiology: Precipitation

What Triggers the Onset of Inflammation at the Time That the Charcot Process Becomes Active?

While affected individuals may have underlying predisposition arising from any of the above processes, it seems that the onset of the active Charcot syndrome is usually triggered by an external event and by trauma in particular—even though the severity of the trauma may often have been thought to be trivial at the time it occurred. Other important triggers are foot ulceration, infection, surgery to the foot [11, 12] but in many cases there is no identified precipitant.

Once triggered, the capacity to mount an exaggerated and persistent inflammatory reaction may be limited to those who produce a more intense response of pro-inflammatory cytokines such as TNF-alpha, IL-1beta and IL-6 [54, 55] or there may be an inadequate capacity to terminate an inflammatory response that has already occurred.

Aetiology: Presentation

The onset of an active Charcot foot is marked by overt clinical inflammation. This will result from increasing activation of pro-inflammatory cytokine pathways and is most likely to be centred on the RANKL/OPG/NFKappaB pathway or, alternatively, the Wnt/β-catenin pathway. The resultant clinical inflammation will only occur if the local microvasculature is capable of responding with the necessary vasodilatation and hence is restricted it to a small minority.

Changes in Pro-inflammatory Cytokine Expression When the Charcot Foot Syndrome Is Active

Active Charcot is associated with increased osteolysis. Baumhauer et al. [56] demonstrated increased expression of the pro-inflammatory cytokines IL-1, IL-6 and TNF-alpha in histological specimens. Mabilleau [57] confirmed these observations in a follow-up study, which also suggested the involvement of a pathway other than that of RANKL and OPG. There is a possibility that this pathway is that centred on the Wnt/β-catenin pathway for which Folestad has since provided independent evidence [58]. High levels of Wnt ligand prevent the breakdown of catenin which in turn promotes osteoblast maturation and therefore bone formation. Low levels therefore would be consistent with bone breakdown. Folestad and colleagues have also confirmed the involvement of TNF-alpha in active Charcot foot, as well as IL-Iβ, IL-6 and other interleukins [59, 60].

Effects of Clinically Overt Inflammation on Bone

Worsening inflammation is associated with increased osteocytic osteolysis with increased bone fragility. In this respect it is worth reflecting that osteolysis is normally a prelude to new bone formation and is a key component of the early phase of a protective response to skeletal injury. The exaggerated osteolysis of the Charcot syndrome must occur only in those in whom the capacity for auto-regulation is defective.

Aetiology: Perpetuation

Once the process is triggered, the person who is already predisposed to an exaggerated inflammatory reaction then enters a phase whereby the inflammation further worsens bone fragility and capsular laxity with the increasing risk of skeletal damage which is itself made more likely by loss of protective sensation and continued weight-bearing [61]. The bone of people with active Charcot syndrome shows inflammatory infiltration with reduced quality of the trabeculae [62].

The process will eventually prove self-limiting and the foot will stabilise once the inflammation settles—provided that irreversible skeletal damage does not lead to limb loss. Expert teams manage the condition by minimising trauma by ensuring effective off-loading as well as management of complications (including secondary

deformity, ulceration and infection). Currently, there is no effective systemic therapy to either prevent or reduce the causative processes or to minimise their effects.

Studies on the Expression of Pro-inflammatory Cytokines During the Course of Active Charcot Syndrome

Folestad et al. [58–60] conducted a detailed analysis of changes in the expression of circulating cytokines in samples collected from 24 to 28 people following the introduction of off-loading for active Charcot syndrome. They were able to demonstrate that changes in the expression of IL-6, IL-8, IL-1β and TNF-alpha were all lower than in controls at the time of presentation with active disease but that IL-6 and TNF-alpha rose slowly and steadily after the introduction of off-loading—suggesting an increased in bone lysis as a prelude to remodelling [58]. In contrast, the concentrations of IL-17A and IL-17E were no different from controls at presentation and then rose slowly over 2–4 months, while those of IL-17F were low at presentation and rose during follow-up to be no different from controls [59]. Finally, they observed that sclerostin, Dkk-1 and Wnt-1 were all low at presentation and rose over 2 years of follow-up and, while concentrations of OPG and RANKL were higher than controls at presentation and fell during follow-up, the ratio of OPG/RANKL did not change [60]. Current knowledge of the detailed interaction of the measured substances is insufficient to allow detailed interpretation to explain these fascinating observations.

Resolution

It is common clinical practice to accept a difference in the temperature of the skin over the area of interest of <2 °C when compared with the non-involved foot as sign of clinical resolution although the data to support this is poor.

Magnetic resonance imaging (MRI), repeated X-rays, repeated bone scans and infrared thermometry have been used to evaluate remission but the lack of validated protocols, standardisation of equipment and high quality studies mean that uncertainty remains about the effectiveness for any [19].

Prognosis

Recurrence

As noted above, some 20% of individuals with Charcot foot syndrome complicating diabetes will have or will develop similar changes on the contralateral foot before, during or after the index presentation. Long term relapse is, however, very rare and this is most likely because the factors that predisposed to or permitted the original attack no longer exist.

Mortality

In one single centre series of 117 cases in the UK, survival was shown to be reduced to a median 7.9 years with a reduction in overall life expectancy of 14.4 years. This reduction in life expectancy was not, however, significantly different from a matched control sample managed for neuropathic foot ulcer and hence is not related to the Charcot syndrome per se [63] but more to the population which is at risk of it.

Footnote

Why Is the Charcot Syndrome So Uncommon?

Given that distal neuropathy is currently thought to affect between a third and a half and of all people with diabetes, it is very remarkable that a syndrome that is thought to be primarily the consequence of neuropathy is so rare. It may be that the primary cause is some particular facet of neuropathy which is itself rare or, as suggested here, that the condition only occurs when a variety of predisposing and potentiating factors co-exist and that such co-existence is uncommon.

Diagnosis of Active Disease

Diagnosis of Active Disease: Clinical

If a health care professional is asked over the phone about a patient who has developed unexplained warmth and swelling of the midfoot, his or her first thought should be to ask two questions: has the person got diabetes and have they got distal neuropathy? If the answer to either is Yes, then active Charcot syndrome must be considered. Early suspicion is essential—not least to minimise weight-bearing until it has been excluded. The single most important stage in the diagnosis of the Charcot foot is to think of it. Most people do not think of it as a possibility because they believe it is rare and that they are unlikely ever to see a case. The Charcot syndrome is uncommon but it is not rare.

Diagnosis of Active Disease: Investigations

Imaging

Once the diagnosis of Charcot syndrome is considered, a plain X-ray should be done immediately and the result reviewed. The foot must be protected by off-loading until a diagnosis is made. Signs that may be seen on a plain film include osteopenia and osteolysis, associated fragmentation of subchondral bone, fractures, dislocations, subluxations and later bony consolidation [64]. Subtle dislocations, joint deformity and collapse may be better visualised on weight-bearing views. The sensitivity of plain X-ray to exclude acute Charcot is not good even on weight-bearing films particularly in the early stages [65].

More advanced imaging techniques have been proposed including MRI, radiolabelled bone scans and more recently ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET). MRI is noninvasive and has much better sensitivity for the detection of early stage acute active Charcot [66] with reported sensitivities of (77–100%) and specificities (80–100%) for the diagnosis [67].

However, the main limitation of MRI lies in its inability to distinguish bone oedema caused by infection (osteomyelitis) from active Charcot, particularly if the two co-exist. A recent retrospective review suggests that if bone infection is suspected in addition, then white blood cell (WBC) scintigraphy had a higher accuracy for the detection of osteomyelitis as long as standardised protocols are used [13] and so may be useful where there is clinical doubt. Other tests involving radiolabelled isotopes such as triple phase bone scans have good sensitivity but lack the specificity of MRI scans for early diagnosis [67]. ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) scanning may be useful for differentiating acute Charcot from osteomyelitis [64] but a recent large series suggests that it lacks the accuracy of WBC scintigraphy and so it is not currently recommended [13].

Other Investigations

There are no other investigations that are useful for the positive diagnosis of active Charcot, unless the intention is to look for other causes of inflammation. While changes in inflammatory cytokines have been described above, none is specific to active Charcot and will be raised in almost any cause of inflammation, whether this be infective or metabolic, as in acute gout, for example.

Diagnosis of Active Disease: Education of the Person with Diabetes

Any person with diabetes and peripheral neuropathy should know that they are at risk of future foot problems. Their risk of foot ulcers far exceeds the risk of developing an active Charcot but it is most important that they know how to contact someone with the necessary expertise should they develop an unexplained red hot swollen foot. It is just as important that the health care professional should think of the diagnosis and make appropriate referrals for investigation and off-loading without delay.

The Bottom Line

The Charcot syndrome is uncommon but not rare and it is important that it is considered in any person with neuropathy who presents with unexplained inflammation of the foot. When considered, the foot should be protected against unnecessary trauma until the diagnosis has been either proved or excluded. If the diagnosis is confirmed, long term off-loading is the current mainstay of management [1].

References

1. Schmidt BM, Wrobel JS, Holmes CM. Physician knowledge of a rare foot condition – influence of diabetic patient population on self-described knowledge and treatment. Clin Diab Endocrinol. 2017;3:2.
2. Chantelau E. The perils of procrastination: effect of early vs. delayed detection and treatment of incipient Charcot fracture. Diabet Med. 2005;22:1707–12.
3. Pakarinen T-K, Laine H-J, Mäenpää H, Mattila P, Lahtela J. Long-term outcome and quality of life in patients with Charcot foot. Foot Ankle Surg. 2009;15:187–91.
4. Wukich DK, Sung W, Wipf SA, Armstrong DG. The consequences of complacency: managing the effects of unrecognized Charcot feet. Diabet Med. 2011;28:195–8.
5. Sanders LJ, Edmonds ME, Jeffcoate WJ. Who was first to diagnose and report neuropathic arthropathy of the foot and ankle: Jean-Martin Charcot or Herbert William Page ? Diabetologia. 2013;56:1873–7.
6. Harris JR, Brand PW. Patterns of disintegration of the tarsus in the anaesthetic foot. J Bone Joint Surg. 1966;48:4–16.
7. Jeffcoate WJ. Charcot foot syndrome. Diabet Med. 2015;32:760–70.
8. Johnson-Lynn SE, McCaskie AW, Coll AP, Robinson AHN. Neuroarthropathy in diabetes: pathogenesis of Charcot arthropathy. Bone Joint Res. 2018;7:373–8.
9. Pitocco D, Scavone G, Di Leo M, et al. Charcot neuroarthropathy: from the laboratory to the bedside. Curr Diabetes Rev. 2019;16:62–72.
10. Chantelau EA, Grützner G. Is the Eichenholtz classification still valid for the diabetic Charcot foot ? Swiss Med Wkly. 2014;144:w139482014.
11. Game FL, Catlow R, Jones GR, Edmonds ME, Jude EB, Rayman G, Jeffcoate WJ. Audit of acute Charcot's disease in UK: the CDUK study. Diabetologia. 2012;55:32–5.
12. Ndip A, Jude EB, Whitehouse R, Prescott M, Boulton AJ. Charcot neuroarthropathy triggered by osteomyelitis and/or surgery. Diabet Med. 2008;25:1469–72.
13. Lauri C, Glaudemans AWJM, Campagna G, et al. Comparison of white blood cell scintigraphy, FDG PET/CT and MRI in suspected diabetic foot infection: results of a large retrospective multicenter study. J Clin Med. 2020;30(9):1645.
14. Rastogi A, Bhansali A, Jude EB. Efficacy of medical treatment for Charcot neuroarthropathy: a systematic review and meta-analysis of randomized controlled trials. Acta Diabetol. 2021;58:687. https://doi.org/10.1007/s00592-020-01664-9.
15. Chapman Z, Shuttleworth CMJ, Huber JW. High levels of anxiety and depression in diabetic patients with Charcot foot. J Foot Ankle Res. 2014;7:22.
16. Fabrin J, Larsen K, Holstein PE. Long-term follow-up in diabetic Charcot feet with spontaneous onset. Diabetes Care. 2000;23:796–800.
17. Stark C, Murray T, Gooday C, et al. 5 year retrospective follow-up of new cases of Charcot neuroarthropathy – A single centre experience. Foot Ankle Surg. 2016;22:176–80.
18. Christensen TM, Gade-Rasmussen B, Pedersen LW, Hommel PE, Svendsen OL. Duration of off-loading and recurrence rate in Charcot osteoarthropathy treated with less restricted regimen with removable walker. J Diabetes Complicat. 2012;26:430–4.
19. Gooday C, Gray K, Game F, Woodburn J, Poland F, Hardeman W. Systematic review of techniques to monitor remission of acute Charcot neuroarthropathy in people with diabetes. Diabetes Metab Res Rev. 2020;21:e3328. https://doi.org/10.1002/dmrr.3328.
20. Rudrappa S, Game F, Jeffcoate W. Recurrence of the acute Charcot foot in diabetes. Diabet Med. 2012;29:819–21.
21. Pop-Busui R, Ang L, Holmes C, Gallagher K, Feldman EL. Inflammation as a therapeutic target for diabetic neuropathies. Curr Diab Rep. 2016;16:29.
22. Tesfaye S, Boulton AJM, Dyck PJ, et al. Diabetic neuropathies: update on definitions, diagnostic criteria, estimation of severity, and treatments. Diabetes Care. 2010;33:2285–93.
23. Gaudio A, Privitera F, Pulvirenti I, Canzonieri E, Rapisarda R, Fiore CE. The relationship between inhibitors of the Wnt signaling pathway (sclerostin and Dickkopf-1) and carotid intima-media thickness in postmenopausal women with type 2 diabetes. Diab Vasc Dis Res. 2014;11:48–52.
24. Brazill JM, Beeve AT, Craft CS, Ivanusic JJ, Scheller EL. Nerves in bone: evolving concepts n pain and anabolism. J Bone Miner Res. 2019;34:1393–406.
25. Jones KB, Mollano AV, Morcuende JA, Cooper RR, Saltzman CL. Bone and brain: a review of neural, hormonal and musculoskeletal connections. Iowa Orthop J. 2004;24:123–32.

[1] Since this manuscript has been submitted, the authors have advanced new speculation to provide an explanation for the observation that the Charcot foot is so uncommon—even though the changes which predispose to it may affect a very high percentage of people with diabetes [68].

26. Saidenberg-Kamanaćh N, Bessis N, Solat MC, De Vernejoul MC, Boissier M-C. Osteoprotegerin and inflammation. Eur Cytokine Netw. 2002;13:144–53.
27. La Fontaine J, Harkless LB, Sylvia VL, et al. Levels of endothelial nitric oxide synthase and calcitonin gene-related peptide in the Charcot foot: a pilot study. J Foot Ankle Surg. 2008;47:424–9.
28. Grässel S, Muschter D. Peripheral nerve fibers and their neurotransmitters in osteoarthritis pathology. Int J Mol Sci. 2017;18:931.
29. Hofbauer LC, Schoppet M. Osteoprotegerin: a link between osteoporosis and arterial calcification. Lancet. 2001;358:257–9.
30. Jeffcoate WJ, Rasmussen LM, Hoffbauer LC, Game FL. Medial arterial calcification in diabetes and its relationship to neuropathy. Diabetologia. 2009;52:2478–88.
31. Jeffcoate W. Vascular calcification and osteolysis in diabetic neuropathy – is RANKL the missing link ? Diabetologia. 2004;47:1488–92.
32. Ndip A, Williams A, Jude EB, et al. The RankL/RANK/OPG signaling pathway mediates medial arterial calcification in diabetic Charcot neuroarthropathy. Diabetes. 2011;60:2187–96.
33. Alexander Y, Heagerty A, Keenan D. Vascular calcification: characteristics and pathological mechanisms. Rec Adv Cardiol. 2008;15:21–42.
34. Witzke KA, Vinik AI, Grant LM, et al. Loss of RAGE defense: a cause of Charcot neuroarthropathy. Diabetes Care. 2011;34:1617–21.
35. Di Marco E, Gray SP, Jandelt-Dahm K. Diabetes alters activation and repression of pro- and anti-inflammatory signaling pathways in the vasculature. Front Endocrinol. 2013;4:68.
36. Nobrega MB, Aras R, Netto EM, et al. Risk factors for Charcot foot. Arch Endocrinol Metab. 2015;59:226–30.
37. Boulton AJ, Scarpello JH, Ward JD. Venous oxygenation in the diabetic neuropathic foot: evidence of arteriovenous shunting ? Diabetologia. 1982;22:6–8.
38. Edmonds ME, Clarke MB, Newton S, Barrett J, Watkins PJ. Increased uptake of bone radiopharmaceutical in diabetic neuropathy. Quart J Med. 1985;57:843–55.
39. Østergaard L, Finnerup NB, Terkelsen AJ, et al. The effects of capillary dysfunction on oxygen and glucose extraction in diabetic neuropathy. Diabetologia. 2015;58:666–77.
40. Sellmeyer DE, Civitelli R, Hofbauer LC, Khosla S, Lecka-Czernik B, Schwartz AV. Skeletal metabolism, fracture risk, and fracture outcomes in type 1 and type 2 diabetes. Diabetes. 2016;65:1757–66.
41. Anthony ML, Cravey KS, Atway SA. Development of Charcot neuroarthropathy in diabetic patients who received kidney or kidney-pancreas transplants. J Foot Ankle Surg. 2019;58:465–9.
42. Dardari D, Dardari R. Why the risk of developing neuroarthropathy is higher after simultaneous kidney and pancreatic transplantation compared to kidney transplantation only: the role of euglycemia. Ann Transpl. 2021;26:e928449.
43. Garcia Barrado F, Kuypers DR, Matricali GS. Charcot neuroarthropathy after simultaneous pancreas-kidney transplantation: risk factors, prevalence, and outcome. Clin Transpl. 2015;29:712–9.
44. Matricali GA, Bammens B, Kuypers D, Flour M, Mathieu C. High rate of Charcot foot attacks early after simultaneous pancreas-kidney transplantation. Transplantation. 2007;83:245–6.
45. Valabhji J. Immunosuppression therapy posttransplantation can be associated with a different clinical phenotype for diabetes Charcot foot neuroarthropathy. Diabetes Care. 2011;34:e135.
46. Ross AJ, Mendicino RW, Catanzariti AR. Role of body mass index in acute Charcot neuroarthropathy. J Foot Ankle Surg. 2013;52:6–8.
47. Bruhn-Olszewska B, Korzon Burakowska A, Wegrzyn A, Jakóbkiewicz-Banecka J. Prevalence of polymorphisms in OPG, RANKL and RANK as potential markers for Charcot arthropathy development. Sci Rep. 2017;29:501.
48. Korzon Burakowska A, Jakóbkiewicz-Banecka J, Fiedosiuk A, et al. Osteoprotegerin gene polymorphism in diabetic Charcot neuroarthropathy. Diabet Med. 2012;29:771–5.
49. Pitocco D, Zelano G, Gioffrè, et al. Association between osteoprotegerin G1181C and T245G polymorphisms and diabetic Charcot neuroarthropathy: a case-control study. Diabetes Care. 2009;32:1694–7.
50. Metcalf L, Musgrove M, Bentley J, et al. Prevalence of active Charcot disease in the East Midlands of England. Diabet Med. 2018;35:1371–4.
51. Edelman SV, Kosofsky EM, Paul RA, Kozak GP. Neuroarthropathy (Charcot's joint) in diabetes mellitus following revascularisation surgery. Arch Intern Med. 1987;147:1504–8.
52. Baker N, Green A, Krishnan S, Rayman G. Microvascular and C-fiber function in diabetic charcot neuroarthropathy and diabetic peripheral neuropathy. Diabetes Care. 2007;30:3077–9.
53. Shapiro SA, Stansberry KB, Hill MA, et al. Normal blood flow response and vasomotion in the diabetic Charcot foot. J Diabetes Complicat. 1992;12:147–53.
54. Gonzalez-Mejia ME, Doseff AI. Regulation of monocytes and macrophages cell fate. Front Biosci. 2009;14:2413–31.
55. Uccioli L, Sinistro A, Almerighi C, et al. Proinflammatory modulation of the surface and cytokine phenotype of monocytes in patients with acute Charcot foot. Diabetes Care. 2010;33:350–5.
56. Baumhauer JF, O'Keefe RJ, Schon LC, Pinzur MS. Cytokine osteclastic bone reception in Charcot arthropathy: an immunohistochemical study. Foot Ankle Int. 2006;27:797–800.
57. Mabilleau G, Petrova N, Edmonds ME, Sakobar A. Increased osteoclastic activity in acute Charcot's osteoarthropathy: the role of receptor activator of nuclear factor-kappa B ligand. Diabetologia. 2008;51:1035–40.

58. Folestad A, Åland M, Asteberg S, et al. Role of Wnt/B-catenin and RANKL/OPG in bone healing of diabetic Charcot arthropathy patients. Acta Orthop. 2015a;86:415–25.
59. Folestad A, Åland M, Asteberg S, et al. IL-17 cytokines in bone healing of diabetic Charcot arthropathy patients: a prospective 2 year follow-up study. J Foot Ankle Res. 2015b;8:39–50.
60. Folestad A, Åland M, Asteberg S, et al. Offloading treatment is linked to activation of proinflammatory cytokines and start of bone repair and remodelling in Charcot arthropathy patients. J Foot Ankle Res. 2015c;8:72–84.
61. Jeffcoate WJ, Game F, Cavanagh P. The role of proinflammatory cytokines in the cause of neuropathic osteoarthropathy (acute Charcot foot) in diabetes. Lancet. 2005;366(9502):2058–61.
62. La Fontaine J, Shibuya N, Sampson HW, Valderrama P. Trabecular quality and cellular characteristics of normal, diabetic, and Charcot bone. J Foot Ankle Surg. 2011;50:648–53.
63. van Baal J, Hubbard R, Game F, Jeffcoate W. Mortality associated with acute Charcot foot and neuropathic foot ulceration. Diabetes Care. 2010;33:1086–9.
64. Rogers LC, Bevilacqua NJ. Imaging of the Charcot foot. Clin Podiatr Med Surg. 2008;25:263–74.
65. Morrison WB, Ledermann HP. Work-up of the diabetic foot. Radiol Clin N Am. 2002;40:1171–92.
66. Schlossbauer T, Mioc T, Sommerey S, Kessler SB, Reiser MF, Pfeifer KJ. Magnetic resonance imaging in early stage Charcot arthropathy - correlation of imaging findings and clinical symptoms. Eur J Med Res. 2008;13:409–14.
67. Milne TE, Rogers JR, Kinnear EM, et al. Developing an evidence-based clinical pathway for the assessment, diagnosis and management of acute Charcot neuro-arthropathy. J Foot Ankle Res. 2013;6:30.
68. Jeffcoate W, Game F. The Charcot foot reflects a response to injury that is critically distorted by pre-existing nerve damage: an imperfect storm. Diabetes Care. 2022;45:1691–7.

Charcot Foot: Conservative Management

18

Armin Koller

Introduction

Conservative treatment in Charcot neuroarthropathy (CN) on the one hand represents an alternative to surgical treatment; on the other hand it is always used before or after operations and therefore an integral part of the treatment algorithm.

Goals of conservative therapy are reduction of inflammation by shielding the foot skeleton from mechanical stress, preservation of foot shape until consolidation of CN, and redressment of foot deformity prior to stabilization.

There are several conceivable scenarios in which conservative treatment would be preferable to surgery. A very morbid patient with high-grade limitation of walking distance due to his medical conditions is not a good candidate for complex and high-risk operative reconstructions. In general, functional improvement from reconstructive surgery has to justify the possibly substantial risk of operation or anesthesia. A foot with mild to moderate deformity which is plantigrade and capable of full weight-bearing in a shoe or an orthosis does not necessarily need operative treatment [1].

Drug treatment is discussed as a complementary anti-inflammatory therapy. There is growing evidence of a link between neuropathy, bone turnover, inflammation, and mechanical stress in Charcot neuroarthropathy [2].

Since neuropathy cannot be reversed and mechanical stress is within the scope of casts and orthoses, different drugs have been utilized to normalize bone turnover and reduce inflammation. Medication can never be a standalone treatment but is intended to shorten time to resolution of the active neuroarthropathic process in combination with standard treatment by means of total contact cast or orthosis. However, none of the drug treatments so far has supplied scientific evidence of a therapeutic effect that would justify unequivocal recommendation. Even adverse effects could be noticed with significant prolongation of the time to resolution using bisphosphonates [3].

Edema typically coming along with the active stages of CN interferes with proper fit of orthotic devices and compromises wound healing. In return, treatment with effective immobilization of foot and lower leg leads to edema regression, unless that is not a consequence of venous, lymphatic, renal, or cardiac insufficiency. Antiedematous therapy includes compression bandages, Unna boot, or semi-rigid casts (Photo 18.1). Additionally, patients should exert complete off-loading of the affected limb, in the sense of completely refraining from weight-bearing, by means of crutches, wheelchair, or even bed rest in the very acute stage of CN, when massive edema

A. Koller (✉)
Department of Technical Orthopedics, Hospital Dr. Guth, Hamburg, Germany
e-mail: info@arminkoller.de

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_18



Photo 18.1 Regression of the previously massive edema of the foot and lower leg after only 1 day of flat positioning and application of a semi-rigid cast (3M™ Scotchcast™ Soft Cast Casting Tape)

with erythematous vulnerable skin makes weight-bearing in a cast or splint impossible anyway. When there is only mild to moderate swelling of foot and lower leg, treatment with casts or orthoses can start.

Charcot neuroarthropathy quite often comes along with pressure ulcers. Both conditions are usually treated by so-called *off-loading*, but the biomechanical principles of treatment are fundamentally different in both cases. That is quite understandable, since one condition affects the soft tissue, the other one the skeleton. Neuropathic ulcers are caused by pressure exceeding a certain threshold, and treatment basically implies reversal of that process. As complete pressure elimination is not always feasible, redistribution of forces acting on the plantar surface has to effect pressure reduction at the ulcer site to a subthreshold level.

Regarding only the mechanical aspects of the complex etiology, CN is not induced or aggravated by forces acting on the skin surface, but by external (walking, standing, and sitting!) and internal (tendon pull) forces acting on the foot skeleton. The result is strain of bones and ligaments. This deformation can only be eliminated or minimized by a device that allows for a permanent rigid three-dimensional fixation of foot and lower leg. With this ensured, weight-bearing and subsequent pressure on soft tissue is not a major obstacle. Not recommended, however, is leaving the device off even for the shortest walk.

Charcot Foot with Fractures

Beyond the contribution of inflammation and deregulated bone metabolism to the multifaceted etiology of CN, the disease has a lot in common with fractures due to repetitive stress or trauma. The basic principles of conservative fracture treatment have been laid down nearly one hundred years ago. *Lorenz Böhler* (1885–1973) [4], one of the godfathers of modern trauma surgery, emphasized that accurate reduction of the displaced fragment is only sensible if subsequent measures are taken to keep the reduced bone fragments in a good position—without any interruption!

Fractures lead to deformity with resulting abnormal plantar pressure and repetitive microtraumata, which in turn are responsible for inflammation, osteoclast activation, and osteopenia, increasing again the risk for further fractures. Casts and orthoses are valuable tools to accommodate deformity and abnormal loading patterns, since it is paramount to interrupt that vicious circle [5].

Since CN rather is a syndrome than a specific nosological entity, orthotic treatment cannot be uniform. Active CN requires permanent stabilization, whereas inactive CN is treated sufficiently with protected weight-bearing. The presence of a plantar ulcer requires additional local pressure relief by plantar insoles or by load transfer to the tibial condyles or patella. A mild to moderate deformity basically can be treated with an off-the-shelf walker, a pronounced deformity must be fitted with a cast or a custom-made orthosis. The plane of the deformity also has to be taken

into consideration. Sagittal plane deformity is easy to accommodate; transverse plane or frontal plane deformity, in particular, makes orthotic fitting and compensation of static alignment quite challenging. Circadian fluctuations of edema due to cardiac or renal insufficiency are usually treated with compression stockings or bandages, but those are not always applicable together with orthoses. As a consequence, the orthotic design should have an adjustment mechanism that enables containment of a lower leg with volume variations without losing proper fit.

Of course, the foot cannot be regarded quite apart from the patient, who will demonstrate different body weight and activity level. Heavy use of an orthosis must be countered with a heavy duty construction.

Orthotic Treatment

General requirements for orthoses in treating Charcot feet include accommodation of any deformity, protection of vulnerable soft tissue, and volume control. Patients should be able to don and doff the orthosis without an auxiliary person to keep their autonomy. Mobility needs range from a few steps at home to long distances in the community. Hence, design of the rocker sole is either geared to stability or to dynamics. Geriatric patients need more safety and active patients more agility.

Specific requirements for orthoses in treating CN depend on the respective pathology to be treated. *Activity* of the neuroarthropathic process needs rigid three-dimensional fixation comprising foot and lower leg. Activity finds its expression in inflammatory signs having a mechanical component due to fracture or joint dislocation which in turn are treated comparable to a skeletal trauma. Ground reaction force during walking and standing is not the major concern, but movements of the foot within the device.

Rotation around the long axis of the leg does not only occur at the hip joint. At the same time the subtalar joint complex accomplishes an inversion-eversion movement which has to be compensated by a contrarotating pronation-supination movement of the midfoot against the hindfoot. This torsion also involves the tarsal bones, so that rigid fixation of that area of the foot skeleton does not only call for a stiff rocker sole, but also for an orthotic design able to control lower leg rotation. The triangular shape of the proximal tibia is the place where rotation can be restricted by an accordingly molded pretibial shell of the orthosis. Counter-pressure at the calf muscles must keep the proximal tibia in the desired position. Large area pressure helps to avoid undue proximal constriction of venous and lymphatic drainage.

The concept of immobilization of foot joints is not new. It was introduced by *Morgan* in 1993 [6]. A long time ago protection from cumulative microtrauma was recognized to be the keynote for orthotic treatment of Charcot feet. Subsequently, this idea had been replaced by a focus on relief of plantar pressure [7]. Orthoses were designed to reduce load transmission to the midfoot or forefoot [8]. Indeed, measurement of high plantar pressure within an orthosis may serve as an indirect proof of mechanical instability or insufficient anatomical fit of the respective device. However, it remains difficult to draw clear conclusions from plantar pressure measurement to joint or fragment movements. The effect of tibial rotation on movement of foot joints cannot be detected by means of plantar pressure measurement. The concept of joint immobilization is consistent with up-to-date hypotheses about the etiology of neuro-arthropathy, but there is still a need for well-designed studies on the mechanical effects of orthoses in a larger cohort of Charcot feet [9].

Deformity of the Charcot foot of a certain extent does not only call for individual fabrication of the ankle foot orthosis, but also has negative impact on biomechanics of walking and standing. Frontal plane deformity at the hindfoot, that is medial or lateral displacement of the calcaneus, calls for an opposed enlargement of the orthotic heel, so that the physiological plumbline of the leg is restored. A deformed but stiff foot is often easier to accommodate with an orthosis than a Charcot foot with *instability*. In particular, when only partial redressment of the deformity is

possible, movements of the foot are responsible for friction within the orthosis causing skin breakdown.

If instability is due to an active neuroarthropathic process (Eichenholtz stage I or II), rigid fixation in an orthosis or cast can support consolidation and transition to Eichenholtz stage III with osseous fusion and permanent stability. But, if instability comes with an inactive, chronic Charcot foot, future stability of the foot skeleton is not guaranteed. In this case, orthotic treatment precedes or replaces an operation, if the patient is too morbid for surgery or does not want operative treatment.

Any bony prominence or exostosis must carefully be protected against excessive pressure, especially if there is only thin soft tissue coverage. If an ulcer occurs at the medial or lateral malleolus, it will take a very long time until wound healing or it will even necessitate surgical wound closure.

Rehabilitation with casts and orthoses means more than to teach autonomous donning and doffing of the device. Partial weight-bearing, which is necessary for postoperative treatment of a wide range of surgical procedures, is not feasible in the presence of peripheral neuropathy coming along with Charcot foot disease. Lack of sensory input interferes with controlled loading of the foot. With this in mind, a stopwatch or a step counter instead of a weighting scale should be used to set stress levels of the foot skeleton. By implication, this means full impact for a few minutes or steps in the beginning. Orthoses or casts have to be stable enough to protect the Charcot foot even with full weight-bearing.

Total Contact Cast (TCC)

The most significant advantage of the TCC is instant availability. It is made of plaster of Paris or fiberglass, cheap in fabrication, and can be produced in most locations. Windowing of the cast allows treating wounds, which should not be infected when using a TCC. The closed construction enforces good compliance. The main disadvantage is that physical examination of the foot requires removal of the cast. For continued treatment, a new cast has to be applied. Frequent replacements of the cast are time-consuming. Well-trained cast technicians, or physicians, who are able to apply a TCC with the least possible risk of skin lesions [10], are not omnipresent. A TCC limits the ability to walk to a greater extent than walkers or orthoses.

Removable TCCs are made by sawing them open into a rear and a front shell. The two halves are then resealed with Velcro or cable ties. In this way, inspections of the foot or dressing changes are possible without having to fit a new cast each time. This is more convenient for the treatment team and often less anxiety-provoking for the patient. However, these advantages are also countered by disadvantages. Mechanical stability is compromised, and the ability for the patient to interrupt therapy increases the risk of therapy failure.

Prefabricated Diabetic Walker (DW)

The prefabricated diabetic walker (DW) is also available immediately if it can be stored. Depending on the model, mechanical stability decreases gradually, and a respective weight limit must be considered. Product information by the manufacturer rarely gives any recommendations for the use in the treatment of Charcot foot. As Charcot feet mostly retain at least some degree of deformity after surgery, the DW is not the orthosis of choice after reconstructive foot surgery in diabetic patients. Particularly high-grade foot deformities are a problem, because the DW has little scope for modifications. Its shape is designed to enclose a foot with some swelling, but not with considerable deformity. Lower legs with edema may be pressed into an unphysiological shape. Air chambers may be damaged and lose function because patients may forget to inflate them, or in contrast, may cause skin lesions by overinflation of the air chambers.

In order to combine the compliance enforced in closed TCC with the simple and fast fitting of a walker, the idea of so-called instant TCC, or iTCC for short, was developed [11]. In this case,

a conventional prefabricated walker is made non-removable with the aid of plaster bandages, for example, but rapid and problem-free removal of the aid remains possible. This therapeutic measure, which has been successful in the treatment of neuropathic ulcers, is also conceivable in principle for Charcot foot, since it is precisely here that consistent immobilization is important. The name iTCC is somewhat misleading, however, since a real TCC can be adapted very precisely to the shape of the foot, which is not the case with the iTCC, which is a ready-made device. In the case of a Charcot foot with a more or less pronounced deformity, an iTCC therefore reaches its limits. To be more precise, there is a quantifiable risk of pressure points in the orthosis.

Charcot Restraint Orthotic Walker (CROW)

The CROW fits more precisely than a TCC or a DW, as it is fabricated individually over a positive model. The device is durable and enables good control of edema. A rocker bottom allows easier ambulation than with a TCC. Load transmission on lower leg depends on the way of fastening the device. High pressure on soft tissues thereby enforces their atrophy, which can lead to worse fit of the orthosis and undesirable motions in the area of the osteosynthesis or the joint to be fused. Provided that the CROW is applied correctly and checked up regularly, it is a useful tool for mobilization of the patient but immobilization of the Charcot joint(s). For physical examination the CROW can be removed without difficulty. Removability of the CROW at the same time involves the risk of noncompliance. Compared to a double-shell TCC, the CROW has a hygienic inner lining that can be easily cleaned and disinfected. This is particularly advantageous if an ulcer is still present at the same time. On the other hand, with the TCC the two shells butt up against each other, with the CROW they overlap, so that this aid allows adjustments to volume fluctuations. The mechanical stability is much better than with the TCC. The CROW should therefore be preferred if long-term use is expected.

Frame Orthosis (FO)

The frame orthosis focuses on immobilizing the joint rather than relieving pressure. A pretibial shell is adapted to the triangular shape of the tibia. Restriction of tibial rotation minimizes transmission of leg motion to the tarsus. The orthotic frame with posterior entry and fixed heel support wedges the lower leg from the tibial plateau to the heel. Axial loading supports fragment fusion in the hindfoot region. Arthrodesis in the midfoot area is effectively protected from bending movements. A lightweight design is available as well as a heavy duty version. Like the CROW and the DW, this type of AFO carries the risk of noncompliance. In the event of soft tissue shrinkage, adjustments are necessary to ensure continued function. Mode of action and medical range are most comparable to the CROW.

A more recent development of the frame orthosis is the combination of an inner semi-rigid socket, comparable to an inner shoe, with an outer rigid monolateral frame. The inner socket can be worn at night when protection is also required during bed rest. It is padded and closes with a zipper. The form-fitting closed construction of the inner socket helps control edema. Putting on is uncomplicated and reproducible. It is virtually impossible for the patient to put the orthosis on incorrectly.

Shoes

Providing footwear is the goal of both conservative and surgical treatment of Charcot foot. In case there is no significant deformity or instability, ready-made shoes may be sufficient for further protection of the foot. Since this protection should primarily consist of shielding the affected joint sections from excessive torsional moments, a stiffened rocker-bottom sole with an early pivot point is required. The apex of the sole roll is even further towards the heel in the case of affection of

Table 18.1 Minimum criteria for orthopedic footwear management of Charcot feet

	Sanders 1	Sanders 2, 3	Sanders 2, 3 + deformity	Sanders 4, 5	Sanders 4, 5 + deformity
Stable	Stiffened rocker sole	Stiffened rocker sole, bottine shoe	Stiffened rocker sole, bilateral ankle support	Stiffened rocker sole, bilateral ankle support	Stiffened rocker sole, stiff boot
Instable	Stiffened rocker sole	Stiffened rocker sole, bilateral ankle support	Stiffened rocker sole, stiff boot	Stiffened rocker sole, stiff boot	Stiffened rocker sole, stiff boot

the hindfoot. At the same time, however, it should be noted that a very pronounced roller reduces the standing area and can thus, in unfavorable cases, also impair gait and stance stability, especially in patients with high-grade polyneuropathy. Full contact insoles trim the foot and work with the shoe to absorb impact forces. Orthopedic custom-made shoes are required in cases of pronounced foot deformity. If the position of the heel is largely physiological and the function of the tibio-talar joint is at least partially preserved, it does not seem necessary to make a boot with a stiff shaft. However, to counter pronator or supinator forces, it is then advisable to make at least a bottine shoe with medial and lateral heel cap.

As a precautionary measure to protect against re-fracture or inflammatory episodes, Charcot feet are usually fitted with a boot with a high and stiffened shaft and a rigid roll-off sole following treatment with TCC or orthotics [12]. Such a type of boot, by its very nature, provides optimal protection, but is nonetheless heavy, uncomfortable, and sweat-inducing. Most importantly, such a uniform shoe fitting lumps together all the different problems of the Charcot foot. A patient with a stable and still mobile ankle joint can benefit from a shoe fitting that still allows mobility in the sagittal plane and only stabilizes the lower ankle joint. However, if a destroyed ankle joint is present, possibly even with deformity or instability in the frontal plane, a high and stiff shank is certainly required for the shoe. In addition to these purely foot-related biomechanical aspects, contextual factors also play a role, which consider the patient's physical activity and weight, the terrain at the place of residence, and, if necessary, special requirements at the workplace (Table 18.1).

Monitoring

Duration of postoperative treatment with orthoses is under debate. One aspect is fracture healing in neuropathic limbs. As it takes up to 3 months for Charcot fractures to heal, this is regarded as the minimum length of time for additional orthotic protection of the extremity. In case of doubt, or when X-rays or CT scans reveal delayed bone fusion, orthotic aftertreatment is continued. Walking without orthosis or with an ill-fitting orthosis before complete bone fusion will lead to loosening and fracture of implanted hardware. Delayed fusion or pseudarthrosis may also occur after external fixation surgery. In either instance functional outcome may be still favorable as long as there is no major relapse of deformity.

The other aspect is CN activity. The terminology "active and inactive CN" is less ambiguous than "acute and chronic CN." Monitoring of activity is even more debatable than duration of orthotic aftertreatment. The key question is when has CN become completely inactive? Eichenholtz stage III on plain X-rays indicates a cooled-off CN. Quite often, a foot with Eichenholtz stage III still shows bone bruise on MRI and some extent of skin temperature rise. Two scenarios have to be differentiated. A foot with congruent joints or a solid bone fusion at the end of treatment is expected to cool off completely, and skin temperature will show no side difference. A foot with incongruent mobile joints ("bag of bones") or a pseudarthrosis at the end of treatment is expected to retain some extent of skin temperature rise, mainly after walking stress. The problem is comparable to a nondiabetic foot with post-traumatic arthritis. Of course, walking without orthosis or with an ill-fitting orthosis has to be excluded.

Patient behavior and function of the device are scrutinized closely unless CN has cooled off after 6 months contrary to expectations.

Just as skin temperature measurement, MRI detects activity of the neuroarthropathic process, but also of other pathological conditions associated with bone marrow edema. Therefore, it has basically the same limitations due to its low specificity. A foot with incongruent mobile joints or with a pseudarthrosis quite often retains bone bruise permanently, so that MRI is not always suitable to determine convenient time to end orthotic treatment. In this regard, bone scans are not superior in differentiating CN activity from other forms of increased metabolic activity.

Doppler spectrum analysis of the first dorsal metatarsal artery may be a modality to monitor the activity of CN. In a study by *Wu* active Charcot feet had a monophasic forward flow in the pedal arteries different from the unaffected contralateral limb [13]. After 6–20 weeks of immobilization Doppler spectra returned to a normal triphasic pattern. Further investigations are necessary to evaluate Doppler spectrum analysis of the foot as a tool for activity monitoring during the rehabilitation process.

It is generally recognized that arthritis or pseudoarthrosis demonstrates swelling or warming during or after mechanical stress of the foot. A so-called inactive Charcot neuroarthropathy nevertheless is often characterized by incongruent joints and pseudarthrotic bone fusion as seen on plain X-rays. Inevitably, walking on an inactive Charcot foot with this radiological picture must result in edema and temperature rise.

Armstrong [14] and subsequently Schon [15] suggested to terminate casting and proceed to shoe fitting when skin temperature difference between the affected site and the corresponding area of the contralateral foot is less than 2°.

However, it is necessary to make a distinction between the areas of the foot where temperature measurements take place. Ankle joint and the small (tarsal) joints behave differently regarding heat production. When it comes to quantification of inflammatory processes of small joints, thermography is stretched to its limits [16]. Evaluation of therapeutic success in terms of skin temperature on a neuroarthropathic process may lead to a false sense of security or, to the contrary, delay termination of orthotic treatment needlessly. Thus, skin temperature measurement cannot be recommended as the only instrument for monitoring CN activity.

MRI

MRI does not only offer an anatomical picture but also different signal intensities that correlate with the activity of an inflammatory process independently of its etiology. Given the diagnosis of neuroarthropathy, signal intensity of bone marrow edema or extent of contrast medium uptake could be used for assessing intensity of inflammation. As with clinical examination, decrease of inflammation may indicate termination of neuroarthropathy in the course of time. Contrast medium uptake correlates with clinical findings as well as with severity of the disease and estimated duration of treatment [17]. Comparable to temperature measurements, the area of the foot with small or big, few or many joints involved must be considered. Another aspect is the presence of fracture and joint dislocation which have influence on duration of offloading treatment. Inclusion of these features into scoring systems helps to identify patients with an expected necessity for longtime treatment [18]. Unfortunately, MRI has comparable limitations to temperature measurements by offering no distinctly quantifiable marker for termination of orthotic or cast treatment. Persistent bone and joint fragmentation after CN consolidation is quite common in Charcot neuroarthropathy. The presence of pseudarthrosis, instability, or deformity with abnormal loading patterns prompts the persistence of mechanical irritation and subsequent inflammation. In those cases, complete remission of bone or soft tissue edema as shown on MRI cannot be expected even if the neuroarthropathic process is no longer active.

Conventional Radiography

Conventional Radiography still has its place in monitoring neuroarthropathy. It is significantly less expensive than MRI and available virtually everywhere in the world. In conjunction with the clinical examination, the X-ray provides valuable information about the consolidation of the neuroarthropathic process. *Eichenholtz* described three stages of osteoarthropathy [19]. The stage of resolution (I) shows joint and soft tissue swelling, bone and cartilage detritus, intraarticular fractures, dislocations, and osteochondral fragmentation. As a result of continued loading of the sensation-impaired foot, persistent microtraumatization occurs, leading to an inflammatory response and increasing deformity.

The stage of reparation (II) shows incipient healing. There is resorption of necrosis, decrease in edema, and fusion of fragments. Sclerosis of bone ends and osteoporosis near the joint are typical. This stage can only begin with unloading of the foot and immobilization of the patient.

The subsequent stage of restitution (III) is characterized by revascularization and "remodeling" of bone ends with the aim of creating stability. In some cases, grotesque joint formations may result. Clinically, stage I is the active phase, while stages II and III are phases of healing [20].

Just like a long persisting bone edema in MRI, swelling and hyperthermia may give the impression that the inflammatory process is still active in the clinical-radiological staging according to Eichenholtz. It should therefore be mentioned again that this is also the case in a burnt-out Charcot arthropathy if this has left considerable mechanical joint destruction.

Postoperative Follow-Up Treatment

We find a combination of conditions with influence on healing time of neuroarthropathy. It is the role of molecules, mechanics, and the mind. On the molecular level, neuropathy impairs bone healing by deregulation of bone turnover where interaction of *nuclear factor kappa b ligand* and *osteoprotegerin* plays an important role. Loss of modulating neuropeptides is responsible for the ignition of an inflammatory process [9]. On the mechanical level, stress and strain around the affected joints can further deteriorate fractures and dislocations and stimulate inflammation that in turn weakens bone—a true vicious circle. Under a technical aspect it is more difficult to control internal and external forces acting around the ankle joint than around the tarsal or midtarsal joint. This may also explain why healing time differs with joint location in CN under conservative treatment [21]. Mechanical disturbances can be caused by ill-fitting orthoses or by leaving them off, occasionally, since neuropathic patients can walk free of pain without orthosis or cast. This is when mind comes in. Not as a synonym for (missing) understanding, but as a complex psychological reaction on peripheral polyneuropathy which is responsible for a neglect-like phenomenon.

Slower bone healing due to neuropathy necessitates a form of follow-up treatment that is different from traumatological standard procedures [22–24]. This is true for internal as well as for external fixation techniques, since in both cases solid bone fusion generally is not completed after 6–8 weeks [25, 26].

Postoperative therapy follows the same principles as in the conservative treatment of active neuroarthropathy. Plaster casts or orthoses are used to protect arthrodesis after internal or also external fixation from damaging mechanical forces until a solid bony fusion is achieved. Only then does the inserted osteosynthesis material no longer have to bear any load. However, if the foot is released for loading before the arthrodesis is fully built up, exactly what happens regularly with repetitive bending loads on metal workpieces happens: it breaks. And this is also true of very massive implants, which are inserted under the assumption that the bone is too soft in Charcot foot. However, as already explained, it is the neuropathy that is responsible for the slower bony fusion. As a rule of thumb, a doubled time until the arthrodesis is completed can be assumed, i.e., at least 3 months. In the case of arthrodesis in the hindfoot, the time can also be half a year or longer. The information available on this in the

literature is quite inconsistent and is based on the experience of the respective centers.

In summary, conservative therapy of Charcot foot is sometimes a possible alternative to surgery, or actually always a complement. Especially the follow-up treatment with casts or orthoses takes into account the specifics of the bone metabolism and the increased mechanical stress in neuropathy and should therefore be familiar to every foot surgeon who deals with Charcot feet.

References

1. Koller A, Springfeld R, Engels G, et al. German-Austrian consensus on operative treatment of Charcot neuroarthropathy: a perspective by the Charcot task force of the German Association for Foot Surgery [published correction appears in Diabet Foot Ankle. 2011;2. doi: 10.3402/dfa.v2i0.14920]. Diabet Foot Ankle. 2011;2. https://doi.org/10.3402/dfa.v2i0.10207.
2. Petrova NL, Petrov PK, Edmonds ME, Shanahan CM. Inhibition of TNF-α reverses the pathological resorption pit profile of osteoclasts from patients with acute Charcot osteoarthropathy. J Diabetes Res. 2015;2015:917945. https://doi.org/10.1155/2015/917945. Epub 2015 Jun 2. PMID: 26137498; PMCID: PMC4468294.
3. Game FL, Catlow R, Jones GR, et al. Audit of acute Charcot's disease in the UK: the CDUK study. Diabetologia. 2012;55:32–5.
4. Böhler L. Technik der Knochenbruchbehandlung. Wien: Wilhelm Maudrich Publisher; 1929. (Technique of fracture treatment).
5. Kaynak G, Birsel O, Güven MF, Oğüt T. An overview of the Charcot foot pathophysiology. Diabetic Foot Ankle. 2013;4. https://doi.org/10.3402/dfa.v4i0.21117.
6. Morgan JM, BiehlL WC, Wagner FW Jr. Management of neuropathic arthropathy with the Charcot restraint orthotic walker. Clin Orthop. 1993;296:58–63.
7. Saltzman CL, Hagy ML, Zimmerman B, et al. How effective is intensive nonoperative initial treatment of patients with diabetes and Charcot arthropathy of the feet? Clin Orthop. 2005;435:185–90.
8. Saltzman CL, Johnson KA, Goldstein RH, et al. The patellar tendon-bearing brace as treatment for neurotrophic arthropathy: a dynamic force monitoring study. Foot Ankle. 1992;13(1):14–21.
9. Jeffcoate WJ, Game F, Cavanagh PR. The role of proinflammatory cytokines in the cause of neuropathic osteoarthropathy (acute Charcot foot) in diabetes. Lancet. 2005;366(9502):2058–61. https://doi.org/10.1016/S0140-6736(05)67029-8. Epub 2005 Aug 10. PMID: 16338454.
10. Guyton GP. An analysis of iatrogenic complications from the TCC. Foot Ankle Int. 2005;26(11):903–7.
11. Piaggesi A, Macchiarini S, Rizzo L, Palumbo F, Tedeschi A, Nobili LA, Leporati E, Scire V, Teobaldi I, Del Prato S. An off-the-shelf instant contact casting device for the management of diabetic foot ulcers: a randomized prospective trial versus traditional fiberglass cast. Diabetes Care. 2007;30(3):586–90.
12. Dahmen R, et al. Therapeutic footwear for the neuropathic foot: an algorithm. Diabetes Care. 2001;24(4):705–9.
13. Wu T, Chen PY, Chen CH, Wang CL. Doppler spectrum analysis: a potentially useful diagnostic tool for planning the treatment of patients with Charcot arthropathy of the foot? J Bone Joint Surg Br. 2012;94(3):344–7.
14. Armstrong DG, Lavery LA. Monitoring healing of acute Charcot's arthropathy with infrared dermal thermometry. J Rehabil Res Dev. 1997;34:317.
15. Schon LC, Easley ME, Weinfeld SB. Charcot neuroarthropathy of the foot and ankle. Clin Orthop Relat Res. 1998;349:116–31.
16. Rajapakse C, et al. Thermography in the assessment of peripheral joint inflammation—a re-evaluation. Rheumatol Rehabil. 1981;20(2):81–7.
17. Zampa V, et al. Role of dynamic MRI in the follow-up of acute Charcot foot in patients with diabetes mellitus. Skelet Radiol. 2011;40:991–9.
18. Berli MC, et al. The "Balgrist Score" for evaluation of Charcot foot. Skelet Radiol. 2021;50:311–20.
19. Eichenholtz SN. Charcot joints. Springfield, IL: Charles C Thomas; 1966.
20. Sanders LJ, Frykberg RG. The Charcot foot (Pied de Charcot). In: Bowker JH, Pfeifer MA, editors. Levin and O'Neal's the diabetic foot. 7th ed. Philadelphia: Mosby Elsevier; 2007. p. 257–83.
21. Sinacore DR. Acute Charcot arthropathy in patients with diabetes mellitus: healing times by foot location. J Diabetes Complicat. 1998;12(5):287–93. https://doi.org/10.1016/s1056-8727(98)00006-3. PMID: 9747646.
22. Armstrong DG, Lavery LA. Acute Charcot's arthropathy of the foot and ankle. Phys Ther. 1998;78(1):74–80.
23. Jones KB, Maiers-Yelden KA, Marsh JL, Zimmerman MB, Estin M, Saltzman CL. Ankle fractures in patients with diabetes mellitus. J Bone Joint Surg Br. 2005;87(4):489–95.
24. Marks RM. Complications of foot and ankle surgery in patients with diabetes. Clin Orthop Relat Res. 2001;(391):153–61.
25. Koller A, Kersken J. Hilfsmittel beim Diabetischen Fußsyndrom. Orthopädie-Technik. 2013;7:1–6.
26. Koller A, Meissner SA, Podella M, Fiedler R. Orthotic management of Charcot feet after external fixation surgery. Clin Podiatr Med Surg. 2007;24(3):583–99.

Charcot Foot: Surgical Management and Reconstruction

19

Dane K. Wukich and Venu Kavarthapu

Introduction

The surgical management of Charcot neuroarthropathy (CN) has evolved over the past several decades. Historically, CN has been treated nonsurgically with offloading and accommodative footwear. Early attempts at surgical reconstruction were associated with high complication rates, and this may have contributed to a longstanding bias against surgical reconstruction. In 1967, Johnson [1] reported on 118 cases of neuropathic fractures and joint injuries. At that time he recognized that inadequately protected fractures, soft tissue sprains, and effusions of neuropathic joints were the precursors of joint destruction. He further stated that trauma in the form of surgery during acute stage could stimulate further resorption. Consequently, Johnson did not advocate surgery until resolution of the acute inflammatory response. Johnson did not advocate surgery specifically for diabetes-related neuropathic foot injuries because of the concern for "circulatory problems."

D. K. Wukich (✉)
Orthopaedic Surgery, University of Texas Southwestern Medical Center, Dallas, TX, USA
e-mail: Dane.Wukich@UTSouthwestern.edu

V. Kavarthapu
Odense University Hospital, University of Southern Denmark, Odense, Denmark

King's College Hospital, London, UK
e-mail: venu.kavarthapu@nhs.net

The growth of surgical intervention in treating CN) appears to parallel the introduction and acceptance of new methods of skeletal fixation. In 1958, "Arbeitsgemeinschaft für Osteosynthesefragen" or AO (translated to Association for the Study of Internal Fixation) was founded in Switzerland. The AO method of employing rigid internal fixation for the treatment of fractures was revolutionary and considered radical by some surgeons, particularly in the USA. After two to three decades of basic science research and outcome studies, AO became widely adopted globally. Specially designed plates and screws offered a significant improvement in managing fractures and dislocations [2]. Contemporaneously, in the Soviet Union, Professor Gavril Abramovic Ilizarov developed an equally revolutionary and radical method of treating musculoskeletal injuries and deformities [3]. Ilizarov's method utilized circular external rings and fine wire transosseous fixation to stabilize fractures and deformities. The true genius of Ilizarov was to create an "external ring fixator" that enabled not only static correction, but gradual dynamic correction of major deformities. Ilizarov's technique greatly expanded the surgical management in treating osteomyelitis, and the recognition that distraction osteogenesis was possible, contributed to success in limb salvage surgery. Ilizarov's methods remained isolated to the Soviet Union and eastern bloc countries until the 1980s when surgeons from Italy were able to

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_19

visit his center in Kurgan, Siberia. Subsequently, the methods of Ilizarov were disseminated across the globe, and circular external fixation has become a widely adopted technique that is often employed in the treatment of CN. Finally, another major advancement in skeletal fixation was developed by Professor Gerhard Kuentscher in Germany. Professor Kuentscher pioneered the intramedullary nailing method for the treatment of long bone fractures. His original book was published in 1947, and the full English translation of "The Marrow Nailing Method" in 2006 [4]. This text was previously unknown until 2004 and gives a remarkable account of his treatment of World War II injuries from the perspective of a German surgeon. Similar to AO principles and the methods of Ilizarov, intramedullary fixation of long bone injuries was initially viewed with skepticism in the USA. Over the past four decades, intramedullary fixation has been universally adopted as the treatment of choice for lower extremity long bone fractures. This technique has been translated to use in CN) reconstruction, and retrograde intramedullary fixation is widely used for complex reconstructions of the ankle and hindfoot. Originally implants designed for the femur were inserted, but now multiple specially designed retrograde ankle arthrodesis nails are available [5].

An early study from the Mayo Clinic (1990) reported on ankle fusion in diabetic neuropathic joints, citing complication rate of 62% including non-union, amputation, and death [6]. The authors cautioned that neuropathic arthropathy contributed to the inordinate complication and failure rates, and ankle arthrodesis should be considered with caution in the diabetic patient. It is now well recognized that patients with CN) may have peripheral artery disease; however, it rarely results in critical limb ischemia. Using noninvasive arterial testing, approximately 13% of patients with CN have ischemia as defined by a great toe pressure of less than 60 mmHg, and only 2.4% of patients had critical limb ischemia defined as a toe pressure of less than 30 mmHg [7]. While adequate perfusion is necessary for successful surgical outcomes, we now recognize the neuropathy and poorly controlled diabetes contribute to high rates of postoperative complications [8–10].

Commensurate with the expanded methods of fixation, enthusiasm for the surgical management of Charcot neuroarthropathy has grown over the past 25 years. Historically, surgical intervention was not recommended until the acute inflammatory response had resolved and consolidation had occurred. One of the earliest reports from Thompson and Clohisy [11] recommended surgical reconstruction in patients whose deformity could not be accommodated in a load sharing orthosis. They also advocated that the skin should be free of ulceration at the time of the procedure.

A systematic review on the surgical management of Charcot neuroarthropathy was published in 2012 [12]. The authors searched databases from 1960 until 2009 and identified 96 articles that met the inclusion criteria of surgical management of Charcot neuroarthropathy. Forty-two of the 96 articles were expert opinion or case reports (44%) and 54 articles were retrospective case series without a control group (56%). The level of evidence for the surgical management of Charcot neuroarthropathy was therefore based on level IV and level V evidence, and there were no controlled retrospective studies or prospective randomized studies. Interestingly, four centers accounted for 51% of all patients reported in this systematic review. The authors offered several conclusions from their study: (1) the evidence for performing or not performing surgery during the acute phase of Charcot neuroarthropathy was inconclusive, (2) the most common locations requiring surgical intervention were the midfoot followed by the ankle, (3) exostectomy was found to be useful to relieve bony pressure that could not be accommodated with orthotics and prosthetics means, (4) Achilles tendon lengthening or gastrocnemius recession reduced forefoot pressure and improved alignment of the ankle and hindfoot relative to the midfoot and forefoot, (5) arthrodesis was indicated for instability, pain, or recurrent ulceration that failed nonsurgical treatment, (6) there was inconclusive evidence to recommend one type of fixation over another (internal versus external fixation).

The same group updated their systematic review searching articles from 2009 until 2014 [13]. An additional 30 manuscripts met the criteria for inclusion, demonstrating that 6.6% of studies were level II prospective comparative studies, 13.3% were level III retrospective case-control study, and 80% were level IV retrospective case series. This updated review demonstrated that the ankle (38.4%) and hindfoot (41.6%) were the most common locations reported for surgery followed by the midfoot (29.6%). The conclusion of this updated systematic review suggested that the published surgical data for Charcot neuroarthropathy was improving as evidenced by higher level studies during the preceding 5 years. The authors also reported that despite improved methods of fixation and improved patient selection, approximately 9% of patients with Charcot neuroarthropathy who underwent surgery required a major amputation.

In 2017 Safavi et al. [14] also performed a systematic review on the outcomes of surgical treatment of midfoot CN. Nine studies were identified, and the authors reported a fusion rate of 91%, amputation rate of 6%, and hardware complication rate of 16%.

One of the most important determinants of a successful Charcot surgical team is to be part of a multidisciplinary program. Cates et al. [15] reported on outcomes of Charcot reconstruction in patients with and without diabetes. The authors are a part of the Georgetown University Diabetic Limb Salvage Program, globally viewed as an excellent multidisciplinary program. Despite their large experience, Charcot reconstruction in diabetic patients was associated with high rates of wound dehiscence (16%), delayed healing (34%), and major lower extremity amputation (26%). When they evaluated their cohort of diabetic patients who were deemed to be well controlled (hemoglobin A1c $\leq$6.5), the rate of major lower extremity amputation was only 10%. There was little difference in the rate of wound dehiscence (15%) or delayed healing (30%) in well-controlled patients.

The King's College Hospital Program in London UK is also widely globally recognized as an outstanding multidisciplinary diabetic foot care team (MDFT) [16]. They have reported their experience in the management of complex midfoot, hind foot, and ankle Charcot neuroarthropathy as well as their protocol for dealing with infected Charcot joints [17–19]. Both the Georgetown and King's College Programs have a collaborative service that includes specialists in reconstructive surgery, vascular surgery, wound care, and internal medicine (diabetologists) with a mission of providing outstanding patient care and service.

Controversies of Surgical Management

Many questions regarding the surgical management of Charcot neuroarthropathy remain unanswered or debated. The decision to proceed with surgical intervention is often debated, and often the anatomic location of Charcot determines whether or not surgery will be done. For example, nonsurgical treatment of midfoot Charcot has been reported to be as high as 60% in a large series [20]. Success was defined as being able to wear standard, commercially available therapeutic depth inlay shoes and custom fabricated accommodative foot orthosis. Deformities at the ankle are less well tolerated and more prone to ulceration, particularly when deformity in the coronal plane is present. A consensus document recommended that for severe Charcot deformity of the ankle, surgical management should be considered a primary treatment because coronal deformity of the ankle is poorly tolerated [21].

Traditionally, surgical intervention was not recommended until the acute inflammatory response had subsided and consolidation occurred. There is little evidence to support this, but the dogma was that surgical intervention during the hyperemic phase was associated with higher complication rates. In 2000 Simon et al. [22] reported on a series of 14 patients with midfoot Charcot who underwent early operative treatment during Eichenholtz stage I. All 14 arthrodesis procedures were successful and the meantime to return to assisted weight-bearing was approximately 10 weeks. In 2010,

Mittlemeier et al. [23] reported on the outcomes in 22 patients (26 ft) that underwent primary surgical reconstruction. The indications for realignment arthrodesis were instability, non-plantigrade foot, and deformity with ulcer or impending ulceration. They experienced nine complications, five hematomas, and four with postoperative instability. Despite this, all patients achieved a stable and plantigrade foot and no recurrent ulcerations occurred. The authors suggested that surgical reconstruction of the Charcot foot should not be limited to salvage procedures, but early surgical intervention in high-risk patients should be considered. One of the potential limitations of this retrospective study is that only four of 22 patients (18%) were treated during Eichenholtz stage 1. Five years later the same center reported that 19 of 21 patients (90%) who underwent late corrective arthrodesis experienced at least one complication [24].

The choice of fixation (i.e., internal or external fixation) depends on several factors, not the least of which is surgeon preference. One of the major determinants is the presence or absence of active bone or soft tissue infection. Most authors agree that internal fixation is not recommended in the setting of active infection. Some surgeons utilize internal fixation in patients with clinically uninfected wounds, while others prefer to achieve ulcer healing prior to operative reconstruction. Our general approach is to use internal fixation in patients without active infection. In patients with open wounds associated with active infection we prefer external fixation, as a primary procedure or staged. Patients with active infection are also treated with culture directed antibiotics and negative pressure wound therapy if indicated. In select cases, a hybrid type of construct is utilized combining both internal and external fixation, particularly in patients with poor bone quality. While external fixation is an invaluable tool in CN, its use can be associated with a high complication rate in patients with diabetes [25].

Dayton et al. [26] published a systematic review comparing the outcomes of CN using internal or external fixation. Procedures using internal fixation achieved an overall successful outcome rate of 87% of patients and 6.5% required major amputation. Procedures on the foot achieved a higher rate of success than the ankle (93% vs. 84%). In contrast, external fixation was associated with successful outcomes in 93% of patients and the major amputation rate was 3.5%. Procedures on the foot achieved a higher rate of success than the ankle (90% vs. 88%).

Additional data demonstrated from Dayton's review included the fact that internal fixation was used in patients with uncomplicated wounds or osteomyelitis. Screws were preferred for the foot and intramedullary fixation for the ankle. Dayton also acknowledged that external fixation was used primarily in more complicated cases with infection. Pooling of data from the 23 studies found that the odds ratio of successful outcome using internal fixation was significantly less likely than when external fixation was used (OR 0.52, 95% CI 0.30–0.90, $p < 0.05$). The conclusions drawn from this study must be viewed in the context of selective bias.

Radiographic Evaluation

Standing X-rays of the ankle and foot should be obtained in all patients to include three views. Hindfoot alignment views are also essential to identify subtle varus and valgus deformities. Contralateral radiographs can be especially helpful to assess the normal anatomy. In some cases, osseous anatomy can be so distorted that radiographs are not optimal for preoperative planning in which case advanced imaging is beneficial. Malalignment of the ankle is typically obvious; however deformities of the hindfoot and midfoot can be less obvious. Measurement of certain angles of the foot can be helpful in preoperative planning and predicting the potential for ulceration. In 2008, Bevan and Tomlinson [27] reported that lateral talar-first metatarsal angle measured on weight-bearing radiographs was a simple means of monitoring patients' risk of development of midfoot ulceration. Another radiographic study found that sagittal plane deformities are more likely to be associated with foot ulcerations than transverse plane deformities

[28]. Lateral column involvement was identified by a decrease in the cuboid height, decreased calcaneal pitch, and decreased lateral calcaneal fifth metatarsal angle. Meyr and Sebag [29] recommended against using a single radiographic parameter to predict midfoot ulceration because of significant positive and negative correlations among various angles that could be measured. Given that limitation, excellent reliability for radiographic measurement of cuboid height on subjects with midfoot Charcot neuroarthropathy has been reported [30].

CT scans provide improved osseous visualization and can identify bone loss and dislocations not seen on radiographs. MRI can identify bone injury beyond the suspected area of Charcot as evidenced by increased signal. MRI can also be useful in cases of suspected osteomyelitis in patients with active or healed wounds as well as following the course of CN.

Nuclear medicine can also be helpful in the evaluation of suspected for infected CN by labeling Leukocytes with either (99m)Tc-HMPAO or (111)In-oxine [31]. In experienced centers accuracy in detecting bone infection can be greater than 95%. Another benefit is that white cell labeled scans may be able to differentiate soft tissue infection versus aseptic inflammation. Single-photon emission computed tomography/computed tomography (SPECT/CT) and bone marrow scanning can also improve anatomic resolution of the foot and ankle [31].

Preoperative Evaluation

Patients with CN often have multiple comorbidities that can increase the perioperative risks of surgery to include cardiovascular disease (hypertension, coronary artery disease, compensated or uncompensated heart failure), diabetic nephropathy or autonomic neuropathy, poorly controlled diabetes, and tobacco use. A thorough preoperative evaluation can predict the risk [32].

Patients undergoing Charcot reconstruction benefit from a structured multidisciplinary evaluation prior to the procedure. At King's College Hospital diabetic foot unit, the preoperative assessment is commenced during their visit to a dedicated "Foot School Clinic" (see figure). The group of patients undergoing Charcot reconstruction procedures are seen along with their personal care providers or family members in the clinic. Detailed and interactive audio-visual presentations are made to the attendees by the members of the MDFT (physician, surgeon, podiatrist, physiotherapist, and occupational therapist), covering the generic information on their perioperative care. This is followed by individual assessment and counseling of each patient, separately, by each member of the MDFT. The physiotherapist provides the information on the prehabilitation regime (PREHAB) whereas the occupational therapist goes through the microenvironment setup at the patient's residence and the regimens used for postoperative mobilization due to the limitation of weight-bearing. All routine perioperative assessments and investigations are completed at this stage.

Routine blood investigations, including CBC, renal and liver profiles, and inflammatory markers (C-reactive protein, ESR, procalcitonin) will provide adequate assessment of surgical fitness. Blood vitamin D levels are often low in this group of patients and it is recommended to routinely provide vitamin D replacement. In the presence of raised inflammatory markers, radiological features of osteomyelitis or a history of previous infection in the Charcot affected region, it is advisable to perform bone biopsies for a definitive diagnosis and microbiological sensitivities.

Bone biopsy can be performed as an outpatient procedure in most patients. The patient should be off antibiotics for at least 2 weeks prior to the biopsy procedure. The location of the bone biopsy target material is determined based on the imaging studies. Local anesthetic infiltration can be applied to the area of skin penetration if the skin sensation is intact. Using aseptic technique, the assembled trocar and cannula of the biopsy instrument is pierced into adequate depth and in the direction based on imaging studies. If an ulcer is present, the biopsy entry point is chosen about 1 cm away from the edge of the ulcer, avoiding areas of active inflammation. Using a standard bone core biopsy technique, the specimen is har-

vested and sent for microbiology (culture and sensitivities) and histological studies.

Vascular studies are routinely considered prior to Charcot reconstruction, to rule out any significant vascular compromise. If identified, this is best addressed by performing the revascularization procedure about 4–6 weeks prior to the deformity correction. The method of revascularization is beyond the scope of this chapter and will be discussed in other chapters.

Charcot Bone

Surgeons should recognize that bone is a dynamic organ, and in normal homeostasis, bone resorption and bone formation are in relative balance. It is well recognized that during the active phase of Charcot neuroarthropathy, circulating osteoclasts are significantly elevated and metabolically active resulting in a net loss of bone. Osteoclasts also express inflammatory cytokines such as interleukin-1 beta, interleukin-6, and TNF alpha which facilitate the recruitment, proliferation, and differentiation of osteoclasts. A histopathological and immunohistochemistry study of bone retrieved from patients undergoing Charcot reconstruction demonstrated that even though patients were beyond Eichenholtz stage 1 (active) and in the remodeling phase, expression of proinflammatory cytokines was still present on pathological examination [33]. This finding has implications in planning surgical reconstruction.

Surgeons planning to reconstruct Charcot neuroarthropathy should have an understanding of the quality of the involved bone. Herbst at al. [34] classified the bone injury pattern as either a fracture, dislocation, or fracture dislocation. Bone mineral density was measured in the contralateral femoral neck or contralateral distal radius, and not measured in the involved foot. The authors found that patients who presented with a fracture pattern had significantly lowered *T*-scores in bone mineral density compared to the dislocation group. In fact, the age adjusted odds ratio of a patient with osteopenia according to the World Health Organization criteria as having a fracture rather than dislocation was 9.5. Dislocations and fracture dislocations had normal bone mineral density as measured in their study. The fracture pattern was more likely to be seen in the ankle and foot, while the midfoot mostly involved dislocations. The hindfoot was represented by fractures, dislocations, and fracture dislocations. The authors opined that the osteopenia seen in the fracture group was not a result of regional Charcot neuroarthropathy, because the decreased bone mineral density was observed in the contralateral extremities. They further stated that the success of midfoot reconstruction may be related to the fact that the dislocation pattern has more of a normal bone mineral density compared to the fracture pattern. Limitations of this article included few patients in the combination fracture dislocation group and inclusion of patients presenting at different Eichenholtz stages of the disease. Nonetheless this study highlights an important point, namely that identification of peripheral osteopenia may be a potentially modifiable systemic risk factor in patients with diabetes and neuropathy.

Petrova at al. [35] studied 36 consecutive patients who were treated for acute Charcot neuroarthropathy. They measured bone mineral density of the calcaneus from the involved foot and compared it to bone mineral density from the contralateral uninvolved foot. The authors found that the bone mineral density of the involved foot was significantly decreased when compared to the contralateral foot at presentation, after 3 months of casting and at clinical resolution. There was a significant decrease in bone mineral density from the time of presentation until the time of casting at 3 months. After 3 months no significant further decrease in bone mineral density occurred. Contrary to the opinions of Herbst et al. [34], the authors felt that this reduced ipsilateral bone mineral density was secondary to proinflammatory induced osteolysis.

Greenhagen et al. [36] prospectively studied central (core) and peripheral bone mineral density in a cohort of diabetic and non-patients. Peripheral bone density was measured in the calcaneus of the extremity affected by CN, while the

core bone density was measured in the lumbar spine. The diabetic cohort was comprised of two groups, one who had Charcot neuroarthropathy and a control of diabetes patients without Charcot. The bone mineral density of the Charcot group was significantly lower in the calcaneus compared to the control group, and there was a strong trend that the Charcot group bone quality was lower than the diabetic control group ($p = 0.08$). Interestingly the core bone mineral density as measured in the lumbar spine was not significantly different between the three groups.

It is important to recognize that tools that measure BMD are quantitative in nature and do not measure the qualitative aspect of bone. Patients with diabetes are at risk for fragility fractures due to decreased bone material strength even in the setting of normal BMD [37]. This increased risk of fracture is secondary to greater cortical porosity, smaller cortical area, and decreased bone strength. The implication in Charcot patients is the obvious potential for stress fractures even without observed trauma. Given the alteration in bone remodeling and turnover seen in diabetic bone, healing after arthrodesis could be impacted as well due to decreased bone quality and reduced biomechanical properties.

It has also been demonstrated that inflammatory and bone turnover markers and acute Charcot neuroarthropathy are elevated in peripheral serum [38]. Inflammatory markers such as C-reactive protein, TNF alpha, and interleukin-6 were found to be significantly higher in patients with Charcot neuroarthropathy when compared to diabetic patients without Charcot neuroarthropathy. Markers of bone turnover such as C-terminal telopeptide, bone alkaline phosphatase, and osteoprotegerin were also significantly elevated at presentation. TNF alpha and interleukin-6 declined significantly after 3 months of casting but did not change during the resolution phase. Markers of bone turnover did not decline significantly after 3 months of casting or at final resolution. Surgeons should recognize that the potential for ongoing bone remodeling can occur regardless of the timing of surgical intervention, even after resolution of Eichenholtz Stage 1.

Indications for Surgery

Traditionally the indications for surgical intervention include:

- Non-braceable deformities
- Instability
- Impending ulceration of the skin
- Non-healing ulcers
- Recurrent ulcers
- Osteomyelitis of the midfoot, hindfoot, and ankle
- Pain

Although symptomatic pain is relatively uncommon, a subset of patients with Charcot neuroarthropathy will complain of significant pain due to instability and deformity. Some patients complain of difficulty ambulating with a rocker bottom deformity. Patients whose foot is non-plantigrade are at high risk of ulceration. For the purposes of this chapter, a non-plantigrade foot/ankle is defined as one in which the patient is bearing weight on skin that is not meant to bear weight. For example, the plantar arch, lateral and medial borders of the foot dorsal to glabrous skin and skin over the medial and lateral malleoli are not designed to bear weight. Midfoot CN commonly results in collapse of the arch with potential skin compromise medially or laterally on the plantar surface. Collapse of the medial column can involve subluxation/dislocation of the talonavicular, naviculocuneiform, or tarsometatarsal joints. Laterally, the prominence is typically a result of subluxation or dislocation of the calcaneo-cuboid joint. Hindfoot and ankle deformities can result in significant varus or valgus malalignment that jeopardizes non-plantar skin (see figure). Final surgical planning and goals of surgery are best discussed by the multidisciplinary team, taking into consideration the factors that have been previously reviewed. While each Charcot case is unique, reconstruction should follow a logical and reproducible plan. We recognize that customization of the approach may be necessary, but in general the following principles guide reconstruction.

1. Perioperative medical optimization measures. A high portion of patients are on anticoagulation treatment and it is often not safe to stop this medication preoperatively.
2. The choice of anesthesia: Peripheral nerve block for pain relief is not considered in most patients, due to the degree of sensory neuropathy. Tranexamic acid administration during induction is usually considered in most patients.
3. Decision on the usage of tourniquet: This is based on the vascular status and previous revascularization procedures. It should be recognized that many patients have medial artery calcinosis that can prevent occlusion with a tourniquet, resulting in a venous tourniquet.
4. Prophylactic antibiotics administration: This is delayed until the intraoperative bone and deep tissue samples are harvested.
5. Surgical approaches: The location of the surgical approaches and their effect on the vascular supply to the soft tissue envelope and bones is discussed. It is preferred to perform the reconstruction using one main surgical approach, supplemented with additional small approaches as required. Foot and ankle surgeons must be comfortable with a 360-degree approach to the pathology, as many patients have compromised skin from previous surgery.
6. Soft tissue releases: The associated soft tissue contractures are assessed, and plans are made for lengthening or release for deformity correction. Commonly performed soft tissue lengthenings in Charcot surgery include Achilles (sagittal plane), posterior tibial (varus deformities), and peroneal (valgus deformities).
7. Bone corrections: The location of the bone osteotomies and the size of the bone wedge/rhomboid resections are discussed based on the assessment of clinical deformity (shape and flexibility) and imaging studies. CT imaging with 3D reconstruction, weight-bearing CT, and 3D printed model of the bone deformity of the foot are useful tools used for this assessment.
8. The fixation devices: Due to the presence of significant bone loss, Charcot foot reconstruction procedures often require a combination of fixation devices to achieve a long-segment and rigid fixation construct. Hindfoot nail fixation may require additional cannulated screw fixation across the hindfoot, and midfoot beams may require supplementary locking plate fixation, to enhance the rotational rigidity to the construct.
9. Wound closure: On occasions, it may not be possible to achieve tension-free primary wound closure, particularly when the degree of the deformity is severe or if concomitant ulcer debridement was done. The need for performing a local rotational flap or other appropriate plastic surgical procedure or usage of NWPT is anticipated. Soft tissue complications are common, and one method of minimizing these complications is to approach the deformity from the convex side. Once the deformity is corrected, the convex side is no longer under tension while the concave side is subjected to tension.
10. Antibiotic regimen: In the presence of an ulcer or previous history of infection, a biodegradable, osseoconductive and local antibiotic eluting calcium sulfate preparation can be used to fill the bone voids and achieve high concentrations of the antibiotic. The postoperative antibiotic regimen can be based on the preoperative bone biopsy microbiology sensitivities and modified according to the sensitivities of intraoperative specimens.
11. Mobility: Postoperative weight-bearing status and the duration is determined based on the complexity of the reconstruction procedure. Consideration is given on the status of the opposite foot, as excessive load bearing carries a risk of activation or re-activation of Charcot changes in this foot.

Exostectomy

Several retrospective case series have described medial or lateral exostectomy to decompress bony deformities of CN and promote healing of

recalcitrant ulcers [39–44]. Advocates of exostectomy cite high healing rates of ulcers; however, Catanzariti et al. [40] reported higher success with medial column exostectomy versus lateral column exostectomy. Molines-Barroso et al. [42] found that sagittal plane radiographic measures worsened after lateral column exostectomy as manifested by a significantly decreased calcaneal inclination angle and significantly increased talar declination angle.

Plantar ulcers due to bone prominence that do not respond to surgical debridement can be considered for exostectomy. The infected ulcer is excised, removing all infected and necrotic tissue, down to the bone prominence. Any associated tendon contractures, particularly of the Achilles tendon is released or lengthened. The area of bone resection is identified by careful palpation and under the guidance of fluoroscopy. All bone prominence is excised completely using an oscillating saw or a sharp osteotome. If there are any areas of residual bone necrosis or bone changes consistent with osteomyelitis, the resection is continued until all these areas are removed. Care is taken not to leave any bone projections or loose bone fragments as this will interfere with ulcer healing. Where available, antibiotic loaded calcium sulfate preparation can be inserted into drill hole channels created in the exposed bone as an injectable form or applied on the bone surface as beads (see figure). Local elution of high concentrations of antibiotic can potentially eradicate any residual infection. The foot is examined after completion exostectomy for the presence of instability due to bone resection. This requires a temporary stabilization of this area with threaded wires or an external fixator for the duration of bone healing. The open wound is managed either with a local rotation flap, free flap, or negative pressure wound therapy and appropriate offloading.

Reconstruction of Active Charcot Foot

Acute (active) CN of foot normally responds to immediate offloading in a total contact cast (TCC) or a well-fitting brace until it reaches an inactive phase. Despite adequate offloading some Charcot deformities continue to progress secondary to the degree of bone fragmentation or joint dislocations. Progressive deformities make the foot and ankle vulnerable to friction and shear forces which can lead to ulceration. If the foot is at risk of ulceration, and consequently infection due to the presence of marked deformity and or instability, it is advisable to perform surgical reconstruction in the active phase of the disease. Although ideally performed after resolution of foot swelling and normalization of local warmth, the degree and location of deformity may accelerate the surgical plan despite the presence of active inflammation. The use of a preoperative compression dressing incorporating cast padding in conjunction with elevation can result in substantial reduction in edema. The reconstruction is performed using internal or external fixation, using the principles described later in this chapter.

Reconstruction of Inactive Charcot foot

Severe Charcot deformity carries a high risk of developing ulceration even with adequate offloading. Associated instability, often noticed in severely affected feet due to non-union of bone fragments effected by the Charcot process, provides additional challenge in preventing a skin breakdown. Ulceration often progresses to developing infection and a chain of events resulting in a major amputation. An ulcerated Charcot foot is 12 times more vulnerable to undergo a major lower limb amputation [45]. Due to the high rate of mortality following a major lower limb amputation in the diabetic population, a functional limb salvage of Charcot foot can potentially save the life of some of these patients.

The aim of Charcot foot reconstruction is to achieve a plantigrade and stable foot that is infection and ulcer free and allows full weight-bearing in a modified shoe or a brace. The incidence of non-union following Charcot foot reconstructions is high, and in general a stable non-union or pseudoarthrosis has been considered as an acceptable out-

come. Some fibrous non-unions achieve adequate stability and are still desirable; however, mobile and unstable non-unions should be avoided in a neuropathic foot, as this can result in recurrence of deformity over a period of time. Ideally, the surgical aim should be to achieve a full bone fusion or a stable fibrous union in every procedure.

Deformity Correction

Charcot foot and ankle deformity correction is achieved by achieving adequate soft tissue balance, through release or lengthening of contracted tendons and other soft tissues, and performing wedge or rhomboid bone resections on the convexity of the deformity, based on surgical planning. The choice of incision and surgical approach depends on the location of the deformity and the vascular status of the angiosomes. Multiple major surgical incisions should be avoided as they carry a significant risk of wound breakdown and infection. Careful deep dissection of the incisions developing thick and deep soft tissue flaps and protecting vascular structures is critical. All joints intended for bone fusion are exposed and thoroughly prepared. Following the desired deformity correction, stabilization of the correction is achieved by using either internal or external fixation methods. Recent systematic review studies revealed no significant advantage of one method over the other (see figure) [46]. With the recent introduction of Charcot-specific internal fixation devices, there has been a recent increase in the usage of this internal fixation method for reconstructions.

Hindfoot and Midfoot Stabilization Using Internal Fixation

The surgical principles for Charcot foot and ankle internal fixation method have evolved since Sammarco et al. [47] described a decade ago, when the term "Super-construct" was introduced for this fixation. This advocated extension of bone fixation beyond the zone of injury, the usage of the strongest fixation device that is tolerated by the soft tissue envelope and application of the fixation devices in a novel position that maximizes its mechanical function. Subsequent studies identified the additional need for the fixation construct to provide rigidity against axial, bending, and rotational forces to improve the fixation outcomes. The current established principle of internal fixation for Charcot reconstruction is "durable long-segment rigid fixation with optimal bone opposition."

Hindfoot Internal Fixation

An intramedullary hindfoot nail (IMHN) is the most accepted method of internal fixation for Charcot hindfoot reconstruction. Biomechanically, IMHN is a load sharing device, provides better mechanical environment, and has higher bending and torsional stiffness compared to other forms of internal fixation. It can also provide intraoperative compression of the bone fragments over the nail and that results in optimal bone opposition. The torsional rigidity of the construct may be suboptimal in the presence of marked bone loss and may require additional fixation (see figure) [18].

A trans-fibular lateral approach provides good access to the ankle and subtalar joints for preparation and wedge resections and is the most common surgical approach. Alternative approaches may be considered for severe valgus deformities or those with compromised lateral soft tissues. Following the soft tissue releases and bone resections, the hindfoot is stabilized temporarily with 2 mm Kirshner wires, to maintain correction. The entry point for the hindfoot nail is determined under fluoroscopy guidance and care is taken to make sure that guide wire goes through the mid-portion of calcaneus. The intramedullary reaming to adequate diameter and depth is performed. The Kirshner wires are then removed and the chosen length and diameter hindfoot nail is inserted, using the recommended standard surgical technique. Correct length and diameter of the nail should be chosen to achieve a good isthmal fit of the nail is the tibial diaphysis. There are varying opinions on whether to use short or long retrograde nails, and IMHN sizes range from 150

to 300 mm in length. Axial compression of the bone fragments over the nail is attained before inserting both proximal and distal locking screws. In the presence of significant bone loss or during severe hindfoot correction that utilizes large bone resections, optimal rotational rigidity cannot be achieved with a standard hindfoot nail construct alone. To enhance the rotational rigidity in such constructs, an additional cannulated screw can be inserted from calcaneum into distal tibia (see figure). Supplemental fixation can also be achieved with a locking plate spanning distal tibial and talus.

Midfoot Internal Fixation

Charcot midfoot deformities generally fall into one of three patterns:

1. rocker bottom forefoot abduction
2. dorsal subluxation/dislocation
3. forefoot adduction (see figure).

The rocker bottom forefoot abduction deformity is the commonest pattern and results from the involvement of the medical column collapse. Significant deformity often results in marked reduction of calcaneal pitch and contracture of Achilles tendon. Sagittal plane deformity can be quite significant.

Midfoot deformity correction often requires posterior muscle group lengthening to achieve soft tissue balance in the sagittal plane. This can be accomplished with required percutaneous tendo Achilles lengthening, open Achilles tendon lengthening, or gastrocnemius recession. This is performed in conjunction with anatomic restoration by performing bone wedge resections on the convex side. Most deformities are associated with rocker bottom and forefoot abduction components. A medial midfoot approach allows performing a plantar and medial based bone wedge resection, with the apex of the wedge placed in the lateral part of the cuboid bone, thereby preserving the cuboid's lateral cortex. This intact lateral cortex of the cuboid allows controlled correction of the forefoot deformity by closing the wedge and permits the application of tension band plating principle for the medial column fixation (see figure). The deformity correction can be provisionally held with two or more 2 mm Kirschner wires.

The deformity correction can be stabilized with a medial column beam or locking plate or a combination of these. For locking plate fixation technique, initial lag screw fixation with one or two cannulated lag screws across the osteotomy is done before using a strong and low profile contoured locking plate spanning across the medial column for neutralization. More recently an intramedullary medial column beam spanning the first metatarsal and talus, inserted either retrograde through the metatarsal head or antegrade through the posterior body of talus, is favored as it provides excellent compressive fixation and requires smaller surgical approach. If any residual rotational instability is noted, this can be enhanced by supplementing the fixation with a locking plate across the medial column (see figure). Most midfoot deformities, involving the medial column, do not require a lateral column fixation, if the lateral cortex of cuboid is left intact. However, for complex deformities, as noted in some dorsal subluxation patterns and those that involve medial and lateral column rocker bottom deformity, additional lateral column fixation is required. This can be achieved by using additional lateral beams inserted from the third and fourth metatarsal into calcaneus, along with an additional plate fixation spanning the base of fourth metatarsal to the anterior part of calcaneum, if required.

Two-Stage Reconstruction

Charcot foot reconstruction is typically carried out as a one-stage procedure, even in the presence of a non-infected ulcer. In the presence of an ulcer, thorough surgical debridement is performed at the beginning of the procedure, followed by the reconstruction using the principles enumerated above. Multiple bone and soft tissue specimens are collected during the procedure for microbiological analysis and empirical antibiotic therapy is com-

menced until the microbiological sensitivity results are obtained. The wound from ulcer debridement is managed with primary closure, a local rotation flap, or NPWT. In some cases, the ulcer wound can be left open and healing occurs rapidly once the osseous deformity has been corrected.

Charcot foot deformity associated with an infected ulcer or deep infection is best managed as a two-stage procedure (to achieve functional limb salvage) [48]. The first stage of this treatment consists of surgical debridement of all infected and necrotic tissues using the principles described above. It is critical that multiple deep tissue and bone specimens from the infected areas are harvested for microbiological culture and sensitivities. Infected bone and prominences are thoroughly excised. In the presence of marked deformity, osteotomy or wedge resection is done to reduce deformity and decompress the soft tissues. The bone voids that are created from debridement and osteotomy are filled with an antibiotic impregnated calcium sulfate preparation, for local antibiotic elution in high concentration to eliminate any residual infection. The choice of the antibiotic used in this preparation is based on the previous microbiological sensitivities. If an osteotomy is done, the associated foot instability is addressed with the application of threaded guidewires or an external fixator temporarily. The open wounds created from ulcer debridement or surgical wounds are managed with negative pressure wound therapy (NPWT).

Infection eradication is achieved by administering empirical intravenous antibiotics that are changed to targeted antimicrobials once the intraoperative specimen microbiology results become available. The duration of antibiotic administration is based on the improvement noted clinically and serologically. After a period of 6–10 weeks of interval treatment that includes advanced wound care and foot offloading, the second stage of treatment is delivered.

The second stage of the reconstruction is typically done using the external fixation option; however, recent reports have shown good results with internal fixation methods using the principles described above (see figure). Repeat debridement of the previously infected areas and further harvesting of deep tissue and bone samples are done during the second stage, followed by soft tissue releases if required, wedge bone resections, joint preparations, and internal fixation using the principle of "long segment and rigid internal fixation with optimal bone opposition," as described above. Gentamycin or Vancomycin impregnated injectable calcium sulfate preparation (Cerament® G or V, Bonesupport, Lund, Sweden) is applied to the bone voids and around the osteotomy sites for local antibiotic elution. Targeted intravenous antibiotics are continued for 2–6 weeks based on the improvements noted clinically and serologically. The postoperative care is similar to the one-stage reconstruction.

Postoperative Care of Reconstructed Charcot Foot

The leg is elevated postoperatively to reduce swelling and the patient mobilized non-weight-bearing in a well-padded below-knee splint. Closed surveillance of the surgical wound is undertaken, and once the wound is stabilized, a total contact cast is applied. Bivalving of the TCC is especially helpful to facilitate regular wound inspections. The patient is discharged home, when safe mobility levels are reached, non-weight-bearing in a TCC. Postoperative radiographs are taken at 6 and 12 weeks and regularly then after as required. The non-weight-bearing TCC is continued for at least 3 months post-surgery. Progression to partial weight-bearing in the cast can be initiated once radiographs demonstrate signs of osseous healing. Ultimately, progression to custom-made orthotics and/or shoes is fabricated to assist in independent ambulation. Some patients may benefit from additional stability by using a cane to help mitigate the consequences of peripheral neuropathy.

References

1. Johnson JT. Neuropathic fractures and joint injuries. Pathogenesis and rationale of prevention and treatment. J Bone Joint Surg Am. 1967;49:1.
2. Mueller ME, Allgower M, Schneider R, Willenegger H. Manual of internal fixation: techniques recommended by the AO-ASIF Group. Berlin: Springer; 1991.
3. Kirienko A, Villa A, Calhoun JH. Ilizarov technique for complex foot and ankle deformities. New York, NY: Marcel Dekker, Inc; 2004.
4. Kuntscher G. The marrow nailing method. Kiel: Stryker Trauma GmbH; 1947, translated 2006.
5. Pinzur MS, Kelikian A. Charcot ankle fusion with a retrograde locked intramedullary nail. Foot Ankle Int. 1997;18:699.
6. Stuart MJ, Morrey BF. Arthrodesis of the diabetic neuropathic ankle joint. Clin Orthop Relat Res. 1990;(253):209.
7. Wukich DK, Raspovic KM, Suder NC. Prevalence of peripheral arterial disease in patients with diabetic Charcot neuroarthropathy. J Foot Ankle Surg. 2016;55:727.
8. Myers TG, Lowery NJ, Frykberg RG, Wukich DK. Ankle and hindfoot fusions: comparison of outcomes in patients with and without diabetes. Foot Ankle Int. 2012;33:20.
9. Wukich DK, Crim BE, Frykberg RG, Rosario BL. Neuropathy and poorly controlled diabetes increase the rate of surgical site infection after foot and ankle surgery. J Bone Joint Surg Am. 2014;96:832.
10. Wukich DK, Shen JY, Ramirez CP, Irrgang JJ. Retrograde ankle arthrodesis using an intramedullary nail: a comparison of patients with and without diabetes mellitus. J Foot Ankle Surg. 2011;50:299.
11. Thompson RC Jr, Clohisy DR. Deformity following fracture in diabetic neuropathic osteoarthropathy. Operative management of adults who have type-I diabetes. J Bone Joint Surg Am. 1993;75:1765.
12. Lowery NJ, Woods JB, Armstrong DG, Wukich DK. Surgical management of Charcot neuroarthropathy of the foot and ankle: a systematic review. Foot Ankle Int. 2012;33:113.
13. Schneekloth BJ, Lowery NJ, Wukich DK. Charcot neuroarthropathy in patients with diabetes: an updated systematic review of surgical management. J Foot Ankle Surg. 2016;55:586.
14. Shazadeh Safavi P, Jupiter DC, Panchbhavi V. A systematic review of current surgical interventions for Charcot neuroarthropathy of the midfoot. J Foot Ankle Surg. 2017;56:1249.
15. Cates NK, Wagler EC, Bunka TJ, Elmarsafi T, Tefera E, Kim PJ, Liu GT, Evans KK, Steinberg JS, Attinger CE. Charcot reconstruction: outcomes in patients with and without diabetes. J Foot Ankle Surg. 2020;59:1229.
16. Manu CA, Mustafa OG, Bates M, Vivian G, Mulholland N, Elias D, Huang DY, Deane C, Cavale N, Kavarthapu V, Rashid H, Edmonds M. Transformation of the multidisciplinary diabetic foot clinic into a multidisciplinary diabetic foot day unit: results from a service evaluation. Int J Low Extrem Wounds. 2014;13:173.
17. Butt DA, Hester T, Bilal A, Edmonds M, Kavarthapu V. The medial column Synthes Midfoot Fusion Bolt is associated with unacceptable rates of failure in corrective fusion for Charcot deformity: Results from a consecutive case series. Bone Joint J. 2015;97-B:809.
18. Siebachmeyer M, Boddu K, Bilal A, Hester TW, Hardwick T, Fox TP, Edmonds M, Kavarthapu V. Outcome of one-stage correction of deformities of the ankle and hindfoot and fusion in Charcot neuroarthropathy using a retrograde intramedullary hindfoot arthrodesis nail. Bone Joint J. 2015;97-B:76.
19. Vasukutty N, Jawalkar H, Anugraha A, Chekuri R, Ahluwalia R, Kavarthapu V. Correction of ankle and hind foot deformity in Charcot neuroarthropathy using a retrograde hind foot nail-The Kings' Experience. Foot Ankle Surg. 2018;24:406.
20. Pinzur M. Surgical versus accommodative treatment for Charcot arthropathy of the midfoot. Foot Ankle Int. 2004;25:545.
21. Rogers LC, Frykberg RG, Armstrong DG, Boulton AJ, Edmonds M, Van GH, Hartemann A, Game F, Jeffcoate W, Jirkovska A, Jude E, Morbach S, Morrison WB, Pinzur M, Pitocco D, Sanders L, Wukich DK, Uccioli L. The Charcot foot in diabetes. Diabetes Care. 2011;34:2123.
22. Simon SR, Tejwani SG, Wilson DL, Santner TJ, Denniston NL. Arthrodesis as an early alternative to nonoperative management of Charcot arthropathy of the diabetic foot. J Bone Joint Surg Am. 2000;82-A:939.
23. Mittlmeier T, Klaue K, Haar P, Beck M. Should one consider primary surgical reconstruction in Charcot arthropathy of the feet? Clin Orthop Relat Res. 2010;468:1002.
24. Eschler A, Gradl G, Wussow A, Mittlmeier T. Late corrective arthrodesis in nonplantigrade diabetic Charcot midfoot disease is associated with high complication and reoperation rates. J Diabetes Res. 2015;2015:246792.
25. Wukich DK, Belczyk RJ, Burns PR, Frykberg RG. Complications encountered with circular ring fixation in persons with diabetes mellitus. Foot Ankle Int. 2008;29:994.
26. Dayton P, Feilmeier M, Thompson M, Whitehouse P, Reimer RA. Comparison of complications for internal and external fixation for Charcot reconstruction: a systematic review. J Foot Ankle Surg. 2015;54:1072.
27. Bevan WP, Tomlinson MP. Radiographic measures as a predictor of ulcer formation in diabetic Charcot midfoot. Foot Ankle Int. 2008;29:568.
28. Wukich DK, Raspovic KM, Hobizal KB, Rosario B. Radiographic analysis of diabetic midfoot Charcot neuroarthropathy with and without midfoot ulceration. Foot Ankle Int. 2014;35:1108.

29. Meyr AJ, Sebag JA. Relationship of cuboid height to plantar ulceration and other radiographic parameters in midfoot Charcot neuroarthropathy. J Foot Ankle Surg. 2017;56:748.
30. Sheth S, Derner BS, Meyr AJ. Reliability of the measurement of cuboid height in midfoot Charcot neuroarthropathy. J Foot Ankle Surg. 2018;57:759.
31. Lauri C, Glaudemans A, Signore A. Leukocyte imaging of the diabetic foot. Curr Pharm Des. 2018;24:1270.
32. Duceppe E, Parlow J, MacDonald P, Lyons K, McMullen M, Srinathan S, Graham M, Tandon V, Styles K, Bessissow A, Sessler DI, Bryson G, Devereaux PJ. Canadian cardiovascular society guidelines on perioperative cardiac risk assessment and management for patients who undergo noncardiac surgery. Can J Cardiol. 2017;33:17.
33. Baumhauer JF, O'Keefe RJ, Schon LC, Pinzur MS. Cytokine-induced osteoclastic bone resorption in Charcot arthropathy: an immunohistochemical study. Foot Ankle Int. 2006;27:797.
34. Herbst SA, Jones KB, Saltzman CL. Pattern of diabetic neuropathic arthropathy associated with the peripheral bone mineral density. J Bone Joint Surg (Br). 2004;86:378.
35. Petrova NL, Edmonds ME. A prospective study of calcaneal bone mineral density in acute Charcot osteoarthropathy. Diabetes Care. 2010;33:2254.
36. Greenhagen RM, Wukich DK, Jung RH, Vardaxis V, Yoho RM. Peripheral and central bone mineral density in Charcot's neuroarthropathy compared in diabetic and nondiabetic populations. J Am Podiatr Med Assoc. 2012;102:213.
37. Lecka-Czernik B. Diabetes, bone and glucose-lowering agents: basic biology. Diabetologia. 2017;60:1163.
38. Petrova NL, Dew TK, Musto RL, Sherwood RA, Bates M, Moniz CF, Edmonds ME. Inflammatory and bone turnover markers in a cross-sectional and prospective study of acute Charcot osteoarthropathy. Diabet Med. 2015;32:267.
39. Brodsky JW, Rouse AM. Exostectomy for symptomatic bony prominences in diabetic Charcot feet. Clin Orthop Relat Res. 1993;(296):21.
40. Catanzariti AR, Mendicino R, Haverstock B. Ostectomy for diabetic neuroarthropathy involving the midfoot. J Foot Ankle Surg. 2000;39:291.
41. Laurinaviciene R, Kirketerp-Moeller K, Holstein PE. Exostectomy for chronic midfoot plantar ulcer in Charcot deformity. J Wound Care. 2008;17:53.
42. Molines-Barroso RJ, Lazaro-Martinez JL, Beneit-Montesinos JV, Alvaro-Afonso FJ, Garcia-Morales E, Garcia-Alvarez Y. Early foot structural changes after lateral column exostectomy in patients with Charcot foot. Int J Low Extrem Wounds. 2019;18:129.
43. Rosenblum BI, Giurini JM, Miller LB, Chrzan JS, Habershaw GM. Neuropathic ulcerations plantar to the lateral column in patients with Charcot foot deformity: a flexible approach to limb salvage. J Foot Ankle Surg. 1997;36:360.
44. Sato T, Ichioka S. Ostectomy and medial plantar artery flap reconstruction for Charcot foot ulceration involving the midfoot. J Foot Ankle Surg. 2016;55:628.
45. Sohn MW, Stuck RM, Pinzur M, Lee TA, Budiman-Mak E. Lower-extremity amputation risk after Charcot arthropathy and diabetic foot ulcer. Diabetes Care. 2010;33:98.
46. Ha J, Hester T, Foley R, Reichert ILH, Vas PRJ, Ahluwalia R, Kavarthapu V. Charcot foot reconstruction outcomes: A systematic review. J Clin Orthop Trauma. 2020;11:357.
47. Sammarco VJ, Sammarco GJ, Walker EW Jr, Guiao RP. Midtarsal arthrodesis in the treatment of Charcot midfoot arthropathy. Surgical technique. J Bone Joint Surg Am. 2010;92(Suppl 1 Pt 1):1.
48. Wukich DK, Sadoskas D, Vaudreuil NJ, Fourman M. Comparison of diabetic Charcot patients with and without foot wounds. Foot Ankle Int. 2017;38:140.

Diagnostic Evaluation of Arterial Disease in Limb Salvage

20

Michael Siah and Cameron M. Akbari

Introduction

Many studies have established the association between diabetes mellitus and peripheral arterial disease (PAD). Although atherosclerosis is a generalized process that can occur in diabetics and non-diabetics alike, the prevalence of PAD is more common in diabetic patients. In patients with diabetes, for every 1% increase in hemoglobin A1c, there is a 26% associated increase in the risk of PAD [1]. In fact, PAD in conjunction with diabetic neuropathy contributes to 50% of diabetic foot ulcerations [2].

The predominant arterial beds impacted by PAD in the diabetic patient are typically infrageniculate, or below the knee. The pathophysiologic mechanism of disease of the anterior tibial, posterior tibial, peroneal, dorsalis pedis, and geniculate arteries is most frequently medial calcinosis [3]. Below the ankle, the infra-malleolar and pedal arch vessels may be impacted by non-enzymatic glycation due to elevated blood sugar [4]. Disease in any vascular bed may impact wound healing. For example, even an incomplete pedal arch is associated with recurrent ulceration within 1 year after primary ulcer healing [5]. These implications highlight the importance of vigilant perfusion screening in both symptomatic and asymptomatic diabetic patients to improve the healing of and prevent new and recurrent ulcerations.

History and Physical Examination

Perfusion assessment of the diabetic patient begins with a complete history and careful physical examination. It should include gross examination of the patient for the stigmata of peripheral vascular disease. Broadly classified, this bedside assessment includes the healing potential of the foot, the details of the foot problem (e.g., ulcer, gangrene, infection, osteomyelitis, etc.), the systemic consequences of diabetes, and any immediate threats to life and/or limb. By carefully following these considerations, the astute surgeon can usually make an accurate diagnosis and reliably start a comprehensive treatment plan without the need for further costly and time-consuming diagnostic tests.

M. Siah (✉)
Surgery, University of Texas Southwestern Medical Center, Dallas, TX, USA

Clements University Hospital, Dallas, TX, USA

Parkland Memorial Hospital, Dallas, TX, USA
e-mail: michael.siah@utsouthwestern.edu

C. M. Akbari
Surgery, Georgetown University Medical School, Washington, DC, USA

Vascular Surgery, Medstar Georgetown University Hospital, Washington, DC, USA
e-mail: cameron.akbari@medstar.net

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_20

The history of the foot problem itself can give valuable insight as to the potential for healing, the presence of coexisting infection or arterial occlusive disease, and the need for further treatment. Any patient presenting with a foot ulceration or gangrene should immediately arouse suspicion of underlying arterial insufficiency, even if neuropathy or infection is present. In the patient with diabetes and arterial insufficiency, the inciting event for a nonhealing foot ulcer may be a seemingly benign event such as cutting a toenail, soaking the foot in a warm bath, or a heating pad.

The duration of the ulcer also provides important clues, insofar as a long-standing, nonhealing ulcer is strongly suggestive of ischemia. Certainly, an ulcer or gangrenous area that has been present for several months is unlikely to heal without some type of further additional treatment, whether it be off-loading of weight-bearing areas, treatment of infection, or, most commonly, correction of arterial insufficiency. Did the present ulcer heal previously, and is the present episode a relapsing problem? A history of intermittent healing followed by relapse should raise suspicion of underlying untreated infection, such as recurrent osteomyelitis, or uncorrected architectural abnormality, such as a bony pressure point or varux deformity.

It is helpful to consider past opinions and treatments, while still formulating an objective treatment plan based on presenting data. Many diabetic patients with correctable foot ulceration and limb ischemia have been told that the only option is limb amputation, usually due to "inherited pessimism" and inadequate knowledge of the advances made in limb and foot salvage. In these circumstances, when sought for an additional treatment opinion, it is best to "start at the beginning" rather than blindly concur with previous actions.

The past history should be first directed to previous foot and limb problems. Recent ipsilateral ulceration or foot surgery that healed in a timely and uncomplicated course may suggest adequate arterial supply; with a more remote history, however, such information becomes less useful. A history of previous leg revascularization (including percutaneous therapies) also provides an important clue as to underlying arterial insufficiency. Other cardiovascular risk factors, such as cigarette smoking or hyperlipidemia, should also be considered, as their presence increases the likelihood that ischemia is contributing to the present foot problem.

Although claudication or rest pain has traditionally been associated with vascular disease, diabetic neuropathy may obscure those symptoms, and their absence in the diabetic patient certainly does not rule out ischemia. Because even moderate ischemia will preclude healing in the diabetic foot, the absence of rest pain is not a reliable indicator of adequate arterial blood supply; moreover, many patients may not ambulate a sufficient distance to develop true vasculogenic claudication. Conversely, some patients with true ischemic rest pain are dismissed for years as having "painful neuropathy."

Because unrecognized infection in the diabetic patient may rapidly progress to a life-threatening condition, attention should be directed toward detecting the subtle manifestations of an infected foot ulcer. Worsening hyperglycemia, recent erratic blood glucose control, and higher insulin requirements all suggest untreated infection. Due to the microvascular and neuropathic abnormalities in the diabetic foot, classical symptoms of infection such as chills or pain are often absent, and hyperglycemia is often the sole presenting symptom of undrained infection. With ongoing infection and hyperglycemia, impending ketoacidosis or nonketotic hyperglycemic hyperosmolar coma may develop, with symptoms of weakness, confusion, and altered mental status.

The history should also include a comprehensive assessment of the patient's overall health, to help stratify perioperative risk should some type of operative intervention be needed. Knowledge of previous cardiac events, such as myocardial infarction or revascularization, and present cardiac status, anginal severity, and heart failure symptoms are all mandatory components of the history taking. Similarly, in the patient with suspected infection and ischemia, a history of worsening renal function or impending need for hemodialysis will help determine the dose and choice of antibiotics and may alter plans for stan-

dard contrast arteriography. Functional status also becomes an important consideration at this point, and the history should carefully determine the ambulatory and rehabilitative potential of the patient, so that appropriate decisions may be made for limb salvage or amputation.

Examination of each limb should identify scars indicating healed arterial or venous ulcers, prior surgical interventions such as saphenous vein harvesting or distal bypass, and biomechanical callous formation. Trophic skin lesions such as pale, cool skin or shiny, thickened nail beds may be visible. Hair loss is an unreliable sign of ischemia and is of little clinical value [6]. Capillary refill in the soft tissue or under the nail bed should be assessed. Atrophy, pallor, and asymmetric peripheral temperatures should be noted. Ulcerations and areas of necrosis or gangrene should be described, measured, and photographed.

The pulse examination, including the status of the foot pulses, is the single, most important component of the physical exam and remains as a cornerstone in the treatment algorithm. As has been emphasized, *ischemia is always presumed to be present in the absence of a palpable pulse*. Identification of diminished or absent pedal pulses provides a general indication as to the presence and level of atherosclerotic disease burden. For example, a palpable popliteal pulse in the setting of absent pedal pulses suggests isolated tibial disease whereas an absent popliteal pulse may suggest a more proximal disease burden. Regardless of the level of disease, the UK NICE National Guidelines for the diabetic foot suggest that the absence of palpable pedal pulses is sufficient for the identification of vascular impairment [7]. Any atherosclerotic disease resulting in the loss of a pulse may cause inadequate perfusion for wound healing [3].

Although not difficult, an accurate pulse examination of the lower extremities is an acquired skill, and time should be devoted to practicing and perfecting the technique. The femoral pulse is palpated midway between the superior iliac spine and the pubic tubercle, just below the inguinal ligament. The popliteal pulse should be palpated with both hands and with the knee flexed no more than 15° (Fig. 20.1).

Great attention should be directed toward the foot pulses, which requires a knowledge of the usual location of the native arteries. The dorsalis pedis artery is located between the first and second metatarsal bones, just lateral to the extensor hallucis longus tendon, and its pulse is palpated by the pads of the fingers as the hand is partially wrapped around the foot (Fig. 20.2).

If the pulse cannot be palpated, the fingers may be moved a few millimeters in each direction, as the artery may have an occasional slight aberrant course. A common mistake is to place a



Fig. 20.1 Proper technique for the palpation of a popliteal pulse



Fig. 20.2 Palpation of the right dorsalis pedis artery

single finger at one location on the dorsum of the foot. The posterior tibial artery is typically located in the hollow just behind the medial malleolus, approximately halfway between the malleolus and the Achilles tendon. The examiner's hand should be contralateral to the examined foot (i.e., the right hand should be used to palpate the left foot and vice versa), so as to allow the hand curvature to follow the ankle (Fig. 20.3).

There are many published scales that may aid in the standardization of physical exam reporting. Consistent use allows for the clinician to track patient improvement or decline. The Fontaine and Rutherford classifications, as well as the University of Texas system, have historically been used to guide wound assessments; however each do not incorporate all the etiologies of threatened limbs. The presence of infection and involvement of deeper structures increases the metabolic requirement of ulcer healing [8]. To account for this, the Society for Vascular Surgery devised the WIfi System to better predict amputation risk and better evaluate outcomes in the treatment of peripheral vascular disease. By integrating the key factors associated with tissue loss, the WIfi classification system is able to combine perfusion and tissue assessment to better predict clinical outcomes than previous scoring systems. Ultimately, the use of any of these scoring systems allows for objective assessment of patients that can guide care and monitor outcomes.



Fig. 20.3 Palpation of the right posterior tibial artery

Noninvasive Perfusion Assessment

Noninvasive testing is beneficial in both the diagnosis of existing peripheral vascular disease and in screening patients for advancing atherosclerotic disease. The simplest of noninvasive exam that can be performed is the ankle-brachial index (ABI) (Fig. 20.4). It is a critical extension of the vascular physical exam and can be performed by the clinician at the bedside. The ABI is a ratio of the ankle and brachial systolic blood pressures. A normal ABI can range from 0.9 to 1.2 [10]. Generally, an ABI of >0.8 is not associated with impaired wound healing [11]. Given the ease with which an ABI can be performed, the American Diabetes Association recommends PAD screening with an ABI every 5 years in patients with diabetes [12].

Unfortunately, ABI values can often be unreliable in the diabetic patient due to the extensive

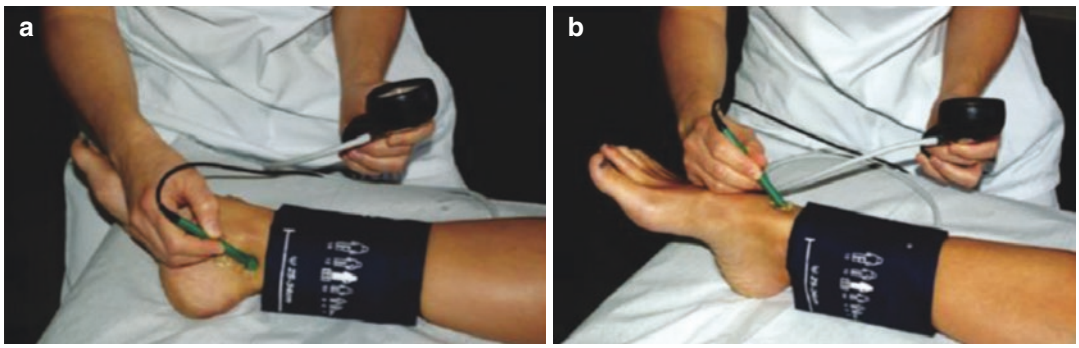


Fig. 20.4 Bedside technique for performed ankle pressure measurement using a Doppler probe at the (**a**) posterior tibial artery and (**b**) dorsalis pedis artery [9]

calcification, or medial calcinosis, of the infrapopliteal blood vessels. This extensive calcification prevents proper compression of the tibial arteries and results in either a falsely elevated ABI or a value that is unattainable due to the inability to achieve a vessel compression at a supra-systolic cuff pressure. Therefore, any abnormal, be it diminished or falsely elevated (non-compressible), ABI indicates the presence of arterial disease that should be further evaluated.

When ABIs are impaired or unattainable, a vascular lab can provide other useful diagnostic tests to assess perfusion in the diabetic patient. Pulse volume recording (PVR), also known as plethysmography, is a noninvasive method to evaluate the arteries of the lower extremity. The pulsed volume recorder (PVR) is a form of volume plethysmography, which measures the pulsatile volume changes that occur in the limb with each heartbeat. A pneumatic cuff is placed around a specific level of the limb (thigh, calf, and ankle) and inflated with air to a preset pressure between 10 and 65 mmHg. During systole, blood enters the limb, the limb expands, this expansion presses upon the cuff, and the pressure within the cuff increases. During diastole, limb volume is reduced and cuff pressure falls. Therefore, volume changes within a specific level of the limb beneath the cuff are indirectly studied by measuring pulsatile pressure changes within the cuff. These changes are converted into a waveform by a strip recorder.

The normal PVR waveform displays a brisk rise during systole, a sharp systolic peak, a dicrotic notch, and a rapid downslope to baseline.

Segmental pressures and waveforms are analyzed to identify the level and degree of potential stenosis. Pressure cuffs are used to measure the pulsatile change in blood pressure at various levels of a limb (Fig. 20.5). Abnormal PVR findings include decreased amplitude, a flattened peak, and an absent dicrotic notch. Amplitudes of less than 5 mm from trough to peak have been used as a criterion for the diagnosis of peripheral vascular disease [13].

Because the PVR measures volume change and not pressure, it is also unaffected by noncompressible arteries and may be a valuable adjunct in the evaluation of the diabetic foot. However, as with all noninvasive tests, the PVR has several limitations. Although there are some semiquantitative criteria, these have not been correlated clinically, and the test is essentially qualitative. Therefore, a completely normal study is helpful, but it is difficult to quantitate the degree of ischemia with any abnormal study. Indeed, one major shortcoming of the PVR test is that it frequently underestimates the severity of proximal arterial disease (due to the presence of collateral vessels). Additionally, the test is affected by several variables, including room temperature (since temperature differences in the air cuff can change the pressure measured by the air-filled plethysmograph). Peripheral edema and obesity will also affect the quality of the waveforms.

Toe systolic pressure measurements (TSP) and transcutaneous partial oxygen pressure measurements ($TcPO_2$) are useful modalities to attain a better understanding of tissue perfusion. Transcutaneous oxygen tension measurements reflect the resting oxygen tension (and the metabolic state) of the underlying tissue. The test involves the placement of a probe (with a sensitized electrode) on the dorsum of the proximal foot, and the local tissue is heated to about 40–42 °C. Following an equilibration period of 20–25 min, the local resting oxygen tension of the skin is recorded in mm Hg. The measurement of toe pressures allows for an accurate assessment of pedal perfusion as digital vessels are often free of atherosclerotic disease burden. Toe pressures are usually 30 mmHg less than ankle pressures and an abnormal toe-brachial index (TBI) is <0.70 [14]. However, digital ulceration or prior amputation may limit the usefulness of the TBI examination.

Transcutaneous measurement ($TcPO_2$) of the partial oxygen pressure is performed at the back of the foot and between the first and second toe space. Normal $TcPO_2$ for a diabetic patient is 50 mmHg [15]. Because hemodynamics are not measured, the test is immune to many of the problems facing other noninvasive tests in the presence of diabetes, such as noncompressible vessels. However, due to the unique considerations of the diabetic foot, $TcPO_2$ measurements are not entirely reliable in the diabetic patient with foot ulceration. Lockhart

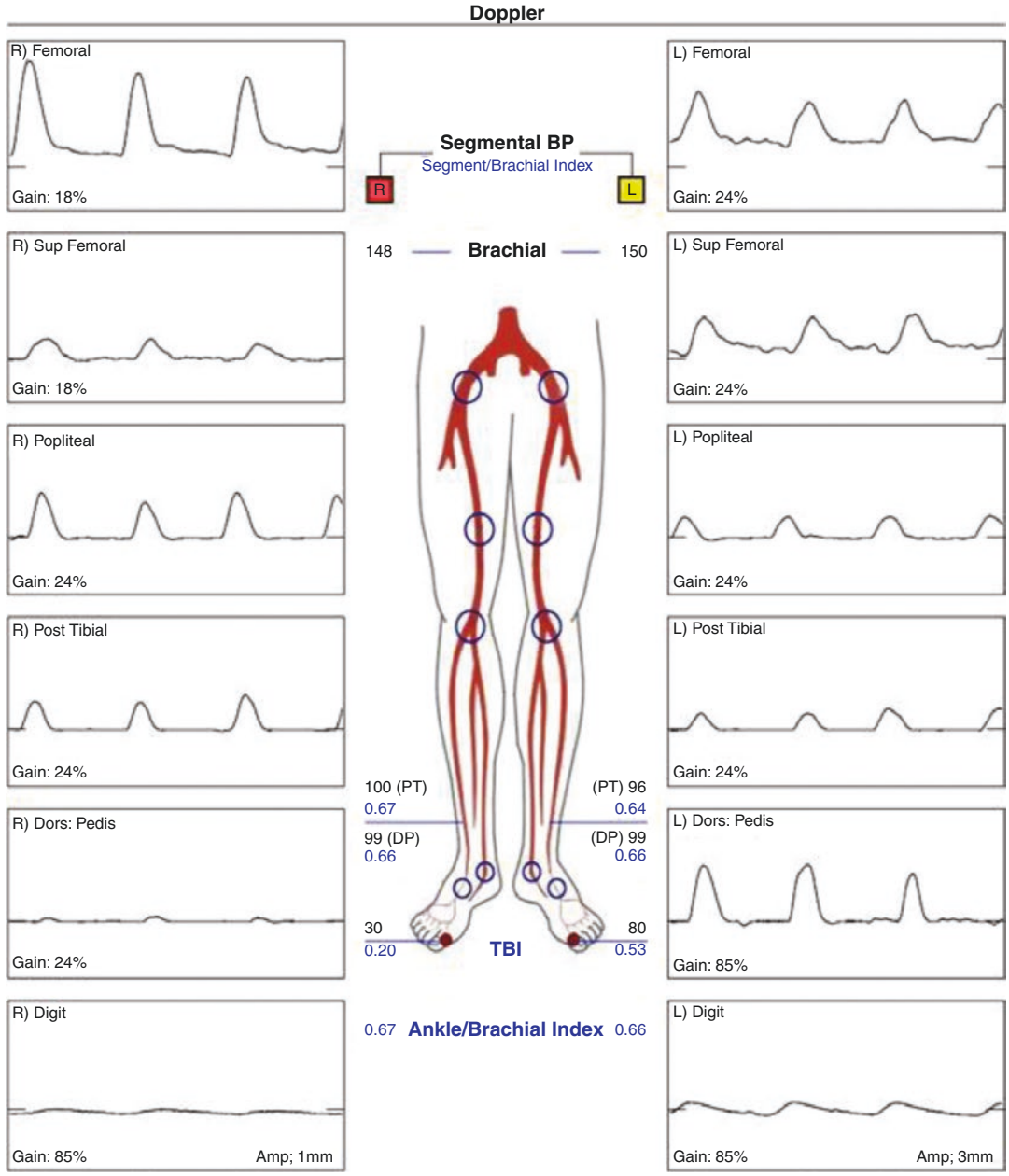


Fig. 20.5 Physiologic study demonstrating segmental pulse volume recording associated with an aortic occlusion

et al. demonstrated pressures <30 mmHg to be associated with severe ischemia, while pressures >40 mmHg are associated with wound healing with conservative therapy [16, 17]. Additionally, Kalani et al. demonstrated that $TcPO_2$ can be a better predictor for ulcer healing than toe pressures in diabetics with foot ulcerations and confirmed a low likelihood of wound healing with pressures <25 mmHg [18]. Therefore, the likelihood of wound healing increases with skin perfusion pressures of >40 mmHg, toe pressures >30 mmHg, or $TcPO_2$ >25 mmHg [19]. Values below these levels suggest a role for invasive diagnostic and therapeutic measures. It should be noted, though, that despite the documented utility of skin perfusion pressure measurements

and $TcPO_2$, they are not typically performed. Even in the patient with a "normal" $TcPO_2$ value, the measurement may not accurately reflect the healing potential at the target area. $TcPO_2$ measurements may be influenced by many technical features, including the type of equipment used, monitor placement, and surface temperature of the measured area.

Hyperspectral Imaging (HSI) has emerged as an additional noninvasive way to assess tissue perfusion and may have a role in predicting wound healing in diabetic patients with tissue loss. HSI identifies tissue oxygenation on a microvascular level and anatomically demonstrates changes in the microcirculation (Fig. 20.6). Unlike $TpCO_2$, HSI measurements

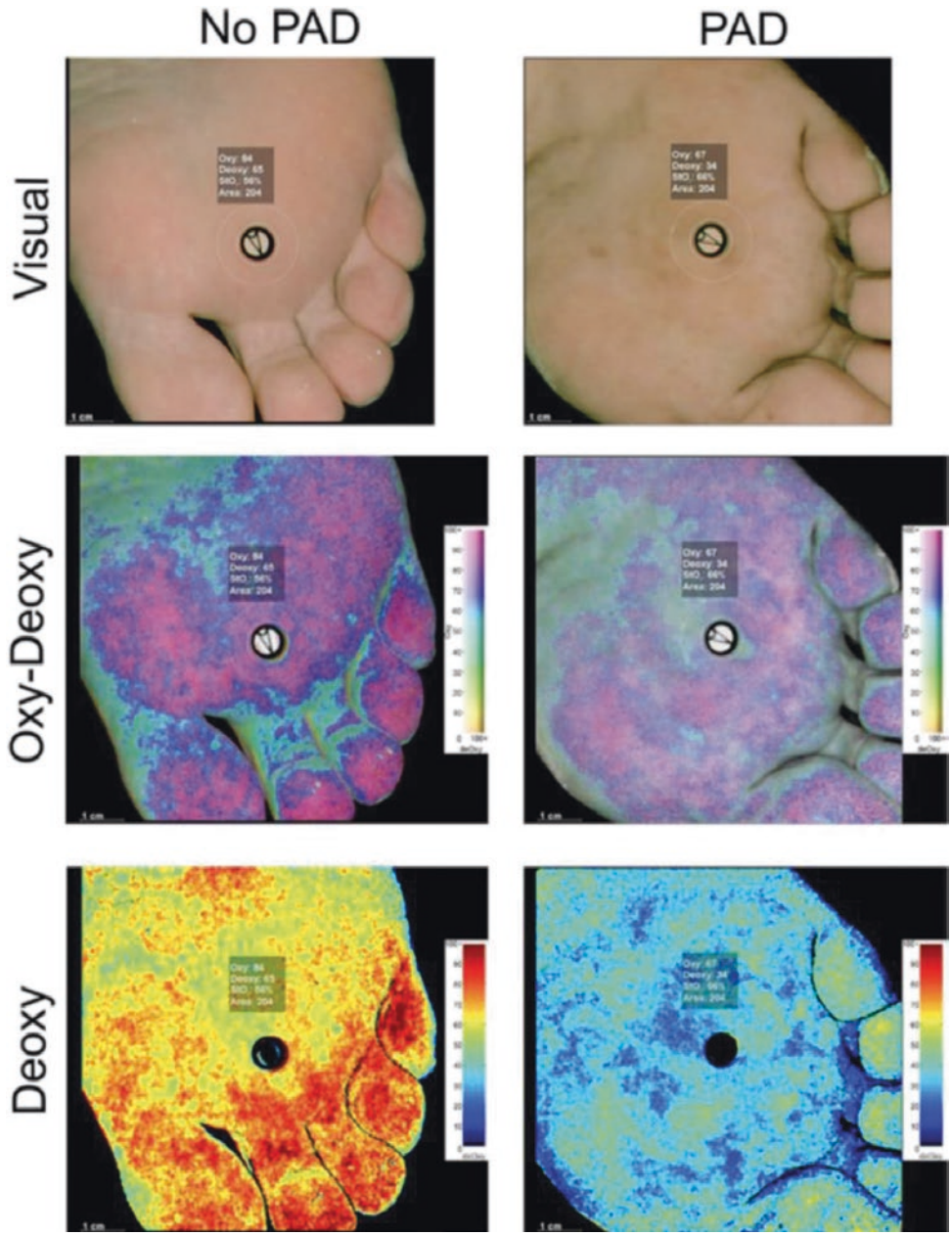


Fig. 20.6 Visual hyperspectral images of pedal perfusion in a foot with no peripheral vascular disease (left) and a foot with peripheral vascular disease (right) [20]

can be performed quickly in the clinic. Additionally, HSI can directly evaluate perfusion in the ulcer bed. One of the major barriers to widespread application of the technology is cost, as the devices are generally very expensive. Additionally, at present time, there is a lack of evidence demonstrating the reliability of HIS measurements in diabetics with tissue loss.

Noninvasive Diagnostic Imaging

Of the many modalities available to assess the arterial supply of the lower extremity, the most commonly utilized are duplex ultrasound, computed tomography angiography (CTA), and magnetic resonance angiography (MRA). In general, these imaging tests should be reserved for patients prior to or after endovascular or surgical therapy. Ultrasound may be considered as the first-line study given its low cost and the lack of potentially adverse side effects.

Duplex scanning employs the dual modalities of B-mode (gray scale) imaging and pulsed wave Doppler spectral frequency analysis. In addition, most Duplex scanners are actually "triplex," with the third modality being color flow imaging. The vessel being insonated may be localized by B-mode imaging, and the pulsed wave Doppler allows for range specificity. Color flow imaging evaluates the Doppler information and determines whether flow is toward or away from the transducer as well as frequency content.

The information obtained from Duplex arterial scanning includes the gray scale ultrasound structural characteristics of the artery (such as wall thickness or type of plaque), as well as Doppler waveform, velocities, and direction of flow. Analysis of the Doppler waveform characteristics is similar to the preceding discussion on segmental waveform analysis (considered as triphasic, biphasic, or monophasic), but the principal advantage of Duplex is that the vessel may be localized by the gray scale ultrasound. Duplex also allows for an estimation of the degree of stenosis based on velocities and degree of spectral broadening: as an artery narrows, there will be a velocity increase in the stenosis with spectral broadening.

Despite the invaluable role of Duplex ultrasound in the diagnosis of carotid arterial disease and for postoperative graft surveillance, there are multiple limitations in its use for the diagnosis of lower extremity arterial disease. There is a large variation in the range of "normal" velocities for the leg arteries, and therefore a significant stenosis may be misinterpreted. Although the femoral and popliteal vessels may be visualized relatively easily, the tibial vessels are more cumbersome to scan, and the velocities in the tibial arteries may be even more difficult to interpret. When one considers the usual pattern of vascular disease in diabetes (with a predilection toward atherosclerotic involvement of the tibial vessels), the limitations of Duplex in the diagnosis of arterial insufficiency in the diabetic patient are realized. Because the study depends on accurate sonographic localization of the vessel, Duplex is quite "operator dependent." Finally, multiple other variables can influence the quality of the image, including medial arterial calcification (which can cause artifactual shadowing), obesity, and peripheral edema (which can preclude imaging of the tibial vessels).

In patients in whom ultrasound is unlikely to be successful, particularly patients that have morbid obesity or extensive dressings or tissue loss, CTA and MRA are reasonable second-line imaging modalities. Both CTA and MRA allow for visualization of supra-inguinal blood vessels, for the localization of infra-inguinal disease burden and the characterization of stenotic or occlusive lesions. Most importantly, they can show the quality of tibial runoff, which is vital for deciding between different interventional strategies. A CTA can be performed rapidly and allows for easy evaluation of previously placed stents and bypasses. However, in the setting of severe calcification, CTA may overestimate the degree of stenosis and lack accuracy of flow assessment of the tibial arteries. Additionally, CTA requires radiation exposure and the use of iodinated contrast agents for vasculature visualization. Such agents are contraindicated in patients with underlying renal dysfunction due to the risk of contrast-

induced nephropathy. However, they can be used in patients with end-stage renal disease (ESRD).

MRA is useful in patients with mild renal dysfunction, as unlike CTA, MRA does not require iodinated contrast. MRA uses a gadolinium-based contrast agent to provide better visualization of the arterial system in the lower extremity. Gadolinium contrast, however, has been associated with the development of nephrogenic systemic fibrosis in patients with impaired creatinine clearance and is contraindicated in patients with ESRD. MRA utilization may be limited in patients with claustrophobia or metallic implants and long acquisition times are associated with more patient-generated motion artifact. Ultimately, the selection between the use of duplex, CTA, or MRA depends upon patient-specific factors, local expertise, and safety profile and is up to the discretion of the clinician.

Invasive Diagnostic Imaging

Invasive diagnostic imaging in diabetics with signs of tissue loss and ischemia should be limited to those patients who would not benefit from primary amputation. Arteriography is the best means of identifying the distribution and extent of PAD. Angiography allows for real-time flow assessment using either carbon dioxide, iodinated contrast, or gadolinium contrast to visualize arterial flow under fluoroscopy. Arterial stenosis, occlusive lesions, and named-vessel collateral reconstitution may all be assessed (Fig. 20.7). Diagnostic imaging may then translate into endovascular intervention or become the basis for open surgical intervention.

Angiography also allows for angiosome characterization. Introduced nearly 30 years ago, an angiosome refers to a 3-dimensional unit of tissue comprised of skin, subcutaneous tissue, muscle, and bone, supplied by a clear arterial source. In the lower leg and foot, there are six angiosomes: three fed by the posterior tibial artery, one fed by the anterior tibial artery, and two supplied by the peroneal artery. Attinger et al. have demonstrated the validity of the angiosome concept in free flap procedures; however the data regarding the angiosome in diabetic patients with PAD is less conclusive.



Fig. 20.7 Diagnostic arteriogram revealing an occlusion of the anterior tibial artery and a patent peroneal and posterior tibial artery

The clinical application of the angiosome concept requires an understanding of perfusion sources of the foot and to consider these as therapeutic targets for intervention. Interventionalists can perform angiosome-directed revascularization procedures, which focus on intervening on the source vessel/angiosome of ulceration, as opposed to indirect revascularization procedures. Some studies have demonstrated more rapid times to healing with angiosome-directed revascularization procedures; however there is no difference in amputation rates. Ultimately, considering the option of angiosome-directed

revascularization should be performed, however revascularization should still be pursued indirectly if no direct revascularization targets are available.

Given the challenge of correlating angiosome and non-angiosome-based perfusion assessment with clinical outcomes, the use of indocyanine green angiography (ICGA) has also emerged as a perfusion assessment tool. ICGA has been studied extensively in free flap creation and has been shown to provide perfusion information that predicts tissue survival in assessing flap viability [21–23]. ICG is administered intravascularly where it binds to serum proteins. The uptake of ICG can be quantified in tissue bed of interest and this value may serve as a surrogate for tissue perfusion. Ongoing studies are being performed to determine the role of IGCA in determining the optimal treatment of peripheral vascular disease, as well as assessing the success of revascularization procedures [24, 25].

Therapeutic Options

There are two modalities to address perfusion deficits in diabetic patients with tissue loss: open and endovascular surgery. Open techniques, namely surgical bypass, historically have been the mainstay of treatment. Bypass with autogenous conduit, most commonly the greater saphenous vein, represents the gold standard for revascularization techniques, as it is associated with better patency and increased amputation free survival compared to bypass using prosthetic conduits [26]. However, endovascular therapies have emerged as an acceptable first line in the surgical management of ischemic diabetic foot ulcerations. This is likely due to the ease with which diagnostic and therapeutic procedures can now be performed, as well as the wide variety of interventionalists who are capable of performing them.

Coming to a decision between bypass first versus an endovascular first strategy is challenging due to the absence of randomized controlled data demonstrating the superiority of either modality in patients with diabetes. The BASIL trial, a randomized controlled trial, compared the results of angioplasty versus bypass and examined amputation rates and survival for the two methods. There was no significant difference between the two techniques, but there was a marked advantage of endovascular techniques in patients with elevated surgical risk, and better results than prosthetic bypasses. Additionally, the trial suggested that bypass outcomes following failed endovascular interventions were worse than those performed prior to endovascular therapy. Since BASIL, there has been little randomized controlled data to guide clinical decision making in the management of critical limb ischemia, but there has been a marked proliferation in the endovascular tools available to the interventionalists. Newer wires, catheters, sheaths, and other devices like drug eluting stents (DESs), drug-coated balloons (DCBs), and atherectomy devices have become readily available and have made treating TASC C and D lesions much easier than before [27–29]. These newer techniques are frequently used to treat PAD despite an absence of level one data. To address the lack of treatment consensus in PAD management, the BEST-CLI (Best Endovascular versus Best Surgical Therapy for Patients With Critical Limb Ischemia) trial is currently being conducted. This trial will compare outcomes of the best endovascular and open surgical revascularization strategies in patients with tissue loss and infrainguinal PAD.

Conclusion

Peripheral arterial disease in the diabetic patient is a growing problem and will continue to represent a tremendous economic and social burden facing modern societies in the twenty-first century. Early recognition of perfusion deficits is critical in curtailing the extent of this problem, and there are a variety of noninvasive tests that allow for the objective identification of PAD. Once diagnosed, referral to a vascular specialist allows for the restoration of arterial perfusion either by open or endovascular techniques.

References

1. Selvin, E, et al. Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. Current neurology and neuroscience reports, U.S. National Library of Medicine, Bethesda, MD 2004. www.ncbi.nlm.nih.gov/pubmed/15381515.
2. Prompers L, Schaper N, Apelqvist J, et al. Prediction of outcome in individuals with diabetic foot ulcers: focus on the differences between individuals with and without peripheral arterial disease. The EURODIALE Study. Diabetologia. 2008;51:747–55.
3. Ho CY, Shanahan CM. Medial arterial calcification. Arterioscler Thromb Vasc Biol. 2016;36:1475. https://doi.org/10.1161/ATVBAHA.116.306717.
4. Schalkwijk CG, Miyata T. Early- and advanced non-enzymatic glycation in diabetic vascular complications: the search for therapeutics. Amino Acids. 2010;42(4):1193–204.
5. Pound N, Chipchase S, Treece K, Game F, Jeffcoate W. Ulcer-free survival following management of foot ulcers in diabetes. Diabet Med. 2005;22:1306–9.
6. Golomb BA, Dang TT, Criqui MH. Peripheral arterial disease: morbidity and mortality implications. Circulation. 2006;114:688–99.
7. Bailey MA, Griffin KJ, Scott DJ. Clinical assessment of patients with peripheral arterial disease. Semin Interv Radiol. 2014;31(4):292–9.
8. NICE. Diabetic foot problems: prevention and management. Guidance and guidelines. London: NICE; n.d.. www.nice.org.uk/guidance/ng19.
9. Aboyans V, et al. Measurement and interpretation of the ankle-brachial index. Circulation. 2012;126(24):2890–909. https://doi.org/10.1161/cir.0b013e318276fbcb.
10. Weitz JI, et al. Diagnosis and treatment of chronic arterial insufficiency of the lower extremities: a critical review. Circulation. 1996;94:3026. https://doi.org/10.1161/01.CIR.94.11.3026.
11. Mills JL. Lower limb ischaemia in patients with diabetic foot ulcers and gangrene: recognition, anatomic patterns and revascularization strategies. Diabetes Metab Res Rev. 2016;32:239–45.
12. American Diabetes Association. Peripheral arterial disease in people with diabetes. Diabetes Care. 2003;26:3333.
13. Sacks D. The TransAtlantic Inter-Society Consensus (TASC) on the management of peripheral arterial disease. J Vasc Interv Radiol. 2003;14(9):351. https://doi.org/10.1097/01.rvi.0000094603.61428.1c.
14. Gerhard-Herman M, et al. Vascular laboratory testing. In: Creager MA, et al., editors. Vascular medicine: a companion to Braunwald's heart disease. Philadelphia, PA: Elsevier/Saunders; 2013. p. 148–65.
15. Vayssairat M. VII. Microcirculatory explorations. J Mal Vasc. 2002;27:2803.
16. Sibley RC, et al. Noninvasive physiologic vascular studies: a guide to diagnosing peripheral arterial disease. Radiographics. 2017;37(1):346–57. https://doi.org/10.1148/rg.2017160044.
17. Hafner J. Management of arterial leg ulcers and of combined (mixed) venous-arterial leg ulcers. In: Hafner J, et al., editors. Management of leg ulcers current problems in dermatology. Basel: Karger; 1999. p. 211–9. https://doi.org/10.1159/00006062.
18. Suzuki K, et al. Skin perfusion pressure and wound closure time in lower extremity wounds. J Am Coll Clin Wound Spec. 2017;9(1–3):14–8. https://doi.org/10.1016/j.jccw.2018.10.001.
19. Kalani M, et al. Transcutaneous oxygen tension and toe blood pressure as predictors for outcome of diabetic foot ulcers. Diabetes Care. 1999;22(1):147–51. https://doi.org/10.2337/diacare.22.1.147.
20. Goodney PP, Beck A, Welch HG, et al. National trends in lower extremity bypass surgery, endovascular interventions and major amputations. J Vasc Surg. 2009;50(1):54–60.
21. Chin JA, et al. Evaluation of hyperspectral technology for assessing the presence and severity of peripheral artery disease. J Vasc Surg. 2011;54(6):1679–88. https://doi.org/10.1016/j.jvs.2011.06.022.
22. Newman MI, Samson MC, Tamburrino JF, Swarrtz KA. Intra- operative laser-assisted indocyanine green angiography for the evaluation of mastectomy flaps in immediate breast reconstruction. J Reconstr Microsurg. 2010;26:487e92.
23. Pestana I, Coan B, Erdmann D, Marcus J, Levin L, Zenn MR. Early experience with fluorescent angiography in free-tissue transfer reconstruction. Plast Reconstr Surg. 2009;123:1239e44.
24. Tsubakimoto Y. TCTAP C-201 successful limb salvage in a CLI patient with scleroderma by complete revascularization of BTA lesions. J Am Coll Cardiol. 2015;65(17):420. https://doi.org/10.1016/j.jacc.2015.03.485.
25. Igari K, et al. Indocyanine green angiography for the diagnosis of peripheral arterial disease with isolated infrapopliteal lesions. Ann Vasc Surg. 2014;28(6):1479–84. https://doi.org/10.1016/j.avsg.2014.03.024.
26. Igari K, et al. Quantitative evaluation of the outcomes of revascularization procedures for peripheral arterial disease using indocyanine green angiography. Eur J Vasc Endovasc Surg. 2013;46(4):460–5. https://doi.org/10.1016/j.ejvs.2013.07.016.
27. Brownrigg JRW, et al. Performance of prognostic markers in the prediction of wound healing or amputation among patients with foot ulcers in diabetes: a systematic review. Diabetes Metab Res Rev. 2016;32:128–35. https://doi.org/10.1002/dmrr.2704.
28. Adam DJ, et al. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. Lancet. 2005;366(9501):1925–34. https://doi.org/10.1016/s0140-6736(05)67704-5.
29. Attinger CE, et al. Angiosomes of the foot and ankle and clinical implications for limb salvage: reconstruction, incisions, and revascularization. Plast Reconstr Surg. 2006;117(Suppl):261S. https://doi.org/10.1097/01.prs.0000222582.84385.54.

21 Arterial Disease Management in the Limb Salvage Patient: Endovascular and Open Bypass

Michael C. Siah, Roberto Ferraresi, Alessandro Ucci, Andrea Casini, Giacomo Clerici, and Cameron Akbari

Introduction

Chronic limb-threatening ischemia (CLTI) represents the most severe manifestation of peripheral arterial disease (PAD) and is defined by the presence of ischemic rest pain, ulceration, or gangrene. It affects over two million Americans and is a global problem of increasing prevalence. The natural history of CLTI is associated with significant morbidity, mortality, and rising health care costs approaching $200 billion annually (1–3). Without revascularization, 20–40% of patients will require amputation and 6-month mortality is greater than 20% (4, 5). As a result, the financial burden posed by patients with CLTI is massive, representing a $3 billion cost to the American health care system annually.

The mainstay of therapy for the management of CLTI is revascularization in an attempt to improve perfusion to an affected limb. Medical therapy is supportive, utilizing lifestyle modification strategies such as smoking cessation, lipid lowering and cardioprotective medications, which are known to decrease adverse cardiac events and mortality in patients with CLTI.

In addition to medical therapy, both open surgery and endovascular therapies are frequently utilized in restoring perfusion in patients with CLTI. Over the course of the last 25 years, invasive therapies for the treatment of PAD have changed dramatically. The frequency of bypass surgery has decreased by 42%, and endovascular therapeutic utilization has increased more than 3 times (6). As a result of the increase in overall procedures performed for PAD, amputation rates have decreased by 29% (6). Ultimately, the choice of procedure should be individualized based on the patient's anatomy, comorbidities, and preoperative assessment, with the goal being to provide the most durable procedure with the least risk.

Open Surgery General Considerations

The approach to the patient with CLTI and the decision as to the type of surgical revascularization depend on the patient presentation and the CLTI classification. The goal of treatment of ischemia in the CLTI patient is to restore maximal perfusion to the foot and ideally restore a palpable foot pulse (7). For example, the patient

M. C. Siah (✉)
Vascular Surgery, UT Southwestern, Dallas, TX, USA
e-mail: michael.siah@utsouthwestern.edu

R. Ferraresi · A. Ucci · A. Casini · G. Clerici
Diabetic Foot Unit, Clinica San Carlo, Paderno Dugnano, Milano, Italy

C. Akbari
Georgetown University Hospital, Washington, DC, USA
e-mail: Cameron.Akbari@medstar.net

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_21

with extensive foot ulceration and/or gangrene will require normal perfusion to the foot for limb salvage, with the goal being to restore a normal foot pulse; in order to maximize the chances of successful limb salvage, targeted revascularization to the specific angiosome should always be the first choice. As the majority of these patients will have diabetes, and because of the pattern of diabetic vascular disease, this will almost always require infrainguinal surgical bypass to the target vessel. Proximal bypass to the popliteal or tibioperoneal arteries may restore foot pulses; however, the characteristic pattern of occlusive disease in the diabetic patient usually requires more distal bypass grafting, often to the dorsalis pedis artery, distal posterior tibial, or plantar arteries.

In contrast, the patient presenting with ischemic rest pain without tissue loss may be significantly ameliorated with more proximal revascularization. This may include femoral endarterectomy with profundaplasty alone in the patient with concomitant superficial femoral artery occlusion, or bypass to an isolated popliteal segment.

In most patients, restoration of the foot pulse usually mandates infrainguinal arterial bypass grafting. The primary goal of infrainguinal arterial reconstruction in the ischemic foot is to bypass to an outflow artery that is in direct continuity with the foot, thereby restoring normal arterial pressure to the target area. Although proximal bypass to the popliteal or proximal tibioperoneal arteries may restore foot pulses, more distal revascularization is often needed to achieve this goal, again owing to the pattern of occlusive disease in the diabetic patient. Similarly, although excellent results have been reported with peroneal artery bypass, the peroneal artery is not in continuity with the foot vessels and may not achieve the maximal flow required for healing, particularly at the forefoot level. Therefore, the authors believe that peroneal artery bypass should be reserved for those rare circumstances in which there is no dorsalis pedis or posterior tibial artery in continuity with the foot, or when limited venous conduit length mitigates against more distal bypass.

Autogenous vein grafting to the dorsalis pedis, distal posterior tibial, and plantar arteries incorporates knowledge of the anatomic pattern of diabetic vascular disease, satisfies the fundamental goal of restoration of the foot pulse, and provides durable and effective limb salvage (7, 8). Indeed, extensive experience with arterial reconstruction to the pedal vessels has established the efficacy, durability, and safety of these procedures, and improved limb salvage rates in the diabetic patient may be directly attributed to the increasing use of pedal bypass (8). Ultimately, the choice of outflow artery should be based on availability of conduit, the location of the foot ulcer, and the quality of the outflow vessel. For example, in the patient with an ischemic heel ulcer, first consideration should be given to the posterior tibial or plantar arteries if they are patent by preoperative imaging. However, absence of a posterior tibial artery should not rule against a dorsalis pedis bypass, as comparable rates of healing and limb salvage for heel ulcers have been reported with the dorsalis pedis artery bypass.

Clinical experience has shown a variety of adjunctive techniques to be of advantage in infrainguinal revascularization among diabetic patients. For example, due to the pattern of lower extremity diabetic atherosclerotic disease, the popliteal or distal superficial femoral artery may be used as an inflow site, thereby allowing for a shorter length of vein to be used and avoiding dissection in the groin and upper thigh, a common location for wound complications. In addition, the shorter length of saphenous vein obviates the need for foot extension of the vein harvest incision, which is parallel to the one required to expose the paramalleolar and inframalleolar arteries; this avoids the resultant skin bridge which may occasionally become ischemic from undue tension.

Although the vein graft may be prepared as in situ, reversed, or nonreversed graft, without any significant difference in outcome, the authors believe that size mismatch may best be minimized with either an in situ or nonreversed technique, particularly for grafts originating from the common femoral artery. Although the valves in the vein graft may be lysed blindly, some sur-

geons prefer to cut the valves under direct angioscopic guidance using a flexible valvulotome. This also allows for assessment of the saphenous vein to detect intraluminal abnormalities, and can help direct endoluminal interventions that upgrade the quality of the conduit and improve patency.

Absence of ipsilateral greater saphenous vein is not a contraindication for bypass; although prosthetic material may occasionally be used for more proximal reconstructions, it should seldom, if ever, be used for extreme distal bypass grafting. When ipsilateral saphenous vein is not available, several alternatives exist for autogenous conduit.

Although the contralateral saphenous vein is an obvious alternative, several considerations limit its use in the diabetic patient. Contralateral leg vein may not always be present in this population of patients who often require multiple cardiovascular interventions. More importantly, diabetes is a strong risk factor for subsequent contralateral limb bypass, with almost 60% of patients requiring contralateral bypass at 3 years. Therefore, the authors' approach has been to use arm vein grafts as the first alternative in the absence of ipsilateral saphenous vein (9). The cephalic, basilic, or upper arm basilic-cephalic loop vein grafts may be harvested. Once the vein has been harvested, angioscopic evaluation is crucial, as many of these patients have undergone multiple venipunctures and cannulations with resultant scarring and web-like synechiae. Angioscopy allows for detection and correction of many of these areas, and allows for precise valve lysis within these thin-walled veins (9).

Active infection in the foot is not a contraindication to paramalleolar bypass grafting, as long as the infectious process is controlled (10). Adequate control implies resolution of cellulitis, lymphangitis, and edema, especially in areas of proposed incisions required to expose the distal artery or saphenous vein. Occasionally, severe circumferential calcification of the distal artery may also be encountered. Strategies include the use of special intraluminal bulb-tipped vessel occluders or tourniquet occlusion, with no attempts made at endarterectomy or "cracking" the plaque. Results of bypasses to calcified vessels are comparable to noncalcified vessels (9–11).

Several reports have summarized the results of the dorsalis pedis artery bypass, of which the most recent summarizes a decade-long experience of more than 1000 cases (11, 12). In that series, 5-year primary patency rates were 57% with a limb salvage rate of almost 80%, confirming the efficacy and durability of these procedures. Additionally, concern regarding perioperative morbidity and long-term outcome in diabetic patients has also been dispelled (12, 13).

Preoperative Surgical Considerations

Essential to the success of surgical revascularization is appropriate and accurate preoperative planning. High-quality arteriography should include visualization of planned target vessels, localization and extent of disease in the proximal vessels (including aorta and iliac arteries), and, if needed, pressure measurements across suspected inflow lesions. Based on the pattern of vascular disease in the diabetic patient, with sparing of the pedal vessels, the arteriogram must include the foot vessels in both the lateral and anterior views for a complete assessment (Fig. 21.1).

Although others have performed distal revascularization based on Duplex ultrasound or CT angiography alone, the author's preference is to always have a high-quality arteriography prior to any infrainguinal bypass.

Autogenous ipsilateral saphenous vein is the preferred conduit for all infrainguinal bypass grafts. High-quality conduit is central to successful bypass and has direct implications for both short-term and long-term patency results. Preoperative bilateral saphenous vein mapping with Duplex ultrasound should always be performed, assessing for caliber and size, phlebitic changes, wall thickening, and accessory branching (Fig. 21.2a, b).

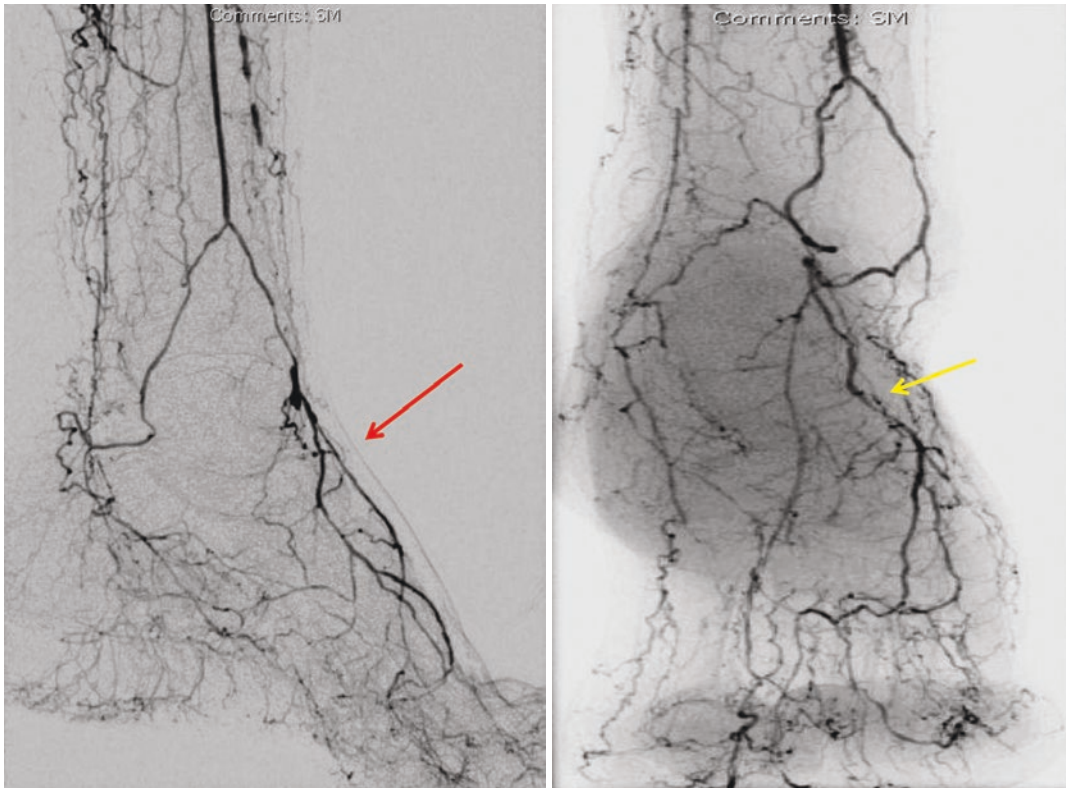


Fig. 21.1 Lateral and AP arteriogram of the foot. Note that on the lateral projection, a vessel which resembles the dorsalis pedis artery is seen (red arrow). However, the AP projection confirms only lateral tarsal runoff (yellow arrow), and no true dorsalis pedis artery is present

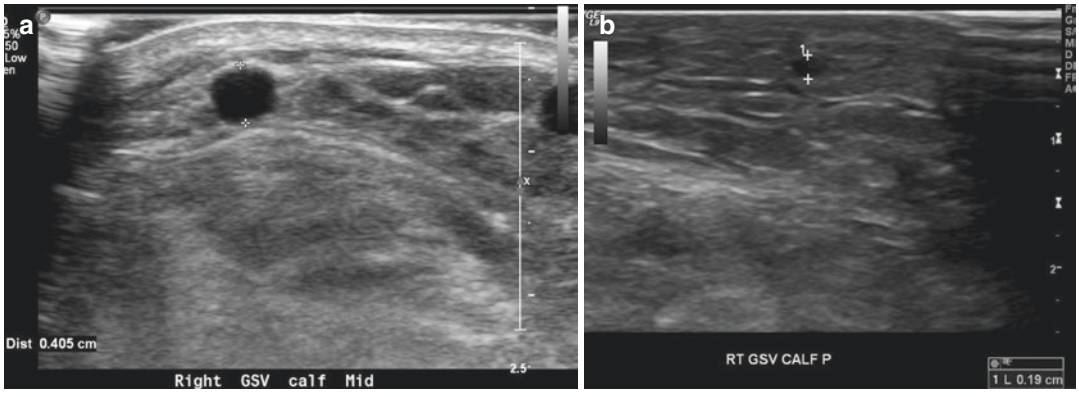


Fig. 21.2 Adequate sized great saphenous vein by Duplex (**a**) in contrast to a nonusable small sized vein (**b**). Duplex can also demonstrate previous phlebitic changes or thrombus within the saphenous vein

A minimum diameter should be 2 mm; experience has shown that smaller veins will yield poor results. If the great saphenous vein is inadequate, consideration may be given to either arm vein or prosthetic graft; if the former is chosen, Duplex scanning should be performed in the upper extremities as well.

As with any major operation, appropriate medical stabilization and optimization of the patient should be performed prior to proceeding with surgical revascularization. This may involve cardiac stress testing, coronary angiography, and echocardiography. Many patients with longstanding foot ulceration may be nutritionally depleted, and preoperative assessment and intervention may prevent postoperative wound and systemic complications.

As noted previously, many patients with CLTI will present with foot ulceration or gangrene, with concomitant foot infection. Control of infection is mandatory prior to surgical revascularization, to prevent the risk of systemic sepsis, wound, and graft infection. In the patient with diabetes, classical signs of infection may not always be present in the infected diabetic foot due to the consequences of neuropathy, alterations in the foot microcirculation, and leukocyte abnormalities. Fever, chills, and leukocytosis may be absent in up to two-thirds of diabetic patients with extensive foot infections, and hyperglycemia is often the sole presenting sign. Infections should be adequately drained, as diabetic patients simply cannot tolerate undrained pus or infection. Because most infections are polymicrobic, cultures should be obtained from the base or depths of the wound after debridement so that appropriate antibiotic treatment may ensue. If adequately controlled with antibiotics and surgical drainage (if necessary), the infectious process can be controlled within 5–7 days, even in patients with systemic sepsis, and subsequent prompt revascularization may ensue.

Surgical Considerations: Inflow Operations

The term inflow operation refers to any procedure performed on a vessel at or proximal to the inguinal ligament, which restores normal flow into the femoral segment. These include aorto-bifemoral bypass, iliac-femoral bypass, common femoral endarterectomy, and profundaplasty, as well as extra-anatomic bypasses such as axillo-femoral and femoral-femoral bypass. Because they are performed on larger vessels with expected higher patency rates, prosthetic grafts are utilized for almost all inflow bypasses. With greater success and application of endovascular procedures, especially in the aorto-iliac segment, these procedures are being performed with marked less frequency. Nevertheless, they continue to be an important component of the treatment plan for revascularization, especially for endovascular failures and infections.

Aorto-bifemoral bypass represents the "gold standard" for patency and durability for inflow operations, with 5-year primary patency surpassing 90%. The aorta is exposed via a midline incision or retroperitoneal incision, and the proximal anastomosis may be performed to the infrarenal aorta in almost all cases. Even if there is occlusive disease present, endarterectomy of the infrarenal aorta may be performed, followed by the proximal anastomosis to the endarterectomized aorta (Fig. 21.3).

Each limb of the graft is tunneled anatomically to the respective groin and the distal anastomosis is performed to the common femoral artery. The author's preference is to extend the anastomosis onto the profunda, so as to prevent late thrombosis of the limb secondary to unrecognized stenoses at the profunda or superficial femoral artery origin. In instances of redo operations or groin infection, the anastomosis may be performed onto the profunda directly, with a lateral approach to the profunda, which avoids the femoral region altogether (Fig. 21.4).

Because of the challenges associated with percutaneous endovascular treatment of common femoral artery disease, common femoral endarterectomy and profundaplasty are utilized commonly, and may be combined with concomitant iliac or superficial femoral-popliteal-tibial angioplasty. The femoral vessels are exposed, and as the occlusive process often extends proximally to

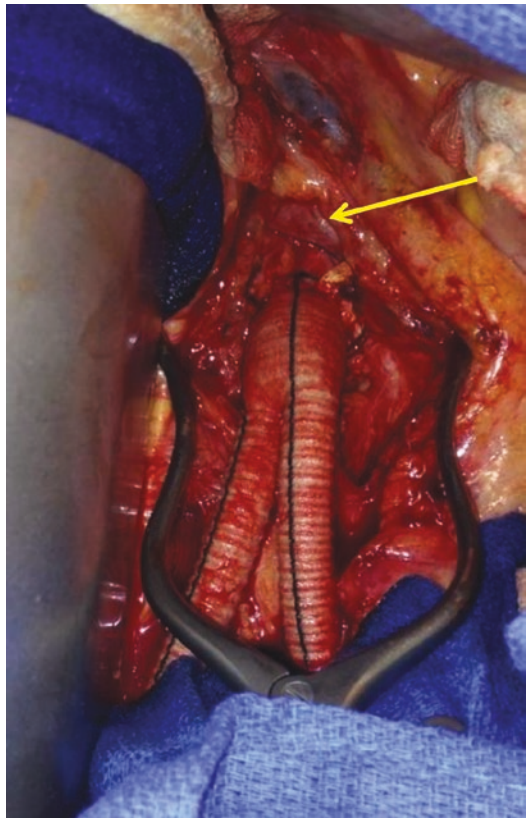


Fig. 21.3 Proximal anastomosis of an aortobifemoral graft sewn to endarterectomized infrarenal aorta. The yellow arrow points to the left renal vein

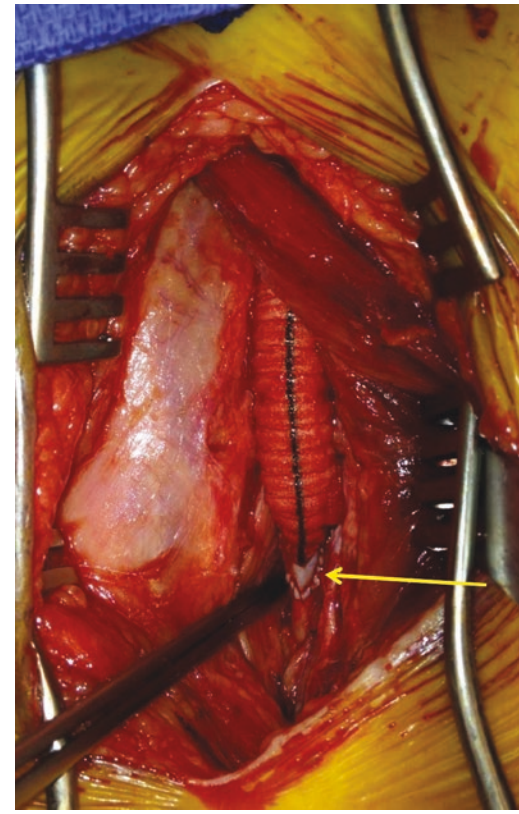


Fig. 21.4 Distal anastomosis of an aortobifemoral graft sewn to the second profunda segment, approached laterally, in a patient with an infected heavily scarred groin from a previous femoral-femoral graft. Note the vein patch onto the profunda (yellow arrow), with the Dacron graft sewn onto the patch

the external iliac artery, the distal external iliac artery above the circumflex branches is also exposed (Fig. 21.5).

Arteriotomy is made extending onto the profunda and all plaque is removed (Figs. 21.6 and 21.7), followed by patch closure with vein, prosthetic patch, or bovine pericardium (Fig. 21.8).

If concomitant iliac or distal endovascular intervention is planned, a sheath may be placed directly through the patch after restoration of flow (Fig. 21.9), and a simple suture used to close the hole after the sheath is removed.

In some cases, the occlusive process within the profunda may be too bulky for endarterectomy, or may result in extensive thinning of the artery. In these instances, a short bypass from the common femoral to the profunda may be performed, with excellent results (Fig. 21.10).

Although axillo-femoral and femoral-femoral bypasses are associated with lower patency rates as compared to the aortobifemoral bypass, their principal advantages lie in the fact that they are markedly less invasive. By avoiding an abdominal incision and aortic cross-clamping, these operations may be performed in high-risk patients with poor cardiopulmonary reserve; in some cases, the operation may be performed under local anesthesia in those patients in whom general anesthetic is contraindicated. In addition, by virtue of their extra-anatomic location, they may be utilized in instances of groin sepsis when placement of a prosthetic graft is undesirable.

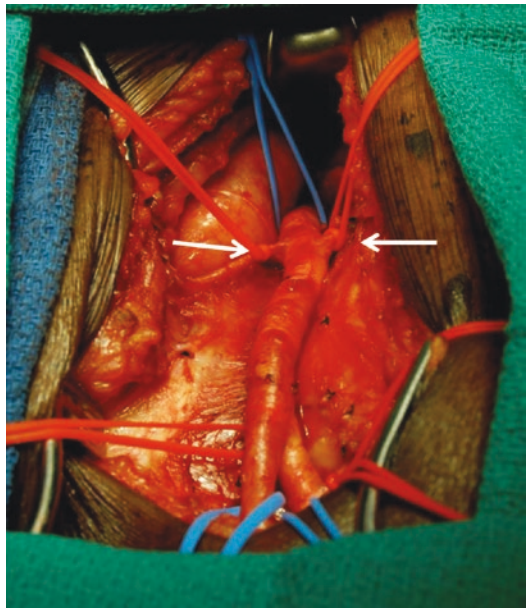


Fig. 21.5 The femoral vessels as well as the distal external iliac artery proximal to the circumflex branches (white arrows) are dissected free prior to femoral endarterectomy

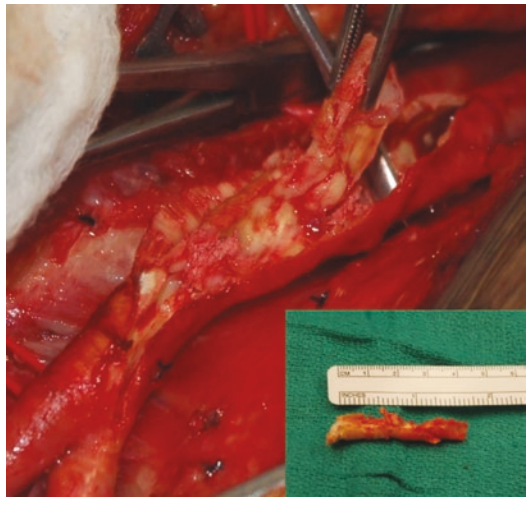


Fig. 21.6 Standard endarterectomy of the common femoral, proximal superficial femoral, and profunda femoris arteries, with inset showing plaque removed

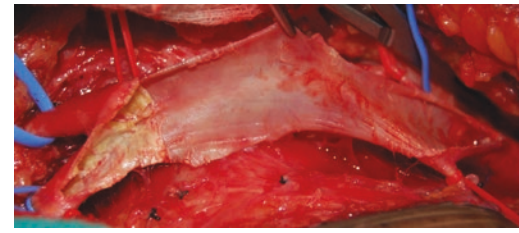


Fig. 21.7 Following complete thromboendarterectomy. Note widely patent orifice of both the superficial femoral and profunda arteries

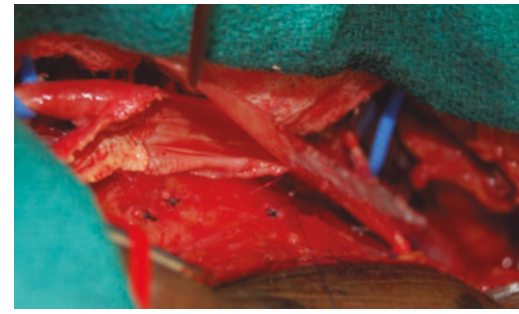


Fig. 21.8 The arteriotomy is closed with a bovine pericardial patch

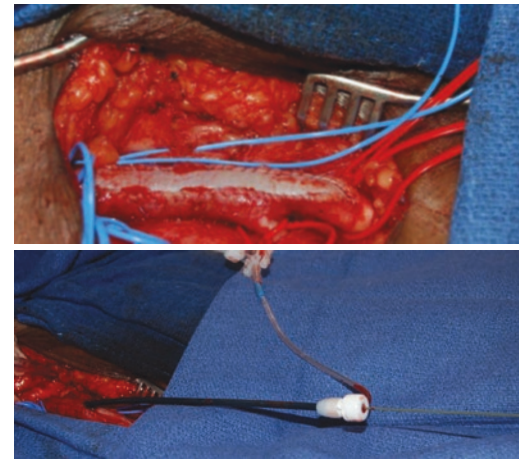


Fig. 21.9 After completion of the patch closure (top panel), a sheath may be inserted for iliac or more distal intervention

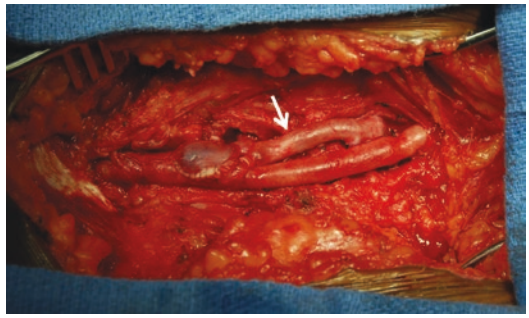


Fig. 21.10 Vein bypass from the common femoral to the profunda (white arrow)

Surgical Considerations: Infrainguinal Bypass

Infrainguinal bypass represents the most commonly performed surgical revascularization among patients with CLI. Several principles are noteworthy. Autogenous saphenous vein is the preferred conduit for all infrainguinal bypass operations, even to the above-knee popliteal artery. In addition to its superior primary patency compared to prosthetic, autogenous vein does not have the disadvantages of associated with prosthetic graft infection, which can be devastating. The saphenous vein graft can be prepared in several ways. The simplest is a reversed configuration, in which the vein is harvested off its bed, reversed, and then placed either subcutaneously or deep to the muscle and fascia after the proximal anastomosis is performed. Because of the inherent disadvantage of the size discrepancy between the smaller distal portion of the vein and the larger proximal artery, the nonreversed and in situ techniques may be employed, in which the valves are rendered incompetent by cutting them with an atraumatic valvulotome. The nonreversed translocated technique is identical to the reversed technique except that the valves are cut, whereas the in situ technique leaves the vein in the bed, with mobilization only of the proximal and distal portions and tributary ligation without harvesting the vein. In both of these, the larger proximal vein is utilized for the proximal anastomosis, allowing for an easier anastomosis both proximally and distally.

The type of configuration utilized—reversed, nonreversed translocated, or in situ—has no effect on patency, and multiple series have confirmed that all yield virtually identical results when performed correctly. Ultimately the decision as to the type of configuration should depend on the surgeon's experience with each technique and vein graft size. Our preference is either a reversed graft when the vein is of a uniformly large caliber and for shorter bypasses, or nonreversed translocated for smaller veins and for long bypasses (such as femoral-tibial). If a nonreversed configuration is used, we prefer to inspect the vein with an angioscope and cut all the valves under direct angioscopic guidance, which allows for precise valve lysis without any risk of intimal injury or retained valve, both of which can have an adverse effect on patency and outcome (Fig. 21.11).

The vein may be harvested through continuous incision, small "skip" incisions, or endoscopically. There has been increasing enthusiasm for endoscopic, minimally invasive techniques for harvest, as it may decrease postoperative recovery time, edema, and wound complications. However, this should be tempered against the risk of occult vein injury during harvest, including vein spasm, which can have implications for patency. Our preference continues to be harvest by a continuous incision which is meticulously created to avoid any skin flaps (Fig. 21.12). This allows for careful vein harvest. Periadventitial papaverine or nitroglycerine injection overcomes vein spasm and the vein is gently distended with solution, then harvested off its bed. With careful incision placement, avoiding skin flaps, and with layered accurate closure, we have found the risk of significant wound complications to be minimal. Additionally, we prefer to place all grafts deep to surgical incisions, such that grafts originating from the femoral artery are tunneled deep to the muscle and fascia down to the below-knee popliteal space. This obviates the risk of graft infection or exposure should a wound complication occur, which is discussed in more detail later in this chapter.

The proximal and distal anastomoses are almost always performed end to side. All adven-

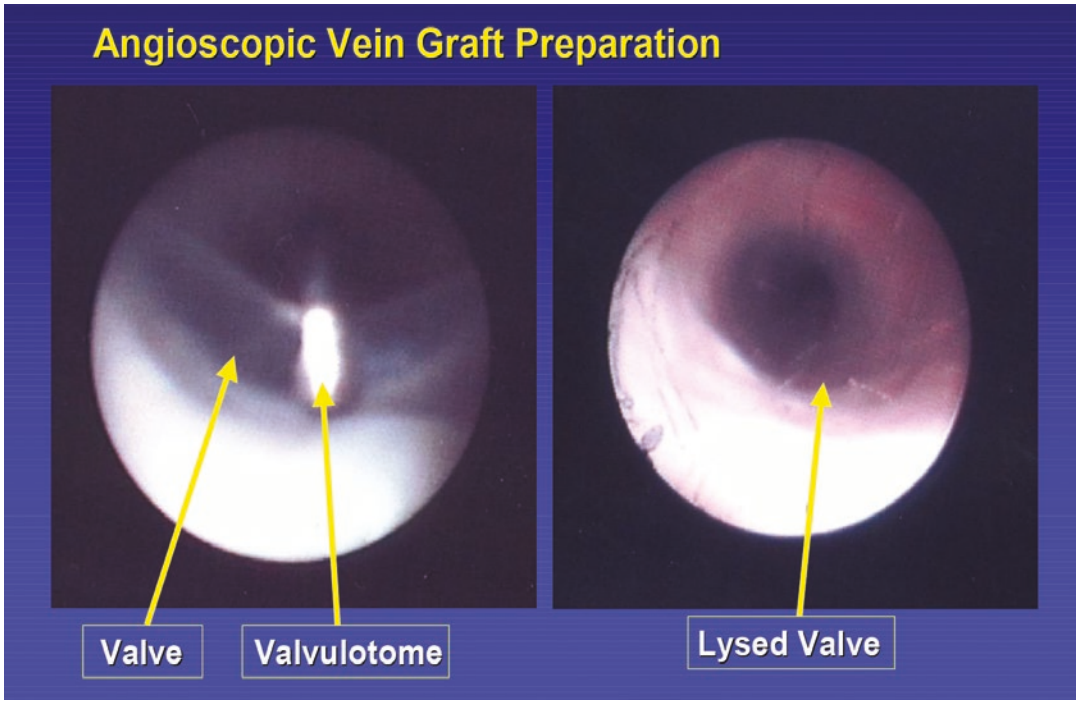


Fig. 21.11 Angioscopic evaluation and angioscopic guided valve lysis (labeled)

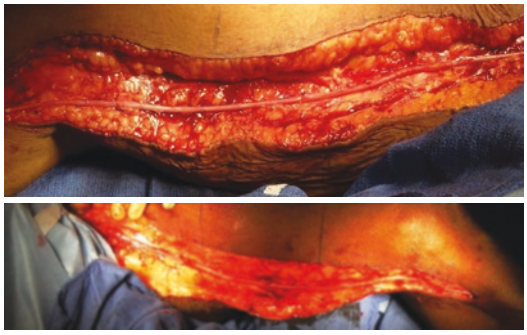


Fig. 21.12 Exposure and harvest of the saphenous vein through a continuous incision without flaps. Note the vein is fully exposed, allowing for meticulous harvest and prevention of spasm. The incision is created directly overlying the vein, and no thin flaps are created, which maximizes the chance for successful wound healing

titia should be removed from the vein at the site of proposed anastomosis to avoid kinking at the "heel" of the graft, which can be a cause of subsequent graft stenosis or failure. Redundancy at the proximal and distal anastomoses should also be avoided. The graft should have a natural curve with the native artery, with the anastomosis on the anterior aspect, so as to minimize twisting of the graft (Fig. 21.13).

Recognizing the pattern of vascular disease in diabetes, in which the femoral-popliteal segment is often spared of the atherosclerotic occlusive process, shorter bypass grafts to the tibial vessels with origin from the popliteal or distal superficial femoral artery may be performed. Extensive experience has shown that, in the absence of more proximal occlusive disease, such grafts yield the same patency results as grafts taken from the common femoral artery. This allows for reconstruction in those patients with limited saphenous vein, shortens operative time and incision length, and avoids potentially troublesome groin wound complications.

As an example of a short bypass graft from the popliteal artery, a typical popliteal to dorsalis pedis bypass graft is illustrated in Figs. 21.14, 21.15, and 21.16. The saphenous vein is harvested from the upper leg and will be translocated subcutaneously in the lower leg, where no incision has been made, which minimizes the risk of graft infection with any wound complication

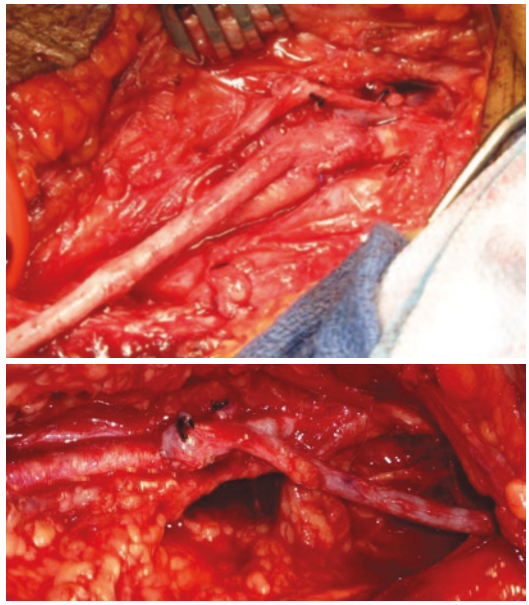


Fig. 21.13 Proximal (top panel) and distal (bottom panel) anastomoses of a femoral-tibial graft. Note absence of kinking or "pull" on the anastomosis, with no redundancy



Fig. 21.14 Popliteal to dorsalis pedis bypass, with translocated vein harvested from the upper thigh (solid dark arrow). Note the vein graft is translocated to a subcutaneous position where no incision has been made in the calf and lower leg (dashed dark arrow)



Fig. 21.15 Same patient as Fig. 21.14, demonstrating the proximal anastomosis to the below-knee popliteal artery



Fig. 21.16 Same patient as Fig. 21.14. The graft has been tunneled subcutaneously to the dorsalis pedis artery and the distal anastomosis has been performed

(Fig. 21.14). After preparation of the graft with angioscopy, the proximal anastomosis is performed in an end vein to side artery fashion to the popliteal artery (Fig. 21.15). After completion of the anastomosis, the graft is placed in the previously created tunnel to the dorsalis pedis incision under arterial pressure (to avoid kinking or twisting of the graft) and the distal anastomosis is then performed (Fig. 21.16). A handheld continuous wave Doppler is used to insonate the distal anastomosis and distal artery. We rarely perform completion arteriography, though some surgeons utilize it routinely. Estimated blood loss is usually 150 mL or less.

In many patients with CLI, the only suitable target for revascularization is a distal inframalleolar vessel, such as the plantar or tarsal artery. Bypass to these vessels, though technically challenging, can be performed successfully through accurate angiographic visualization preoperatively, anatomic knowledge of the plantar and tarsal vessels, and by incorporating meticulous surgical and vein harvest techniques (Figs. 21.17, 21.18, and 21.19). Increasing experience has shown excellent short-term and long-term patency and limb salvage rates, which is highly encouraging in this particular subset of patients who are often advised to undergo limb amputation.

When ipsilateral saphenous vein is not available, the decision for an alternative source of conduit should be made with consideration of the patient's comorbidities. Contralateral saphenous vein may be used, though up to 60% of patients will require contralateral revascularize-

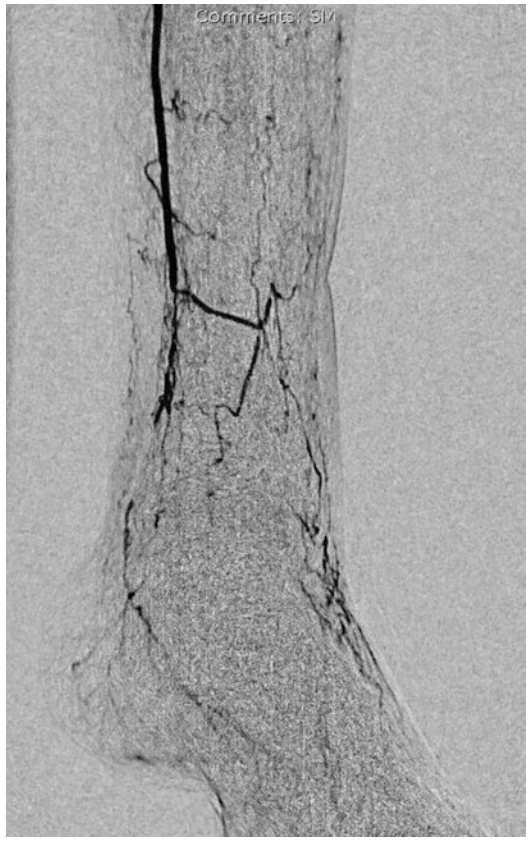


Fig. 21.17 Arteriogram of the foot in a 60-year-old patient with a gangrenous hallux, demonstrating only a plantar vessel in the foot

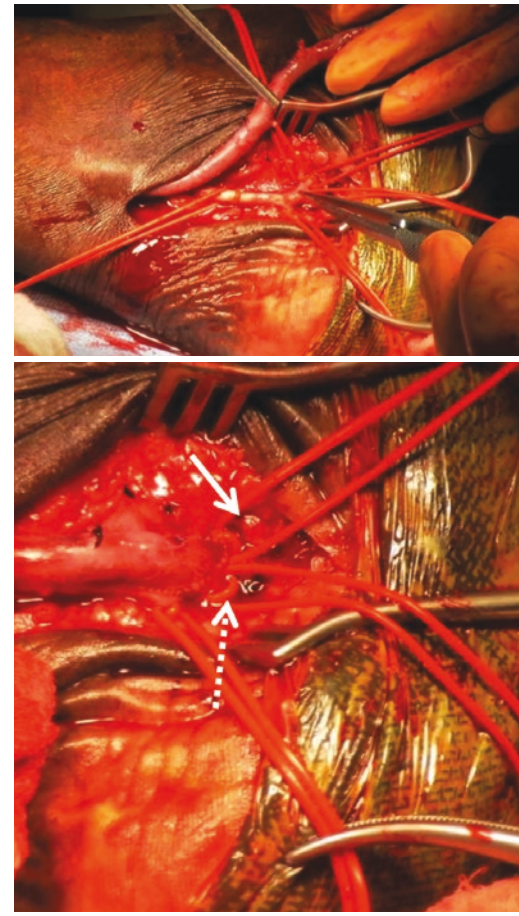


Fig. 21.18 Same patient as Fig. 21.17. The plantar vessels have been exposed and the vein graft is prepared for distal anastomosis (top panel). Distal anastomosis performed to the junction of the medial and lateral plantar arteries (solid and dashed arrows) (bottom panel)

tion within 2 years. Several reports also have attested to the success of arm vein grafts; however, enthusiasm is tempered by their limited length. In addition, an increasing number of patients with CLI will have either chronic renal insufficiency or end-stage renal disease, and the arm vein should not be sacrificed in these patients in whom optimal angioaccess is essential for survival.

Based on these limitations, prosthetic grafts have been increasingly used in the tibial location for patients with limited autogenous conduit, with encouraging results. Newer developments and advancing techniques, such as heparin-bonded polyfluorotetraethylene (PTFE) and vein cuffs/patches at the distal anastomosis, have resulted in improved patency rates in some series.

Our preference is to use the contralateral saphenous vein only in those patients who have a palpable foot pulse or near-normal noninvasive arterial studies. Our second preference is a prosthetic PTFE graft which I modify by performing a vein patch at *both* the proximal and distal anastomosis. The patch is sewn widely onto the recipient vessel, with a generous PTFE anastomosis on the top of the patch (Fig. 21.20). By performing this at the proximal anastomosis, we have not encountered a patient who presents with severe limb ischemia from proximal propagation of thrombus should the graft occlude.

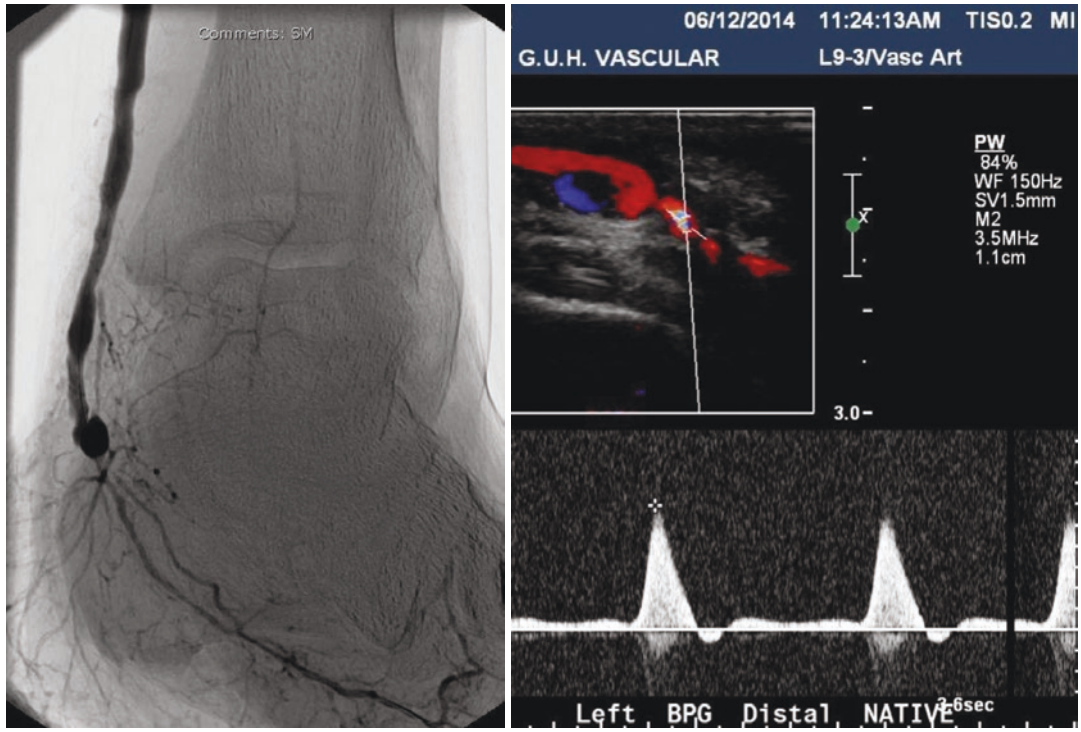


Fig. 21.19 Angiogram 1 year postoperative and Duplex 2 years postoperative of the patient from Fig. 21.17, demonstrating a widely patent graft

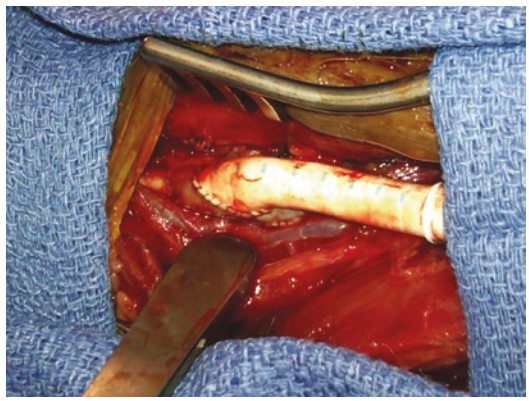


Fig. 21.20 Distal anastomosis of a PTFE graft with distal vein patch to the peroneal artery. Note the wide vein patch on the native artery with the PTFE graft anastomosed to the patch

Complications

Both systemic and local complications may occur after surgical revascularization. Perioperative cardiac complications are the most common systemic complication, occurring in up to 5% of patients, and include arrhythmias, congestive heart failure, and myocardial infarction. Perioperative use of beta-blockers may reduce this risk. Judicious use of fluids, intraoperative monitoring with liberal use of nitrates, and a high index of suspicion for myocardial ischemia remain as important tenets of postoperative care.

The incidence of early (immediate) postoperative graft occlusion varies according to the loca-



Fig. 21.21 Four weeks following left femoral to tibial bypass, complicated by a superficial wound dehiscence, this patient presented with bleeding in the groin incision (top panel) with a large infected pseudoaneurysm by CT scan. This necessitated emergent groin exploration with debridement and graft removal (bottom panel)

tion and obviously varies among individual surgeons; most series report a rate of approximately 2–5%. Unless otherwise dictated at the time of the original operation, or otherwise mitigating circumstances, all patients with early graft occlusion should be re-explored and graft thrombectomy performed. Most importantly, an underlying cause (such as an anastomotic flap or clamp injury) should be sought and addressed, as the outcome is more favorable when the cause is corrected.

Wound complications are often underreported, and probably the most frequent complication after infrainguinal bypass surgery. The spectrum ranges from simple cellulitis which may be treated with antibiotics alone, to extensive soft tissue infection with graft involvement. Most often, the sequence is that of an indolent infection which results in a small area of wound dehiscence and fibrinous exudates. Unfortunately, this can mask deeper involvement, which can result in a catastrophic outcome if the graft is involved (Fig. 21.21). The most important treatment is prevention. Accurate and precise tissue approximation and closure, avoidance of flaps, judicious use of antibiotics, prevention of lymph leaks, and clean dressings all can help prevent wound complications. Additionally, as stated previously, we will avoid placing grafts in the subcutaneous space of a surgically created incision. In the femoral location, use of a rotational sartorius muscle flap is quite helpful to cover the graft prophylactically.

Results

Patency rates and limb salvage after surgical revascularization vary widely, principally according to the anatomic location, though other factors (such as re-do procedures, type of conduit, and indication) also are important determinants. The highest patency rates are seen with in-line (anatomic) inflow operations, with 5-year and 10-year patency for aortobifemoral bypass being 90% and 80% respectively. Similar rates are seen following isolated profundaplasty or femoral endarterectomy. For extra-anatomic bypass, the results are obviously lower, with 5-year patency for femoral-femoral bypass averaging 65%. Among axillo-bifemoral grafts, the patency rates are even lower, averaging between 40% and 60% at 3 years.

Bypass grafts with saphenous vein provide the highest patency rates among infrainguinal revascularization. In situ and reversed vein graft primary patency at 1 year and 4 years averages approximately 85% and 65% respectively, again with no difference based on vein configuration. For paramalleolar bypass grafts, secondary patency is approximately 60% at 5 years, with limb salvage rates in excess of 80% at 5 years.

The reported patency data for prosthetic grafts vary widely, with expected 1 year patency between 35% and 75%. Multiple factors may explain this wide variation. At least some of the reports are 20 years or older; additionally, variables such as use of a distal vein cuff, anticoagulation, and outflow are widely discrepant or not even reported. More recent data are more encouraging, and certainly support the use of prosthetic grafts to the popliteal or tibial location when good quality autogenous vein is not available.

In addition to patency, quality of life scores need be considered after any intervention, but especially after infrainguinal bypass among patients with foot ulceration. In this subset of patients, time for healing can take up to 3–6 months, with only 50% reporting "back to normal" at 6 months. Significantly, approximately 15% of patients who were independent preoperatively require some level of dependence at 6 months postoperatively. Finally, the best measure of quality of life is freedom from major amputation, as amputation is uniformly associated with the lowest quality of life score.

Choice of Surgical Revascularization or Endovascular Procedure

The decision for surgical revascularization or percutaneous endovascular intervention is dependent on multiple variables, including both patient variables and the skill of the interventionalist/surgeon. Notwithstanding the debates on which should be performed first, it is axiomatic that the patient with CLI is best served by an aggressive approach to limb salvage, which, by definition, incorporates both endovascular and surgical approaches.

A suggested approach to the patient with limb ischemia may be guided by the results of the BASIL trial, which was the first and only intention to treat randomized controlled trial comparing endovascular intervention to surgical bypass as "first treatment" among patients with severe limb ischemia. At follow-up of 7.7 years, 56% of patients had died, emphasizing the precarious medical condition of these patients. At 2 years, there was no difference in amputation free survival or overall survival among the two treated groups, with a slight increase in overall survival and amputation free survival favoring bypass surgery at 3 years. Hospital costs were significantly higher for bypass surgery, but this had equalized at 3 years among the two groups. Finally, in the analysis of quality of life, the worse outcome was seen among patients undergoing major limb amputation, again emphasizing an aggressive approach to limb salvage in these patients.

The results of these and other smaller nonrandomized series suggest that an endovascular-first approach is warranted in almost all patients, provided that it may be performed without "burning a bridge" for future surgical revascularization. This is especially applicable for patients who are expected to live less than 2 years, based on the BASIL results. Conclusively, it can be stated that limb amputation should be avoided, and surgical revascularization plays an integral part of that goal.

General Considerations in Endovascular Revascularization

In 2000, the TransAtlantic Inter-Society Consensus on the management of PAD, authored by vascular surgeons, cardiologists, angiologists, and interventional radiologists aimed to address the variation in therapy among individual patients with identical conditions, with an aim to promote uniform high-level care across different countries. The document stated that "in general, if there is a balanced choice between an endovascular and a surgical procedure for a particular lesion, then the former is preferred because it usually avoids a general anaesthesia, poses a

lesser systemic stress, and has fewer serious complications" (14). Encouraged by this vision, in the next 20 years we observed a widespread increase of endovascular procedures in patients with CLTI, with many authors advocating an "angioplasty first" revascularization strategy (15–20).

Interventional physicians rode this endovascular wave, developing new technical approaches, such as endoluminal and subintimal crossing of long occlusion and retrograde approaches able to increase procedural success. Manufacturers of medical devices followed them, producing new dedicated tools, able to ablate and dilate long and often calcified lesions, to scaffold vessel wall preventing recoil and dissection, and to deliver antiproliferative drugs to avoid restenosis.

Despite this huge effort, even in high-income countries with advanced health care systems, such as Germany and the United States, many patients with CLTI do not always undergo angiography or any attempt at revascularization (21, 22). For this reason, it is important to keep in mind that a low-cost balloon angioplasty with uncoated balloons and bailout stenting has been demonstrated from the beginning to be effective in preventing amputation in the majority of patients with CLTI (15, 23–26).

Instead of pursuing a high-cost and high-tech angioplasty in few fortunate patients our duty should be to promote and guarantee a widespread access to basic endovascular revascularization to the vast majority of patients with CLTI, independently from census and country. In line with this assumption, the purpose of this chapter is not to describe the newest and most advanced devices and techniques, but to overview the basic technical strategy that should be used everywhere by skilled physicians for changing the fate of CLTI at a reasonable cost.

Targets of Endovascular Revascularization

According to the new Global Vascular Guidelines (GVGs) a successful revascularization in CLTI, particularly in patients with tissue loss, nearly always requires restoration of pulsatile in-line flow to the foot (27). In presence of diffuse BTK disease, typical of CLTI, the first step is to identify the target arterial path (TAP) in each patient by high-quality imaging, selecting a preferred infrapopliteal artery. The TAP is generally based on the least diseased crural artery providing runoff to the foot and other relevant factors, such as angiosome preference or avoidance of a previously instrumented vessel (27).

In the last years multiple studies have supported the concept that direct revascularization (DR) of the angiosome affected by tissue lesion leads to improved healing and limb salvage rates in patients with CLTI (28–35). In line with the angiosome concepts, the endovascular treatment of patients with CLTI has evolved toward extreme approaches, and BTA interventions are proposed as a new strategy to improve the clinical outcomes of revascularization (36, 37).

In summary, the key point in our revascularization strategy is to identify the proper TAP in each patient with CLTI, considering many factors such as anatomy, obstructive disease pattern, and technical hurdles that must be overcome to achieve, if possible, a successful recanalization.

Anatomic Considerations in Endovascular Revascularization

The TAP must be evaluated by high-quality imaging, applying standard foot projections and digital post-processing methods. About 7% of the patients present some type of anatomical abnormality in the distribution of BTK vessels at the ankle: anterior or posterior dominance of peroneal artery or a single peroneal artery (38). Moreover about 20% of the patients have some variations in the foot vessel anatomy with dominant dorsalis pedis or plantar artery or a tarsal loop. Every patient is different and to recognize the true underlying anatomy is of fundamental importance in guiding our procedure (38).

Evaluation of the Collateral Vessel Network

Angiosomes are interconnected by a collateral vessel network which guarantees blood flow to the entire foot in case of occlusion of one or more arteries (39, 40). In cases when diffuse disease prevents the DR of the injured angiosome, some authors suggest to seek a collateral-vessel-guided revascularization (41, 42). Other authors demonstrated that indirect revascularization through collaterals can effectively promote the healing of ulcers and decrease the amputation rate (34, 35, 43).

The evaluation of collateral vessels is a key point in guiding our revascularization strategy in patients with CLTI. The value of an angiosome-oriented revascularization is directly correlated to the degree of SAD affecting the foot distribution system, and inversely correlated with the expansion of the collateral vessel network (38).

Metabolic Demands of Tissue Loss

According to the GVGs, angiosome-guided revascularization may be of importance in the setting of endovascular intervention in patients with significant wounds (e.g., WIfI wound grades 3 and 4), particularly those involving the midfoot or hindfoot, but is likely to be irrelevant for ischemic rest pain and of marginal value for most forefoot lesions and minor ulcers (27). Wounds have a different blood flow requirement for healing. The value of revascularization, and particularly an angiosome-targeted revascularization, varies according to the type of wound (38).

Multivessel Versus Single-Vessel Revascularization

Every lesion starts generally well localized; however delayed referral and infection lead to its enlargement, invading surrounding tissues and adjacent angiosomes (44). Spillerova et al., evaluating patients with CLTI and foot lesions, observed that the wound interfered with one angiosome in 24.2% legs, two angiosomes in 46.6%, three angiosomes in 26.1%, four angiosomes in 2.5%, and five angiosomes in 0.6% legs (45). They concluded that the tissue lesion of CLTI affects several angiosomes in majority of the cases, suggesting that consensus needs to be achieved for the accurate definition of angiosome-targeted revascularization when more than one angiosome is clinically involved. Some authors suggest to pursue a multiple BTK vessel recanalization, because this approach can obtain a better wound perfusion, improving healing speed and compensating for restenosis of one of the treated vessels. On the other hand, it is suspected that the procedure may carry a higher risk due to greater contrast volume, longer procedure time, radiation exposure, and potential complications (46–48). The GVGs assert that multivessel (tibial) revascularization may be reasonable in selected patients with advanced limb-threatening lesions (e.g., WIfI stages 3 and 4) undergoing endovascular therapy if it can be safely accomplished without risking loss of a bypass target or compromising runoff to the foot (27).

Technical Approaches in Endovascular Revascularization

This is not meant to be a treatise on the endovascular treatment of inferior limb vessels; it merely highlights the key technical elements to consider when facing patients with CLTI.

Chronic Total Occlusions (CTOs) Crossing Strategy

CTOs represent the majority of the obstructive lesions encountered in patients with CLTI (49). Crossing the lesion is the first step of endovascular recanalization. Independently of the site of the lesion (above-the-groin inflow, femoro-popliteal or infra-popliteal) we recommend a step-by-step approach. The first attempt is endoluminal crossing. In many cases a soft tip, hydrophilic wire can cross the occluded lumen, also in very long occlusion, finding easily the true distal lumen.

The explanation of this success resides in a softer core of the occluding material, surrounded by stiffer and often calcified walls: the wire slides inside the core, supported by dedicated low profile catheters or balloons. In case of resistant fibrous cap or focal calcification, the soft tip wire can be exchanged with a CTOs dedicated wire. The stiffer and often tapered tip can pierce the tough material, oriented by the operator in the correct direction.

In case of failure of the endoluminal approach, the subintimal approach offers an effective alternative. The wire is typically advanced in a looped shape, and instead of crossing the lumen, the operator dissects the subintimal space. The discovery of the subintimal space by Bolia was a major development in angioplasty technique (51, 52). At the end of the CTO, reentry inside the true distal lumen can be achieved by pushing the wire; however, due to the risk of damaging the distal vessel, especially in case of a diseased target, retrograde approaches are preferred.

The retrograde approaches have demonstrated to be safe and effective, and to increase by 20% the success rate of peripheral endovascular procedures (53, 54). Every vessel below the CTO can be used for a retrograde approach, from the metatarsal arteries to pedal, tibial, and peroneal artery. The retrograde puncture of tibioperoneal, popliteal, and superficial femoral artery can be performed without changing the supine position of the patient on the radiological table. In the majority of the cases it is possible to use a sheathless approach, supporting the wire with low profile catheters or balloons. Rendezvous with the antegrade approach can be accomplished in the endoluminal or subintimal space, sometimes with the help of balloons dilatation.

Other approaches were described, transcollateral, pedal-plantar loop, and can be used in particular cases with the advice to respect what is functioning and to preserve the potential landing zone of bypass.

Endoluminal, subintimal, and retrograde approaches in CTOs crossing are key elements of a successful percutaneous revascularization. Every center treating CLTI must be familiarized with these techniques and must have a workload sufficient to keep the skill of the operators at a high level.

Endovascular Strategy in the Vascular Territories of the Lower Leg

The concept of target arterial path implies that a partial revascularization, limited to the arterial inflow or the femoro-popliteal segment, leaving an untreated diffuse BTK vessel disease, is generally insufficient to obtain healing; a successful revascularization in CLTI requires restoration of pulsatile in-line flow to the foot. While in bypass surgery this is generally an achievable target due to the size and low resistance of the bypass conduit, in the endovascular treatment of multivessel diffuse disease this target is more difficult to obtain. Every segment of the vascular tree of the inferior limb requires a different and specific approach.

Treatment of Inflow Disease: The Aortoiliac System

The endovascular treatment of iliac obstructive disease represents the first choice of revascularization if done by an experienced team and if it does not compromise subsequent surgical options. A recent metanalysis compared endovascular and open surgical approaches in iliac obstructive disease: the endovascular approach reduced the length of hospital stay and the postoperative morbidity, while, in the long-term follow-up, open surgical approach demonstrated a better primary patency and lower reintervention rate (54).

The procedure must be planned according to the characteristic of the obstructive lesion: site of lesion (common or external iliac artery), type of lesion (stenosis or occlusion), length of lesion, calcium burden, soft plaque. Whenever possible, the internal iliac artery should be preserved. The involvement of common iliac ostium often requires a bilateral kissing stenting technique, in order to avoid plaque prolapse and contralateral ostium stenosis, and to optimize blood flow in the aortic bifurcation (55–57).

Simple balloon angioplasty is now abandoned in favor of primary stenting, which represents the gold standard in iliac treatment, due to better results in terms of patency and complications (58–63). Different types of stents are available on the market: bare metal stents and covered stents, both in the balloon expandable and self-expandable configuration. Drug elution has a marginal role in iliac arteries, limited to restenotic lesions (64).

Balloon expandable stents offer a higher radial force, able to scaffold calcified lesions, and precise deployment; self-expandable stents have lower radial force and less precise deployment; however the adaptable geometry and the higher flexibility facilitate the treatment of longer lesions and maintain the natural movements of external iliac artery (65–67).

Covered stents reduce the risk of distal embolization and repair arterial wall ruptures, demonstrating safety and good long-term results in comparison with uncovered stents (68–71).

Treatment of Inflow Disease: The CFA

Open endarterectomy is considered the standard of care for treatment of atherosclerotic stenosis of the CFA due to the scarce invasiveness of the procedure, durable results, and possibility to spare the bifurcation. The endovascular approach is limited to patients at high surgical risk or with hostile groin because the CFA is a hyperdynamic region with risk of stent fracture; obstructive plaque is often heavily calcified and difficult to dilate, and in case of bifurcation involvement stenting can jeopardize the ostium of one main femoral branch (27).

Nevertheless, there is significant morbidity and mortality resulting from open surgery in CFA, and in recent times the endovascular approach has demonstrated to compete with surgery. In a recent systematic review and meta-analysis of 28 studies, endovascular treatment with routine stenting has demonstrated comparable 1-year primary patency and target lesion revascularization as CFA endarterectomy, with a lower complication rate (72). Another meta-analysis involving more than 3000 patients confirmed these positive 1 year results; however, after this duration, the patency of the endovascular treatment was significantly lower than open repair and the overall rate of stent fracture was 3.6% (73).

Waiting for further studies, dedicated materials and a broader consensus, endovascular treatment of CFA should be considered in selected patients with contraindication for surgery and a favorable anatomy.

Treatment of Femoro-Popliteal (FP) Segment

The new GVGs affirm that, "individual lesion-based schemes correlate poorly with effective revascularization in CLTI, vascular specialists must integrate approaches for arterial segments into a management strategy for the whole limb." According to this global strategy, complex FP lesions should be considered for a surgical approach; however the final decision relies on the surgical patient's risk, type of foot lesion, autologous vein availability, and the evaluation of BTK and BTA vessel disease.

In the last 20 years, the endovascular strategy for the FP segment is radically improved, with outcomes approaching that of surgical bypass. After initial experiences with balloon angioplasty, the introduction of the "drug delivery" technology, drug coated balloons (DCB) and drug eluting stents (DES), and covered stents has significantly improved the outcomes of the endovascular treatment of the FP segment in terms of primary patency and freedom from target lesion revascularization (TLR), becoming the first treatment option in the FP segment (74–78).

A recent meta-analysis comparing drug-coated devices versus saphenous vein graft bypass in FP arterial occlusive disease concluded that there is no significant difference in short-term efficacy, short- and long-term mortality (79). Despite traditional saphenous vein bypass remaining the gold standard, drug coated devices provide a reasonable alternative therapy with

lower short-term morbidity associated with the procedure (79).

Despite the evolution of materials and techniques, there are still several critical issues regarding the endovascular treatment of the FP segment, essentially represented by calcium and motion.

Heavily calcified lesions are a barrier for every step of endovascular revascularization: crossing, dilatation, scaffolding, and drug elution. New devices are available to overcome calcium resistance to dilatation, starting with high pressure balloons, cutting and scoring balloons. Orbital atherectomy has demonstrated to be effective in modifying the calcified lesions facilitating easier balloon inflation and intravascular drug elution. A new approach of intravascular lithotripsy to treat severely calcified lesions in a real-world study demonstrated low residual stenosis, high acute gain, and a low rate of complications despite the complexity of disease. A different solution is represented by the "pave and crack technique" which requires stent-graft implantation and aggressive dilatation of the arterial segment (80).

The second issue is represented by the dynamic properties of popliteal artery. The whole FP segment is affected by torsion, compression, and bending forces during the walking movement or sitting position. Furthermore, from cadaveric studies, these forces seem to be lower in the proximal and mid-superficial femoral artery and higher in the distal portion in the abductor channel and in the popliteal artery (81). Individual characteristics regarding the muscle modeling, different for each patient, modify the bending forces acting on the popliteal artery, and the presence of arterial wall calcification influences its curvature. Moreover, the endovascular treatment, both with angioplasty and stenting, modifies the dynamic characteristics of the FP segment (82).

The choice of the treatment method is a key point: while angioplasty results in a more flexible artery, suggesting priority to a "leaving nothing behind" strategy, stents interfere more with FP dynamic properties (83, 84). Depending on the anatomical position of the stents, the axial stiffening of the arteries may lead to chronic kinking and stent fractures, both responsible for restenosis and occlusion and, consequently, affecting the long-term success of the procedure (82, 85–87).

To overcome these problems, in the last years different technical approaches have been proposed. Atherectomy, with or without DCB, does not seem to confer any significant additional clinical benefit compared with balloon angioplasty or stenting (88–92). However, several authors disagree with this conclusion (93, 94).

A self-expandable nitinol stent (Supera™, Abbott), with a peculiar geometry that allows conformability to the FP segment during flexion, showed good results in terms of patency, freedom from TLR and stent fracture rate (95–99).

Treatment of Below the Knee (BTK) Arteries

BTK arteries are extensively diseased in patients with CLTI, so to be considered the most challenging field. The first line of treatment is plain old balloon angioplasty with uncoated balloon with optional bailout stenting. Balloons now are available in tapered shape and length up to 30 cm, allowing a homogeneous dilatation of the vessel. Calcification is a common problem in BTK vessels and non-compliant high-pressure balloons, able to support 25 atm, represent an important tool in BTK treatment. Cutting, scoring balloons, and atherectomy could play a role in optimal vessel dilatation. Long dissection after balloon angioplasty can be corrected by the focal implantation of dedicated stent.

Also in the BTK district, after initial experiences with balloon angioplasty, DESs and DCBs were proposed in order to improve the outcomes of the endovascular treatment in terms of primary patency and freedom from TLR; however the results were promising but also conflicting. The reasons for this situation of uncertainty are essentially two. First, while studies on FP segment were predominantly done on claudicants, studies on BTK vessels were done on patients with CLTI, resulting in a higher complexity of the clinical scenario and confounding factors such as wound severity and comorbidities. Secondly the popula-

tions enrolled in BTK angioplasty studies present a selection bias based on matching the target lesion length on the type of studied device.

Studies on stenting, evaluating balloon expandable and self-expandable stents, bare metal and DESs, were focused on short and proximal BTK lesions, while studies on uncoated and DCBs enrolled longer BTK lesions extended to the distal third of the tibial vessels.

In summary, for short (<5 cm) and proximal BTK lesions DCBs have demonstrated better results in terms of patency, TLR, and amputations and improved wound healing compared to uncoated balloon angioplasty and bare metal stent (100–102).

Treatment of Below the Ankle (BTA) Arteries

If the best strategy in revascularizing patients with CLTI is restoration of pulsatile in-line flow to the foot vessel, possibly a DR to the wounded angiosome, BTA vessel disease represents the final obstacle. Many authors proposed BTA intervention as a new strategy to improve clinical success of revascularization.

A recent systematic review and meta-analysis concluded that the currently available evidence suggests that additional BTA angioplasty is a safe and feasible procedure, and there is a potential benefit in wound healing (103).

Despite these positive findings, before going aggressively into BTA vessels, we believe it extremely important to consider a critical appraisal of this literature.

Studies on FP and BTK endovascular treatment include thousands of patients, many randomized control trials, and long-term follow-up. The amount of data on BTA vessel angioplasty is much lower: the only metanalysis by Huinzig et al. included 10 studies of moderate quality, reporting a total of 478 patients with BTA angioplasty performed in 524 legs (103). Moreover, these studies are heterogeneous, the authors applied different techniques such as endoluminal or subintimal approaches, antegrade, retrograde and pedal-plantar loop technique, plain old balloon angioplasty with uncoated balloons and DCBs, and stenting. We lack data on restenosis rate and long-term follow-up and no randomized control trials are available. In conclusion BTA angioplasty is still in an artisanal era, and we can share only anecdotal advice based on our experience.

In line with the GVGs, the first advice is to study BTA vessel disease with high-quality imaging. BTA vessels represent the main obstructive target of SAD, which is strongly associated with diabetes, hemodialysis, and CLTI (104). To evaluate the presence and the degree of SAD is a key point in defining the prognosis and the strategy of any revascularization procedure in patients with CLTI. Due to the difficulty of obtaining a high-quality imaging of the BTA vessels and quantifying SAD (repeated contrast dye injection, movement artifacts), we proposed a calcium score on the plain radiographs of the foot, which has demonstrated a high sensitivity and specificity for SAD (105). SAD and MAC scores are both strong predictors of major adverse limb events in patients with CLTI.

The second advice is to respect what is, more or less, function. After treating big artery disease to the ankle level, before going BTA, consider the disease extension and the collateral vessel function. We suppose that SAD is not a yes or no phenomenon; it should take months or years to slowly progress in the vascular tree. The quantitative evaluation of SAD is an open question, for which we lack standardized angiographic systems, and we rely on peripheral perfusion tests such as transcutaneous oxygen tension and toe pressure. In case of doubts, stop the procedure and wait days or weeks for the clinical response to big artery disease treatment, looking at wound evolution and tissue perfusion indexes. Go BTA only with clear clinical indications and angiographic targets.

"No-Option" Patients with CLTI

Not every patient with CLTI can be revascularized due to vascular and clinical factors. The fate of these no-option patients with CLTI is poor,

with rates of limb loss up to 46% at 1 year (106–111). Moreover, these patients suffer from a low quality of life and higher rates of mortality in comparison to other patients with CLTI (106, 110).

Kim et al. proposed a new classification of no-option patients with CLTI in five types: type I—severe and pedal occlusive disease (desert foot anatomy) for which there is no accepted method of repair; type II—lack of suitable venous conduit for bypass in the setting of an acceptable target for bypass; type III—extensive tissue loss with exposure of vital structures that renders salvage impossible; type IV—advanced medical comorbidities for which available revascularization options would pose a prohibitive risk; and type V—presence of a nonfunctional limb (106).

Type I no-option patients are characterized by the desert foot anatomy, which is the final expression of SAD-MAC. Their prevalence in patients with CLTI varies from 20% to 45% and is associated with aging, diabetes, and ESRD (110). In these patients, alternative therapies should be considered such as primary major amputation, palliative care, or foot vein arterialization (FVA). FVA was proposed as the last attempt, obtaining a limb salvage rate between 55% and 75% at 1 year, with very with few complications.

In recent years, following the evolution of the therapy toward less invasive approaches, some authors proposed totally percutaneous techniques of FVA, describing positive single center case series, treated with off-label devices (111–113). These are quite complex and difficult maneuvers, whose reproducibility is as yet unknown.

The main attempt in developing a totally percutaneous deep vein arterialization was realized by the LimFlow company through a series of dedicated tools designed to perform an arteriovenous fistula at the tibial artery level, diverting blood flow to the deep venous plantar system through dedicated covered stents. The preliminary studies showed >96% technical success rate and 70% amputation-free survival at 1 year and multicentric studies are ongoing. In the near future, FVA could be proposed as a standard procedure in no-option patients with CLTI, before proceeding with a major amputation (114–117).

Conclusion

The management of a CLTI patient is exceedingly challenging. Interventionalists are armed with a host of medical, open surgical, and endovascular tools to treat this complex disease process. The decision between open and endovascular therapy delivery is nuanced, and even in the best interventionalists hands, avoiding major amputation and cardiovascular morbidity remains a challenge. Continued developments and advancements may provide new options for the treatment of CLTI, in the hopes of achieving effective and durable therapies for patients.

22

Venous Disease Management in the Limb Salvage Patient: Diagnostics, Compression, and Ablation

Bianca Cutler, Nikita Patel, and Misaki Kiguchi

Introduction

Chronic venous disease (CVD) of the lower extremities encompasses a wide range of disease pathologies. Venous hypertension generally occurs as a result of either a structural or obstructive pathophysiology, or a combination of both. Structural obstruction of venous outflow is seen in various disease states including May-Thurner's, deep vein thrombosis (DVT), and retroperitoneal fibrosis, whereas CVD related to functional reflux occurs due to a dysfunction of vein valves. Healthy veins carry blood towards the heart, and competent valves prevent retrograde venous flow. However, the failure of vein valves to close appropriately allows backflow (e.g., reflux) of blood, preventing the reduction in venous pressure that normally occurs with walking or exercising. This reflux of venous blood ultimately results in venous hypertension [1] (Fig. 22.1). Excessive venous hypertension can produce a wide distribution of symptoms described by the CEAP classification, ranging from asymptomatic to clinical findings of edema, skin changes, or venous ulcers to the legs [2].

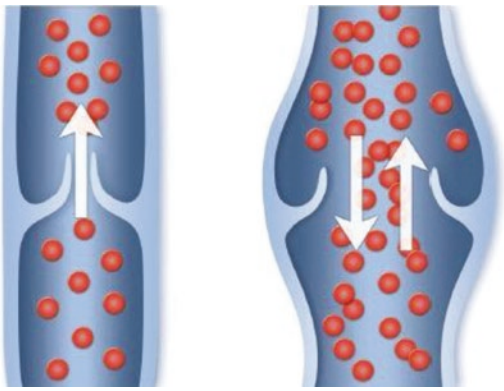


Fig. 22.1 Valves in a normal vein and diseased vein. (Reprinted with permission from Medtronic, Inc.)

The progression and sequelae of venous insufficiency in the setting of chronic venous disease contributes significantly to the economic healthcare burden and negatively impacts patient quality of life [3]. Fortunately, the emergence of minimally invasive, safe, and effective office-based treatments has significantly improved outcomes in chronic venous disease progression and has largely improved patient satisfaction.

B. Cutler · M. Kiguchi (✉)
Department of Vascular Surgery, MedStar Washington Hospital Center, Washington, DC, USA
e-mail: Misaki.M.Kiguchi@medstar.net

N. Patel
Piedmont Heart Institute, Division of Vascular Surgery, Piedmont Atlanta Hospital, Atlanta, GA, USA

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_22

Anatomy

The lower extremity venous system is divided into three major components: the superficial, deep, and perforating systems. The superficial leg veins are located between the dermis and muscle fascia, while the deep veins run just below the muscle fascia. The deep and superficial systems are connected by a network of perforating veins.

Superficial veins include major truncal veins: the great saphenous vein (GSV) and the small (lesser) saphenous vein (SSV), accessory veins (anterior and posterior), and any tributaries or branches that originate from the superficial venous system [4]. Excluding any anatomical variants, the GSV is a continuation of the dorsal venous arch in the foot, traveling anteriorly along the medial malleolus and ascending along the medial aspect of the leg. It drains into the deep system via the saphenofemoral junction (SFJ) and perforating veins. The SSV begins on the lateral aspect of the foot and travels posteriorly along the back of the calf, ultimately draining into the popliteal vein at the saphenopopliteal junction (SPJ). Anatomical variants include draining into a posterior medial tributary of the GSV, femoral vein or a vein of Giacomini [5] (Fig. 22.2).

Deep veins include the iliac, femoral, profunda, popliteal, peroneal (fibular), soleal, tibial, and plantar (foot) veins. These veins course from the foot to the upper thigh. Approximately 85% of the total lower extremity blood volume is transported via the deep venous system [4].

Perforating veins are bridging channels that link the superficial and deep venous systems through the fascia (Fig. 22.3). Competent perforator veins support unidirectional blood flow from the superficial to the deep system. They are

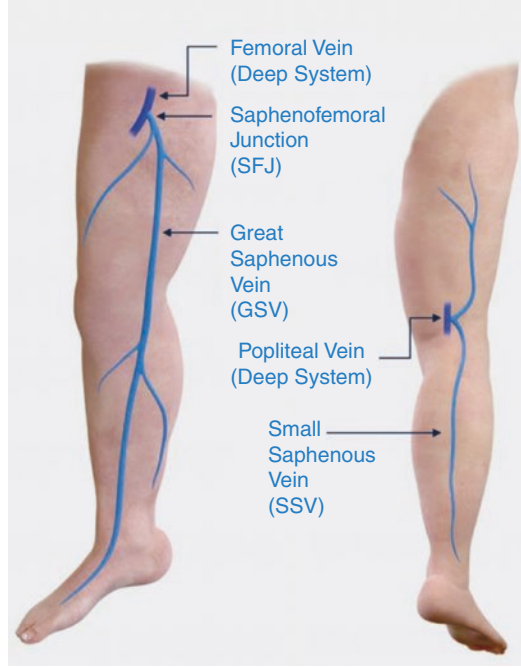


Fig. 22.2 Superficial venous anatomy. (Reprinted with permission from Medtronic, Inc.)

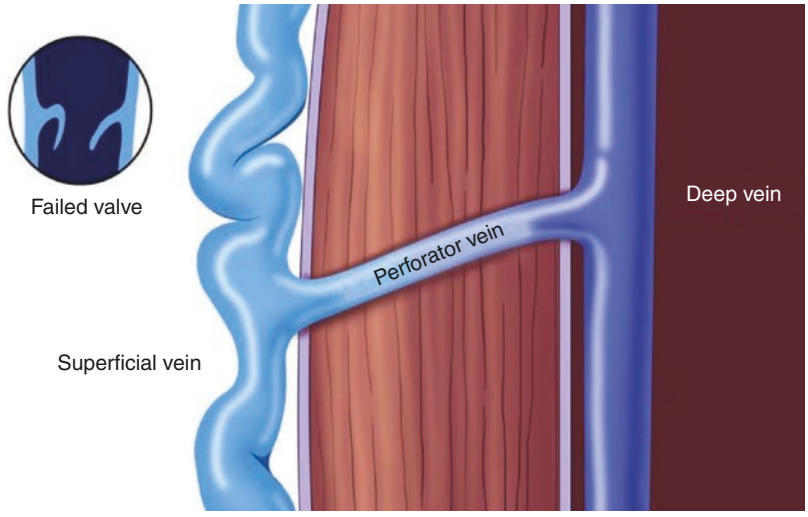


Fig. 22.3 Perforator veins. (Reprinted with permission from Medtronic, Inc.)

integral in equilibrating blood flow during calf-muscle contraction (walking) by facilitating venous outflow from superficial veins as the deep system pressure drops. However, it is important to note that perforators may have physiologic bidirectional capabilities depending on the phase of the calf-pump activity, and thus "reflux" of the perforator veins alone is not considered a cause for venous hypertension [5]. There are approximately 60 perforating veins in a lower extremity, excluding anatomical variants [6]. However, there are four clinically important perforator groups that have been identified, grouped by distribution: upper thigh (Hunterian), lower thigh (Dodd's), at knee level (Boyd's), and in the calf region (Cockett's) [5].

Normal Venous Valves

Venous valves are integral in maintaining unidirectional venous circulation against gravity and intra-abdominal pressure [7]. Normal venous valves are bicuspid and promote blood flow from peripheral superficial veins to the central deep veins, preventing pathologic reflux [5]. These valves are more frequent in distal veins, located the farthest from central venous circulation. There are approximately 10–20 valves in the GSV and 10–12 valves in the SSV [8].

Valves in the deep system vary in number and location as well; both the tibial and the peroneal veins have numerous valves, spaced apart at approximately 2 cm intervals. Most popliteal veins have one to two valves. The femoral veins may contain an average of five valves across the mid and distal femoral veins, though there are generally one or no valves in the common femoral vein above the level of the saphenofemoral junction. The inferior vena cava and the external iliac veins may be absent of valves altogether [9, 10]. Thus, the deep system relies heavily on adequate use of the calf-pump muscle contraction that occurs with walking to promote venous return.

Perforating veins have been shown to have between one to three venous valves [9]. Dysfunction of these critically important valves in any component of the lower extremity veins causes retrograde flow, ultimately resulting in chronic venous insufficiency.

Pathophysiology

The etiology of valvular incompetence resulting in venous hypertension is generally classified as either venous reflux or venous obstruction, or a combination of both derangements [4]. Venous disease from reflux results from progressive venous remodeling due to persistent hemodynamic stress. Obstructive incompetence occurs due to valve damage and limited venous recanalization after deep venous thrombosis or due to extrinsic compression [5]. Mechanical contributions to venous hypertension include the failure of an effective calf muscle pump, thus limiting effective venous return [11].

Inflammatory changes to the venous vessel wall are thought to be largely involved in the development and progression of venous reflux and related valve incompetence. There is evidence to suggest that inflammatory changes precede the development of observable valvular incompetence and varicose veins [5]. Low shear stress within the vein as a result of vein dilation and venous reflux can promote release of inflammatory markers, increased collagen, and decreased elastin content. The resulting chronic inflammation ultimately progresses to the clinical manifestations of chronic venous insufficiency (CVI) [4].

Deep system valvular venous disease has multiple etiologies, the most common of which (approximately 30%) is primary valvular incompetence. Deep venous reflux may also occur due to post-thrombotic injury after DVT, extramural compression (most commonly left common iliac vein compression by the right common iliac artery, e.g., May-Thurner's syndrome), and more rarely, congenital valve agenesis or hypoplasia [12–14].

Regardless of a reflux-related or obstructive pathology, the resulting inflammation and dysfunction of vein walls and valves within both the

superficial and deep venous systems cause chronic venous hypertension and dilation, resulting in a repeating cycle of pathologies that potentiate one another (abnormal venous flow, increased local venous pressure, damaged venous valves, and continued inflammatory response to the venous endothelial cells), ultimately contributing to CVD progression [15].

Epidemiology

CVD is a common condition, although its overall reported prevalence is difficult to capture as the disease clearly remains underdiagnosed. The European Society of Vascular Surgery estimates the prevalence of CVD in the adult population to be as high as 60%, particularly among populations in developed countries [16]. There is great variability depending on the study population and demographics, and the condition itself is thought to be largely underreported due to variability of symptoms. To better detect and stratify an accurate diagnosis, venous disease is stratified according to severity using the CEAP classification system, which is recommended for clinical practice. The CEAP classification was introduced in 1994 by the American Venous Forum (AVF) (later revised in 2020). The classification is based on clinical signs of venous disease (C), etiology (E), anatomy (A), and the underlying pathophysiology (P) (Fig. 22.4) [17].

The linchpin of appropriate diagnosis and subsequent management of CVD is establishing the accurate clinical class of the disease. Clinical class describes the full spectrum of venous disorders, ranging from no physical signs of venous disease to venous ulceration, which represents the most severe form of venous disease. The clinical classification stratifications are as follows: no signs of visible or palpable venous disease (C0), telangiectasia or reticular veins (C1), varicose veins (C2), edema (C3), skin changes, including hyperpigmentation or eczema (C4a), lipodermatosclerosis, atrophie blanche (C4b) or corona phlebectatica (C4c), presence of healed ulceration (C5), or presence of active ulceration (C6). The presence or absence of symptoms is documented as S (symptomatic) or A (asymptomatic). Etiology is either congenital (Ec), primary (Ep), secondary (Es), or no cause identified (En). Anatomic classification refers to the superficial system (As), perforator involvement (Ap), deep system (Ad), or no location identified (An). Pathophysiology is classified under reflux (Pr), obstruction (Po), or both [16].

With standardized clinical reporting (using the C of the CEAP scale), it is possible to provide more accurate reports of disease prevalence for each clinical class, as well as progression rates though clinical classes over time and the relation-

C class	Description
C_0	No visible or palpable signs of venous disease
C_1	Telangiectasias or reticular veins
C_2	Varicose veins
C_{2r}	Recurrent varicose veins
C_3	Edema
C_4	Changes in skin and subcutaneous tissue secondary to CVD
C_{4a}	Pigmentation or eczema
C_{4b}	Corona phlebectatica
C_{4c}	Lipodermatosclerosis or atrophie blanche
C_5	Healed
C_6	Active venous ulcer
	Recurrent active venous ulcer

CVD, Chronic venuous disease.
Each clinical class subcharacterized by a subscript indicating the presence (symptomatic, *s*) or absence (asymptomatic, *a*) of symptoms attributable to venous disease.

Fig. 22.4 CEAP classification system. (Reprinted with permission from the Journal of Vascular Surgery: Venous and Lymphatic Disorders. License Number 502659091955 [18])

ship to risk factors, which impacts the development of CVD. The European Society for Vascular Surgery published the most recent and comprehensive data in 2015 from updated epidemiologic studies: telangiectasia and spider veins (C1) have been reported to affect up to 80% of the population. Varicose veins (C2) are common, with a variable reported incidence ranging from 20% to 64%. C3-C6 affects approximately 5% of the population, with the prevalence of severe symptoms (C5-6) estimated at approximately 1–2% [16].

Causes and Risk Factors

While the development of primary CVI of the superficial or deep venous system can be idiopathic, there are many known risk factors that contribute to its progression.

Obstructive disease affecting the deep system is generally due to the aforementioned post-thrombotic disease and/or extramural compression of the iliac vein. After development of DVT, spontaneous lysis occurs in the acute period, while venous recanalization occurs over months to years after sustaining the thrombus [19]. Although the extent of recanalization depends on a myriad of factors (including extent of original thrombus, location, inflammation and inflammatory mediators), the process itself generates relative obstruction and reflux in the deep and superficial systems. Incomplete recanalization may lead to outflow obstruction, further potentiating venous hypertension [20].

Primary valvular incompetence that occurs in the superficial system is thought to be due to a variety of factors. The European Society for Vascular Surgery's 2015 updated clinical practice guidelines report older age as the most important risk factor for both symptomatic and asymptomatic varicose veins and CVI [16]. Historically, gender was thought to be a significant risk factor, although more recent studies demonstrate inconclusive gender influence. While several studies have highlighted that women have a higher risk for development of varicose veins (approximately 2–3 times higher risk) than men, a similar prevalence of varicose veins has been documented among both men and women who have not been pregnant, which suggests that pregnancy is an influential risk factor in development of C2 disease [21]. However, existing literature remains conflicted in gender influence: the notable Edinburg Vein study reports that C2 disease may be even more common among male subjects in the general population. While there is no obvious gender influence concerning development of venous disease, the gender influence diminishes with age [16].

Obesity is known to have a damaging effect on venous return. A body mass index greater than 25 kg/m^2 significantly increases the risk for CVI. Excess weight, particularly around the abdominal area, increases intra-abdominal pressure and thus alters the hemodynamics of the lower extremity veins that are already under stress to counteract gravity [22]. Additionally, a positive family history also increases the prevalence of CVI among individuals. Many studies have revealed a correlation between positive family history and the risk of developing venous disease; however, a responsible specific genetic disturbance has not been identified to explain the heredity [16].

Ethnicity is thought to play a role in CVI, but most studies are based on figures from developed countries in the western world. More studies are needed to evaluate evidence from other geographical locations. Existing data reveals prevalence of C1-C6 disease in all demographics, with unequal distributions of C5-C6 by region [16]. Some recent studies on the impact of race on CVI demonstrate that African-American patients present with more advanced venous disease at a younger age, compared to Caucasians [23]. In addition, lower socioeconomic status portended to a more advanced venous disease presentation, reflecting a possible delay in diagnosis and intervention [24]. Other risk factors for CVI include damage to the deep veins (secondary to DVT or trauma), and poor function of the calf muscle pump through inactivity, immobility, or abnormal gait [1]. Thus, lifestyles or careers that include prolonged periods of standing or sitting, with limited use of the calf-muscle pump, increase the risk for vein damage.

Clinical Presentation of Venous Hypertension

The clinical presentation of CVI and resulting CVD runs the gamut from asymptomatic to lifestyle-limiting subjective symptoms. While objective manifestations of CVD are encompassed in the CEAP classification system, the subjective symptoms often correlate to disease severity.

CEAP C0-C2 patients may often be asymptomatic. Symptom presentation becomes prevalent in CEAP C1-C2 with spider veins, telangiectasias, and development of small varicosities <3 mm [4]. Varicosities are manifestations of CVD, defined as dilated subcutaneous veins (arising from superficial veins: GSV, SSV, or tributaries) measuring >3 mm in the upright position. While often a result of primary venous disease, varicosities can also manifest due to secondary causes including venous obstruction, previous DVT, superficial thrombophlebitis, or arteriovenous fistula [17]. Varicosities may be tender or nontender.

Subjectively, patients with CVI at the CEAP C3 score often report lower extremity heaviness, achiness, fatigue, and edema that is progressive throughout the day or with prolonged leg exertion, with improvement of symptoms with leg elevation [16]. There is a tendency for these patients to report pruritus, pain, and/or nocturnal leg cramps. As venous disease progresses to the CEAP C4 level, the increased truncal vein diameter in conjunction with erythrocyte extravasation and dermal hemosiderin deposition result in hyperpigmentation [4]. These trophic skin changes are generally seen in the gaiter distribution of the lower leg, defined as the circumferential region between the medial malleolus and upper part of the calf [7]. Severe CEAP C4 manifestations include lipodermatosclerosis, atrophie blanche, and stasis dermatitis, often presenting as erythema, fibrosis, and induration. Patients often describe symptoms of pruritus and pain to the affected area [4].

CEAP C6 patients may present with a combination of any of the subjective and objective findings from previous CEAP classifications; however, criteria for this category is presence of an ulceration. CEAP C5 classification is reserved for those with successful healing of venous ulcers; however, the patient may continue to have subjective symptoms consistent with CVI/CVD [4].

Diagnostic Workup

The Society of Vascular Surgery (SVS) guidelines recommend a comprehensive workup of venous disease including a thorough review of HPI and clinical exam, in combination with noninvasive diagnostic imaging techniques. Symptoms that suggest CVD may include throbbing, heaviness, edema, fatigue, restlessness of the lower extremities, often exacerbated with standing and sitting for prolonged periods of time and relieved with elevation. Venous claudication symptoms occur in both primary and secondary venous diseases. Pertinent medical history includes a review of DVT or thrombophlebitis history, self or family history of thrombophilia and hypercoagulable disorders, tobacco or hormone use (including pregnancy), and family history of venous diseases. Physical exam should be comprehensive for varicosities, discoloration (including atrophie blanche, lipodermatosclerosis, pigmentation), edema, telangiectasias, ulcer (active or healed), and ankle mobility. Pedal pulses and sensory/motor function of the leg and foot should be evaluated to rule out any arterial insufficiency and neuropathy etiologies, respectively. The patient should also be evaluated for compressive abdominal masses or lymphadenopathy for consideration of extrinsic venous compression.

The SVS recommends using the CEAP classification system to evaluate CVD severity on clinical exam. If CVD is suspected, a duplex scan should be completed. Venous duplex is the gold standard, first-line diagnostic imaging test to evaluate for valvular incompetence and obstructive disease, with or without the presence of acute venous thrombosis. A comprehensive duplex scan includes visibility, compressibility, venous flow, and augmentation of the venous vessels. The SVS defines venous reflux in the superficial system veins as >500 ms, which aligns with previous international consensus recommendations of 0.5 s as a cutoff value for lower extremity vein incompetence. The iliac, femoral, and popliteal veins of the deep system cutoff are slightly longer at 1 s. Perforating veins have previously suggested cutoff values of 350 and 500 ms, and thus, perforator vein diameter is included in defining pathologic reflux. The SVS and AVF Guideline Committee defines pathologic perforating veins as those with an outward flow of ≥500 ms, with a diameter of ≥3.5 mm, with presence of a current or previous ulceration (CEAP class C5-C6).

CT venography is recommended for patients in which deep venous obstruction, iliac vein compression, or post-thrombotic syndrome is suspected, as well as for patients planning to undergo endovenous or surgical treatment of deep system veins [17].

Economic Burden and Quality of Life

Although a condition of low mortality, venous insufficiency and its complications significantly impact patient quality of life and the overall economic healthcare burden. Varicose veins affect up to 40% of the population, with up to 4% of patients older than 65 suffering from venous ulcers [26]. It is estimated that the direct medical cost of CVD may exceed over $1 billion annually in the United States [17]. A systematic review published in the *European Journal of Endovascular Surgery* suggests that venous ulcers alone contribute to 2% of the total healthcare budget in developed countries [26]. This figure is expected to increase with the rising population of older adults and the growing prevalence of obesity [27]. Symptomatic varicosities alone can be a source of chronic pain, discomfort, loss of working days, disability, and decreased quality of life. Infrequently, severe CVD can lead to loss of limb or life [17]. An increased awareness among healthcare providers of venous disease, early detection, lifestyle coaching, and prompt referral to vein specialists will aid in preventing the progression of venous disease and curb treatment expenditure [27].

Recognizing the quality of life burden of severe venous insufficiency and disease, numerous standardized outcomes of patient reported quality of life measures are used to quantify the degree of venous disease disability. The Venous Clinical Severity Score (VCSS), for example, is a scoring tool that standardizes the clinical assessment of venous-specific disease severity. The tool uses ten gradable symptom categories that may change in response to treatment, rendering the VCSS an ideal instrument for longitudinal surveillance and evaluation of venous disease. The ten clinical descriptors include: pain, varicose veins, venous edema, skin pigmentation, inflammation, induration, number of active ulcers, duration of active ulcers, ulcer size, and compression use. Each category is scored from 0 to 3 with a total possible score of 30 (Fig. 22.5). With the introduction of the VCSS and other venous disease specific quality of life measures, both venous clinical severity and its impact on quality of life can be quantified, allowing for an outcomes evaluation that cannot be captured by a CEAP score alone. The venous disease specific quality of life measures are being increasingly studied and used in the clinical setting [28].

Clinical descriptor	Absent (0)	Mild (1)	Moderate (2)	Severe (3)
Pain	None	Occasional	Daily not limiting	Daily limiting
Varicose veins	None	Few	Calf or thigh	Calf and thigh
Venous oedema	None	Foot and ankle	Below knee	Knee and above
Skin pigmentation	None	Limited perimalleolar	Diffuse lower 1/3 calf	Wider above lower 1/3 calf
Inflammation	None	Limited perimalleolar	Diffuse lower 1/3 calf	Wider above lower 1/3 calf
Induration	None	Limited perimalleolar	Diffuse lower 1/3 calf	Wider above lower 1/3 calf
Number of active ulcers	None	1	2	≥ 3
Ulcer duration	None	< 3 month	3-12 month	> 1 year
Active ulcer size	None	< 2 cm	2-6 cm	> 6 cm
Compression therapy	None	Intermittent	Most days	Fully comply

Fig. 22.5 Venous Clinical Severity Score (VCSS) Tool. License Number: 5444480868116

Conservative Management

All treatment and management strategies for venous disease have a common aim of achieving reduced venous hydrostatic pressure. When supine, and not counteracting effects of gravity, lower extremity venous pressure is around 10–20 mmHg. Hydrostatic pressure changes dramatically during postural changes from supine to erect, as the body must now counteract an increased gravitational column. Thus, the lower extremity veins are subject to a pressure increase as high as 90–100 mmHg. In the absence of any functional venous pathology, utilization of the calf muscle pump of the leg can reduce hydrostatic pressure in the lower legs to as low as 22 mmHg, after an average of only 7–12 steps [29, 30].

Elevation

Leg elevation is recommended to mitigate venous stasis, provide symptomatic relief, reduce edema and inflammation, and promote ulceration healing in CVD patients. Leg elevation in patients with C3-C6 disease has been shown to reduce leg swelling and venous pressures [16, 31]. While there is no correlation between elevation and compression use regarding ulcer size reduction, elevation remains recommended for patients unable to tolerate compressive therapy alone. Some studies suggest that patients who elevate their legs throughout the day have reduced ulcer healing times [32, 33]. Additionally, elevation can help reduce lower extremity edema prior to donning compressive garments or bandages, allowing for easier application and compliance.

Compression Therapy

Compression therapy remains the gold standard in the conservative management of CVD and has been shown to improve the healing rate of ulcers. Compression modalities include elastic stockings, non-elastic bandages, non-elastic compression systems (self-adjusted Velcro devices), and intermittent pneumatic compression pumps

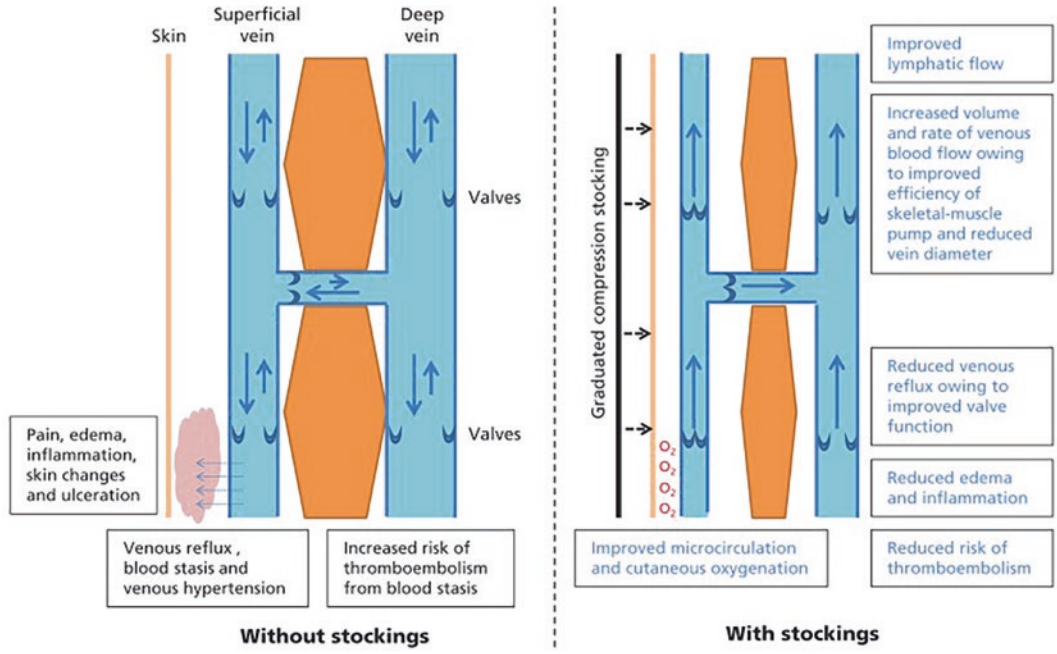


Fig. 22.6 Effect of compression on venous macrocirculation. (Reprinted with permission: http://creativecommons.org/licenses/by/4.0/ [34, 66])

(IPC). However, elastic graduated compression is the hallmark of conservative management for C0-C4 disease, which improves calf muscle pump function and thus reduces venous pressures and edema (Fig. 22.6) [16, 31]. Most importantly, the degree of compression must be medical-grade to be considered clinically significant in the treatment of venous hypertension. While further research is needed to evaluate the benefit of elastic compression directly on venous valve function, what is well established in the literature is the improvement in venous hemodynamics with compression use. Venous hemodynamics can be directly evaluated via air plethysmography (APG), which measures volume changes in the leg and calf-pump effectiveness with ambulation. The residual volume fraction (RVF), a direct reflection of ambulatory venous pressure, is significantly reduced in patients with CVI with the use of graduated elastic compression. APG has also demonstrated that compression garments exerting a higher pressure on the calf versus the ankle demonstrate a greater efficacy in increasing the venous ejection fraction from the leg [35–37]. The SVS and the AVF recommend a minimum pressure of 20–30 mmHg for C2 disease and above [17].

Compression stockings are the most common form of compression. The main disadvantage of stockings is that they produce less extrinsic pressure increases compared to compression bandages when standing up and walking and, therefore, are less effective with respect to their hemodynamic effects. However, compression stockings have been shown to be effective in reducing edema and pain versus no stockings and are thought to have anti-inflammatory properties [31]. Patients should be advised of the recommendation to replace compression stockings at 3–4 month intervals to promote optimal pressure and avoid overstretching the elastic compression gradient [16].

If elastic medical-grade compression socks (Fig. 22.7) cannot be tolerated due to difficulty donning or discomfort, non-elastic compression (such as bandages and adjustable Velcro bands) can be considered, although non-elastic compression is not as clinically effective as elastic compression systems. Compression bandages are multilayer and have been shown to promote the wound healing rates of ulcers when compared to standard wound care without the utilization of compressive therapy [16].

Common compression bandages include the Unna boot, Profor, Comprifore, and Coban. An important consideration with bandage compression is to avoid applying the dressing too loosely, which results in an ill-fitting, non-effective dressing.

Another non-elastic compression system consists of Velcro bands, which facilitate higher compression levels during ambulation, thus reducing venous stasis and edema. Compliance is improved with Velcro wraps due to ease of donning and can be easily adjusted as leg edema is reduced or loosened as discomfort occurs.

Adherence to treatment recommendations is particularly low in patients requiring long-term management. Compression therapy is essential to prevent the recurrence of ulcers, and the most benefit is derived from high-grade compression. The main concerns reported by patients include difficulties donning and doffing stockings, improper fitting bandages that are loose, and concerns for hygiene, as dressings are often worn for extended periods of time. Hence, the technical ability for patients to don and doff must be considered in compression treatment choice.

Significant peripheral arterial disease is a contraindication to compression therapy use, but unfortunately may be concomitant in many patients with venous ulcers or venous disease. Compression can compromise arterial perfusion to limbs, and it is recommended to limit compression use in patients with an ankle brachial index of less than 0.5 or if absolute ankle pressure is <60 mmHg [31].



Fig. 22.7 Medical grade compression. (Reprinted with permission: Lim CS, Davies AH. Graduated compression stockings. *CMAJ*. 2014;186(10):E391–E398. doi:10.1503/cmaj.131281 [38])

Treatment of Superficial Refluxing Veins

The era of open ligation and stripping of refluxing superficial saphenous veins has been replaced by more minimally invasive safe and effective endovenous closure techniques to decrease venous hypertension. These endovenous closure techniques can be done without general anesthesia and are often performed in the office. Although open ligation and stripping continues to be appropriate for superficial saphenous veins (>1 cm) from the skin, dilated >2.5 cm, etc., regular advancements in endovenous closure techniques have broadened indications for venous treatment.

Thermal Endovenous Closure

Either laser or radiofrequency can accomplish thermal closure of refluxing superficial veins. Both techniques require access to the vein under ultrasound guidance after local anesthetic is administered. With regard to the GSV, access is performed slightly below the knee to avoid thermal injury to the saphenous nerve in the distal calf. Similarly with the small saphenous vein, precautions should be taken to avoid the sural nerve. A microwire is used to gain access into the vein through the access needle. Once confirmed to be intraluminal by ultrasound, the catheter is introduced, often through a sheath, into the vein and advanced to a point of 2 cm away from the sapheno-femoral/popliteal junction. Tumescent anesthesia is then administered around the perivenous tissue, mitigating risks of thermal injury. Thermal energy is then initiated. For laser ablation, the fiber and sheath are withdrawn simultaneously and continuously, treating the entire length of the vein in a pull-back fashion. For radiofrequency ablation, the catheter treats a segment (3 or 7 cm) at a time. The heat causes irreversible cellular damage of the refluxing vein, collagen contraction, fibrosis, and ultimately, induces collapse of the vein.

With regard to endovenous laser ablation (EVLA), the treatment was first approved by the FDA in 2001, but as it gained popularity through its minimally invasive convenience, safety, and efficacy; its technology and procedural modifications to power, linear endovenous energy density, wavelength, and fiber type have resulted in improvements in treatment success. The International Endovenous Laser Working Group evaluated long-term outcomes of endovenous treatment. Failure rates were 7.7% at 1 year and 5.4% at 2 years [39].

Radiofrequency ablation (RFA) of refluxing superficial veins was introduced in the early 1990s (Fig. 22.8). The alternating electrical current emits heat due to its electrical resistance. The newest iterations can automatically adjust the power output to ensure consistent treatment throughout the treating section by maintaining a target temperature of 120 °C. Several studies have shown success rates >90% [40–42].

Not surprisingly, comparisons between RFA and high open ligation with stripping have demonstrated RFA to be less painful, require less time off work, and increase quality of life, without any difference in efficacy [41, 43, 44]. Across all modalities, including thermal and nonthermal endovenous closure, a meta-analysis demonstrated RFA and EVLA to consistently be more durable than sclerotherapy at 36 months to close refluxing saphenous veins [45]. A pivotal randomized control trial by Rasmussen et al. demonstrated low procedural failure at 1 year with RFA and EVLA compared to sclerotherapy [46]. Comparison studies between EVLA and RFA groups confirmed that post-procedural discomfort is higher in the EVLA group [40].

Mechanochemical Endovenous Closure (MOCA)

The need for tumescent anesthesia to mitigate periprocedural pain and thermal injury with RFA and EVLA techniques has catapulted nonthermal techniques for endovenous saphenous vein closure to the forefront of emerging techniques for treatment of chronic venous insufficiency since tumescent anesthesia prolongs procedural time and adds to patient discomfort. Furthermore, thermal tech-

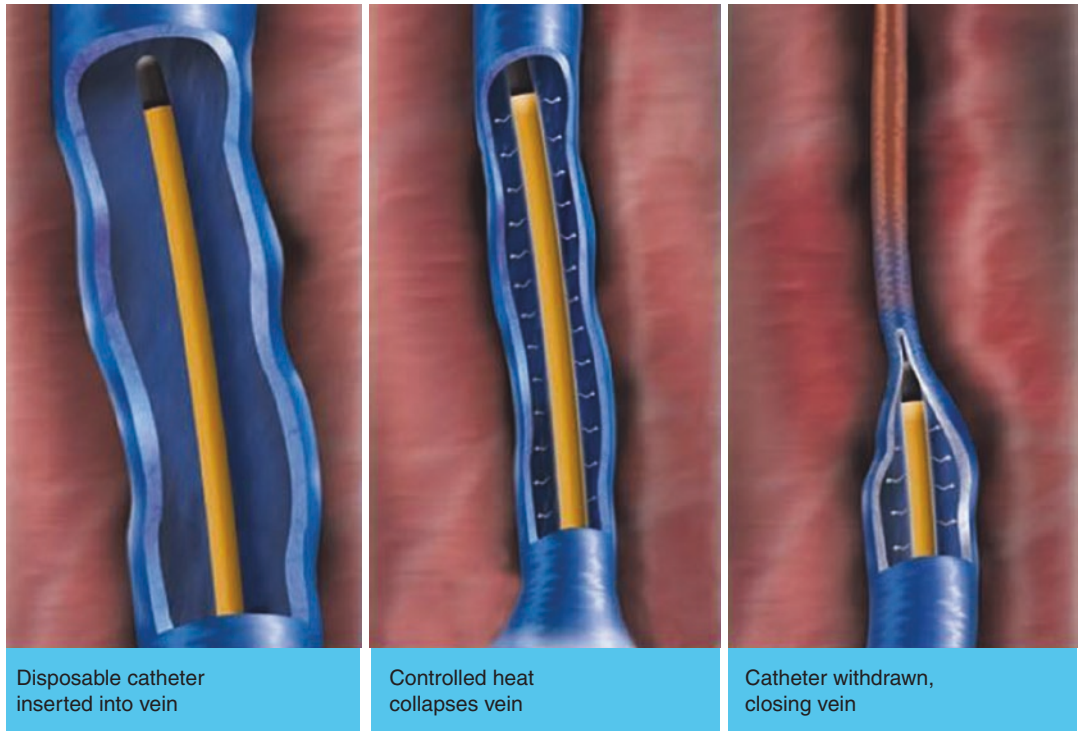


Fig. 22.8 RFA catheter. (Reprinted with permission from Medtronic, Inc.)

niques avoid treatment of reflux in the distal saphenous veins due to risk of thermal injury. MOCA, on the other hand, produces inflammatory changes to endothelial wall, fibrosis, and subsequent closure by utilizing mechanical injury with chemical irritation with typical sclerosant without the need for tumescent anesthesia and can treat the entire length of the saphenous vein. Furthermore, sclerosant tends to dissipate into the superficial varicosities of the vein being treated, maximizing treatment efficacy.

Access for MOCA treatment with a microneedle and microwire can be at the ankle. The MOCA device is introduced through the sheath to the saphenojunction, 1 cm away. The first 2–3 cm is treated with the mechanical ablation to induce vasospasm and closure of the junction to limit dispersion of sclerosant into the deep system. The delivery catheter is activated with the rotating mechanical tip to withdraw at a constant speed while delivering sclerosant.

MOCA, compared to thermal techniques, have lower long-term closure rates. Van Eekeren et al. published 1-year results of MOCA with 88.2% closure rate [47]. Despite consistent higher recanalization rates compared to thermal endovenous closure, MOCA can treat the entire length of the refluxing vein without risk of thermal nerve injury and does not require tumescent anesthesia, lending to a more favorable patient experience. The venous clinical severity score (VCSS) post-procedure also significantly improved, even at 1 year.

In a randomized trial comparing MOCA with RFA, the MOCA cohort experienced significantly less post-procedural pain compared to RFA, and thus, an earlier return to activity [48]. The Maradona trial compared MOCA with RFA. MOCA was reported to be less painful of a procedure than RFA with a faster improvement in venous clinical severity scores. However, more anatomic failures were reported with MOCA due to recanalization, but similar clinical success rates at 1 and 2 years between the two techniques [49]. The LAMA trial compared MOCA to EVLA. As predicted, the MOCA procedure was

a less painful procedure, though degree of post-procedural pain was similar between both groups [50, 51].

Adhesive Endovenous Closure

Given the efficacy and safety of cyanoacrylates in endovascular procedures for abdominal aortic aneurysms, arteriovenous malformations, and pelvic congestion syndrome, this chemical adhesive is delivered directly into the lumen of the refluxing vein to incite an inflammatory response and eventually leads to fibrosis. The access and delivery are similar to MOCA, and as it is non-thermal, the use of tumescent is not necessary and the entire length of the vein can be treated without risk of nerve injury.

A microwire is inserted into the access needle and confirmed to be intraluminal under ultrasound guidance. A 7Fr introducer sheath is placed into the vein over the microwire. The 7Fr delivery system is also introduced close to the saphenojunction. The delivery catheter, primed with glue, is inserted through the introducer sheath and is positioned 5 cm away from the saphenojunction. While putting pressure on the junction, the trigger of the dispensing gun is pulled to deliver the adhesive, squeezing once to deliver 0.10 mL of adhesive, pulling back 1 cm, and the trigger is squeezed again. Pressure is maintained at the junction for 3 min. The catheter is then pulled back 3 cm for another delivery of 0.10 mL of adhesive with manual compression above the catheter for 30 s. This pull back and adhesive delivery is continued until the entire length of the target vein is treated.

The first clinical trial of cyanoacrylate adhesive closure involved 38 patients. The complete occlusion rate immediately post-procedure was 100% and at 1 year, 92.1%. Using Kaplan-Meier life table analysis, the closure rate at 2 years was 92% [52]. A multicentered European study treated refluxing GSVs with cyanoacrylate adhesive. At 1 year, the complete venous closure rate was 92.9%. Venous Clinical Severity Score improved significantly with acceptable safety profile [53]. A more recent post-market evaluation of the cyanoacrylate adhesive closure system reported a 97.2% closure rate of the great saphenous vein at 1 year, compared to the nearly identical closure rate of 97% with RFA. Other trial studies using cyanoacrylate adhesive have also demonstrated similar closure efficacy without the need for post-procedural compression. Mean return to work time was significantly shorter for cyanoacrylate adhesive closure [54, 55]. Additionally, a randomized trial comparing adhesive to RFA showed treatment noninferiority in closure of incompetent GSV at 3 months post-procedure. At 3-months post-procedure, the closure rate for adhesive was 99% and RFA was 96% [56].

Post-procedural Care

For thermal and MOCA endothermal closure techniques, patients are discharged from the office with 20–30 mmHg compression stockings to wear continuously for approximately 48 h. Subsequently, patients are advised to wear daytime compression for at least 2 weeks. Patients are encouraged to walk immediately post-procedure and resume normal activities, including daily walking. Post-procedural ultrasounds should be scheduled within 7–14 days.

With cyanoacrylate adhesive closure, post-procedural compression is not required. Patients should continue to walk immediately post-procedurally and resume normal activities, including daily walking. Post-procedural ultrasounds should be scheduled within 7–14 days [17].

Complications

The advent of minimally invasive endovenous closure techniques has allowed for superficial vein treatments to be performed in the outpatient setting. Though generally safe and well-tolerated, superficial closure techniques carry inherent risks.

Endovenous thermal closure complications include post-procedural pain, bruising, hematoma, phlebitis, and adjacent skin burn/discoloration.

Post-procedural duplex ensures diagnosis of possible deep vein thrombosis or endothermal heat-induced thrombosis (EHIT) [57]. EHIT is unique to thermal closure techniques and is referred to a thrombus that propagates more proximally than the treated segment, towards the junction. Taking extra care in treating a safe distance from the saphenojunction, including distal to the superficial epigastric vein for GSV treatment, is imperative to prevent post-procedural thrombus propagation.

In recent years, efforts have been made to standardize a classification system and guidelines for treatment of EHIT. Given that an acute thrombus of an EHIT behaves differently than a de novo DVT, there is some controversy surrounding the treatment algorithm for this complication, and ongoing research is required for a consistent consensus on treatment approach. The AVF and SVS published updated EHIT grading and recommendation guidelines in 2020. The recommendations are summarized below [57] (Fig. 22.9).

Furthermore, unique to thermal closure is nerve injury. For RFA, focal paresthesias were noted in 12% of limbs in the first limb, improving over time. However, for below-knee GSV treated patients, the paresthesia rate was 7.7% at 5 years. Dermody et al. have showed a lower risk of nerve injury with RFA compared to EVLA (3.8% vs. 5.5%) [58]. Due to the proximity of the saphenous vein to the saphenous nerve below the knee, most physicians limit RFA treatment to the proximal third of the GSV below the knee and supply sufficient tumescent fluid to separate the vein from the nerve [58].

MOCA complications include hyperpigmentation, bruising, hematoma, and phlebitis. The incidence of phlebitis is reported to be lower than endothermal techniques [46]. The risk of paresthesia is rare with MOCA as the technique does not use heat. DVT and PE are also known complications to MOCA. Neurological side effects are unique to MOCA. The sclerosant may travel systemically and can potentially cause

Classification and Treatment of Endothermal Heat Induced Thrombosis

Recommendations from the American Venous Forum (AVF) and the Society for Vascular Surgery (SVS)

AVF EHIT CLASS	DEFINITION	TREATMENT RECOMMENDATION	STRENGTH OF RECOMMENDATION* AND LEVEL OF EVIDENCE**
I	Thrombus without propagation into deep vein a. Peripheral to superficial epigastric vein b. Central to superficial epigastric vein, up to and including the deep vein junction	No treatment or surveillance.	2C
II	Thrombus propagation into the adjacent deep vein, but comprising <50% of the deep vein lumen	No treatment, weekly surveillance until thrombus resolution. In high risk patients consider antiplatelet therapy vs. anticoagulation. Discontinue treatment following thrombus retraction or resolution	2C
III	Thrombus propagation into the adjacent deep vein but comprising >50% of the deep vein lumen	Therapeutic anticoagulation, weekly surveillance. Discontinue treatment following thrombus retraction or resolution	1B
IV	Occlusive deep vein thrombosis contiguous with the treated superficial vein	Treatment should be individualized, taking into account risks and benefits to patient. Reference may be made to CHEST guidelines for treatment of DVT.	1A

* 1=Strong, 2=Weak. ** A=High, B=Moderate, C= Low to very low

JVS-VL Journal of Vascular Surgery Venous and Lymphatic Disorders

Kabnick et al. *J Vasc Surg Venous Lymphat Disord, January 2021*

Copyright © 2021 by the Society for Vascular Surgery®

LinkedIn @TheJVascSurg @JVascSurg

Fig. 22.9 Classification and treatment of endothermal heat-induced thrombosis. License #: 5447820045253

cerebrovascular accidents or transient ischemic attacks [59].

Complications of endovenous adhesive closure include bruising and phlebitis. The phlebitis can sometimes be severe, requiring high dose NSAIDs, compression, and warm compress therapy. Care should also be taken to ensure there is no allergy to adhesive, or history of autoimmune disease, prior to treatment as the cyanoacrylate is considered an implant. Furthermore, endovenous glue-induced thrombus (EGIT) also can occur due to extension of thrombus into the deep system [60].

Treatment of Incompetent Perforator Veins

In addition to closure of refluxing superficial saphenous veins, incompetent perforator vein closure has contributed to decreasing venous hypertension, directly near wounds. The Linton procedure had severe wound complications and was largely replaced by subfascial endoscopic perforator vein surgery (SEPS) when introduced by Hauer in 1985 [61, 62]. SEPS became the procedure of choice due to fewer incisions farther away from the already compromised area around the ulcer. However, in recent years, thermal ablations and US-guided sclerotherapy of refluxing perforators for associated venous ulcers have become the mainstay.

Societal guidelines have recommended treatment of pathologic perforators near the ulcer with a diameter of >3.5 mm and with a reflux time of >0.5 s.

Percutaneous thermal ablation of incompetent perforators involves placing the laser or RFA stylet directly into the offending vein under ultrasound guidance. The directed heat damages the endothelium, collapsing and fibrosing the vein.

Under RFA, the stylet is directly placed into the vein 2 mm away from the deep system. Tumescent anesthesia is administered around the perivenous tissue. A spot-welding ablative technique is recommended, treating all four quadrants of the venous wall for 60 s each. The stylet is then withdrawn 3–5 mm and RF is performed in all four quadrants. This is repeated throughout the length of the perforator.

For laser, a 1470 nm, 400-mm laser fiber is placed through a micropuncture needle, directly into the vein, 2.0–3.0 mm away from the deep system. Perivenous tissue is infiltrated with tumescence. The vein is treated in a pulsed technique at 6 W with 50–100 J per 2 mm through the entire length of the perforator.

Ultrasound-guided sclerotherapy of perforator veins involves a 25-gauge butterfly needle accessing the perforator vein or a tributary off the perforator vein. Ultrasound-guided compression is applied to the junction of the deep vein and the perforator vein while the sclerosant is delivered.

Lawrence et al. reported on a large series of patients refractory to wound healing and eligible for perforator treatment. The study demonstrated a subgroup of patients that may benefit from perforator ablation. Forty-five patients underwent perforator ablation and healed in 71% of cases at a mean of 193 days [63].

Treatment of Deep Venous Obstruction

Patients with advanced venous disease presentation (e.g., CEAP C4-6) have a higher incidence of concomitant deep venous disease. The deep venous disease can either be reflux and/or obstruction. In symptomatic patients, both can occur simultaneously in up to 55% of patients [16]. Thus, to optimize treatment of venous hypertension, patients need to be evaluated and treated for both deep and superficial venous disease. Classification, based on signs and symptoms, can be either “reflux dominant” or

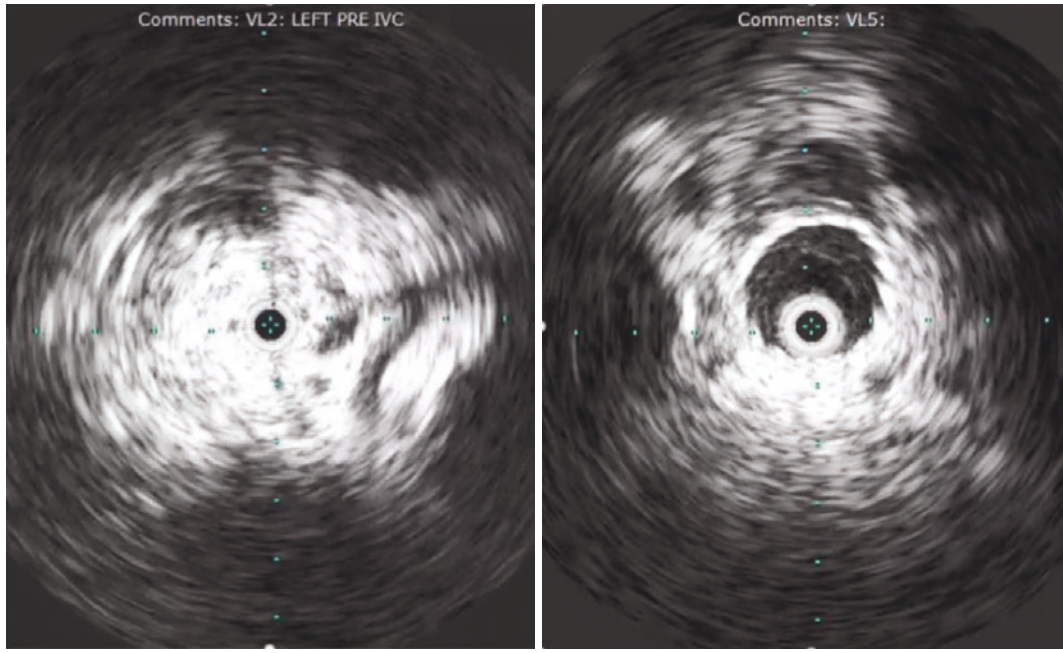


Fig. 22.10 Pre- and post-treatment IVUS of occluded iliac vein

"obstructive dominant." This separation can guide treatment options to maximize outcomes.

Deep venous thrombosis is the most common cause of venous outflow obstruction causing venous hypertension in the lower extremities. However, other structural abnormalities such as May-Thurner's and retroperitoneal fibrosis can also impede venous outflow as well. Although collateralization may occur to mitigate outflow obstruction, its compensation is often inadequate and can result in chronic venous hypertension.

Current endovascular techniques to recanalize the inferior vena cava and iliac vein obstruction to reduce venous hypertension in the lower extremities rely heavily on preoperative planning with CT venograms. Peri-procedurally, access is often antegrade and retrograde. Crossing total occlusion requires patience by the interventionalist and a myriad of different wires and supportive catheters. The use of intravascular ultrasound (IVUS) to diagnose and guide sizing of stents is critical for optimizing chances of success in maintaining venous outflow (Fig. 22.10).

Commercially available venous stents are self-expanding nitinol stents (Fig. 22.11). Each venous stent varies in design to offer a balance

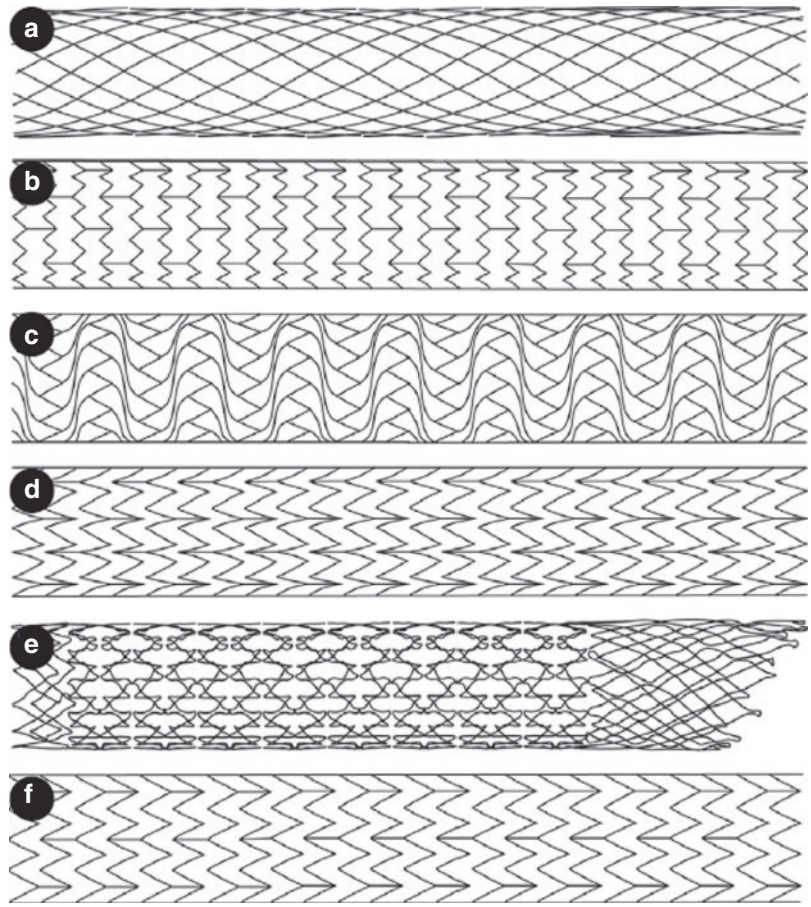


Fig. 22.11 Commercially available self-expanding venous stents. (**a**) Boston Scientific Wallstent Endoprosthesis. (**b**) Cook Zilver Vena Venous Stent. (**c**) Boston Scientific Vici Venous Stent. (**d**) Bard Venovo Venous Stent. (**e**) Optimed sinus-Obliquis Venous Stent. (**f**) Medtronic Abre Venous Stent [64]. (Reprinted with permission: License Number 5026661464274)

between radial force, flexibility, and deployment accuracy. Long-term clinical efficacy studies of the various stents are still under investigation.

Venous stenting, however, can be performed with low morbidity and mortality with acceptable patency rates. Furthermore, it results in major symptomatic relief in patients with CVD, including ulcer healing. Neglen et al. demonstrated a primary, assisted-primary, and secondary cumulative patency rates of 79%, 100%, and 100%, respectively, at 72-months after ileocaval stenting with significant decreases in venous clinical severity score [65]. In an additional study, sustained ulcer healing was achieved in 60% of all limbs after ileocaval stenting (Fig. 22.12) [66].

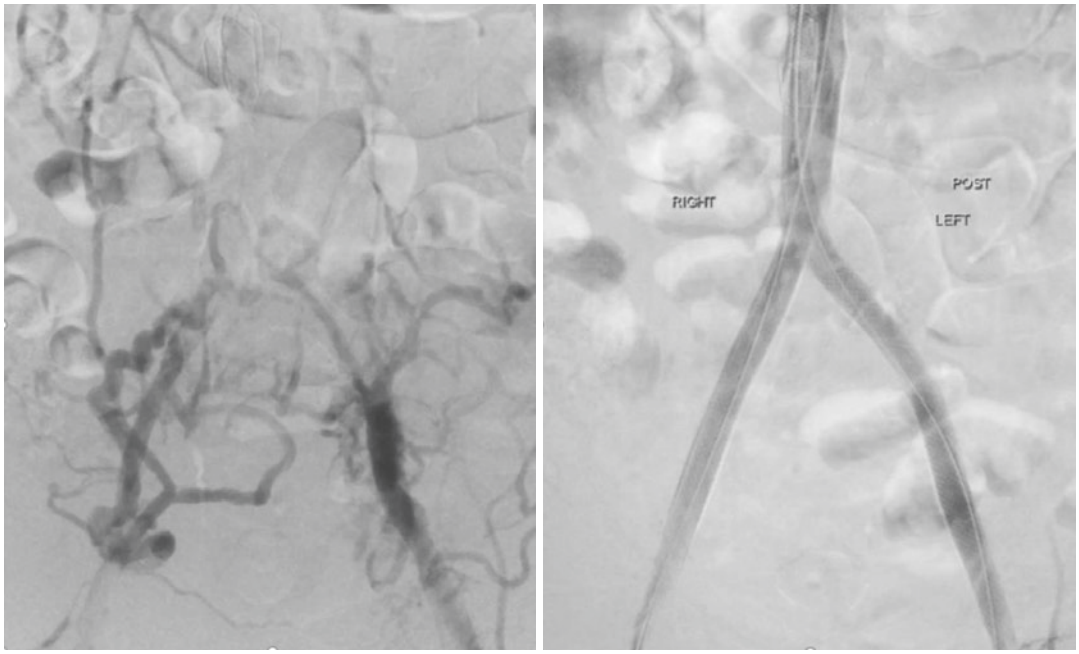


Fig. 22.12 Pre- and post-treatment venogram for ileocaval obstruction

Conclusion

Venous disease is an often under-recognized but treatable condition that significantly impacts patients' quality of life. Emerging minimally invasive techniques to address functional and structural venous disease have allowed increased access to treatments with significantly improved outcomes for patients suffering with venous hypertension, who otherwise would rely on compression and elevation therapy alone.

References

1. Spiridon M, Corduneanu D. Chronic venous insufficiency: a frequently underdiagnosed and undertreated pathology. Maedica (Bucur). 2017;12(1):59–61.
2. Launois R. Health-related quality-of-life scales specific for chronic venous disorders of the lower limbs. J Vasc Surg Venous Lymphat Disord. 2015;3(2):219–27.e1–3.
3. Davies AH. The seriousness of chronic venous disease: a review of real-world evidence. Adv Ther. 2019;36(Suppl 1):5–12.
4. Santler B, Goerge T. Chronic venous insufficiency—a review of pathophysiology, diagnosis, and treatment. J Dtsch Dermatol Ges. 2017;15(5):538–56.
5. Baliyan V, Tajmir S, Hedgire SS, Ganguli S, Prabhakar AM. Lower extremity venous reflux. Cardiovasc Diagn Ther. 2016;6(6):533–43.
6. Thomson H. The surgical anatomy of the superficial and perforating veins of the lower limb. Ann R Coll Surg Engl. 1979;61(3):198–205.
7. Youn YJ, Lee J. Chronic venous insufficiency and varicose veins of the lower extremities. Korean J Intern Med. 2019;34(2):269–83.
8. Kachlik D, Pechacek V, Baca V, Musil V. The superficial venous system of the lower extremity: new nomenclature. Phlebology. 2010;25(3):113–23.
9. Meissner MH. Lower extremity venous anatomy. Semin Intervent Radiol. 2005;22(3):147–56.
10. LePage PA, Villavicencio JL, Gomez ER, Sheridan MN, Rich NM. The valvular anatomy of the iliac venous system and its clinical implications. J Vasc Surg. 1991;14(5):678–83.
11. Bonkemeyer Millan S, Gan R, Townsend PE. Venous ulcers: diagnosis and treatment. Am Fam Physician. 2019;100(5):298–305.
12. Tassiopoulos AK, Golts E, Oh DS, Labropoulos N. Current concepts in chronic venous ulceration. Eur J Vasc Endovasc Surg. 2000;20(3):227–32.
13. Morano JU, Raju S. Chronic venous insufficiency: assessment with descending venography. Radiology. 1990;174(2):441–4.
14. Plate G, Brudin L, Eklof B, Jensen R, Ohlin P. Congenital vein valve aplasia. World J Surg. 1986;10(6):929–34.
15. Labropoulos N. How does chronic venous disease progress from the first symptoms to the advanced stages? A review. Adv Ther. 2019;36(Suppl 1):13–9.

16. Wittens C, Davies AH, Baekgaard N, Broholm R, Cavezzi A, Chastanet S, et al. Editor's choice—management of chronic venous disease: clinical practice guidelines of the European Society for Vascular Surgery (ESVS). Eur J Vasc Endovasc Surg. 2015;49(6):678–737.
17. Gloviczki P, Comerota AJ, Dalsing MC, Eklof BG, Gillespie DL, Gloviczki ML, et al. The care of patients with varicose veins and associated chronic venous diseases: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. J Vasc Surg. 2011;53(5 Suppl):2S–48S.
18. Lurie F, Passman M, Meisner M, Dalsing M, Masuda E, Welch H, et al. The 2020 update of the CEAP classification system and reporting standards. J Vasc Surg Venous Lymphat Disord. 2020;8(3):342–52.
19. Killewich LA, Bedford GR, Beach KW, Strandness DE Jr. Spontaneous lysis of deep venous thrombi: rate and outcome. J Vasc Surg. 1989;9(1):89–97.
20. Saha P, Humphries J, Modarai B, Mattock K, Waltham M, Evans CE, et al. Leukocytes and the natural history of deep vein thrombosis: current concepts and future directions. Arterioscler Thromb Vasc Biol. 2011;31(3):506–12.
21. Ismail L, Normahani P, Standfield NJ, Jaffer U. A systematic review and meta-analysis of the risk for development of varicose veins in women with a history of pregnancy. J Vasc Surg Venous Lymphat Disord. 2016;4(4):518–24 e1.
22. Willenberg T, Schumacher A, Amann-Vesti B, Jacomella V, Thalhammer C, Diehm N, et al. Impact of obesity on venous hemodynamics of the lower limbs. J Vasc Surg. 2010;52(3):664–8.
23. Dua A, Desai SS, Heller JA. The impact of race on advanced chronic venous insufficiency. Ann Vasc Surg. 2016;34:152–6.
24. Natour AK, Rteil A, Corcoran P, Weaver M, Ahsan S, Kabbani L. Socioeconomic status and clinical stage of patients presenting for treatment of chronic venous disease. Ann Vasc Surg. 2022;83:305–12.
25. Schleimer K, Barbati ME, Grommes J, Hoeft K, Toonder IM, Wittens CHA, et al. Update on diagnosis and treatment strategies in patients with post-thrombotic syndrome due to chronic venous obstruction and role of endovenous recanalization. J Vasc Surg Venous Lymphat Disord. 2019;7(4):592–600.
26. Tan MKH, Sutanto SA, Onida S, Davies AH. The relationship between vein diameters, clinical severity, and quality of life: a systematic review. Eur J Vasc Endovasc Surg. 2019;57(6):851–7.
27. Nicolaides AN, Labropoulos N. Burden and suffering in chronic venous disease. Adv Ther. 2019;36(Suppl 1):1–4.
28. Passman MA, McLafferty RB, Lentz MF, Nagre SB, Iafrati MD, Bohannon WT, et al. Validation of venous clinical severity score (VCSS) with other venous severity assessment tools from the American Venous Forum, National Venous Screening Program. J Vasc Surg. 2011;54(6 Suppl):2S–9S.
29. Raju S, Knight A, Lamanilao L, Pace N, Jones T. Peripheral venous hypertension in chronic venous disease. J Vasc Surg Venous Lymphat Disord. 2019;7(5):706–14.
30. Meissner MH, Moneta G, Burnand K, Gloviczki P, Lohr JM, Lurie F, et al. The hemodynamics and diagnosis of venous disease. J Vasc Surg. 2007;46 Suppl S:4S–24S.
31. Lurie F, Lal BK, Antignani PL, Blebea J, Bush R, Caprini J, et al. Compression therapy after invasive treatment of superficial veins of the lower extremities: clinical practice guidelines of the American Venous Forum, Society for Vascular Surgery, American College of Phlebology, Society for Vascular Medicine, and International Union of Phlebology. J Vasc Surg Venous Lymphat Disord. 2019;7(1):17–28.
32. Barnes M, Mani R, Barret D, White JE. Changes in skin microcirculation at periulcerous sites in patients with chronic venous ulcers during leg elevation. Phlebology. 1992;7(1):36–9.
33. Dix F, Reilly B, David M, Simon D, Dowding E, Ivers L, et al. Effect of leg elevation on healing, venous velocity and ambulatory venous pressure in venous ulceration. Phlebology. 2005;20(2):87–94.
34. Xie T, Ye J, Rerkasem K, Mani R. The venous ulcer continues to be a clinical challenge: an update. Burns Trauma. 2018;6:18.
35. Dezotti NRA, Dalio MB, Ribeiro MS, Piccinato CE, Joviliano EE. The clinical importance of air plethysmography in the assessment of chronic venous disease. J Vasc Bras. 2016;15(4):287–92.
36. Ibegbuna V, Delis KT, Nicolaides AN, Aina O. Effect of elastic compression stockings on venous hemodynamics during walking. J Vasc Surg. 2003;37(2):420–5.
37. Mosti G, Partsch H. Compression stockings with a negative pressure gradient have a more pronounced effect on venous pumping function than graduated elastic compression stockings. Eur J Vasc Endovasc Surg. 2011;42(2):261–6.
38. Lim CS, Davies AH. Graduated compression stockings. CMAJ. 2014;186(10):E391–8.
39. Spreafico G, Kabnick L, Berland TL, Cayne NS, Maldonado TS, Jacobowitz GS, et al. Laser saphenous ablations in more than 1,000 limbs with long-term duplex examination follow-up. Ann Vasc Surg. 2011;25(1):71–8.
40. Goode SD, Chowdhury A, Crockett M, Beech A, Simpson R, Richards T, et al. Laser and radiofrequency ablation study (LARA study): a randomised study comparing radiofrequency ablation and endovenous laser ablation (810 nm). Eur J Vasc Endovasc Surg. 2010;40(2):246–53.
41. Lurie F, Creton D, Eklof B, Kabnick LS, Kistner RL, Pichot O, et al. Prospective randomized study of endovenous radiofrequency obliteration (closure procedure) versus ligation and stripping in a selected patient population (EVOLVeS Study). J Vasc Surg. 2003;38(2):207–14.

42. Nordon IM, Hinchliffe RJ, Brar R, Moxey P, Black SA, Thompson MM, et al. A prospective double-blind randomized controlled trial of radiofrequency versus laser treatment of the great saphenous vein in patients with varicose veins. Ann Surg. 2011;254(6):876–81.
43. Subramonia S, Lees T. Radiofrequency ablation vs conventional surgery for varicose veins—a comparison of treatment costs in a randomised trial. Eur J Vasc Endovasc Surg. 2010;39(1):104–11.
44. Rautio T, Ohinmaa A, Perala J, Ohtonen P, Heikkinen T, Wiik H, et al. Endovenous obliteration versus conventional stripping operation in the treatment of primary varicose veins: a randomized controlled trial with comparison of the costs. J Vasc Surg. 2002;35(5):958–65.
45. Van Den Bos RR, Neumann M, De Roos KP, Nijsten T. Endovenous laser ablation-induced complications: review of the literature and new cases. Dermatol Surg. 2009;35(8):1206–14.
46. Rasmussen LH, Lawaetz M, Bjoern L, Vennits B, Blemings A, Eklof B. Randomized clinical trial comparing endovenous laser ablation, radiofrequency ablation, foam sclerotherapy and surgical stripping for great saphenous varicose veins. Br J Surg. 2011;98(8):1079–87.
47. van Eekeren RR, Boersma D, Holewijn S, Vahl A, de Vries JP, Zeebregts CJ, et al. Mechanochemical endovenous Ablation versus RADiOfrequeNcy Ablation in the treatment of primary great saphenous vein incompetence (MARADONA): study protocol for a randomized controlled trial. Trials. 2014;15:121.
48. van Eekeren RR, Boersma D, Konijn V, de Vries JP, Reijnen MM. Postoperative pain and early quality of life after radiofrequency ablation and mechanochemical endovenous ablation of incompetent great saphenous veins. J Vasc Surg. 2013;57(2):445–50.
49. Holewijn S, van Eekeren R, Vahl A, de Vries J, Reijnen M, group Ms. Two-year results of a multicenter randomized controlled trial comparing Mechanochemical endovenous Ablation to RADiOfrequeNcy Ablation in the treatment of primary great saphenous vein incompetence (MARADONA trial). J Vasc Surg Venous Lymphat Disord. 2019;7(3):364–74.
50. Leung CC, Carradice D, Wallace T, Chetter IC. Endovenous laser ablation versus mechanochemical ablation with ClariVein((R)) in the management of superficial venous insufficiency (LAMA trial): study protocol for a randomised controlled trial. Trials. 2016;17(1):421.
51. Mohamed AH, Leung C, Wallace T, Smith G, Carradice D, Chetter I. A randomized controlled trial of endovenous laser ablation versus mechanochemical ablation with ClariVein in the management of superficial venous incompetence (LAMA trial). Ann Surg. 2021;273(6):e188–95.
52. Almeida JI, Javier JJ, Mackay E, Bautista C, Proebstle TM. First human use of cyanoacrylate adhesive for treatment of saphenous vein incompetence. J Vasc Surg Venous Lymphat Disord. 2013;1(2):174–80.
53. Proebstle TM, Alm J, Dimitri S, Rasmussen L, Whiteley M, Lawson J, et al. The European multicenter cohort study on cyanoacrylate embolization of refluxing great saphenous veins. J Vasc Surg Venous Lymphat Disord. 2015;3(1):2–7.
54. Morrison N, Gibson K, Vasquez M, Weiss R, Cher D, Madsen M, et al. VeClose trial 12-month outcomes of cyanoacrylate closure versus radiofrequency ablation for incompetent great saphenous veins. J Vasc Surg Venous Lymphat Disord. 2017;5(3):321–30.
55. Gibson K, Ferris B. Cyanoacrylate closure of incompetent great, small and accessory saphenous veins without the use of post-procedure compression: initial outcomes of a post-market evaluation of the VenaSeal System (the WAVES Study). Vascular. 2017;25(2):149–56.
56. Morrison N, Gibson K, McEnroe S, Goldman M, King T, Weiss R, et al. Randomized trial comparing cyanoacrylate embolization and radiofrequency ablation for incompetent great saphenous veins (VeClose). J Vasc Surg. 2015;61(4):985–94.
57. Kabnick LS, Sadek M, Bjarnason H, Coleman DM, Dillavou ED, Hingorani AP, et al. Classification and treatment of endothermal heat-induced thrombosis: recommendations from the American Venous Forum and the Society for Vascular Surgery. J Vasc Surg Venous Lymphat Disord. 2021;9(1):6–22.
58. Dermody M, O'Donnell TF, Balk EM. Complications of endovenous ablation in randomized controlled trials. J Vasc Surg Venous Lymphat Disord. 2013;1(4):427–36 e1.
59. Ceulen RP, Sommer A, Vernooy K. Microembolism during foam sclerotherapy of varicose veins. N Engl J Med. 2008;358(14):1525–6.
60. Cho S, Gibson K, Lee SH, Kim SY, Joh JH. Incidence, classification, and risk factors of endovenous glue-induced thrombosis after cyanoacrylate closure of the incompetent saphenous vein. J Vasc Surg Venous Lymphat Disord. 2020;8(6):991–8.
61. Creager MA, Creager MA, Beckman JA, Loscalzo J, ScienceDirect. Vascular medicine: a companion to Braunwald's heart disease. 2nd ed. Philadelphia, PA: Elsevier/Saunders; 2013.
62. Bergan JJ, Murray J, Greason K. Subfascial endoscopic perforator vein surgery: a preliminary report. Ann Vasc Surg. 1996;10(3):211–9.
63. Lawrence PF, Alktaifi A, Rigberg D, DeRubertis B, Gelabert H, Jimenez JC. Endovenous ablation of incompetent perforating veins is effective treatment for recalcitrant venous ulcers. J Vasc Surg. 2011;54(3):737–42.
64. Shamimi-Noori SM, Clark TWI. Venous stents: current status and future directions. Tech Vasc Interv Radiol. 2018;21(2):113–6.
65. Neglen P, Hollis KC, Olivier J, Raju S. Stenting of the venous outflow in chronic venous disease: long-term stent-related outcome, clinical, and hemodynamic result. J Vasc Surg. 2007;46(5):979–90.
66. George R, Verma H, Ram B, Tripathi R. The effect of deep venous stenting on healing of lower limb venous ulcers. Eur J Vasc Endovasc Surg. 2014;48(3):330–6.

Science and Practicality of Tissue Products in Limb Salvage

23

Alexandra N. Verzella, Allyson R. Alfonso, and Ernest Chiu

Introduction

In 2017, the CDC estimated that the total direct and indirect expenditure on *diagnosed* diabetes in the USA was $327 billion, an increase of $56 billion dollars since 2012 [1]. Globally, the estimated cost in 2019 was 760 billion, and that is projected to reach 825 billion in 2030 [2]. The crude estimate of Americans with diabetes in 2018 was 34.1 million or 13.0%, and 7.3 million (21.4%) of whom were not aware of the diagnosis, with diabetic complications being the greatest contributor to healthcare expenditure in these patients [3, 4]. Some of these diabetes-related complications include kidney disease, ocular disease, death, and hospitalizations secondary to major cardiovascular disease, hyperglycemia, hypoglycemia, and diabetic ulcers. Foot ulcers develop in up to 34% of patients with diabetes, and failure of these ulcers to heal can lead to limb amputation [3, 4]. In fact, up to 5.6 out of 1000 adults with diabetes underwent a lower-extremity amputation for a total of 130,000 people in 2016 alone, underlining the importance of finding a way to better heal diabetic wounds and salvage limbs in these individuals [4].

Current Treatments

Diabetic wounds are precipitated by motor, sensory, and autonomic neuropathy. Motor deficits include atrophy of intrinsic muscles of the foot and dislocated metatarsophalangeal joints caused by unopposed power of the long flexors and extensors of the foot [5]. Sensory neuropathy decreases the protective ability to sense pain and impairs proprioception, causing balancing deficits. Autonomic system dysregulation then further contributes to the formation of diabetic foot ulcers through decreased sweat and oil gland secretions, which predisposes patients to cracks and fissures in the skin barrier [5].

According to guidelines from the American Diabetes Association, there are 6 vital components to the treatment algorithm for a diabetic wound which include: wound off-loading, surgical debridement of the wound early and often, maintenance of a moist wound bed, treatment of active infections, vascular assessment with correction of ischemia, and strict glycemic control [6–13]. Though there are a multitude of imperative components to healing a diabetic wound, the standard of care (SOC) for these wounds is limited to saline washes and vaseline gauze [14].

A. N. Verzella · A. R. Alfonso · E. Chiu (✉)
Hansjörg Wyss Department of Plastic Surgery, New York University Grossman School of Medicine, New York, NY, USA
e-mail: Alexandra.verzella@nyulangone.org; Allyson.alfonso@nyulangone.org; Ernest.chiu@nyulangone.org

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_23

In addition to the standard practices of care, the clinical practice guidelines published by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine also recommend negative pressure therapy, hyperbaric oxygen therapy, and biologics as adjunctive therapy for wounds recalcitrant to current SOC alone [15, 16]. However, before biologics like tissue products can be considered for use, the wound bed must be optimized through demonstrating adequate perfusion, debridement, and edema control.

Tissue Product Definition

In this chapter, tissue products are defined as anything that substitutes for skin and incorporates into the healing wound. The ideal tissue product for a diabetic foot ulcer should resist infection, prevent water loss, withstand the shearing forces endured by native skin, conform to irregular wound surfaces, lack significant antigenicity, and possess flexible thickness. It should also be cost-effective, widely available, easy to apply, durable and stable, and easy to store with a long shelf-life. Unfortunately, the ideal tissue product with all of these qualities does not currently exist.

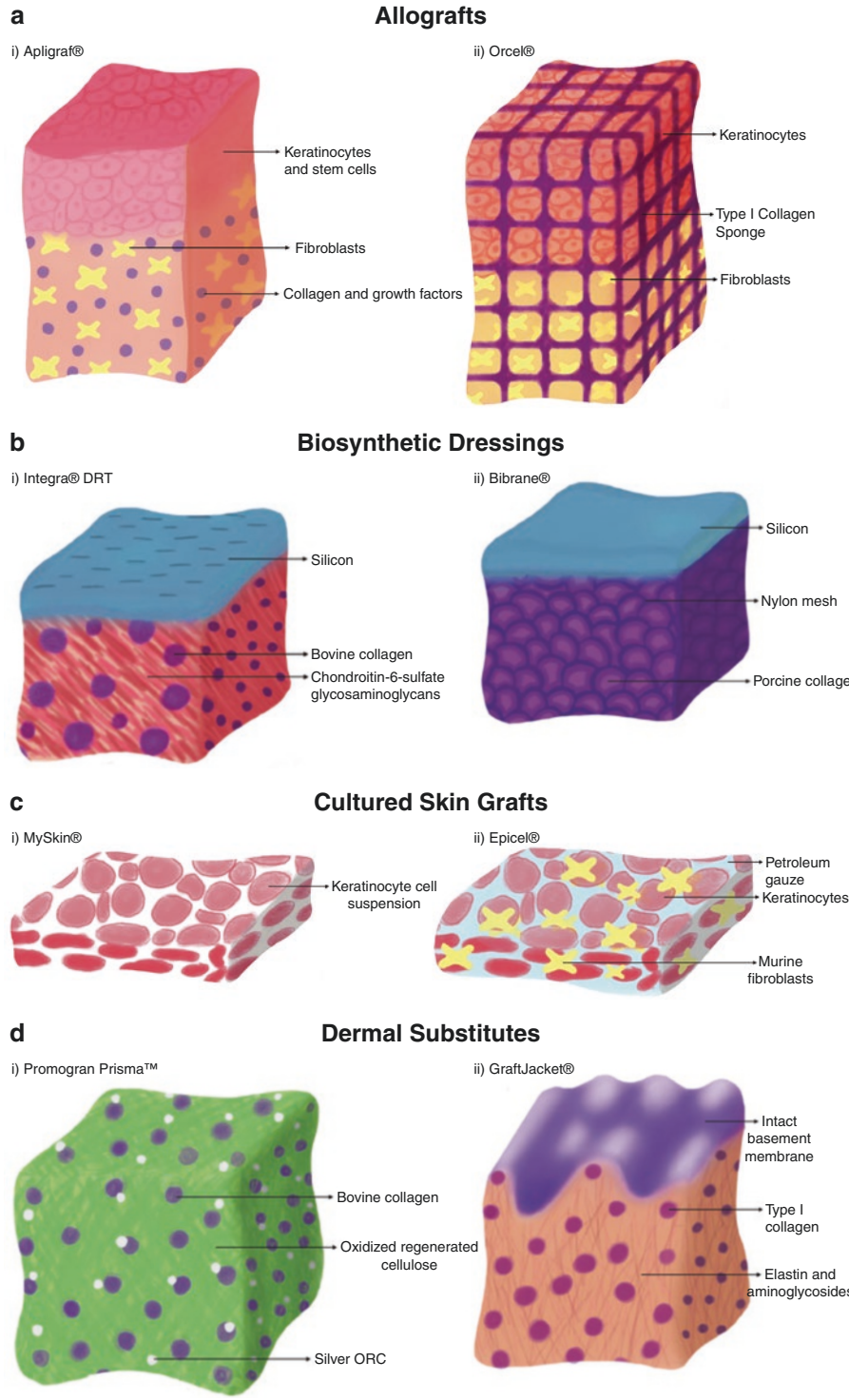
Several systems of classification for tissue products have been proposed such as Kumar's 3 classes that divide the products into temporary impervious dressing materials, single-layer durable substitutes, and composite skin substitutes or Dieckman et al.'s 2 classes of biomaterial or cellular products with allogenic, xenogenic, and autologous subcategories [17, 18]. Because there is a lack of consensus in these classification systems, in this chapter, biologic tissue products will be organized into their individual brand product and will be placed into 4 broader categories: (1) allografts/xenografts, (2) dermal substitutes, (3) biosynthetic dressings, and (4) cultured skin grafts. We will also highlight some of the currently commercially available products and do not endorse one over another.

Science and Practicality of Allografts and Xenografts

Allografts and xenografts are skin substitutes that are harvested from human and animal sources, respectively, that act as temporary skin grafts [19, 20].

Allografts can be either cellular or acellular and are exclusively derived from human sources, most commonly from neonatal foreskin. Cellular allografts contain living cells like fibroblasts and keratinocytes that encourage wound healing through secretion of growth factors and cytokines that promote the ingrowth of native host cells and neovascularization. Because these grafts retain non-autologous living cells, they can provoke an immunologic response in the host.

Apligraf® (Organogenesis, Inc., Canton, MA), previously called Graftskin, is a bilayer composite allograft that is indicated for full-thickness neuropathic diabetic foot ulcers that have been present for greater than 3 weeks and have not responded to SOC [21, 22] (Fig. 23.1a, Table 23.1). While Apligraf can be used in wounds that extend through the dermis, it is not indicated for diabetic ulcers that involve tendon, muscle, joint, or bone [22]. Its epidermal layer is comprised of living human neonatal foreskin-derived keratinocytes and stratum corneum, and its dermal layer contains bovine type I collagen and neonatal fibroblasts that produce growth factors and cytokines like VEGF, IL-6, and IL-8. These components function to activate host keratinocytes at the edge of the wound, regulate growth factors signals, provide a barrier against further wound damage and infection, control fibrosis and scar formation, and revitalize fibroblasts in the base of the wound—correcting ECM and matrix metalloproteinase balance. Because of the impact on fibrosis and scar formation, Apligraf also has reports of improved cosmesis and functional outcomes when used in chronic wounds [21, 23]. While Apligraf preserves many extracellular matrix (ECM) proteins and cytokines native to human skin, it does not contain Langerhans cells, melanocytes, macrophages, lymphocytes, blood vessels, or hair follicles [22]. In addition, Apligraf's allogenic cells are not able to survive long-term in



Adapted from Vig K, Chaudhari A, Tripathi S, et al. Advances in Skin Regeneration Using Tissue Engineering. *Int J Mol Sci.* 2017;18(4):789. Published 2017 Apr 7. doi:10.3390/ijms18040789

Fig. 23.1 Biologic skin substitutes. (**a**) Allografts: (i) Apligraf®, (ii) Orcel®. (**b**) Biosynthetic dressings: (i) Integra® DRT, (ii) Biobrane®. (**c**) Cultured skin grafts: (i) MySkin®, (ii) Epicel®. (**d**) Dermal substitutes: (i) Promogran Prisma™, (ii) GraftJacket®

Table 23.1 Biologic skin substitutes

	Manufacturer	Source	Intact cells	Application schedule	Shelf-life	Storage temperature	Difference over SOC	Indications
Allografts								
Apligraf®	Organogenesis, Inc., Canton, MA	Neonatal foreskin-derived keratinocytes with stratum corneum (epidermis) and bovine type-I collagen and neonatal fibroblasts (dermis)	Yes	Weekly	10 days	Room temperature	Yes	PMA[a] (1998)— Non-infected partial and full-thickness skin ulcers secondary to venous insufficiency >1 month resistant to standard therapies PMA (2001)—full-thickness neuropathic diabetic foot ulcers >3 weeks that have not responded to SOC [95] Off-label—epidermolysis bullosa [96], recurrent hernia repair, pressure sores, burn reconstruction [39]
Orcel®	Forticell Bioscience, Inc., NY, USA	Neonatal foreskin-derived epidermal keratinocytes and dermal fibroblasts cultured on bovine type-I collagen	Yes	One-time use	9 months	Room temperature	No	HDE[b] (2001)—burns (partial and full thickness) and recessive dystrophic epidermolysis bullosa with hand deformities PMA—fresh, clean, split-thickness, donor-site wounds in burn patients Off-label—chronic wounds (venous and diabetic ulcers) [20, 95]
Dermal substitutes								
GraftJacket®	Wright Medical Technologies, Inc., Memphis, TN	Cadaveric allogenic acellular dermis with an intact basement membrane and dermal matrix with ECM components	No	As needed	2 years	Room temperature	No	PHS 361—full-thickness diabetic foot ulcers that have been present for >1 week and extend through the dermis [95, 97] Off-label—superficial wounds, wounds with sinus tracts, and tendon and osteal repairs [98]
DermACELL®	LifeNet Health, Virginia Beach, VA	Decellularized cadaveric regenerative dermal matrix	No	As needed	1.5–4 years	Room temperature	No	PHS 361—chronic non-healing wounds (diabetic and venous ulcers), acute burns, breast reconstruction, and other soft tissue trauma and can be used on exposed joints, muscles, bones, and tendons [97]

	Manufacturer	Source	Intact cells	Application schedule	Shelf-life	Storage temperature	Difference over SOC	Indications
Amnioband®	MFT Biologics, Edison, NJ	Dehydrated human amnion and chorion allograft	Non-viable	Weekly	3 years	Room temperature	Yes	Partial and full-thickness neuropathic diabetic foot ulcers >6 weeks with no capsule, tendon, or bone exposure Internal and external tissue defects, including acute, chronic, and surgical wounds
Epifix®	MiMedx, Marietta, GA	Dehydrated human amnion and chorion membrane with epithelial cells, basement membrane, and avascular connective tissue	Non-viable	Minimal disruption is ideal but change as needed	5 years	Room temperature	Yes	Neuropathic ulcers, venous stasis ulcers, pressure ulcer, trauma wounds, and surgical wounds
Allopatch Pliable®	MFT Biologics, Edison, NJ	Acellular human reticular dermal tissue	No	Weekly	3 years	Room temperature	–	Partial and full-thickness neuropathic diabetic foot ulcers >6 weeks without exposed tendon or bone [97]
Epicord®	MiMedx, Marietta, GA	Dehydrated human umbilical cord allograft on an ECM of hyaluronic acid and collagen	Non-viable	As needed	5 years	Room temperature	Yes	Management of chronic and acute, including diabetic and other leg ulcers; burns treatment and tendon protection
Grafix®	Smith + Nephew Osiris Therapeutics, Inc., Columbia, MD	Cellular placental-based skin substitute	Yes	Weekly	3 years	−75 to −85 °C	No	"Wound cover" for management of chronic and acute wounds (diabetic foot ulcers, venous stasis ulcers, pressure ulcers), deep chronic wounds, tendon repair, burns [97]
AmnioExcel®	Integra Lifesciences, Plainsboro, NJ	Trilayered human allograft membrane (chorion–amnion–chorion)	Non-viable	Weekly	5 years	Room temperature	No	Management of complex chronic and acute wounds, including diabetic and venous/arterial ulcers, pressure ulcers, trauma wounds, surgical wounds, burns, and wounds with exposed muscle, tendon, bone and vital structures

(continued)

Table 23.1 (continued)

	Manufacturer	Source	Intact cells	Application schedule	Shelf-life	Storage temperature	Difference over SOC	Indications
Oasis®	Cook Biotech, Lafayette, IN	Acellular ECM from porcine jejunal submucosa	No	Weekly	2 years	Room temperature	No	510(k) (2006)—"management of wounds including: partial and full-thickness wounds; pressure ulcers; venous ulcers; diabetic ulcers; chronic vascular ulcers; tunneled, undermined wounds; surgical wounds (donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence); trauma wounds (abrasions, lacerations, second-degree burns, and skin tears); draining wounds" [95]
Promogran Prisma®	3M, Saint Paul, MN	Collagen, oxidized regenerated cellulose, and silver on a sponge	No	Daily	Use by date printed on packaging	<25 °C	No	510(k)—"intended for the management of exuding wounds including: diabetic ulcers, venous ulcers, pressure ulcers, ulcers caused by mixed vascular etiologies, full thickness and partial thickness wounds, donor sites and other bleeding surface wounds, abrasions, traumatic wounds healing by secondary intention, dehisced surgical wounds" [95, 99]
Kerecis®	Kerecis, Arlington, VA	Decellularized Icelandic codfish skin that has been harvested, lyophilized, and freeze-dried	No	When previous Kerecis is absorbed and no longer visible	3 years	Room temperature	–	510(k) (2013)—"management of partial and full-thickness wounds, pressure ulcers, venous ulcers, chronic vascular ulcers, diabetic ulcers, trauma wounds, surgical wounds, and draining wounds" [95, 100]

	Manufacturer	Source	Intact cells	Application schedule	Shelf-life	Storage temperature	Difference over SOC	Indications
Biosynthetic dressings								
Biobrane®	Smith and Nephew, St. Petersburg, FL	Porcine collagen in nylon mesh with semipermeable outer layer of silicone	No	Typically one time use	~3 years (see use by date on packaging)	Room temperature	–	510(k) (2009)—clean superficial burn wounds, donor sites after hemostasis, protective covering for meshed autografts [95] Off-label—dermabrasions, skin-graft harvesting, laser resurfacing, chronic wounds, venous ulcers [20, 101]
Transcyte®	Shire Regenerative Medicine, San Diego, CA	Neonatal foreskin fibroblasts seeded on bioabsorbable nylon mesh and covered with a layer of silicone	Yes	Typically one time use	18 months	−70 to −20 °C	–	PMA (1997)—temporary wound cover for surgically excised full-thickness and deep partial-thickness thermal burn wounds [21] Off-label—chronic legs ulcers, diabetic foot ulcers lasting >6 weeks, venous ulcers, pressure ulcers [21]
Integra®	Integra Lifesciences, Plainsboro, NJ	Bilayer of bovine collagen cross-linked with chondroitin-6-sulfate glycosaminoglycans with a semipermeable silicone outer layer	No	Minimal disruption is ideal but change as needed	6 months	Room temperature	Yes	510(k) (2002)—"management of wounds including: partial and full-thickness wounds, pressure ulcers, venous ulcers, diabetic ulcers, chronic and vascular ulcers, surgical wounds (donor sites/grafts, post-Mohs surgery, post-laser surgery, podiatric, wound dehiscence), trauma wounds (abrasions, laceration, second-degree burns, skin tears), and draining wounds" [95]
Dermagraft®	Shire Regenerative Medicine, Inc., San Diego, CA	Cryopreserved neonatal foreskin fibroblasts cultured on a bioabsorbable polyglactin polymer mesh scaffold	Yes	Weekly	6 months	−75 °C +/- 10	Yes	PMA (2001)—"full-thickness diabetic foot ulcers >6 weeks' duration which extend through the dermis, but without tendon, muscle, joint capsule, or bone exposure" [20, 21, 39, 91] Off-label—chronic wounds, uninfected wounds, temporary or permanent covering prior to STSG graft on burn wounds [21, 75, 102]

(continued)

Table 23.1 (continued)

	Manufacturer	Source	Intact cells	Application schedule	Shelf-life	Storage temperature	Difference over SOC	Indications
Cultured skin grafts								
Hyalograft 3D®	Fidia Advanced Biopolymers, Abano Terme, Italy	Autologous fibroblasts seeded on a 3D hyaluronic matrix	Yes	One-time application	Several days	–	No	Non-infected chronic lower extremity ulcers (diabetic foot ulcers)
MySkin®	CellTrain Ltd., UK	Cell suspension of autologous sub-confluent keratinocytes	Yes	One-time application	2–3 days [103]	−90 °C	No	Burns and non-healing wounds
Laserskin®	Fidia Advanced Biopolymers, Abano Terme, Italy	Autologous sub-confluent keratinocytes and fibroblasts biopsy on a biodegradable benzyl esterified hyaluronic acid matrix	Yes	One-time application	2 days	–	No	510(k) (2001)—"management of wounds in the granulation phase such as pressure ulcers, venous and arterial ulcers, diabetic ulcers, surgical incisions, second degree burns, skin abrasions, lacerations, partial-thickness grafts and skin tears, wounds and burns treated with meshed grafts. It is intended for use as a temporary coverage for wounds and burns to aid in the natural healing process" [95]
Epicel®	Vericel Co., Cambridge, MA	Autologous keratinocytes and murine fibroblasts from epidermal biopsy seeded on petroleum gauze	Yes	One-time application	1 day	13–23 °C	–	HDE (2007)—deep dermal or full thickness burns comprising a total body surface area of at least 30% for use with split-thickness autografts or alone; post nevus excision [95] Off-label—diabetic and venous ulcers [21]
Kaloderm®	Tegoscience, Seoul, Korea	Allogenic keratinocytes from neonatal foreskin	Yes	One-time application	2 years	−60 °C	No	Non-infected diabetic foot ulcers and burns

[a]PMA-FDA premarket approval to evaluate the safety and effectiveness of products and devices that are integral in preventing serious illness or injury
[b]*HDE* humanitarian device exemption: regulatory pathway for products intended for use in rare/infrequent conditions

the host wound and are gradually replaced by native cells as the ulcer heals [21]. Small wounds are likely to only require one application, which increases the financial feasibility of using this product [21]. However, a disadvantage of Apligraf is that wounds require new applications once per week, decreasing its cost-effectiveness [21]. On average, Apligraf costs $86,226 per avoided amputation, and the direct costs associated with a lower-extremity amputation are roughly $50,000, a price that is considerably higher when the indirect costs of amputation are also considered [24, 25]. Another limitation of the allograft is its shelf-life of only 10 days at ambient temperatures [22]. It also requires debridement down to healthy bleeding tissue, but then, hemostasis must be achieved before application [22]. Use of Apligraf is contraindicated in infected wounds, patients allergic to bovine products (specifically bovine collagen), and individuals with a hypersensitivity to the agarose medium used for storage [22].

Orcel® (Forticell Bioscience, Inc., NY, USA), indicated in the treatment of chronic diabetic ulcers, is a composite allograft composed of a bilayered cellular matrix in which allogenic epidermal keratinocytes and dermal fibroblasts from neonatal foreskin are cultured in 2 distinct layers on a type I bovine collagen sponge [19, 27] (Fig. 23.1a, Table 23.1). As the wound heals, native host cells replace the allogenic keratinocytes and fibroblasts and fill in the collagen sponge scaffold [21, 25, 26]. Orcel has a shelf-life of 9 months, but it must be cryopreserved and is not indicated for use in infected wounds or in patients with allergies to penicillin, gentamycin, streptomycin, amphotericin B, or any animal products due to Orcel's processing [21, 27]. Additional allogenic tissue products are discussed in the dermal substitutes, biosynthetic dressings, and cultured skin graft sections.

While allografts are widely used and have many benefits, they can be limited by their availability, and xenografts can help to offset any shortage of allografts due to their constant supply [28]. Xenografts are made from acellular nonliving tissue that is derived from different species (most commonly bovine or porcine) and are composed of dermis in a variety of thicknesses or bilayered dermal–epidermal composites [29]. They must be acellular to avoid rejection and severe inflammation in the host, and because they are derived from non-human sources, they require increased processing to decrease their immunogenicity [6, 30]. However, there are a variety of different preparations for xenografts that can impact their contents and ultimate effect in patients [28]. Fresh, fresh frozen, lyophilized, and irradiated preparations all maintain the epidermal and dermal layers of the xenograft [28]. A more recent modification to xenograft processing includes the incorporation of aldehyde cross-linking and silver ions to amplify the antimicrobial properties of the graft, prolong its lifespan, decrease its antigenicity, and inhibit collagenase to prevent collagen breakdown [29–36]. Aldehyde cross-linking also removes the epidermis and the dermal appendages, resulting in an acellular dermal matrix that can be applied with either side down on the wound bed [28]. However, this cross-linking also can prolong inflammation and delay graft incorporation into the wound, effectively transforming the behavior of the graft from a biologic material into a more synthetic one [30].

Xenografts can be used as a temporary dressing before an autologous graft, and in partial thickness burns, xenograft matrices can be used as a permanent dressing [28]. Xenografts can be left in place until they naturally separate away from the healing skin of the underlying wound, but dressing changes should be done every 2–4 days in order to monitor the wound closely [28, 29]. However, given their immunogenicity, xenografts have increased potential for scarring and immunogenic rejection [37, 38]. Xenogeneic tissue products will be discussed in further detail in the dermal substitute and biosynthetic dressing sections.

Science and Practicality of Dermal Substitutes

Dermal substitutes are any tissue products that effectively act as dermis. They can be comprised of human or non-human-derived tissue that has then been processed to create an acellular scaf-

fold with a basement membrane and a complete extracellular matrix [17, 39]. Because of the complex nature of the dermal layer, dermal substitutes can be classified into cellular or acellular and living or nonliving [17, 39].

Acellular dermal matrix is composed of collagen, elastin, laminin, and glycosaminoglycans and derived from a decellularized cadaveric or xenogenic source. The tissue has no living cells remaining in the graft and therefore has the advantage of being immunologically inert, and revascularization begins within 1–2 weeks after implantation of the graft [5, 40]. They are better for use in fields that may be contaminated because they incorporate into a wound and achieve revascularization more rapidly, making them more resistant to any potential infection [40].

Graftjacket® (Wright Medical Technologies, Inc., Memphis, TN) is a cadaveric allogenic acellular dermal matrix which consists of an intact basement membrane and dermal matrix with ECM components, including type I collagen, elastin, and various aminoglycosides (Fig. 23.1d, Table 23.1). The dermal scaffold and intact basement membrane aid in adhering the tissue product to the wound and encourage ingrowth of cells and neovascularization through release of cytokines and growth factors [21, 41]. It is indicated for deep and superficial wounds, wounds with sinus tracts, and tendon and osteal repairs [21, 29, 41]. Because the product is allogenic and acellular, it can be used as a permanent skin substitute when autograft is not available in partial thickness wounds, but it can also be utilized for immediate reconstruction as a temporary dressing prior to autograft skin grafting [19, 21]. Graftjacket® helps to optimally prepare the wound prior to autograft placement by increasing wound bed vascularity and decreasing infection potential and fluid loss in the area [19]. Graftjacket® can also be applied concurrently with an autograft using the sandwich grafting technique in order to prevent wound desiccation and reduce bacterial colonization of the autograft [19]. The dermal substitute also comes premeshed for ease of clinical application and transudate drainage and has a shelf-life of 2 years at ambient temperatures [21, 41]. Graftjacket® should not be used in patients with autoimmune connective tissue disease or in infected wounds [41]. Moreover, because the tissue product is sourced from a human cadaver, there is always the potential for disease transmission despite extensive screening of donors [41].

DermACELL® (LifeNet Health, Virginia Beach, VA) is another example of an allogenic acellular dermal matrix that contains a nonliving dermal scaffold of matrikines, growth factors, cytokines, and extracellular matrix components such as collagen, elastin, and glycosaminoglycans [42–44] (Table 23.1). The intact structure acts a scaffold for host cells, and the signaling factors serve to promote cell ingrowth, proliferation, and angiogenesis [45]. The acellular dermal matrix (ADM) also contains fibroblast receptors that aid the cells in attaching to the scaffold, strengthening the matrix, and allowing it to withstand sheering forces comparable to those endured by healthy, intact dermis [42–44]. DermACELL® is indicated for diabetic foot ulcers and chronic non-healing wounds and can be used on exposed joints, muscles, bones, and tendons [30]. >97% of donor DNA is removed from the product during processing to mitigate disease transmission and minimize immunogenicity, and the product is then sterilized with radiation and low temperatures [42]. DermACELL® has a shelf-life of 1.5–4 years, depending on the exact product utilized, at room temperature [42]. However, DermACELL® is not to be used in patients with allergies to any of the antibiotics that are used in the processing and preparation of the product [42].

Placental membrane- and umbilical-derived products like Amnioband® (MFT Biologics, Edison, NJ) (ADM), Epifix® (MiMedx, Marietta, GA) (umbilical cellular dermal substitute) (ADM), Amniopatch Pliable® (cellular dermal substitute), Epicord® (umbilical cellular dermal substitute) (MiMedx, Marietta, GA), and Grafix® (Smith + Nephew Osiris Therapeutics, Inc., Columbia, MD) (cellular placental-derived skin substitute) can also act as dermal substitutes in chronic and diabetic wounds [46–48] (Table 23.1). These products can be preserved in a variety of different ways, including cryopreser-

vation in liquid nitrogen, silver nitrate, antibiotics, glycerol sheets, dried sheets, and gamma-irradiated sheets [49]. Umbilical and placental products decrease rates of infection and minimize loss of proteins, electrolytes, and fluids from wounds [19, 29]. The products are rich in growth factors, ECM proteins such as fibronectin and collagen, and cytokines that promote neovascularization, dermal fibroblast proliferation, and mesenchymal stem cell recruitment, allowing these products to perform dermal functions and closely mimicking the composition of human skin [49–51]. Placental and umbilical products undergo minimal processing to ensure that they maintain their inherent dermal scaffold, functional properties, and progenitor cells (in the case of the cellular products) [29]. These dermal substitutes are also able to conform to wounds with more complex anatomies [46–48, 51]. Grafix, specifically, can also be directly applied to exposed bone, tendons, and muscles [48]. While they are able to conform to complex anatomies, they are minimally adherent and have poor mechanical properties, necessitating more frequent dressing changes [29]. They also have a high biodegradability rate [51, 52]. Like other allogenic tissue products, there is always the risk of contamination and disease transmission despite donor screening [19, 29].

Oasis® (Cook Biotech, Lafayette, IN) is a xenogeneic non-cross-linked acellular dermal matrix (ADM) derived from processed porcine jejunum and indicated for use in diabetic ulcers and partial- and full-thickness wounds [53, 54] (Table 23.1). The processing required for this product is more extensive than that required for allogenic products because of the increased immunogenic potential of xenogeneic products. The processing removes cells from the porcine jejunum but leaves a scaffold of ECM components (glycosaminoglycans, fibronectin, proteoglycans, basic fibroblast growth factor, and transforming growth factor beta) intact [28, 53]. Because Oasis® lacks aldehyde cross-linking, it is less likely to cause scarring and inflammation, but is also does not possess the strength, prolonged lifespan, or decreased antigenicity that the cross-linking provides [30–36]. Dehydrated Oasis® can be stored for up to 2 years at room temperature and requires rehydration with normal saline once the product has been applied to the wound [29, 37]. However, because of its xenogeneic origin, no angiogenesis occurs, and the product does not take [28]. Therefore, it is only indicated for use as a temporary skin substitute and cannot be used permanently [29]. The product can remain on the wound until it sloughs off with the ingrowth of native epithelial cells to the wound [29]. However, many physicians prefer to change out the ADM every 2–4 weeks in order to more closely monitor the healing process because Oasis® is not a semi-transparent material [29]. Oasis® should not be used in patients with known porcine allergies, and patients from various religious backgrounds may be opposed to the use of a porcine product [21].

Like Oasis®, Promogran Prisma™ (3 M, Saint Paul, MN) is a xenogenic acellular dermal matrix, but instead of being derived from porcine components, it is composed of 55% bovine collagen, 44% oxidized regenerated cellulose, and 1% silver oxidized regenerated cellulose freeze-dried into a sponge [55, 56] (Fig. 23.1d, Table 23.1). Promogran™ works to heal wounds through minimizing protease activity, and, therefore, protecting growth factors from degradation [24]. The silver serves as an antimicrobial [promogran]. It is indicated for wounds that have been debrided of any necrotic tissue, including diabetic ulcers and trauma wounds [56]. Promogran Prisma™ should not be used in patients with known sensitivities or allergies to bovine products [56].

Kerecis® (Kerecis, Arlington, VA) is another example of a xenogeneic acellular dermal substitute. It is made from the skin of decellularized Icelandic codfish skin that has been harvested, lyophilized, and freeze-dried, and it is indicated for chronic vascular ulcers, trauma wounds, and partial- and full-thickness wounds, including diabetic ulcers [50, 57] (Table 23.1). The dermal substitute maintains its fat, protein, elastin, and glycans and has an abundant supply of antimicrobial agents such as omega-3 polyunsaturated fatty acid, eicosapentaenoic acid, and docosahexaenoic acid [50, 58]. Fish have dermis with

structures comparable to that of humans, but they also possess rich supplies of type I collagen and noninfectious microbiota that aid in the wound healing process [50, 59]. Through epidermal growth factors and fibroblast growth factors, the native collagen in the fish skin has the ability to promote collagen synthesis in the host's wound bed and stimulates fibroblast and keratinocyte migration, proliferation, and differentiation [50, 60]. Fish collagen is also able to be degraded and absorbed into the wound because of its high level of biocompatibility with human tissues [50, 60]. Kerecis® adheres well to the wound bed, which minimizes the number of applications necessary for wound healing [50]. Fish products also do not risk prion transmission like bovine and porcine derived skin substitutes. Kerecis® can easily be stored at ambient temperature for 3 years [50, 61, 62]. It also does not have the same restriction against placement on potentially infected wounds that many other skin substitutes possess, given its indication for use in trauma wounds. However, Kerecis® cannot be used in patients with fish sensitivities or allergies.

Science and Practicality of Biosynthetic Dressings

Biosynthetic dressings are acellular tissue products engineered to contain both biologic and nonbiologic non-degradable materials such as silicone, nylon, and polyglactin [19, 29, 63–65]. The dressings act as scaffolds to promote cell growth and generate neodermis [29]. A major advantage of biosynthetic dressings is that their compositions can be controlled and growth factors and cytokines can be added as needed. The biosynthetic outer layer acts as the epidermis, preventing loss of moisture and wound contamination. However, they are not able to mimic the architecture of the skin and do not have a basement membrane. Another disadvantage of these biosynthetic dressings is their ability to cause a robust inflammatory response in the tissue, causing significant scarring or even immune rejection of the product.

Biobrane® (Smith and Nephew, St. Petersburg, FL) is a bilaminar dressing with an inner layer of porcine collagen embedded in a nylon mesh covered by a semipermeable outer layer of silicon, which is indicated for use in the treatment of chronic wounds [5, 19, 21, 66] (Fig. 23.1b, Table 23.1). The layer of nylon mesh provides a scaffold for fibrovascular growth into the tissue product and wound, and the outer silicone-based layer serves as a microbial barrier and retains moisture. While Biobrane® is able to retain moisture, it is also sufficiently porous to allow for exudate drainage and antibiotic penetration to the wound when applied on top of the dressing [21]. Biobrane's structure and collagen binding work together to recruit fibrin and fibroblasts from the wound bed, helping the product securely adhere to the wound [28]. As the wound heals and the native skin regenerates and grows inward, the Biobrane® naturally separates away from the wound and can be trimmed away [21]. This process makes dressing changes painless [28]. The trimming process also decreases risk of infection as it prevents fluid accumulation, providing an outlet for drainage from the wound [28]. Because Biobrane® is not composed of human-derived allogeneic material, it does not pose the same risk of disease transmission as allogenic products. However, Biobrane® does have drawbacks of its own, including its immunogenicity and ability to cause scaring due to the synthetic materials [19]. Because of the antigenic potential of Biobrane®, it is not indicated for use as a permanent skin substitute and must be removed [19]. Its use is also limited to wounds without evidence of infection or eschar and wounds with an intact basement membrane and dermis because its architecture does not closely approximate that of normal skin and, therefore, cannot replace it effectively on its own [19].

Transcyte® (Shire Regenerative Medicine, San Diego, CA) is a biosynthetic dressing composed of allogeneic fibroblasts from neonatal foreskin that have been seeded onto a bioabsorbable nylon mesh scaffold covered with silicone, which is indicated for diabetic foot ulcers lasting more than 6 weeks [21] (Table 23.1). The fibroblasts are cultured ex vivo for 4–6 weeks on the scaffold, and when used on a diabetic wound, secrete ECM components and local growth factors [21,

67]. Transcyte® has a shelf-life of 1.5 years and is easier to remove than allografts, which is an important feature of a biosynthetic dressing given that they must be removed and cannot be used as permanent skin substitutes [21].

Integra® Dermal Regeneration Template (Integra Lifesciences, Plainsboro, NJ) is a bilayered matrix composed of bovine collagen cross-linked with chondroitin-6-sulfate glycosaminoglycans with a semipermeable silicone outer layer that acts as the epidermis (Fig. 23.1b). Integra® DRT is FDA approved for use in the healing of diabetic wounds [21] (Fig. 23.1b, Table 23.1). The porous matrix serves as a scaffold for autologous cell ingrowth, effectively regenerating a functional dermal layer [69]. Neovascularization of the dermal component of the membrane is expected to be completed at 3 weeks, and the top layer of silicone can be removed at 2–4 weeks in preparation for skin grafting, which happens roughly 3 weeks after the initial procedure in which Integra® DRT was placed [21, 68, 69]. Integra® DRT facilitates the migration of macrophages and fibroblasts into the wound and promotes the formation of granulation tissue, increasing the survival potential of both the wound and any graft that will be placed [21, 70]. Once the neodermis has formed in the healing wound, Integra's silicone layer can be removed, allowing for split-thickness skin graft placement on the neodermis [21, 70]. While Integra® can be used as an interim wound coverage until an autograft is ready, it can also act as an absorbable implant or a permanent skin substitute in full-thickness or deep partial thickness wounds [21]. However, for Integra® DRT to be used in wound healing, complete wound excision is required as it will not take on nonviable tissue and should not be applied on an infected wound [21, 69]. Because the tissue product is avascular, there is a high risk of infection and graft loss [21]. Integra® DRT should not be used in patients with hypersensitivities to bovine products or chondroitin [20]. Integra® DRT should ideally be placed on the same day as an excision or debridement because any delays can decrease the tissue products' ability to take.

Very similar to Integra® DRT, Integra® Bilayer Matrix (Integra Lifesciences, Plainsboro, NJ) is composed of a cross-linked bovine collagen-glycosaminoglycan biodegradable matrix and an outer layer of semipermeable polysiloxane (Figs. 23.1, 23.2, Table 23.1). The silicone helps to prevent water loss from the wound and improves durability of the tissue product [71]. The biodegradable matrix serves as a scaffold for neovascularization and cell ingrowth [71]. It indicated for partial- and full-thickness diabetic ulcers and wounds and is immediately available for wound coverage [29, 71]. Integra® Bilayer Matrix has also demonstrated better cosmesis and tissue elasticity than STSG alone [29]. Other advantages of Integra include a reduction in wound site morbidity, including reduced infection when compared to SOC alone [29]. This biosynthetic dermal substitute can be used in conjunction with negative-pressure wound therapy to decrease time to graft placement and increase take rates of skin grafts [29, 72]. While there are a multitude of advantages, Integra® also has a steep learning curve for use, and there is a significant risk of seroma or hematoma formation with Integra® (likely due to its use in acute wounds) [29]. However, surgeons can mitigate this risk by meshing the skin substitute prior to application to allow for improved wound drainage [29].

Dermagraft® (Shire Regenerative Medicine, Inc., San Diego, CA) is another example of a biosynthetic dressing, and it is composed of cryopreserved neonatal foreskin fibroblasts cultured on a bioabsorbable polyglactin polymer mesh scaffold [21, 29, 70] (Table 23.1). The allogenic fibroblasts then multiply and secrete growth factors such as collagen, tenascin, vitronectin, glycosaminoglycans, and other extracellular matrix proteins, encouraging granulation tissue production and migration of the patient's own cells into the wound bed [29, 73, 74]. The donor cells of the dressing are gradually replaced with fibrovascular tissue from the host over 3– 4 weeks [74]. Dermagraft® is indicated for full-thickness diabetic lower-extremity wounds that extend through the dermis but do not reach tendon, muscle, our bone and have been present for at least 6 weeks



Fig. 23.2 Clinical images calcaneal foot view. (**a**) 54-year-old NIDDM with persistent chronic non-healing calcaneal wound for 3 years with normal pre-op vascular surgery evaluation and an HgA1c of 6.3. (**b**) A 2 cm wound/scar excision was performed to the calcaneal bone and (**c**) Integra® graft matrix was applied to accelerate healing over bone/tendon and increase heel pad thickness. (**d**) Negative-pressure wound therapy was utilized and (**e**) full-thickness skin graft was applied after 3 weeks. (**f**) Wound at 2 month follow-up visit

[21, 39]. The growth factors and cytokines are essential for building granulation tissue, stimulating matrix production, and angiogenesis. The polyglactin mesh has several advantages over collagen-based materials including improved strength and its ability to be broken down in vivo by hydrolysis [73]. The semi-transparency of Dermagraft® also allows for continuous wound surveillance during dressing changes [21]. Despite the xenogeneic and synthetic components of Dermagraft®, there has been very low incidence of rejection and infection [21, 75]. However, Dermagraft® is contraindicated in infected wounds, patients with bovine allergies, infected ulcer, ulcers with sinus tracts, and in wounds that have not yet been debrided [21]. Dermagraft® has a shelf-life of 6 months and is contraindicated in patients with bovine allergies, infected ulcers, and ulcers with sinus tracts [21]. Moreover, Dermagraft® is only used as a temporary coverage [21].

Science and Practicality of Cultured Skin Grafts

Cultured skin grafts are allogenic or autologous human keratinocytes or fibroblasts that have been expanded in culture onto a collagen matrix to produce a sheet suitable for grafting [76, 77]. The basal keratinocytes in cultured skin grafts are able to augment wound epithelialization [19]. However, there are significant disadvantages of using cultured skin grafts. They are fragile, and, therefore, difficult to manipulate during the application process and are challenging to handle while doing dressing changes [19]. Due to the fragility of the sheet, the take rate of cultured skin grafts can be difficult to predict and strict surgical immobilization is required to maximize adhesion. Additionally, cultured skin grafts cannot be applied to full-thickness wounds with exposed fat or fascia due to their inability to adhere to the wound without the anchoring fibrils and other dermal regenerative components located at the base of pilosebaceous layer of the dermis [19]. Another limitation of cultured skin grafts is their infection potential [19].

Hyalograft 3D® (Fidia Advanced Biopolymers, Abano Terme, Italy) is an example of a cultured skin graft that its derived from autologous fibroblast cells that have been seeded on a 3D hyaluronic acid matrix [78, 79] (Table 23.1). Similarly, Hyalomatrix® is composed of autologous fibroblasts on a hyaluronic acid base, but it covered by a silicon layer that helps to retain moisture, acting as a temporary epidermis [78]. Hyaluronic acid is one of the most common polysaccharides found in the native dermal extracellular matrix and acts to attract and proliferate fibroblasts and keratinocytes to the wound. These products, because they provide elements necessary for the formation of an ECM, are commonly used prior to split-thickness skin grafts [80]. In clinical practice, Hyalograft 3D® is commonly used in combination with Laserskin® for the treatment of diabetic foot ulcers [80]. However, the take rate of the product is unpredictable [19].

MySkin® (CellTrain Ltd., UK) is a cell suspension of sub-confluent autologous keratinocytes delivered on a polymer silicone scaffolds or as a spray (Fig. 23.1c, Table 23.1). The silicone substrate improves the grafts' ability to withstand the tearing and sheering forces that occur when manipulating cultured skin grafts. Additionally, the polymer substrate allows it to cover a larger wound than sub-confluent cells alone would have the potential to [81]. However, as of 2012, MySkin® was sold as a spray due to physician preference, simplifying the application process. In addition to ease of application, the use of a sprayed cell suspension has the added benefit of avoiding dispase, which is an enzyme that is necessary to release the epidermal sheets from the culture but also likely removes surface proteins on keratinocytes, decreasing the adhesive capacity of the cells [28]. As opposed to sheets of keratinocytes, the cell suspensions also contain melanocytes and papillary fibroblasts in variable ratios and quantities [28]. Use of a delivery substrate or spray and sub-confluent cells decreases the cell culture time necessary prior to application [28]. The time needed to culture a sufficient sub-confluent quantity of cells for use with diabetic foot ulcers is usually 15 days but can range between 11 and 19 days [28]. However, because

MySkin is cultured from autologous cells, preparation and culture time will always be required and will delay treatment of the wound, which is a significant disadvantage of MySkin and other autologous-based products.

Laserskin® (Fidia Advanced Biopolymers, Abano Terme, Italy) is composed of autologous sub-confluent keratinocytes and fibroblasts, tissue acquired from skin biopsy, that have then been cultured on a laser-microperforated biodegradable matrix of benzyl esterified hyaluronic acid, and it is indicated for diabetic foot ulcers [21, 29, 82, 83] (Table 23.1). The Laserskin® matrix allows for cell proliferation and migration into the wound, and the micro-perforations allows for drainage of wound exudate [21]. Like other autologous products, Laserskin has the advantage of negating any potential for rejection but also necessitates a premanufacture skin biopsy and culture time [21]. Because the cells are not confluent on the matrix, the time needed to culture is decreased in comparison to confluent cultured skin substitutes. The matrix of Laserskin lends to easier manipulation and handling during both initial application and dressing changes, and the transparency of the dressing allows for wound visualization and monitoring during dressing changes. Because the autologous cells are cultured on the scaffold that is then used as a part of the skin substitute, the use of the enzyme dispase is not required to remove keratinocyte sheets from culture flasks, mitigating disruption to keratinocyte surface proteins and adhesive potential of the cells [21]. Due to the preserved adhesive potential of the cells, Laserskin has good graft take and does not demonstrate the fragility that other cultured epithelial autografts possess. It has also demonstrated low rates of infection [21]. Laserskin® is limited by its availability in the USA, as it is currently only available for use in Europe [21]. Moreover, Laserskin® is also limited by its 2-day shelf-life [21].

Epicel® (Vericel Co., Cambridge, MA), indicated for use in diabetic foot ulcers, is a sheet of cultured skin substitute made from autologous keratinocytes with murine fibroblasts obtained from epidermal skin biopsy that is then placed on petroleum gauze [21, 84, 85] (Fig. 23.1c, Table 23.1). Epicel® is frequently used as an adjuvant therapy with an autologous split-thickness skin graft (STSG), but it can also be used when STSGs cannot be obtained due to the extent of an injury or wound (more likely in the setting of a burn, not a diabetic foot ulcer) [21]. Like other autologous grafts, the risk of rejection is mitigated. Epicel® can also permanently provide coverage of extensive wounds. However, Epicel® requires a premanufacture epidermal biopsy and about 3 weeks to culture a sufficient number of cells [21]. After 3 weeks of culturing, the graft has a shelf-life of only 1 day, complicating the application process [21, 86]. The take rate of Epicel can vary, and the long-term results of the product have shown variable efficacy [21]. The skin substitute also carries the risks of blistering, contractures, and infection [21].

Kaloderm® (Tegoscience, Seoul, Korea) is a cultured skin substitute composed of allogenic keratinocytes from the foreskin of a circumcised infant [87] (Table 23.1). Kaloderm® consists of an ECM, cytokine- and growth factor-secreting keratinocytes, and collagenases to encourage wound healing and decrease scar formation [87]. It is indicated for non-infected diabetic foot ulcers, and it can be stored for up to 24 months at -60 °C or 3 months at -15 °C [87]. After thawing for 10 min, Kaloderm can be directly applied to the wound, providing a skin substitute that can be used acutely without waiting for cells to propagate or culture [87].

Impact of Tissue Products for Diabetic Foot Wound Healing

Neuropathic foot ulcers are a significant complication of diabetes that can greatly increase health care costs due to wound care and the potential for hospitalizations and amputations.

Impact on Wound Healing

Tissue products do provide an advantage over SOC alone when measuring complete wound closure at 12 weeks [3, 88]. The mean number of

applications generally range from 1.2 to 10.1 [89]. Healing rates with tissue products at 12 weeks range from 24 to 100%, while healing rates with SOC alone ranged between 0 and 69% [88]. Diabetic ulcers treated with tissue products were 1.67 times more likely to demonstrate complete closure than ulcers treated with SOC alone [88, 90]. When the proportion of healed ulcers at 6 weeks is investigated, tissue products still demonstrate an advantage over SOC alone. The risk ratio for complete ulcer closure at 6 weeks is 2.81, favoring tissue products [88].

While all tissue products work to target various steps in the wound healing process, and, overall, they show an advantage over SOC for promoting complete wound closure, not all categories or brands of tissue products demonstrate an improvement in diabetic ulcer healing [88]. Among the tissue products, *dermal substitutes and biosynthetic dressings* were the two categories that demonstrated a statistically significant wound healing advantage over SOC [88, 89, 91]. The individual dermal substitutes that demonstrated significantly improved healing over SOC at 12 weeks were *Dermagraft and Apligraf/Graftskin*, but no difference was observed for Healaderm and Orcel [88]. The biosynthetic dressings with significant advantages over SOC were *Amnioband, Amniopatch Pliable, Epicord, and Epifix*, while Grafix, Graftjacket, Promogram, and Oasis showed no advantage over SOC [88]. In contrast to dermal substitutes and biosynthetic dressings, cultured skin grafts (as an overall tissue product category) showed no significant difference over SOC, as was the case with the individual cultured skin grafts that were studied (Hyalograft, Kaloderm, and MySkin) [88, 89]. Of the individual products studied when examining closure of ulcers at 6 weeks, *Amnioband, Allopatch Pliable, and Integra* showed significant advantages over SOC alone, but Amnioexcel did not [88]. Other individual tissue products may also show a significant advantage in diabetic wound healing over SOC, but there are currently insufficient studies for some individual brands to draw a significant conclusion.

Both dermal substitutes and biosynthetic dressings demonstrated improvement over SOC alone, but when compared against each other, the studies do not definitely demonstrate superiority of one product over the other [88, 92, 93]. In order to definitively determine a gold standard of skin substitutes, more prospective comparative trials are required to allow providers to make evidence-based decisions on which skin substitute to use in their practice [88].

Overall, tissue products show a modest decrease in healing time of diabetic ulcers when compared to standard care alone, and dermal substitutes demonstrate the most significant effects over SOC. However, given the varying evidence for these tissue products, at this time, it is difficult to draw a definitive conclusion about which product to use, and therefore, tissue product choice remains individual physician preference dependent.

Determining and comparing time to complete healing has remained a challenge in the field due to heterogeneity of data collection and reporting [88]. However, the majority of studies do favor use of skin substitutes for wound healing [88].

Impact on Limb Salvage

There is a small absolute risk reduction for amputation when comparing SOC and tissue products [90]. In patients with lower-extremity diabetic ulcers, there was a significant reduction in the number of minor amputations in the tissue product group, with a 3.9% rate of amputation in the advanced treatment group compared to the 4.3% rate of amputation in the standard of care group [3]. The difference in major amputations between the two groups was more significant with a 50% decrease in major amputations in the advanced treatment tissue product group when compared to SOC alone with amputation rates of 1.6% and 3.2%, respectively [90]. Despite some evidence of minimally decreasing rates of amputation, the data is insufficient to draw definitive conclusions about the efficacy of tissue products in preventing amputations [3].

In addition to modest decreases in amputation rates, other practical aspects of tissue product implementation in diabetic wound healing

include lower readmission rates (6.4% vs. 4.0%) and fewer ED visits (23.1% vs. 18.3%) [3]. There is also no significant increase in length of hospital stay for patients treated with tissue products over the length of hospital stay for patients treated with SOC alone [3].

Financial Comparison

While there are an abundance of studies that focus on the wound healing abilities of various tissue products, only recently there has been an increase in studies researching the cost-effectiveness of these tissue products to determine if there is an economic incentive for our healthcare system and patients. While tissue product treatments may cost an average of an additional $1058 over SOC alone, this increase is offset by their ultimate long-term impact on wound healing through decreased minor and major lower-extremity amputations, increased ulcer-free weeks, and fewer ED visits and hospital readmissions [90, 94]. Amputations themselves can cost up to 10–40x the amount that would be required to treat diabetic foot wounds before they necessitate an amputation [94]. Tissue products can also provide a modest impact on quality adjusted life years (QALYs), providing an increase of 0.022 QALYs and 6.69 ulcer-free weeks over SOC alone [94]. Additionally, tissue products provided an incremental cost-effectiveness ratio of $48,242 per QALY when compared with SOC alone [94].

All tissue products examined demonstrate decreased cost-effectiveness in the hospital outpatient setting when compared to treatment in a physician's office due to higher application costs [89] (Table 23.2). A single diabetic foot wound, when treated with tissue products in the hospital outpatient setting cost an average of $2001–$14,507, whereas the average cost of treatment in an office ranged between $1207 and $8791 [89]. The allogenic dermal matrices GraftJacket, Integra DRT, and Dermagraft are capable of healing more ulcers for $1000 per patient than the other products studied by Samsell et al., demonstrating the highest level of cost-efficiency of the skin substitutes investigated [89].

In order to evaluate whether tissue products are an economically sustainable option for diabetic ulcers, the cost of the skin substitutes, as well as the long-term impact of wound closure, limb salvage, and patient satisfaction with limb function should be taken into consideration. In addition, the cost that patients will need to pay out-of-pocket should also be taken into consideration when determining treatment method and tissue product selection (Table 23.3).

Table 23.2 Parameters utilized to determine incurred costs of various tissue products to heal a single DFU

Tissue product	Mean number of applications	Product cost per application on 5cm^2 wound	Jan 2018 CMS ASP cost/cm^2	Cost of product per treated wound
ApliGraf	2.5	$1,359.34	$30.89	$3,398.34
DermACELL	1.2	$1,060.96	$66.31	$1,273.15
Dermagraft	6.3	$1,241.63	$33.11	$7,822.24
EpiFix	3.5	$990.08	$165.01	$3,465.27
Grafix	8.7	$805.70	$134.28	$7,009.62
GraftJacket	1.3	$774.74	$96.84	$1,007.17
Integra DRT	2.0	$901.01	$128.72	$1,802.02
Oasis ultra	10.1	$115.58	$11.01	$1,167.40

CMS centers for medicare and medicaid services, *ASP* average selling price

Table 23.3 Costs of treating DFUs in hospital outpatient departments and physicians' offices and estimated costs to patients for various biologic skin substitutes

Tissue product	Cost of treating one DFU in physician's office	Estimated patient cost in physician's office	Bundled HOPD payment	Cost of treating one DFU in HOPD	Estimated patient cost in HOPD
ApliGraf	$3,781.74	$756	$3,921.08	$4,168.58	$834
DermACELL	$1,457.18	$291	$1,882.12	$2,000.92	$400
Dermagraft	$8,791.41	$1,758	$9,022.90	$9,648.54	$1,930
EpiFix	$4,002.03	$800	$5,489.51	$5,836.01	$1,167
Grafix	$8,343.85	$1,669	$13,645.34	$14,506.64	$2,901
GraftJacket	$1,206.54	$241	$2,038.96	$2,167.66	$434
Integra DRT	$2,108.74	$422	$3,136.86	$3,334.86	$667
Oasis Ultra	$2,716.33	$543	$4930.82	$5,930.72	$1,186

HOPD hospital outpatient department

Conclusion

The shear magnitude of tissue products on the market, with new skin substitutes continually being developed, complicates the synthesis and analysis of these products. The information in this chapter only scratches the surface of tissue products available for diabetic wound healing, attempting to highlight the tissue products that are most commonly used. Some tissue products were able to show an improvement in wound closure over SOC, while others made no significant impact on healing time. However, tissue products overall did show a very modest benefit in limb salvage, decreasing rates of both minor and major lower-extremity amputations.

Not only do allogenic dermal matrices demonstrate a greater ability to heal diabetic ulcers than their other tissue product counterparts, but they also exhibit the greatest cost-efficiency of the tissue products examined in this study [3, 89]. However, the absence of standardized metrics in diabetic foot wound literature poses a considerable problem with drawing conclusions and comparing study results. There is no standardization of the categorization of skin substitutes, with various studies putting the same tissue product in different categories, confusing the results and diminishing comparability of studies. Inconsistency in reported healing endpoints and study timelines in concert with new tissue products rapidly being released on the market also complicate study comparison. Twelve weeks was traditionally the endpoint used in studying diabetic wound healing, whereas now studies have started to use 16 weeks, which may be a more appropriate endpoint for wound closure. Additionally, more studies are needed to determine the long-term impact of tissue products on these chronic wounds.

While this chapter works to investigate the impact of skin substitutes on healing diabetic foot ulcers, we are not able to draw definitive conclusions on the long-term effects of these products or post-closure adverse events. Future studies should continue to focus on the potential of tissue products in diabetic wound closure to better understand the long-term implications of using these products. There is also a relative paucity of research on the impact of tissue products on amputation rates and limb salvage, an important endpoint to measure long-term impacts of tissue product efficacy.

As we move toward further evidence-based medicine and efficiency, it is important that we choose a product that will continue to evolve and be mindful of the cost as we move to bundle payment and cost-efficiency.

Acknowledgments No acknowledgments are made.

References

1. American Diabetes Association. Economic costs of diabetes in the U.S. in 2017. Diabetes Care. 2018;41(5):917–28. [cited 2021 Jul 24]: 11p. https://diabetesjournals.org/care/article/41/5/917/36518/Economic-Costs-of-Diabetes-in-the-U-S-in-2017.
2. Williams R, Karuranga S, Malanda B, et al. Global and regional estimates and projections of diabetes-related health expenditure: results from the International diabetes federation diabetes atlas, 9th edition. Diabetes Res Clin Pract. 2020;162:108072.
3. Armstrong DG, Boulton AJM, Bus SA. Diabetic foot ulcers and their recurrence. N Engl J Med. 2017;376(24):2367–75.
4. Centers for Disease Control and Prevention. National diabetes statistics report, 2020. Atlanta, GA: Centers for Disease Control and Prevention, U.S. Department of Health and Human Services; 2020. [cited 2021 Oct 16]. https://www.cdc.gov/diabetes/data/statistics-report/index.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fdiabetes%2Fdata%2Fstatistics%2Fstatistics-report.html.
5. Reddy G. Foot ulcers. In: Janis JE, editor. Essentials of plastic surgery. 2nd ed. Boca Raton, FL: CRC Press/Quality Medical Publishing, Inc.; 2014. p. 667–81.
6. Boulton AJM, Armstrong DG, Kirsner RS, et al. Diagnosis and management of diabetic foot complications. Arlington, VA: American Diabetes Association; 2018. https://doi.org/10.2337/db20182-1. [cited 2021 Jan 8]. 20p. https://www.ncbi.nlm.nih.gov/books/NBK538977/pdf/Bookshelf_NBK538977.pdf.
7. Boulton AJM, Armstrong DG, Albert SF, Frykberg RG, Hellman R, Sue Kirkman M, et al. Comprehensive foot examination and risk assessment: a report of the task force of the foot care interest group of the American Diabetes Association, with endorsement by the American Association of Clinical Endocrinologists. Diabetes Care. 2008;31(8):1679–85.
8. Aldana PC, Khachemoune A. Diabetic foot ulcers: appraising standard of care and reviewing new trends in management. Am J Clin Dermatol. 2020;21(2):255–64.
9. Lavery LA, Davis KE, Berriman SJ, Braun L, Nichols A, Kim PJ, et al. WHS guidelines update: diabetic foot ulcer treatment guidelines. Wound Repair Regen. 2016;24(1):112–26, 112.
10. Everett E, Mathioudakis N. Update on management of diabetic foot ulcers. Ann N Y Acad Sci. 2018;1411(1):153–65.
11. Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG, et al. 2012 Infectious diseases society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2012;54(12):e132–e73. https://doi.org/10.1093/cid/cis346. [cited 2021 Nov 6]. https://academic.oup.com/cid/article/54/12/e132/455959.
12. Bakker K, Apelqvist J, Lipsky BA, Van Netten JJ, International Working Group on the Diabetic Foot. The 2015 IWGDF guidance documents on prevention and management of foot problems in diabetes: development of an evidence-based global consensus. Diabetes Metab Res Rev. 2016;32(Suppl 1):2–6.
13. Vatankhah N, Jahangiri Y, Landry GJ, Moneta GL, Azarbal AF. Effect of systemic insulin treatment on diabetic wound healing. Wound Repair Regen. 2017;25(2):288–91.
14. Margolis DJ, Kantor J, Berlin JA. Healing of diabetic neuropathic foot ulcers receiving standard treatment. A meta-analysis. Diabetes Care. 1999;22(5):692–5.
15. Hingorani A, LaMuraglia GM, Henke P, Meissner MH, Loretz L, Zinszer KM, et al. The management of diabetic foot: a clinical practice guideline by the society for vascular surgery in collaboration with the American podiatric medical association and the society for Vascular Medicine. J Vasc Surg. 2016;63(2 Suppl):S3–21.
16. Janis JE, Harrison B. General management of complex wounds. In: Janis JE, editor. Essentials of plastic surgery. 2nd ed. Boca Raton, FL: CRC Press/Quality Medical Publishing, Inc; 2014. p. 10–6.
17. Kumar P. Classification of skin substitutes. Burns. 2008;34(1):148–9.
18. Dieckmann C, Renner R, Milkova L, Simon JC. Regenerative medicine in dermatology: biomaterials, tissue engineering, stem cells, gene transfer and beyond. Exp Dermatol. 2010;19(8):697–706.
19. Halim AS, Khoo TL, Mohd Yussof SJ. Biologic and synthetic skin substitutes: an overview. Indian J Plast Surg. 2010;43(Suppl):S23–8.
20. Gupta S, Mohapatra DP, Chittoria RK, et al. Human skin allograft: is it a viable option in management of burn patients? J Cutan Aesthet Surg. 2019;12(2):132–5, 132.
21. Vyas KS, Vasconez HC. Wound healing: biologics, skin substitutes, biomembranes and scaffolds. Healthcare (Basel). 2014;2(3):356–400.
22. Apligraf®. Package insert. Canton, MA: Organogenesis Inc.; 2016.
23. Waymack P, Duff RG, Sabolinski M. The effect of a tissue engineered bilayered living skin analog, over meshed split-thickness autografts on the healing of excised burn wounds. The Apligraf burn study group. Burns. 2000;26(7):609–19.
24. Chow I, Lemos EV, Einarson TR. Management and prevention of diabetic foot ulcers and infections: a health economic review. Pharmacoeconomics. 2008;26(12):1019–35.
25. Ulbrecht JS, Cavanagh PR, Caputo GM. Foot problems in diabetes: an overview. Clin Infect Dis. 2004;39(Suppl 2):S73–82.
26. Kanokpanont S, Damrongsakkul S, Ratanavaraporn J, Aramwit P. An innovative bi-layered wound dress-

ing made of silk and gelatin for accelerated wound healing. Int J Pharm. 2012;436(1–2):141–53.
27. Orcel™. (Bilayered cellular matrix) instructions for use for managing donor sites in burn patients. New York, NY: Ortec International, Inc.; 2001. Orcel; [cited 2021 Dec 3]; 12p. https://www.accessdata.fda.gov/cdrh_docs/pdf/P010016c.pdf.
28. Sharma KS, Ralston D, Giblin V, MacNeil S. Engineering of accepted skin-equivalent tissue for tissue repair: current state and perspectives. In: Reis IL, editor. Encyclopedia of Tissue engineering and regenerative medicine. 1st ed. San Diego, CA: Academic Press, Inc.; 2019. p. 285–98.
29. Shores JT, Gabriel A, Gupta S. Skin substitutes and alternatives: a review. Adv Skin Wound Care. 2007;20(9 Pt 1):493–510.
30. Wan D, Potter J. Biomaterials. In: Janis JE, editor. Essentials of plastic surgery. 2nd ed. Boca Raton, FL: CRC Press/Quality Medical Publishing, Inc.; 2014. p. 87–106.
31. Turza KC, Butler CE. Adhesions and meshes: synthetic versus bioprosthetic. Plast Reconstr Surg. 2012;130(5 Suppl 2):206S–13S.
32. Patel KM, Bhanot P. Complications of acellular dermal matrices in abdominal wall reconstruction. Plast Reconstr Surg. 2012;130(5 Suppl 2):216S–24S.
33. Dunn RM. Cross-linking in biomaterials: a primer for clinicians. Plast Reconstr Surg. 2012;130(5 Suppl 2):18S–26S.
34. Novitsky YW, Rosen MJ. The biology of biologics: basic science and clinical concepts. Plast Reconstr Surg. 2012;130(5 Suppl 2):9S–17S.
35. Bengtson B. Discussion: use of dermal matrix to prevent capsular contracture in aesthetic breast surgery. Plast Reconstr Surg. 2012;130(5 Suppl 2):137S–41S.
36. Butler CE, Burns NK, Campbell KT, Mathur AB, Jaffari MV, Rios CN. Comparison of cross-linked and non-cross-linked porcine acellular dermal matrices for ventral hernia repair. J Am Coll Surg. 2010;211(3):368–76.
37. Liu Y, Panayi AC, Bayer LR, Orgill DP. Current available cellular and tissue-based products for treatment of skin defects. Adv Skin Wound Care. 2019;32(1):19–25.
38. Catalano E, Cochis A, Varoni E, Rimondini L, Azzimonti B. Tissue-engineered skin substitutes: an overview. J Artif Organs. 2013;16(4):397–403.
39. van der Veen VC, van der Wal MB, van Leeuwen MC, Ulrich MM, Middelkoop E. Biological background of dermal substitutes. Burns. 2010;36(3):305–21.
40. Clemens MW, Kronowitz SJ. Acellular dermal matrix in irradiated tissue expander/implant-based breast reconstruction: evidence-based review. Plast Reconstr Surg. 2012;130(5 Suppl 2):27S–34S.
41. Graftjacket®. Regenerative tissue matrix instructions for use [package insert]. Memphis, TN: Wright Medical Technology; 2015.
42. Dermacell AWM. Instructions for use [package insert]. Virginia Beach, VA: LifeNet Health; 2019.
43. Dermacell AWM®. Human acellular dermal matrix (hADM). Virginia Beach, VA: LifeNet Health; 2020. [cited 2021 Dec 19]. https://www.lifenethealth.org/sites/default/files/files/68-65-040-01.pdf.
44. Dermacell AWM®. Technical overview. Virginia Beach, VA: LifeNet Health; 2019. [cited 2021 Dec 19]. https://www.lifenethealth.org/sites/default/files/files/DermACELL%20AWM%20Technical%20Overview(1).pdf.
45. Capito AE, Tholpady SS, Agrawal H, Drake DB, Katz AJ. Evaluation of host tissue integration, revascularization, and cellular infiltration within various dermal substrates. Ann Plast Surg. 2012;68(5):495–500.
46. MFT allograft tissue instructions for use [package insert]. Edison, NJ: Musculoskeletal Transplant Foundation; 2016.
47. Epifix dehydrated human amnion/chorion membrane allograft information/instructions for use [package insert]. Marietta, GA: MiMedx Tissue Services, LLC; 2017.
48. Grafix®. Cryopreserved placental membrane [package insert]. Columbia, MD: Smith + Nephew; 2021.
49. Bujang-Safawi E, Halim AS, Khoo TL, Dorai AA. Dried irradiated human amniotic membrane as a biological dressing for facial burns: a 7-year case series. Burns. 2010;36(6):876–82.
50. Bay C, Chizmar Z, Reece EM, Yu JZ, Winocour J, Vorstenbosch J, et al. Comparison of skin substitutes for acute and chronic wound management. Semin Plast Surg. 2021;35(3):171–80.
51. DiDomenico LA, Orgill DP, Galiano RD, Serena TE, Carter MJ, Kaufman JP, et al. Aseptically processed placental membrane improves healing of diabetic foot ulcerations: prospective, randomized clinical trial. Plast Reconstr Surg Glob Open. 2016;4(10):e1095. https://doi.org/10.1097/GOX.0000000000001095. [cited 2021 May 11]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5096542/pdf/gox-4-e1095.pdf.
52. Farhadihosseinabadi B, Farahani M, Tayebi T, et al. Amniotic membrane and its epithelial and mesenchymal stem cells as an appropriate source for skin tissue engineering and regenerative medicine. Artif Cells Nanomed Biotechnol. 2018;46(sup2):431–40.
53. Hodde JP, Ernst DM, Hiles MC. An investigation of the long-term bioactivity of endogenous growth factor in OASIS wound matrix. J Wound Care. 2005;14(1):23–5.
54. OASIS®. Matrix product guide. Fort Worth, TX: Smith + Nephew Inc.; 2019. [cited 2021 Dec 17]. https://www.smith-nephew.com/documents/education%20and%20evidence/literature/2020/awm/us%20customer%20support%20collections/bio%20tissue%20products/oasis%20portfolio%20product%20guide.pdf.
55. Cullen B, Smith R, McCulloch E, Silcock D, Morrison L. Mechanism of action of PROMOGRAN, a protease modulating matrix, for the treatment of diabetic

foot ulcers. Wound Repair Regen. 2002;10(1):16–25, 16.
56. Promogran Prisma™. Wound balancing matrix indications and applications. St. Paul, MN: 3M; 2020. [cited 2021 Dec 15]. https://www.acelity.com/healthcare-professionals/global-product-catalog/catalog/promogran-prisma-wound-balancing-matrix.
57. Kerecis. Omega3 wound instructions for use. Isafjordur: Kerecis Limited; 2020.
58. Alam K, Jeffery SLA. Acellular fish skin grafts for management of split thickness donor sites and partial thickness burns: a case series. Mil Med. 2019;184(Suppl 1):16–20, 16.
59. Lima-Junior EM, de Moraes Filho MO, Costa BA, Fechine FV, de Moraes ME, Silva-Junior FR, et al. Innovative treatment using tilapia skin as a xenograft for partial thickness burns after a gunpowder explosion. J Surg Case Rep. 2019;2019(6):1–4. [cited 2021 Apr 22]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6565829/pdf/rjz181.pdf doi:10.1093/jscr/rjz181.
60. Chen J, Gao K, Liu S, Wang S, Elango J, Bao B, et al. Fish collagen surgical compress repairing characteristics on wound healing process in vivo. Mar Drugs. 2019;17(1):1–12. https://doi.org/10.3390/md17010033. [cited 2021 Mar 17]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6357035/pdf/marinedrugs-17-00033.pdf.
61. Kerecis. Kerecis intact fish-skin technology. Isafjordur: Kerecis; 2010. [updated 2021; cited 2021 Dec 17]. https://www.kerecis.com/omega3-fishskin.
62. Kerecis. Fish-skin graft rich in omega3 fatty acids. Iceland: Kerecis; 2010. [updated 2021; cited 2021 Dec 17]. https://www.kerecis.com/omega3-wound.
63. Cassidy C, St Peter SD, Lacey S, Beery M, Ward-Smith P, Sharp RJ, et al. Biobrane versus duoderm for the treatment of intermediate thickness burns in children: a prospective, randomized trial. Burns. 2005;31(7):890–3.
64. Demling RH. Burns. N Engl J Med. 1985;313(22):1389–98.
65. Ferreira M, Paggiaro A, Isaac C, Neto N, Santos G. Skin substitutes: current concepts and a new classification system. Rev Bras Cir Plást. 2011;26(4):696–702.
66. Smith + Nephew. Biobrane. Fort Worth, TX: Smith + Nephew Inc.; 2021. [cited 2021 Dec 26]. https://www.smith-nephew.com/key-products/advanced-wound-management/other-wound-care-products/biobrane.
67. Bello YM, Falabella AF, Eaglstein WH. Tissue-engineered skin. Current status in wound healing. Am J Clin Dermatol. 2001;2(5):305–13.
68. Arteche Pujana M, Pérez-Álvarez L, Cesteros Iturbe LC, Katime I. Biodegradable chitosan nanogels crosslinked with genipin. Carbohydr Polym. 2013;94(2):836–42.
69. Integra®. Dermal regeneration template Integra® Meshed dermal regeneration template [package insert]. Princeton, NJ: Integra LifeSciences Co.; 2020.
70. Hansen SL, Voigt DW, Wiebelhaus P, Paul CN. Using skin replacement products to treat burns and wounds. Adv Skin Wound Care. 2001;14(1):37–46, 37.
71. Integra®. Meshed bilayer wound matrix instructions for use [package insert]. Plainsboro, NJ: Integra LifeSciences Co.; 2013.
72. Jeschke MG, Rose C, Angele P, Füchtmeier B, Nerlich MN, Bolder U. Development of new reconstructive techniques: use of Integra in combination with fibrin glue and negative-pressure therapy for reconstruction of acute and chronic wounds. Plast Reconstr Surg. 2004;113(2):525–30.
73. Organogenesis. Dermagraft human fibroblast-derived dermal substitute directions for use. La Jolla, CA: Organogenesis Inc.; 2015. [cited 2021 Nov 18]. https://dermagraft.com/pdf/Dermagraft-Directions-for-Use.pdf.
74. Mansbridge J, Liu K, Patch R, Symons K, Pinney E. Three-dimensional fibroblast culture implant for the treatment of diabetic foot ulcers: metabolic activity and therapeutic range. Tissue Eng. 1998;4(4):403–14.
75. Hansbrough JF, Mozingo DW, Kealey GP, Davis M, Gidner A, Gentzkow GD. Clinical trials of a biosynthetic temporary skin replacement, Dermagraft-transitional covering, compared with cryopreserved human cadaver skin for temporary coverage of excised burn wounds. J Burn Care Rehabil. 1997;18(1 Pt 1):43–51, 18, 43.
76. Greenwood JE. Hybrid biomaterials for skin tissue engineering. In: Albanna MZ, Holmes IV JH, editors. Skin Tissue engineering and regenerative medicine. 1st ed. San Diego, CA: Academic Press, Inc.; 2016. p. 185–210.
77. Eisenberg M, Llewelyn D. Surgical management of hands in children with recessive dystrophic epidermolysis bullosa: use of allogeneic composite cultured skin grafts. Br J Plast Surg. 1998;51(8):608–13.
78. Vig K, Chaudhari A, Tripathi S, Dixit S, Saho R, Pillai S, et al. Advances in skin regeneration using tissue engineering. Int J Mol Sci. 2017;18(4):1–19. https://doi.org/10.3390/ijms18040789. [cited 2021 Jun 7]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5412373/pdf/ijms-18-00789.pdf.
79. Límová M. Active wound coverings: bioengineered skin and dermal substitutes. Surg Clin North Am. 2010;90(6):1237–55.
80. Shevchenko RV, James SL, James SE. A review of tissue-engineered skin bioconstructs available for skin reconstruction. J R Soc Interface. 2010;7(43):229–58.
81. Savoji H, Godau B, Hassani MS, Akbari M. Skin tissue substitutes and biomaterial risk assessment and testing. Front Bioeng Biotechnol. 2018;6(86):1–18. https://doi.org/10.3389/fbioe.2018.00086. [cited

2021 Apr 5]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6070628/pdf/fbioe-06-00086.pdf.
82. Ramos-e-Silva M, Ribeiro de Castro MC. New dressings, including tissue-engineered living skin. Clin Dermatol. 2002;20(6):715–23, 715.
83. Uccioli L, TissueTech Autograph System Italian Study Group. A clinical investigation on the characteristics and outcomes of treating chronic lower extremity wounds using the tissuetech autograft system. Int J Low Extrem Wounds. 2003;2(3):140–51.
84. Vacher D. Autologous epidermal sheets production for skin cellular therapy. Ann Pharm Fr. 2003;61(3):203–6.
85. Epicel cultured epidermal autograft instruction for use [package insert]. Cambridge, MA: Vericel Co; 2021.
86. Horch RE, Kopp J, Kneser U, Beier J, Bach AD. Tissue engineering of cultured skin substitutes. J Cell Mol Med. 2005;9(3):592–608.
87. Tego Science. Kaloderm®. Seoul: Tegoscience; 2010. [updated 2019; cited 2021 Jul 16]. http://www.tegoscience.com/eng/product/view.do?prdSeq=11.
88. Gordon AJ, Alfonso AR, Nicholson J, Chiu ES. Evidence for healing diabetic foot ulcers with biologic skin substitutes: a systematic review and meta-analysis. Ann Plast Surg. 2019;83(4S Suppl 1):S31–44, S31.
89. Samsell B, McLean J, Cazzell S, Dorsch K, Moyer PM, Moore M. Health economics for treatment of diabetic foot ulcers: a cost-effectiveness analysis of eight skin substitutes. J Wound Care. 2019;28(Sup9):S14–26.
90. Santema TB, Poyck PP, Ubbink DT. Skin grafting and tissue replacement for treating foot ulcers in people with diabetes. Cochrane Database Syst Rev. 2016;2(2):CD011255. https://doi.org/10.1002/14651858.CD011255.pub2. [cited 2021 Dec 21]. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6464524/pdf/CD011255.pdf.
91. Álvaro-Afonso FJ, García-Álvarez Y, Lázaro-Martínez JL, Kakagia D, Papanas N. Advances in dermoepidermal skin substitutes for diabetic foot ulcers. Curr Vasc Pharmacol. 2020;18(2):182–92.
92. Zelen CM, Gould L, Serena TE, Carter MJ, Keller J, Li WW. A prospective, randomised, controlled, multi-Centre comparative effectiveness study of healing using dehydrated human amnion/chorion membrane allograft, bioengineered skin substitute or standard of care for treatment of chronic lower extremity diabetic ulcers. Int Wound J. 2015;12(6):724–32, 12.
93. Zelen CM, Serena TE, Gould L, Le L, Carter MJ, Keller J, et al. Treatment of chronic diabetic lower extremity ulcers with advanced therapies: a prospective, randomised, controlled, multi-centre comparative study examining clinical efficacy and cost. Int Wound J. 2016;13(2):272–82.
94. Kabali C, Higgins C, Guo J, Li C, Mistry J. Skin substitutes for adults with diabetic foot ulcers and venous leg ulcers: a health technology assessment, vol. 4. Ontario, CA: Ontario Health (Quality); 2021. [cited 2021 Dec 23]. 165p. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8210978/.
95. Snyder DL, Sullivan N, Schoelles KM. Skin substitutes for treating chronic wounds. Rockville, MD: Agency for Healthcare Research and Quality; 2012. [cited 2021 Nov 28]. 203p. https://www.ncbi.nlm.nih.gov/books/NBK248353/pdf/Bookshelf_NBK248353.pdf/.
96. Falabella AF, Valencia IC, Eaglstein WH, Schachner LA. Tissue-engineered skin (Apligraf) in the healing of patients with epidermolysis bullosa wounds. Arch Dermatol. 2000;136(10):1225–30.
97. Aetna. Skin and soft tissue substitutes. Hartford, CT: Aetna, Inc.; 2021. [updated 2021 Dec 22; cited 2021 Dec 31]. http://www.aetna.com/cpb/medical/data/200_299/0244.html.
98. Papanas N, Eleftheriadou I, Tentolouris N, Maltezos E. Advances in the topical treatment of diabetic foot ulcers. Curr Diabetes Rev. 2012;8(3):209–18.
99. Witten CM. Promogran matrix wound dressing 510(k) summary. Rockville, MD: Department of Health and Human Services; 2002. [cited 2021 Dec 24]. 5p. https://www.accessdata.fda.gov/cdrh_docs/pdf/K014129.pdf.
100. Krause D. Kerecis 510k summary. Rockville, MD: Department of Health and Human Services; 2013. [cited 2021 Dec 30]. 6p. https://www.accessdata.fda.gov/cdrh_docs/pdf13/k132343.pdf.
101. Whitaker IS, Prowse S, Potokar TS. A critical evaluation of the use of biobrane as a biologic skin substitute: a versatile tool for the plastic and reconstructive surgeon. Ann Plast Surg. 2008;60(3):333–7.
102. Purdue GF, Hunt JL, Still JM Jr, Law EJ, Herndon DN, Goldfarb IW, et al. A multicenter clinical trial of a biosynthetic skin replacement, Dermagraft-TC, compared with cryopreserved human cadaver skin for temporary coverage of excised burn wounds. J Burn Care Rehabil. 1997;18(1 Pt 1):52–7, 18, 52.
103. Moustafa M, Bullock AJ, Creagh FM, et al. Randomized, controlled, single-blind study on use of autologous keratinocytes on a transfer dressing to treat nonhealing diabetic ulcers. Regen Med. 2007;2(6):887–902.

24 Limb Wounds of Dermatologic Disease: Dermatopathology, Biopsy, and Medical Management

Helena B. Pasieka, Nicholas Logemann, Felix Yang, and Alexandra Gosh

Wound Differential

Please note: This chapter will work to provide examples of patients with different skin tones at every opportunity.

The differential diagnosis for dermatologic wounds are:

- Autoimmune and inflammatory diseases
- Opportunistic infection
- Allergic contact dermatitis
- Cutaneous malignancy
- Calciphylaxis and other vascular diseases

Autoimmune and Inflammatory Diseases

This section will cover sterile/noninfectious etiologies of atypical wounds that are the result of autoimmune diseases (e.g. discoid lupus erythematosus) or aberrant inflammatory reactions (e.g. pyoderma gangrenosum). An awareness of these diagnoses is critical as they can be a source of diagnostic confusion if the diagnosis of an autoimmune process is not considered and "missed" and the patient then is not appropriately treated for an autoimmune process. Treatment of an autoimmune process can differ greatly from other causes of chronic wounds and likely will require the involvement of a specialist from dermatology or rheumatology to adequately manage these diseases.

An important note on tissue submission: The evaluation and workup of several autoimmune diagnoses will require an investigation to determine if there are fixed immune deposits in the skin biopsy. The study to evaluate for this is called direct immunofluorescence (DIF) and it requires that the sample be sent in a fixative

H. B. Pasieka (✉)
Department of Dermatology, Georgetown University School of Medicine, Washington, DC, USA

Department of Dermatology, Walter Reed National Military Medical Center, Bethesda, MD, USA

Department of Dermatology, Uniformed Services University, Bethesda, MD, USA

Department of Medicine, Uniformed Services University, Bethesda, MD, USA
e-mail: helena.pasieka@usuhs.edu

N. Logemann
Department of Dermatology, Walter Reed National Military Medical Center, Bethesda, MD, USA

Department of Dermatology, Uniformed Services University, Bethesda, MD, USA
e-mail: nicholas.f.logemann.mil@mail.mil

F. Yang
School of Medicine, Uniformed Services University, Bethesda, MD, USA
e-mail: felix.yang@usuhs.edu

A. Gosh
Department of Dermatology, Georgetown University School of Medicine, Washington, DC, USA

Department of Dermatology, Uniformed Services University, Bethesda, MD, USA
e-mail: alexandra.gosh@usuhs.edu

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_24

called Michel's transport medium (Zeus transport media, a commercial product, is similar). Michel's/Zeus medium is designed to facilitate the transport of fresh tissue biopsies obtained in the office to the lab where the immunohistochemical analysis will be performed.

Clinical pearl: Ensure that you have your transport medium at the ready prior to obtaining the sample; a commonly seen error is to place the peripheral sample into formalin and then move it into the Michel's/Zeus fixative. As formalin instantaneously destroys the diagnostic immune deposits, even a transient exposure (such as a brief dip in error) will render the sample useless. Recommended biopsy technique and transport are main takeaway points of this chapter and will be summarized at the end.

Pyoderma Gangrenosum

Clinical scenario: Patients often recollect that the wound began as a tender and inflamed pustule. Often, they attribute this early pustule to a spider bite (see Fig. 24.1a). In the event that the patient attempts to "pop" the pustule, they find that to find that the resultant wound starts to expand (see Fig. 24.1b).

A spider bite is rarely the cause. This case is an example of pathergy in the setting of pyoderma gangrenosum. Pathergy is the phenomenon of a wound enlarging after manipulation and is a hallmark feature of certain autoimmune skin diseases.

Pyoderma gangrenosum presents as an expansile lesion that results from neutrophil derangement. On examination, pyoderma gangrenosum manifests as a painful ulcer with a wet central cribriform appearance in the central portion of the ulcer, circumscribed by a violaceous/gun-metal gray border (see Fig. 24.2). This violaceous border is of clinical importance because it is an indication of actively expanding pyoderma gangrenosum.

Pyoderma gangrenosum that has ceased to expand will present with retraction of the borders and once healed may take on an atrophic appearance with thin skin and marked pigmentary alterations (see Fig. 24.3). In instances where pyoderma gangrenosum is suspected it is of paramount importance for the wound care provider to recognize that there is the potential for reactivation of pyoderma gangrenosum (i.e. "pathergy") with additional trauma (e.g. debridement).

Pyoderma gangrenosum can occur anywhere on the body, but is common on the lower extremities. When pyoderma gangrenosum is suspected, a thorough clinical history should be obtained.

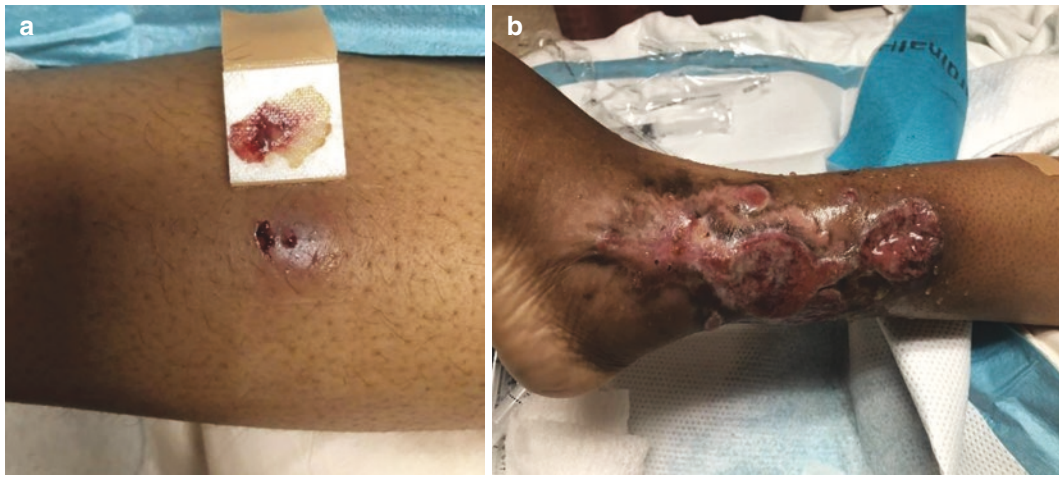


Fig. 24.1 (**a**) Initial presentation of a pustule with a violaceous border and central cribriform appearance on a patient with deeply pigmented skin, (**b**) 2–4 weeks later, after the patient attempted to "pop" the pustule. This rapid expansion and intense inflammation after minor trauma or manipulation is a classic example of "pathergy"



Fig. 24.2 Pyoderma gangrenosum in a patient with a light skin tone. Note the presence of a violaceous border on the proximal side of the wound (arrow), indicative of an actively expanding wound. The characteristic cribriform ("sieve-like") appearance of the base of the ulcer is apparent



Fig. 24.3 Typical appearance of a healed pyoderma gangrenosum wound with atrophy, dyspigmentation, and a "wrinkled tissue paper" appearance



Fig. 24.4 (**a**) Typical progression of PG from tiny inflammatory pustule (May 24th), to (**b**) cribriform ulcer of several centimeters (July 1st), to (**c**) atrophic healed scar (July 29th) in a patient with underlying multiple myeloma

Up to 50% of pyoderma gangrenosum is associated with an underlying systemic disease and may be associated with inflammatory bowel disease, rheumatoid arthritis, or hematologic disorders [1]. For this reason, a review of systems should be conducted to identify any clues to these occult diagnoses. In terms of demographics, the vast majority of pyoderma gangrenosum presents in adults.

Clinical pearl: When a patient has PG, conduct a focused and detailed review of systems and any diagnostic studies (such as colonoscopy or laboratory studies) to identify an underlying, driving diagnosis. In such cases, the PG is unlikely to respond to treatment until the underlying etiology is also treated.

For example, the patient below (see Fig. 24.4a–c) was found to have underlying multiple myeloma and an elevated IgA level, who developed numerous lesions of pyoderma gangrenosum which persisted despite systemic steroid therapy and intravenous immunoglobulin. It was not until he began treatment for his multiple myeloma, and a resultant drop in his IgA level that his wounds began to respond to treatment.

Evaluation of suspected pyoderma gangrenosum involves histopathology and deep tissue culture. A wedge excision of the ulcer edge is of the highest yield and should be performed to obtain a sample for pathologic evaluation, ideally by an experienced dermatopathologist. As pyoderma gangrenosum is the result of sterile neutrophilic derangement, identification of a neutrophilic infiltrate is essential for the diagnosis of pyoderma gangrenosum. The Maverakis diagnostic criteria can be used to aid in the diagnosis of pyoderma gangrenosum and they are listed below:

Maverakis Diagnostic Criteria [2]

Diagnosis of pyoderma gangrenosum requires 1 major criterion: biopsy-proven neutrophilic infiltrate of ulcer edge. Additionally, 8 additional minor criteria have been established, with at least 4 out of 8 minor criteria providing 86% sensitivity and 90% specificity.

Major criterion: Biopsy of ulcer edge demonstrates neutrophilic infiltrate (see Fig. 24.5).

Minor criteria:

1. Exclusion of infection
2. Pathergy
3. History of inflammatory bowel disease or inflammatory arthritis
4. History of papule, pustule, or vesicle ulcerating within 4 days of appearance
5. Peripheral erythema, undermining border, and tenderness at ulceration site
6. Multiple ulcerations with at least 1 ulcer on an anterior lower leg
7. Cribriform or "wrinkled paper" scar(s) at healed ulcer sites
8. Decreased ulcer size within 1 month of initiating immunosuppressive medication(s)

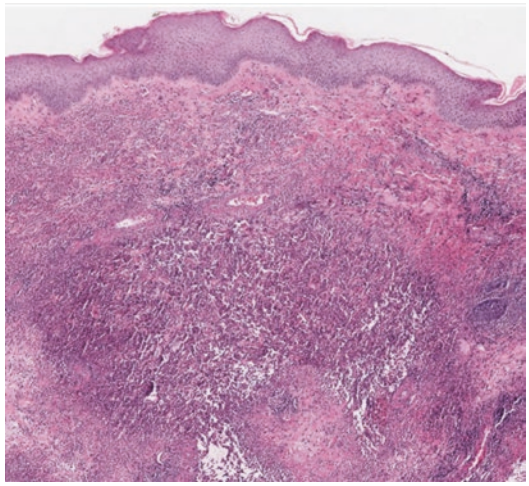


Fig. 24.5 This image shows the classic histopathology of pyoderma gangrenosum with sheet-like aggregates of neutrophils nearly consuming the entirety of the dermis. The intensity of inflammation ultimately can lead to ulceration of the overlying epidermis. With this histopathologic picture, infection must always be carefully excluded with the use of special stains and appropriate tissue cultures [3].

Expert tip: Consider pyoderma gangrenosum in patients with hidradenitis suppurativa (HS)/acne inversa. Patients with a history of hidradenitis suppurativa may have a predisposition to develop pyoderma gangrenosum [4]. HS is another neutrophilic disorder of aberrant immune response. Classically, HS presents as recurrent abscesses and sinus tracts in the intertriginous regions of the body (e.g. groin or axillae) (see Fig. 24.6a). Rarely, a patient will demonstrate HS/PG overlap and may demonstrate both classic HS lesions in the typical areas and ulceration on the lower extremity with tracts and fistulae (such as typically seen in HS) (see Fig. 24.6b).

Autoimmune Bullous Diseases of the Skin

As the skin is an organ of immunity, it is a common target in autoimmune diseases.

Autoimmune blistering diseases are rare skin conditions in which the body's own immune system actively targets adhesion proteins in the epidermis resulting in bullae formation. Several autoimmune disorders (e.g. bullous pemphigoid or pemphigus vulgaris) and other connective tissue diseases such as cutaneous lupus erythematosus may manifest as blisters on the skin. It is helpful to consider that most autoimmune blistering diseases tend to be symmetric and bilateral. While initially sterile, with friction, pressure, or superinfection, these bullae may persist leading to chronic wounds.

One of the most important steps in excluding an autoimmune blistering disease is by performing a full skin and examination of mucous membranes including ocular and oral mucosa. If

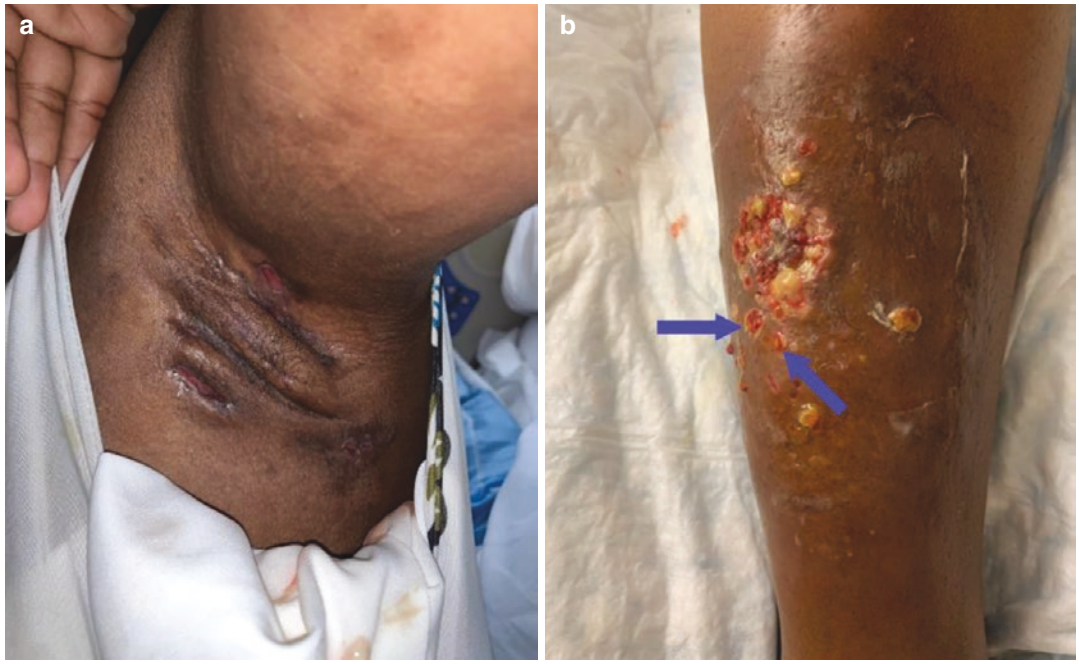


Fig. 24.6 (**a**) Typical presentation of hidradenitis suppurativa in the axilla with sinus tracts and scarring, (**b**) 6 cm cribriform lesion centrally with fistulous tracts (*blue arrows*) on the leg surrounded by erythema. This is a rare variant of hidradenitis suppurativa/pyoderma gangrenosum overlap

multiple areas of blister formation and/or erosion/ulceration are noted, this should raise concern for an underlying autoimmune blistering disease. Further workup (discussed later) includes a skin biopsy for both hematoxylin and eosin (H&E) evaluation and a direct immunofluorescence (DIF) study.

Bullous pemphigoid (BP) traditionally presents as tense and firm bullae with mild to severe pruritus in patients over age 60 (see Fig. 24.7a, b). Bullous pemphigoid may present in a limited fashion below the knees. Of the several types of autoimmune blistering diseases that have been described, it is one of the most common. Circulating immunoglobulins recognize hemidesmosomes (a protein that connects keratinocytes to one another) as foreign, destroying them, which results in dermal–epidermal disadhesion and blister formation that eventually could result in formation of shallow friction ulcers and nonhealing wounds [6]. The blisters of BP are distinctive, very tense, and circular, with a shiny surface, reminiscent of the clear plastic "bubble wrap" included in fragile packages.

If bullous pemphigoid is suspected, skin biopsy with evaluation by H&E (see Fig. 24.7c) and DIF should be considered, with special care given to the appropriate transport media used for each specimen. For detailed recommendations, please refer to the Workup section at the end of this chapter (see Table 24.3).

Clinical pearl: A note on trimming: A wound care provider may be tempted to trim bullae, but this increases the risk for infection (see Fig. 24.7d). Bullae fluid is sterile. The epidermal blister roof, if intact, can serve as a barrier to infection. If a blister is voluminous and uncomfortable for the patient, the blister should be punctured with a sterile needle and the contents drained, with the now deflated blister roof remaining over the top. The small fenestration can be dressed with antimicrobial ointment and dressed with a bandage.

Discoid Lupus Erythematosus

While many forms of cutaneous lupus exist, discoid lupus erythematosus (DLE) is probably the most common lupus type to cause an ulcer. DLE tends to manifest as annular erythematous lesions

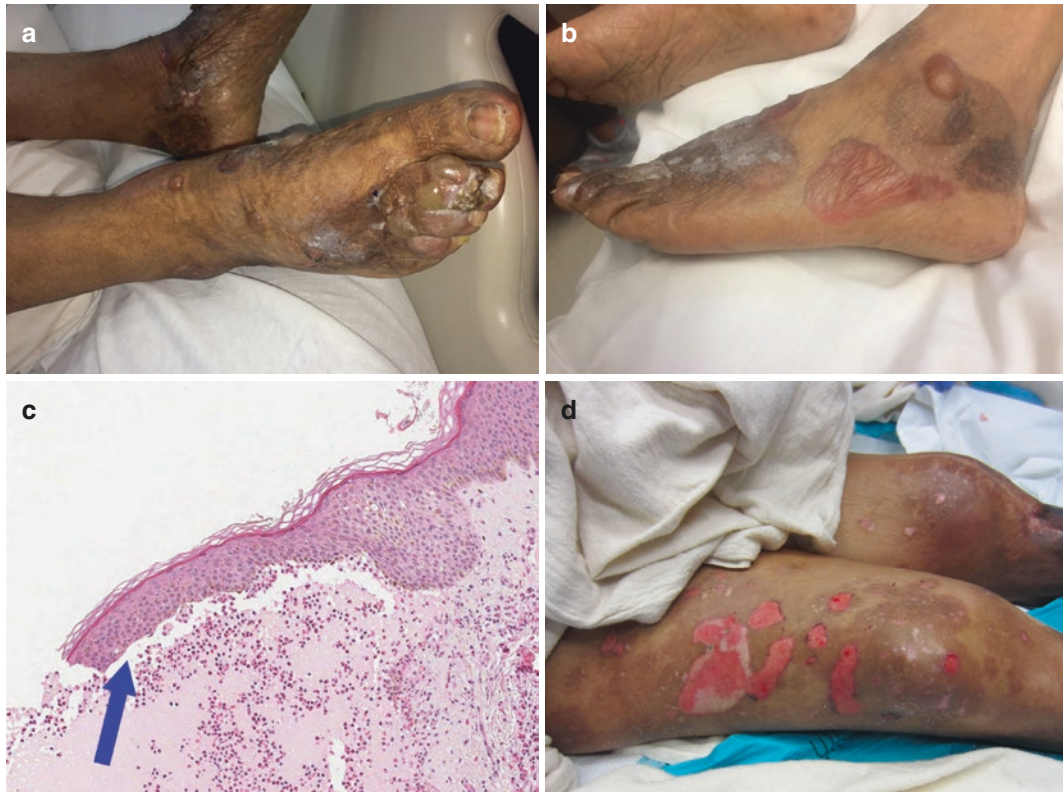


Fig. 24.7 (**a**) Bullous pemphigoid on the digits of the lower extremities. You can see here how fresh bullae reflect light. On palpation these bullae are tense and firm to palpation. Note the hyperpigmentation of the proximal nail fold of the second digit, suggestive of a previous bulla associated with bullous pemphigoid, (**b**) resolving bullae are less reflective and are not as tense and firm as active lesions. Note that the circular hyperpigmentation around the lateral malleolus suggests previously healed bullae in this area, (**c**) histopathology of bullous pemphigoid with subepidermal blister formation (arrow). As the epidermis loses its connection with the underlying dermis, the epidermis will slough off, resulting in ulceration [5], (**d**) appearance of blisters after the blister roof has been removed by trimming, revealing round, shallow ulcerations to the depth of the dermis beneath

that resolve with hypopigmented scarring. These lesions will rarely present on lower extremities if the more common facial manifestations are not present.

While discoid lupus erythematosus tends to be a disease limited to the skin [7], it can on occasion be associated with underlying systemic lupus erythematosus, a well-known multisystem disease. Delphi criteria for the disease as determined by the American College of Rheumatology in 2019 include arthralgias, fever, leukopenia, thrombocytopenia, psychosis, and proteinuria [8]. As is the case with other autoimmune disorders, a thorough history will guide diagnosis toward or away from DLE, in particular DLE associated with systemic disease. If DLE is suspected, a skin biopsy for H&E and DIF evaluation should be performed.

Opportunistic Infections

Opportunistic infection may also be considered in the evaluation of wounds. Breakdown in the skin barrier may also yield easier entry to invasive organisms, such as atypical mycobacterial or fungal species. This section will review common microorganisms and associated opportunistic infections along with associated patient history, risk factors, and presentation.

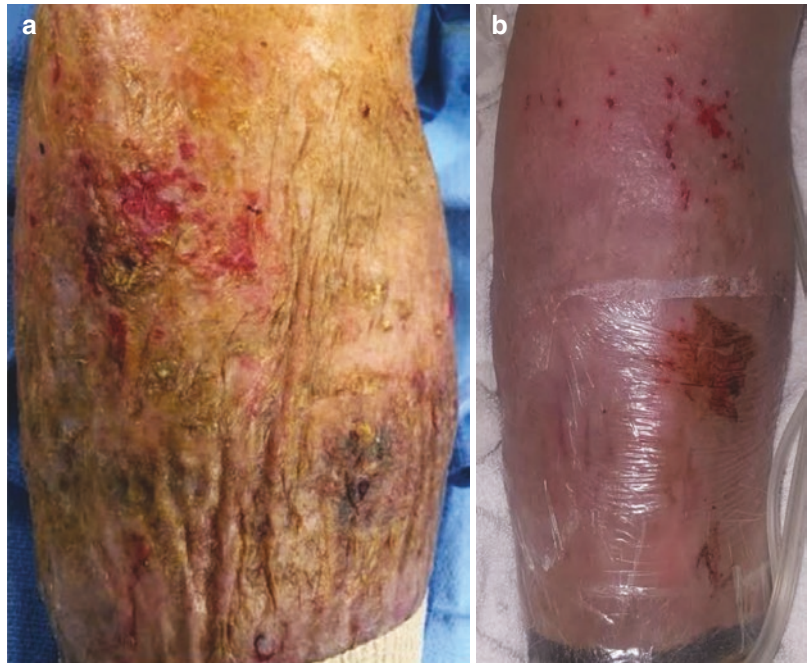


Fig. 24.8 (**a**) This figure demonstrates the effect of over-the-counter Domeboro compresses and 40% urea from initial presentation, in which the provider desired to disinfect the limb before attempting wound closure, (**b**) after 2 days of twice daily application of urea and compresses

If an infectious etiology is suspected, a tissue culture specimen should be obtained and cultured for aerobic and anerobic bacteria, atypical mycobacteria, and fungi. Deep tissue cultures, such as those obtained via punch or excisional biopsy technique, are typically sent to the pathology lab in a sterile cup. They can be placed on a saline dampened sponge or directly into the sterile cup with a splash of normal saline to prevent the tissue from desiccation. Tissue for culture should not encounter formalin. Tissue cultures need to be sent to the lab as soon as possible for processing, ideally within an hour or two of procurement. Unlike tissue placed in formalin, tissue cultures cannot be placed on a shelf and await transport the following day.

In terms of management, debridement and/or antimicrobials tailored to culture data are eminent treatment options.

Clinical pearl: The sequential application of Burow's solution, an antiseptic/astringent compresses, followed by 40% urea cream qHS can be very beneficial in swollen, inflamed, or thickened skin (see Fig. 24.8a, b). Burow's solution can be obtained over-the-counter or can be purchased as a convenient powdered formulation in packets to be mixed with water. The astringent property decreases swelling and weeping. Additionally, aluminum acetate is active against S. aureus and P. aeruginosa, decreasing bacterial colonization and decreasing inflammation at the site. Urea is a potent keratolytic with humectant properties, effective at gently lifting and removing retained hyperkeratosis while hydrating the skin. This combination can be used to promote de-novo healing, or prior to planned grafting or amputation to promote a healthy closure. The urea should be discontinued once the skin is resolved of hyperkeratosis and smooth.

Another useful tool to prevent colonization and infection is the use of gentian violet. Gentian violet has recently gained popularity as a topical antiseptic due to its effectiveness, low cost, and availability as an FDA-approved over-the-counter medication. Well known for its antimicrobial properties, gentian violet has been used to treat

oral candidiasis and in coating urinary catheters to reduce the risk of urinary tract candidiasis [9, 10]. In terms of antibacterial properties, gentian violet has been used in the treatment of impetigo as well as demonstrated in randomized controlled trials to be more effective than iodine in killing MRSA [9].

Clinical pearl: Gentian violet is also a useful indicator of patient adherence, as it turns the skin a characteristic violet after application.

Atypical Mycobacterial Infection

Atypical mycobacterial infections manifest as single or multiple erythematous lesions. See Table 24.1 for a summary of clinical presentations and history. In immunocompromised patients, atypical mycobacterial infections may induce a distal to proximal "sporotrichoid spread": suppurative/ulcerated/inflamed nodules which usually present at the distal upper extremities and produce successive proximal lesions along lymphatic drainage [11, 12] (See Fig. 24.9a–c).

Fungal Infections

The workup of wounds should also include fungal cultures, especially in transplant recipients, patients with HIV, or other immunocompromised patients such as patients with uncontrolled diabetes mellitus. See Table 24.2 for a relevant summary [14].

Clinical pearl: A note on Tinea incognito: Tinea incognito is a dermatomycosis that can be exacerbated by the use of systemic or local corticosteroids. Use of these anti-inflammatory agents promotes the proliferation of the dermatophyte and encourages the *Tinea* dermatophytes to dive

Table 24.1 Summary of atypical mycobacteria with relevant clinical presentation and history

Mycobacterium	Cutaneous presentation	History
M. marinum	Sporotrichoid spread from point of inoculation	"Swimming pool granuloma," cleaning fish tanks, swimming in freshwater lakes or unchlorinated swimming pools
M. ulcerans	Firm, painless, mobile subcutaneous module, may progress to necrosis, destruction of nervous, musculoskeletal, vascular tissue	Central/West Africa, Japan, SE Asia, Australia, South America
M. avium complex (MAC)	Rare cutaneous involvement, but presents as necrotic papules with sporotrichoid spread	History of AIDS/immunocompromised
M. fortuitum/chelonae complex	Erythematous subcutaneous nodules with sporotrichoid spread	Recent trauma, surgery, injection

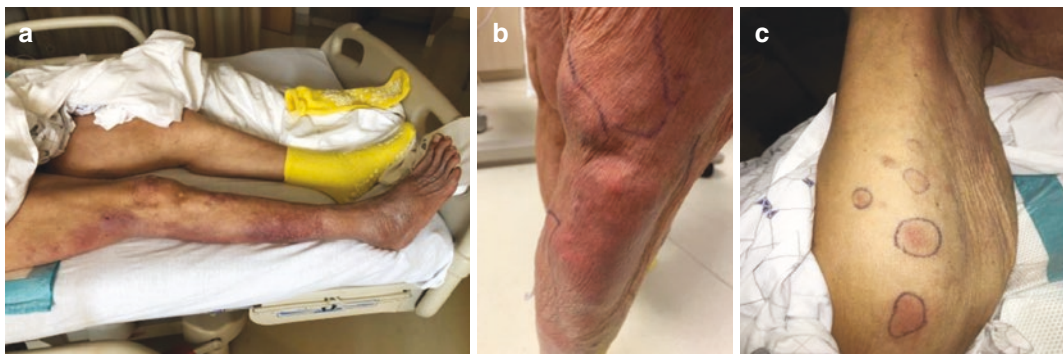


Fig. 24.9 (**a**) A patient with an erythematous right lower extremity with distinct skip areas and nodularity, inconsistent with venous stasis dermatitis or dermatosclerosis, (**b**) skin markings/wrinkles over lesions in the same patient, inconsistent with lymphedema, (**c**) deep-seated indurated nodules with sporotrichoid spread from the same patient, suggestive of atypical mycobacterial infection

Table 24.2 Summary of fungal infections in wound care

Fungal organism	Cutaneous presentation	History
Aspergillus flavus/fumigatus	Necrotic papules/nodules	Immunocompromised, impaired skin barrier due to wounds, burn, trauma
Mucormycetes spp.[a] (formerly *Zygomycetes*)	Dark eschar at point of inoculation, commonly in facial/sinus areas	Immunocompromised, neutropenia, poorly controlled diabetes
Candida albicans[b]	Interdigital superinfection with satellite lesions	Immunocompromised, high moisture wound dressing
Tinea pedis	Annular superficial erythematous plaques of the feet with scale	Male sex, walking barefoot in locker rooms, gyms
Tinea incognito[c]	Annular erythematous macules/plaques with hypopigmentation and diminished/absent scale	Misuse of systemic or local corticosteroids

[a]See Fig. 24.10a–d
[b]See Fig. 24.11
[c]See Fig. 24.12

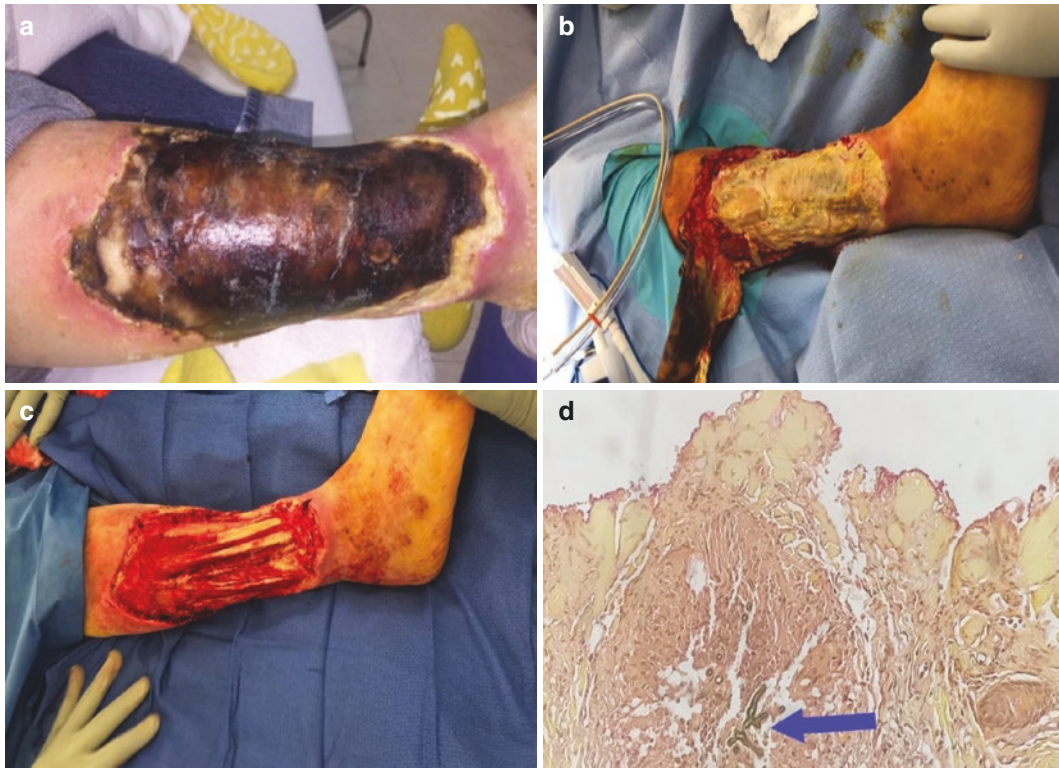


Fig. 24.10 (**a**) Ulcer with dry, necrotic eschar that had slowly expanded over the course of months in a patient with poorly controlled diabetes mellitus [13], (**b**) removal of the eschar revealed significant amounts of necrosis [13], (**c**) removal of necrotic tissue down to tendon [13], (**d**) histology demonstrates broad, non-septate hyphae consistent with mucormycosis (*blue arrow*). (d, Courtesy, Arash Radfar, MD)



Fig. 24.11 Erosio interdigitalis blastomycetica due to *C. albicans infection*



Fig. 24.12 Confluent faint erythematous patch without scale overlying the lateral left lower extremity from a patient with *Tinea incognito*

into adnexal structures such as hair follicles [9] causing a fungal folliculitis. See Fig. 24.12.

When situated in the dermis, *Tinea* may be more difficult to detect as the characteristic erythema and round morphology may be obscured. Additionally, tinea treated with steroids is usually lacking the characteristic scale on the surface of the skin. Fungal folliculitis usually requires systemic antifungal medications for several weeks to cure, as antifungal medications applied topically do not reach the depth of the infection. Therefore, dermatologists generally discourage the use of combination or concomitant use of anti-inflammatory/antifungal creams.

Ecthyma Gangrenosum

Ecthyma gangrenosum is a cutaneous manifestation of septic *Pseudomonas aeruginosa* angioinvasion. Lesions may initially develop on the extremities as hemorrhagic vesicles/bullae that progress into a central black eschar surrounded by tender and erythematous tissue [15].

Allergic Contact Dermatitis

Allergic contact dermatitis is another useful consideration in the management of atypical wounds. In contrast to pyoderma gangrenosum and DLE, allergic contact dermatitis is a sterile reaction to a foreign but innocuous antigen. The type IV delayed hypersensitivity reaction associated with allergic contact dermatitis can hinder wound healing. Furthermore, the impaired protective skin barrier in the setting of wound care may further facilitate sensitization to allergens.

Several components of routine wound care are potential causes of allergic contact dermatitis: topical antibiotics such as neomycin and bacitracin, ointments containing balsam of Peru, hydrogels containing propylene glycol, and hydrocolloids containing colophonium. Moisturizing substances such as lanolin or wood alcohols can cause periwound maceration [16].

According to North American Contact Dermatitis Group (NACDG) patch testing data from 2017 to 2018, balsam of Peru and topical antibiotics are the most common causes of allergic contact dermatitis. Balsam of Peru is of particular concern to the wound care provider because it may

be found in combination ointments [16], whether applied in clinic or at home. Per NACDG patch testing data from 2017 to 2018, 7.1% of allergic contact dermatitis patients experienced reactions to balsam of Peru [16]. Colophonium/resin may be found in some hydrocolloid dressings and may cross react with balsam of Peru [16].

Antibiotics constitute a key component of wound care, although common topical antibiotics such as neomycin and bacitracin may induce allergic contact dermatitis and impede normal wound healing (see Fig. 24.13). Of the two, neomycin is especially of note as it is the most used topical antibiotic. NACDG patch testing results up to 2018 have demonstrated that 5.4% to 13% of patch-tested patients exhibit a contact dermatitis reaction to this aminoglycoside and that it consistently appears within the top 15 most common causes of contact dermatitis [17–19]. The associated contact dermatitis reaction can manifest with extensive inflammation and skin breakdown, but neomycin reaction may not necessarily be the first thought that comes to mind.

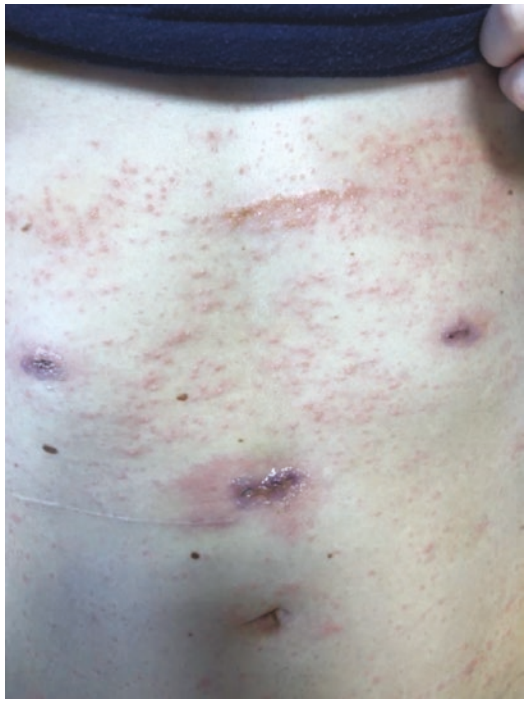


Fig. 24.13 Contact dermatitis on the abdomen of a patient who had laparoscopic surgery. He was applying Neosporin™ to his surgical sites. You can see the intense inflammation at the site of his surgical wounds and also an "id reaction," also known as an "autoeczematous response," manifesting as innumerable small papules, in the surrounding skin. The treatment for both conditions is withdrawal of the offending topical allergen

In addition to neomycin and bacitracin, other antibiotics that may cause contact dermatitis include polymyxin B and gentamicin, a known cross-reactant with neomycin.

Removing the offending allergen and continued avoidance will alleviate allergic contact dermatitis. Use of topical steroid ointment such as clobetasol or triamcinolone twice daily can speed the resolution of the eruption and provide relief of pruritus. Be sure to avoid placing steroid ointment directly on surgical incisions in the immediate post-operative period; we recommend sparing the area 1cm around the incision. Discontinue steroids as soon as the rash is no longer pruritic to avoid side effects from topical steroids. If these allergens constituted a component of previous wound care, the wound care provider may need to consider non-allergy-provoking substitutes. Patch testing is a further step that can establish a patient's allergy profiles and personalize wound treatment regimens going forward.

Clinical pearl: It is important to distinguish irritant contact dermatitis from allergic contact dermatitis. Irritant contact dermatitis is caused by direct tissue damage following exposure to a known irritant—for this reason irritant contact dermatitis tends to be localized. Because allergic contact dermatitis is mediated through immunologic mechanisms, *allergic contact dermatitis tends to involve skin beyond the area of application*. Allergic contact dermatitis also tends to be intensely pruritic.

Cutaneous Malignancy

The wound care provider should also consider that skin malignancies may be another source of wounds. The protective skin barrier that is caught in the vicious cycle of barrier disruption and chronic inflammation may continue to deteriorate, or it may exit the cycle via malignant transformation. Lesions in these cases tend to present as fungating wounds.

Squamous Cell Carcinoma

Areas which have undergone radiation or thermal treatment are at heightened risk for squamous



Fig. 24.14 (**a**) Multinodal cutaneous squamous cell carcinoma in a patient with a history of pyoderma gangrenosum, with a fungating central lesion suggestive of squamous cell carcinoma, deemed unresectable, (**b**) Post-treatment appearance after administration of systemic immunotherapy

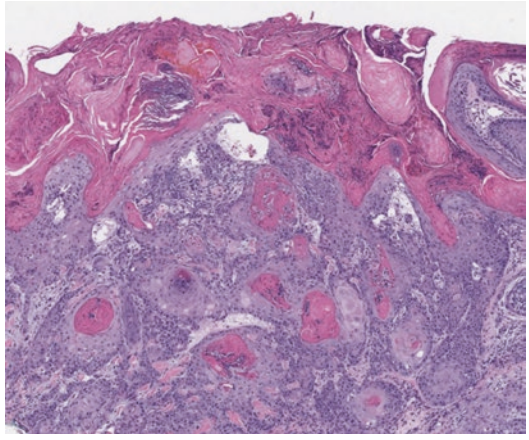


Fig. 24.15 Depicted is an example of squamous cell carcinoma on histopathology which shows a markedly atypical with a lack of maturation, large keratinocytic islands and squamous eddies as well as thick overlying crust [20]



Fig. 24.16 Here on the left buttock of a young man is a large, crateriform non-healing wound at the center of surrounding sinus tracts. Biopsy revealed that this was a Marjolin's ulcer. This poorly differentiated squamous cell carcinoma developed after several years of uncontrolled hidradenitis suppurativa. Further workup revealed metastatic disease

cell carcinoma due to increased keratinocyte activity. Persistent ulceration or inflammation in the context of hidradenitis suppurativa, especially in the inguinal folds, may be another driver of keratinocyte activity and risk for squamous cell carcinoma. See Figs. 24.14a, b and 24.15.

Marjolin's Ulcer

Marjolin's ulcer describes a delayed malignant transformation associated with scarred tissue. Most Marjolin's ulcers are squamous cell carcinomas and occur over lower extremity scars. While Marjolin's ulcer is primarily associated with old burn trauma and secondarily with osteomyelitis, they may also arise from venous stasis ulcers, pressure ulcers, hidradenitis suppurativa (see Fig. 24.16), or trauma.

Malignant transformation takes on average 30–35 years to manifest, but acute variations of

Marjolin's ulcer exist with some reports of disease following 6 months after injury [15]. Given this variable range, a patient who presents with more than 3 months of a triad including nodularity, induration, and ulceration over an area of scarring should warrant consideration of Marjolin's ulcer.

Other forms of skin cancer that could present as a non-healing wound include basal cell carcinoma and rarer malignancies such as epithelioid angiosarcoma. Nonmalignant causes of fungating wounds include pseudoepitheliomatous hyperplasia, a close, but benign mimic of squamous cell carcinoma. For this reason, we prefer that such biopsies be sent to an experienced dermatopathologist.

Vascular Diseases

Venous and arterial ulcers are commonly seen and therefore will not be discussed here. This section will focus on less common dermatologic entities caused by vascular diseases such as calciphylaxis, vasculopathy, and vasculitis.

A common and nonspecific manifestation of vascular disease in the setting of atypical wounds is retiform purpura, a net-like lesion with non-blanching and visible hemorrhage into the skin and mucous membranes. The non-blanching purpuric characteristic of retiform purpura differentiates it from livedo reticularis, another net-like lesion.

Retiform purpura occurs from thrombus formation in small cutaneous vessels and carries with it a broad differential ranging from vasculitis to vessel occlusion. When the wound care provider suspects a vascular etiology with retiform purpura, a sample for direct immunofluorescence should be obtained and sent in Michel's/Zeus transport media in addition to a sample for hematoxylin and eosin staining.

Calciphylaxis

Calciphylaxis typically presents as extremely painful, edematous, retiform, non-blanching purpura, plaques, or livedo reticularis. Of note, retiform purpura is not a specific finding of calciphylaxis and heads a broad differential, which will be covered further in this chapter.

In later stages of calciphylaxis, the wound may form a central, leathery, bound down eschar with a surrounding dusky, reticular plaque (see Fig. 24.17a–c). Traditional locations of calciphylaxis have a predilection for areas with high amounts of adipose tissue, such as the thigh, buttocks, trunk, and upper extremities, but may involve atypical locations like the penis, digits, and lower extremities.

Calciphylaxis can be further characterized into uremic and nonuremic disease. Risk factors for uremic disease revolve around hypercalcemic conditions such as end-stage renal disease and secondary hyperparathyroidism to calcium and/or vitamin D supplementation (see Fig. 24.18a). Nonuremic etiologies can arise due to liver dis-

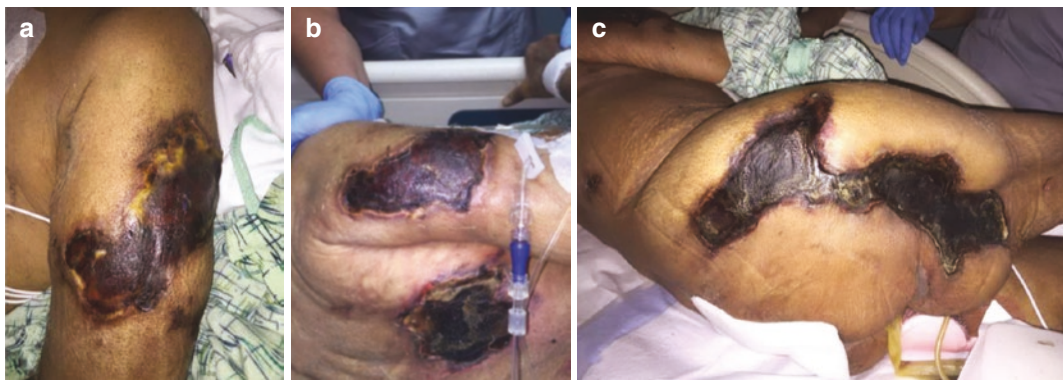


Fig. 24.17 (**a**–**c**) Retiform, "star-like" eschar as seen in calciphylaxis

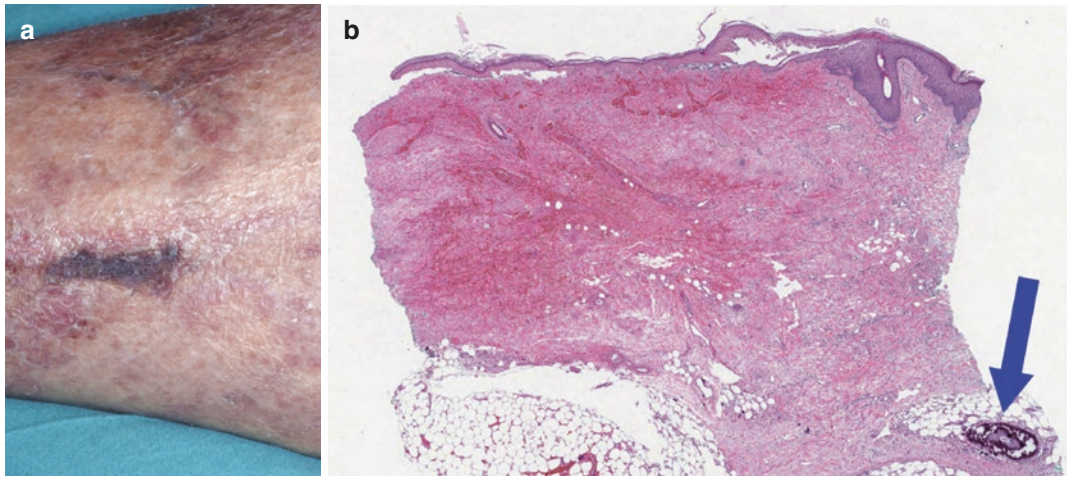


Fig. 24.18 (**a**) Faint dusky retiform plaques with overlying dried serosanguineous crust on leg of a patient with renal failure, early calciphylaxis lesion, (**b**) this photomicrograph shows calciphylaxis with calcium deposits in the vessel in the deep dermis (see arrow) which have resulted in overlying dermal and epidermal necrosis [21]

ease, warfarin, or malignancy. Elevated alkaline phosphatase and low serum albumin have also been identified as risk factors for calciphylaxis. Patients undergoing hemodialysis or the use of calcium-based phosphate binders such as calcium carbonate will place patients at a higher risk of vascular calcium deposition and calciphylaxis (see Fig. 24.18b). Additional risk factors identified include female gender, hyperphosphatemia, obesity, and diabetes mellitus [22].

Management of calciphylaxis focuses on removing the underlying source of hypercalcemia and preventing secondary infection of wounds. Whether to debride the wounds is debated, as in some cases this causes pathergy. Partnership with dermatology is recommended.

Vasculitis

Small to medium vessel vasculitis describe endothelial inflammation in postcapillary vasculature that can cause retiform purpura [23].

IgA vasculitis/Henoch-Schönlein purpura is thought to induce retiform purpura through IgA immune complex deposition.

ANCA vasculitis such as microscopic polyangiitis, granulomatosis with polyangiitis/Wegener's granulomatosis, and eosinophilic granulomatosis with polyangiitis/Churg-Strauss syndrome may also present with retiform purpura [24]. Both microscopic polyangiitis and granulomatosis with polyangiitis may present with glomerulonephritis.

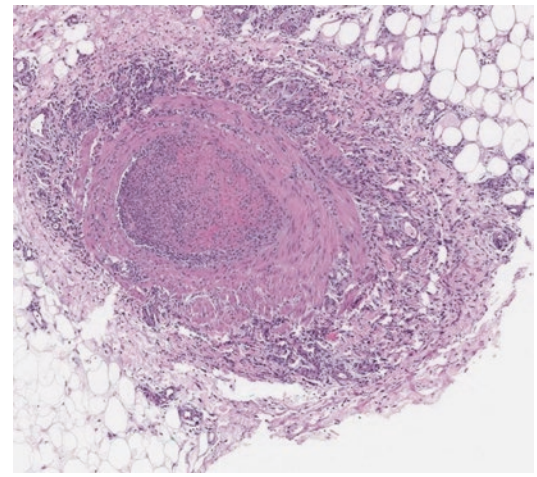


Fig. 24.19 This figure shows a massively inflamed medium caliber artery in the subcuticular tissues characteristic of vasculitis/polyarteritis nodosa. Inflammation of vessels can lead to vessel destruction which eventually can result in ulceration of the skin [25]

Polyarteritis nodosa (PAN) is a medium vessel vasculitis (see Fig. 24.19) that may exhibit systemic manifestations with fever, arthralgias,

myalgias, abdominal pain, and renovascular hypertension or may simply be limited to cutaneous signs like retiform purpura. Cutaneous PAN tends to be a chronic and benign disease and recently has been theorized to be an altogether separate process from systemic PAN [26].

Other vasculitides that can cause retiform purpura include rheumatoid vasculitis or septic vasculitis.

Vasculopathies

In contrast to vasculitis, vasculopathies describe an occlusion of the vasculature that can manifest as retiform purpura. This can arise from angioinvasive organisms or occlusive conditions such as calciphylaxis or thrombophilia.

Heparin-induced thrombocytopenia (HIT) may induce platelet activation and subsequent thrombocytopenia and should be consistent with the patient's medication history.

Cryoglobulinemia/cryofibrinogenemia describes the excessive vascular deposition of antibodies or fibrinogen in response to cold temperature.

Underlying coagulation disorders such as protein C/S deficiencies, antiphospholipid syndrome [27], livedoid vasculopathy, and use of levamisole-adulterated cocaine may also contribute toward a presentation of livedo reticularis.

Angioinvasive organisms include fungi such as *Aspergillus* and *Mucor* spp. These infections and their associated cutaneous manifestations are covered in the "Opportunistic Infections" section above.

The context of thrombophilia as well as an accurate patient history is important to the consideration of thrombophilia.

Workup

This section ties together a summary of biopsy locations and appropriate media to use for dermatopathology evaluation. Once the wound care provider has considered the possibility of a dermatologic wound before debridement, the next step is to obtain three specimens for histopathologic analysis (see Table 24.3).

It is important to keep each specimen organized in its correct transport media. A common mistake is to send a sample in an inappropriate medium, such as a sample intended for DIF or culture, incorrectly sent in formalin rather than correctly sent in Michel's/Zeus transport media or sterile cup, respectively.

All specimen containers should be labeled with the patient's name and the site from which they were procured. It is also helpful for the clinician to provide an adequate history (i.e. concern for calciphylaxis) along with the specimen, as this can focus pathology evaluation.

Obtaining Specimens: Recommended Sites and Transport Media

For larger wounds, the main specimen should be obtained via an elliptical wedge incision at the ulcer edge (see Fig. 24.20). This specimen should be from a wound that is over 72 h old and should be sent in a formalin bottle for H&E analysis.

A tissue culture specimen should be obtained from a representative site and should be about 4–6 mm in size. This should be submitted in a sterile urine cup with sterile gauze/saline with orders for tissue culture for bacteria, fungi, and

Table 24.3 Summary of the three different biopsy specimens, sites, and recommended transport media

	Main specimen	Tissue culture specimen	Peripheral specimen
Purpose	Is there pyoderma gangrenosum, malignancy, or calciphylaxis?	Is there an opportunistic infection?	Is there underlying vasculitis, vasculopathy, or autoimmune process?
Specimen site	Elliptical wedge incision at ulcer edge, >72 h old	Representative site, 4–6 mm	Representative site, <24 h old
Media	Formalin	Sterile urine cup with sterile gauze/saline	Michel's/Zeus transport media
Orders	H&E	Mycobacterial, fungal, and bacterial cultures	DIF

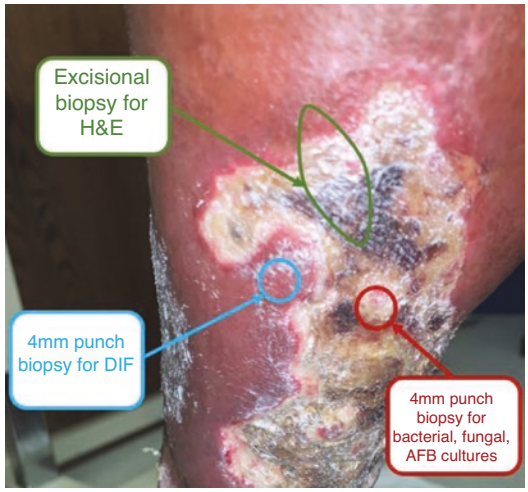


Fig. 24.20 Representative specimen sites for H&E, tissue culture, and DIF analysis

acid-fast bacilli. Tissue cultures need to be sent to the lab as soon as possible for processing, ideally within an hour or two of procurement. Unlike tissue placed in formalin, tissue cultures cannot be placed on a shelf and await transport the following day.

A peripheral specimen for DIF should be obtained from a new specimen under 24 h old when concern for vasculitis exists. This should be submitted in Michel's/Zeus transport media for direct immunofluorescence to ascertain the presence of autoimmune skin disease or vasculitis.

Michel's/Zeus transport media is a hyperosmolar sucrose solution which will allow any immune components in the sample to remain bound. It is important not to expose the peripheral specimen to formalin at all, as formalin will instantly destroy antibodies and subsequent DIF will return a false negative result. This inaccurate reading will also require a second biopsy and more tissue.

If possible, it is best to have stains read by a board-certified dermatopathologist. There is frequent overlap in the histopathological findings of atypical wounds: for example, a surface-level reading of "neutrophilic invasion present" does not resolve the question of pyoderma gangrenosum vs. bacterial infection. Histopathology may occasionally make a definitive diagnosis, however, frequently the biopsy provides more information, but not a definitive diagnosis and therefore, the wound care provider should also draw from clinical and historical clues to solidify the diagnosis.

Further Management

Pyoderma Gangrenosum

If an atypical wound is suspected, the patient should be counseled to:

- Check wound frequently.
- Avoid disturbing the wound by picking/popping lesion.
- Use non-stick dressings to avoid pathergy with dressing changes.
- Return to clinic in the event of pathergy/enlarging wound.

Atypical Mycobacterial Infection

Atypical mycobacterial infections are difficult to treat and require partnership with infectious disease to determine targeted systemic antimicrobial therapy. The duration of treatment necessary is often several months.

Fungal Infection

When weighing fungal vs. autoimmune wound etiologies, it is important to never combine steroids and antifungal medications as this runs the risk of Tinea incognito, as discussed in the fungal infections section above.

Our recommendation is to trial topical antifungals first before attempting topical immunomodulatory agents.

Contact Dermatitis

Remove offending allergen with continued avoidance and consider alternative wound care modalities. Document the allergen and patient reaction in the electronic medical record.

Malignancy

Marjolin's ulcer and SCC should be preferably excised via wide local excision.

Multinodal SCC deemed unresectable may be managed by PD-1 inhibitory therapy.

Calciphylaxis

After a diagnosis of calciphylaxis, management extends beyond routine wound care considerations such as removal of triggers, maximizing blood flow and nutrition, preventing infection, and promoting healing:

- Remove triggers.
  - Warfarin can be changed to apixaban.
  - Sources of exogenous calcium should be replaced with alternatives such as low Ca2+ dialysate or non-calcium phosphate binders like Sevelamer.
- Check protein C and S levels.
- Assess venous and arterial insufficiency on lower extremities.
- Maximize blood flow with pentoxifylline, compression.
- Maximize nutrition with high protein diet.
- Utilize medications to prevent calcium deposition such as IL and/or IV sodium thiosulfate, cinacalcet.
- Prevent infection with silver impregnated dressings.
- Optimize wound healing with advanced wound dressings, HBO.
- Pain management: gabapentin, Cymbalta, opioids.

Clinical Pearls

Diagnostic pearls

- Violaceous border in pyoderma gangrenosum suggests an actively expanding lesion.
- Retiform purpura with pain out of proportion suggests calciphylaxis.
- If an atypical wound is suspected, the wound care provider should consider obtaining three specimens:
  - Main specimen from lesion >72 h old, obtained by elliptical wedge incision and submitted for H&E analysis in formalin bottle.
  - Tissue culture specimen submitted in sterile urine cup/gauze and submitted for bacterial, fungal, and acid-fast bacilli cultures.
  - Peripheral specimen from lesion <24 h old, submitted for direct immunofluorescence in Michel's/Zeus transport media.

Management pearls

- Counsel patient on wound care with low threshold to return to clinic if concerned for pyoderma gangrenosum.
- Neomycin is a common contact allergen, avoid if possible.
- Do not combine antifungal and topical steroids due to the risk of tinea incognito.
- Restore skin barrier function with topical moisturizers containing ceramides.
- Domeboro compressions/soaks +40% urea as astringent/antibacterial.
- Gentian violet as an antifungal agent.

Acknowledgment This chapter contains images that were reproduced from the Michigan Medicine Department of Pathology Virtual Slide Box Dermatopathology collection (https://www.pathology.med.umich.edu/slides/search.php?collection=DermPath&dxview=show) with permission from the Regents of the University of Michigan.

Disclaimer The opinions and assertions expressed herein are those of the author(s) and do not reflect the official policy or position of the Uniformed Services University of the Health Sciences or the Department of Defense.

Conflicts of Interest None.

References

1. Davis Mark DP, Moschella SL. Neutrophilic dermatoses. In: Bolognia JL, Schaffer JV, Cerroni L, editors. Dermatology. 4th ed. Amsterdam: Elsevier Limited; 2018. p. 453–471.e2.
2. Maverakis E, Ma C, Shinkai K, et al. Diagnostic criteria of ulcerative pyoderma Gangrenosum: a Delphi consensus of international experts. JAMA Dermatol. 2018;154:461–6.
3. McClintock D. Slide 48552: Pyoderma gangrenosum. In: University of Michigan Medicine Department of Pathology Virtual Slide Box, Dermatopathology Collection. https://www.pathology.med.umich.edu/slides/oldfilmstrip.php?loc=QXJwcyUyRkFycHMlMjUyMHNsaWRlcyUyNTIwMzMwJTI1MjB0aHJ1JTI1MjAzMzUlMkZIJTI2RV80ODU1Mm5sLnN2cw==&myname=48552&stain=H%26E. Accessed 19 Dec 2021.
4. Tannenbaum R, Strunk A, Garg A. Overall and subgroup prevalence of pyoderma gangrenosum among patients with hidradenitis suppurativa: a population-based analysis in the United States. J Am Acad Dermatol. 2019;80:1533–7.
5. McClintock D. Slide 63036: Bullous pemphigoid. In: University of Michigan Medicine Department of Pathology Virtual Slide Box, Dermatopathology Collection. https://www.pathology.med.umich.edu/slides/oldfilmstrip.php?loc=RGVybVBhdGglMkZEZXJtUGF0aCUyNTIwQ29uZmVyZW5jZSUyRkFuZGVhJTI1MjAyMDE2MDcyOSUyRkglMjZFXzYzMDM2bmwuc3Zz&myname=63036&stain=H%26E. Accessed 19 Dec 2021.
6. Bernard P, Borradori L. Pemphigoid group. In: Bolognia JL, Schaffer JV, Cerroni L, editors. Dermatology. 4th ed. Amsterdam: Elsevier Limited; 2018. p. 510–526.e2.
7. Elman SA, Joyce C, Nyberg F, et al. Development of classification criteria for discoid lupus erythematosus: results of a Delphi exercise. J Am Acad Dermatol. 2017;77:261–7.
8. Aringer M, Costenbader K, Daikh D, et al. 2019 European league against rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. Arthritis Rheumatol. 2019;71:1400–12.
9. Maley AM, Arbiser JL. Gentian violet: a 19th century drug re-emerges in the 21st century. Exp Dermatol. 2013;22(12):775–80. https://doi.org/10.1111/exd.12257.
10. Hachem R, Reitzel R, Borne A, Jiang Y, Tinkey P, Uthamanthil R, Chandra J, Ghannoum M, Raad I. Novel antiseptic urinary catheters for prevention of urinary tract infections: correlation of in vivo and in vitro test results. Antimicrob Agents Chemother. 2009;53:5145–9.
11. Ramos-e-Silva M, Ribeiro de Castro MC. Mycobacterial infections. In: Bolognia JL, Schaffer JV, Cerroni L, editors. Dermatology. 4th ed. Amsterdam: Elsevier Limited; 2018. p. 1296–318.
12. Rapini, R. P. Practical Dermatopathology, Third edition.; Elsevier: Philadelphia, PA, 2021.
13. Coerdt KM, Zolper EG, Starr AG, Fan KL, Attinger CE, Evans KK. Cutaneous mucormycosis of the lower extremity leading amputation in two diabetic patients. Arch Plast Surg. 2021;48(2):231–6. https://doi.org/10.5999/aps.2020.00549. Epub 2021 Mar 4. PMID: 33657778; PMCID: PMC8007453.
14. Elewski BE, Hughey LC, Hunt KM, Hay RJ. Fungal diseases. In: Bolognia JL, Schaffer JV, Cerroni L, editors. Dermatology. 4th ed. Amsterdam: Elsevier Limited; 2018. p. 1329–63.
15. Sommer LL, Reboli AC, Heymann WR. Bacterial diseases. In: Bolognia JL, Schaffer JV, Cerroni L, editors. Dermatology. 4th ed. Amsterdam: Elsevier Limited; 2018. p. 1259–95.
16. Smart V, Alavi A, Coutts P, Fierheller M, Coelho S, Linn Holness D, Sibbald RG. Contact allergens in persons with leg ulcers: a Canadian study in contact sensitization. Int J Low Extrem Wounds. 2008;7:120–5.
17. DeKoven JG, Silverberg JI, Warshaw EM, et al. North American contact dermatitis group patch test results: 2017-2018. Dermatitis. 2021;32:111–23.
18. DeKoven JG, Warshaw EM, Zug KA, et al. North American contact dermatitis group patch test results: 2015-2016. Dermatitis. 2018;29:297–309.
19. Gehrig KA, Warshaw EM. Allergic contact dermatitis to topical antibiotics: epidemiology, responsible allergens, and management. J Am Acad Dermatol. 2008;58:1–21.
20. McClintock D. Slide 51174: Invasive, well-differentiated squamous cell carcinoma. In: University of Michigan Medicine Department of Pathology Virtual Slide Box, Dermatopathology Collection. https://www.pathology.med.umich.edu/slides/oldfilmstrip.php?loc=bmV3c2NhbnMlMkZIJTI2RV81MTE3NG5sLnN2cw==,RGVybVBhdGglMkYyMDE1JTI1MjBWU0IlMkZIJTI2RV81MjI5NW5sLnN2cw==&myname=51174,52295&stain=H%26E,H%26E. Accessed 20 Dec 2021.
21. McClintock D. Slide 61317: Calciphylaxis. In: University of Michigan Medicine Department of Pathology Virtual Slide Box, Dermatopathology Collection. https://www.pathology.med.umich.edu/slides/oldfilmstrip.php?loc=RGVybVBhdGglMkZBbG9tYXJpLUd1dG1hcmslMjUyMENvbGxlY3Rpb24lMkZBbG9tYXJpX3JlcSUyNTIwMTM4Nl9KdW5lJTI1MjAyMDE2JTJGSCUyNkVfNjEzMTdubC5zdnM=&myname=61317&stain=H%26E. Accessed 5 Dec 2021.
22. Kroshinsky D, Fairley JA. Calcifying and ossifying disorders of the skin. In: Bolognia JL, Schaffer JV, Cerroni L, editors. Dermatology. 4th ed. Amsterdam: Elsevier Limited; 2018. p. 784–792.e1.
23. Wetter DA, Dutz JP, Shinkai K, Fox LP. Cutaneous vasculitis. In: Bolognia JL, Schaffer JV, Cerroni L,

editors. Dermatology. 4th ed. Amsterdam: Elsevier Limited; 2018. p. 409–439.e3.
24. Valerio Marzano A, Raimondo MG, Berti E, Meroni PL, Ingegnoli F. Cutaneous manifestations of ANCA-associated small vessels vasculitis. Clin Rev Allergy Immunol. 2016;53(3):428–38. https://doi.org/10.1007/s12016-017-8616-5.
25. McClintock D. Slide 91398: Polyarteritis nodosa. In: University of Michigan Medicine Department of Pathology Virtual Slide Box, Dermatopathology Collection. https://www.pathology.med.umich.edu/slides/oldfilmstrip.php?loc=SCUyNkVfOTEzOThubC5zdnM=&myname=91398&stain=H%26E. Accessed 15 Dec 2021.
26. Alibaz-Oner F, Koster MJ, Crowson CS, Makol A, Ytterberg SR, Salvarani C, Matteson EL, Warrington KJ. Clinical spectrum of medium-sized vessel vasculitis. Arthritis Care Res (Hoboken). 2017;69:884–91.
27. Weinstein S, Piette W. Cutaneous manifestations of antiphospholipid antibody syndrome. Hematol Oncol Clin North Am. 2008;22:67–77.

25 Prosthetics, Orthotics, and Amputation Rehabilitation

Benjamin G. Higgs

Collaboration with Medstar

The Medstar Georgetown University Hospital (MGUH) Center for Wound Healing (CWH) collaborates with a variety of specialists to create a comprehensive environment for patient care, providing an avenue for patients with at-risk limbs to meet with an extensive limb salvage team. A prosthetist in clinic is one part of this team that also includes podiatry, vascular, plastic, orthopedic, hyperbaric, and rheumatoid specialties. At each clinic visit, the patient has an opportunity to consult with several team members in an effort to provide an inclusive plan to optimize care. Since this is a specialized limb salvage team, the patient can rest assured knowing that the route of amputation either provides optimum function above what would be obtained when saving the limb or will occur as the last result after other treatment modalities are explored. This chapter will focus on the prosthetic and orthotic intervention assisting with limb preservation or providing care throughout the amputation process when limb salvage is no longer the most practical option.

Preventative Measures

Comorbidities and other detrimental health outcomes for patients with diabetes are well documented, including neuropathy, dysvascularity, and an increased susceptibility of limb loss [1]. As of 2020, there are 34.2 million Americans, nearly 1 in 10, living with diabetes mellitus (DM) [2]. Furthermore, an individual with diabetes is 28 times more likely to receive an amputation than an individual without diabetes, and two-thirds of the 2.1 million Americans living with limb loss have diabetes [1–3].

In diabetes related lower extremity amputations, 85%, are preceded by foot ulcerations [1, 4]. Each year, ulcerations develop in 5% of diabetic patients, and 1% require amputation. Importantly, the ulcerative recurrence rate is 66% in this patient population and the likelihood of amputation rises from 1% to 12% with these subsequent ulcers [5]. The 5-year survival rate of a major amputation is 50% [6]. Mortality is double among diabetic patients with ulcerations than that among diabetic patients without [1, 7]. Considering the time required in treating ulcerations, there is a great societal cost due to loss of productivity and lesser quality of life for these patients and their families. Chronic wounds impact 6.5 million patients at a cost of $25 billion annually [5].

The majority of patients that require care through the CWH is part of this neuropathic, dys-

B. G. Higgs (✉)
Hanger Clinic, Washington, DC, USA
e-mail: bhiggs@hanger.com

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_25

vascular, diabetic patient population. Due to the associated comorbidities and considering the mortality rate, prevention is the utmost priority—beginning with gait salvage. The challenge lies in how to salvage gait and improve mobility. Many of the above-mentioned complications are compounded when a patient is stagnant and immobile. Pressure ulcers are a localized injury to the skin and/or underlying tissue as a result of pressure or pressure combined with shear or friction forces. Skin integrity is weakened and deconditioned without frequent stresses, thus leaving a non-ambulatory patient at higher risk for ulcerations. Coincidentally, an ulcerative compromised limb is also a limiting factor in the ability to ambulate. It is proven that increased activity is beneficial in the treatment of the at-risk foot. However, a sudden increase in loading the foot might explain why a foot ulcer could develop, unable to tolerate the additional stresses [8]. In order to maintain skin integrity and optimize the success of this patient population, pressure distribution combined with a slow re-introduction of pressure and shear forces is imperative [9]. Mitigating the chance of ulceration formation would have a cascade effect of reducing the comorbidity amputation potential. A prosthetist in clinic allows the provision of prompt care when preventative measures are needed in treating contractures and deformations leading to wounds. There are a number of orthotic modalities that can help accomplish this task [10, 11]:

Total Contact Cast (TCC): provided by technicians within the clinic. It has been identified that ulcer healing is significantly better when irremovable devices like the TCC are used [12]. It mitigates noncompliance and is sufficiently padded to offload wounds appropriately. However, there are a number of circumstances where a TCC is no longer appropriate, ideal, or preferred. Access to monitor the limb is challenging. Hygiene is problematic. Limited weight bearing, mobility, and possibility of lesser quality of life are factors to be considered.

Diabetic Healing Shoe (DH Shoes): Typically intended for short-term use, DH shoes are designed to distribute pressure across the plantar surface of the foot. These lightweight shoes accommodate mild contractures or deformations of the foot that can create excessive pressure and hot spots leading to skin breakdown and provides ample space to accommodate soft dressings. They lack any significant composition to stabilize to ankle and are a basic means of plantar pressure distribution.

Diabetic Healing Boot (DH Boot): Also designed to distribute pressure across the plantar surface of the foot. The DH boot provides increased integrity and leverage when compared to the DH shoe. This taller design accommodates or corrects contractures of both the foot and the ankle, promotes enhanced ankle stability, and further offloads the plantar surface utilizing proximal compression of the shank.

Pressure Relief Ankle Foot Orthosis: (PRAFO): Available as several designs both off-the-shelf (OTS) or custom fabricated versions. The PRAFO family of ankle foot orthoses (AFO) ideally maximize pressure distributions and accommodate or correct mild to severe deformations or contractures while either in seated or supine positions, or for ambulation. Advancements in the ambulatory design include an adjustable tibial shell which accommodates edematous fluctuations or soling cutouts for optimal forefoot or hindfoot offloading. One such robust design is also known as a Charcot Restraint Orthotic Walker (CROW) due to the severe deformation associated with the Charcot joint and the common need of this AFO design to help accommodate it. Total contact, depressions of the midfoot, and a rocker bottom soling help facilitate movement while stabilizing the joint and mitigating plantar pressure that could otherwise cause ulcerations or wounds.

Diabetic Shoes and Pedorthic Care: A key modality in preventative measures. Off-the-shelf (OTS) shoes, custom molded shoes, and custom foot orthoses are all options designed to provide long-term protection of the at-risk limb as a physical barrier to foreign objects and through reduction of pressure and friction. Shoes should have few to no internal stitches, mitigating any contact points that could breakdown the skin [13]. Wear and tear or stretching of the shoe upper material and gradual deterioration of soling along with

insole compression is expected as with any shoe frequently used. Annual replacement is encouraged to replace degraded shoes and insoles in order to maintain optimal foot protection.

With neuropathy, or a lack of sensation, impact does not always register as pain and therefore indicate a problem. Trauma to the foot arises from ill-fitting footwear, undetected foreign objects inside the shoes, and accidental injury through impact. Poor vascularity can delay healing, allowing for infection to cultivate and propagate. Over half of ulcers with vascular origin are infected on presentation [12, 14]. Infections precede about two-thirds of lower extremity amputations [15]. Appropriate education along with donning/doffing procedures will help mitigate these issues [16]. However, less than one-third of those with appropriately fitting footwear actually use these items [17]. Diabetic foot disease is a lifelong condition predisposing the patient to risk of a new ulcer, amputation, or early death. A holistic treatment approach is required for optimal prevention and wound management.

The primary objective of the integrated team at Wound Center is mobility and functionality obtained via gait salvage—typically accomplished with preventative measures in an effort to preserve the limb. The prosthetist's clinical presence opens the lines of communication and enables discussion in mapping out current orthotic treatments to aide in wound closure. Gait salvage and limb salvage are not mutually exclusive. While limb salvage is typically an appropriate approach, in order to meet the primary objective, gait salvage, early amputation, and setting realistic expectations might be a more viable solution for an active patient [18].

Pre-amputation Consultation

Approximately two million people in the USA live with limb loss and 185,000 amputations occur yearly in the USA [3]. Amputation etiology includes neuropathic and vascular 81.9%, trauma 16.4%, cancer 0.9%, and congenital 0.8% and is a life changing event for a patient [19]. Each etiology presents challenges during the recovery process, due to the undeniable physical and psychological toll. Many patients experience limb loss in the same fashion as the loss of a loved one—progressing through the phases of grief, particularly lingering in depression [20–22]. Individuals with diabetes are at increased risk for psychological distress due to a lack of psychological support and contending with comorbidities prior to amputation [23]. There is limited research on the psychological aspects for patients with diabetes, particularly for those also experiencing limb loss [20]. While an ideal treatment modality would include the addition of a psychiatrist to the interdisciplinary team [21], the ability for prosthetists, peer supporter, and a specialized Amputee Care Coordinator (ACC) to meet with patients in advance provides patients with additional resources to aide their recovery. See Fig. 25.1 for General Rehabilitation Timeline [24].

Prosthetist Consultation

Unlike patients with traumatic amputation, those with diabetes and dysvascularity typically have an opportunity to prepare for surgery and the associated lifestyle changes. A pre-amputation consultation with a prosthetist is the first time a patient discusses definitive next steps surrounding the prosthesis. While the discussions of this encounter vary, it is common to share and set realistic expectations, inclusive of both short- and long-term recovery. This is also the initial opportunity for the patient to convey thoughts and concerns, to ask questions, and to discuss functional design options with their prosthetist. An open dialogue is important to bridge the gap between potentially divergent patient desires and initial prosthetists assessments.

Peer Support

An often overlooked, yet vital role in an amputee's recovery is peer support. While prosthetists work with amputees daily, most have not experienced the event of an amputation. Only a fellow amputee can truly appreciate and understand the

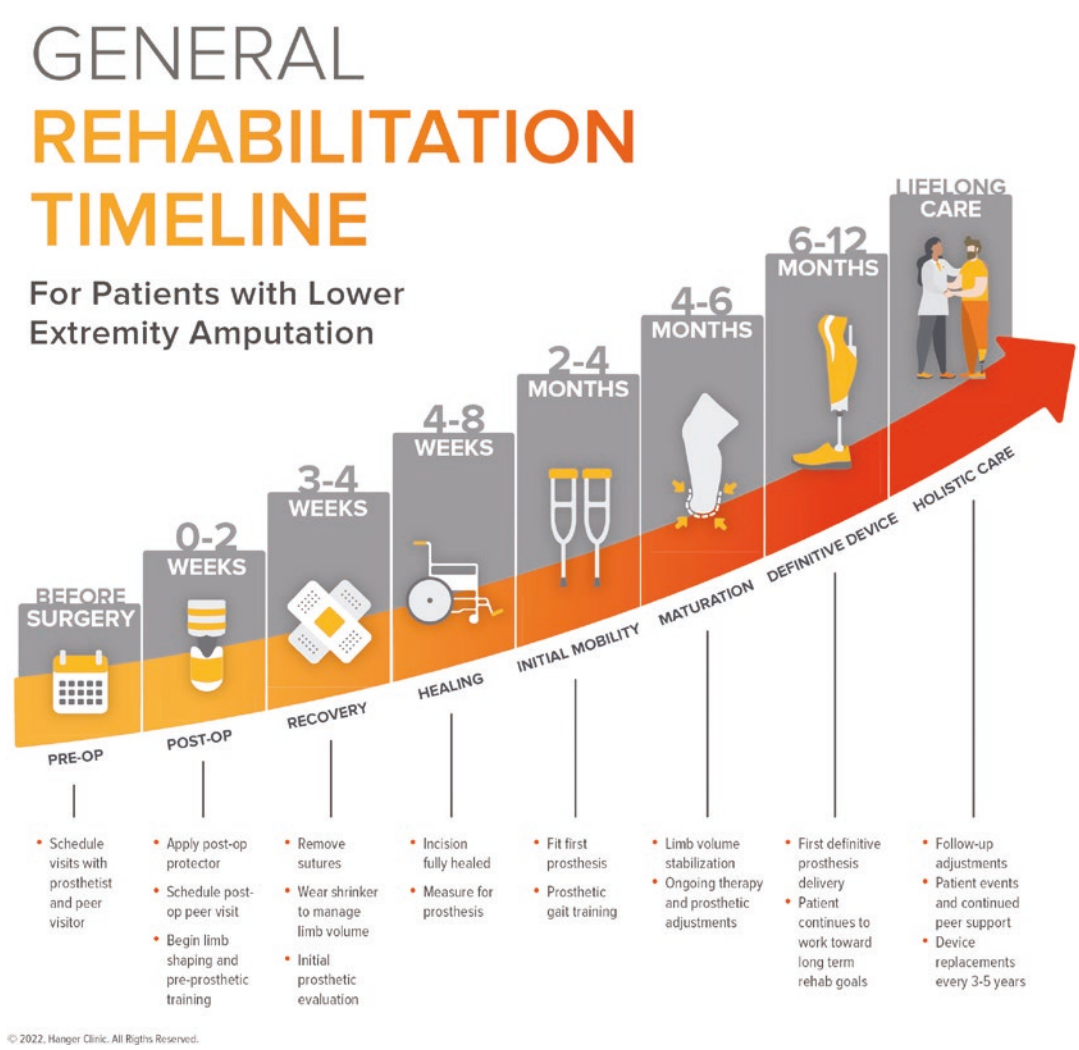


Fig. 25.1 General rehabilitation timeline

journey and obstacles that lie ahead. This does not negate the ability for a prosthetist to successfully provide clinical care; however, connecting amputees to one another provides a valuable resource that can be monumental in the outcomes and success of a patient [20, 22].

Not surprisingly, given the implications of ulceration treatment and its adverse effects on mobility, coupled with the feelings of anger and resentment [5], depression is 2x more likely in patients with DM [25]. Pairing the patient with a peer in a similar demographic can improve morale and confidence while aiding in the recovery and outcomes post-amputation. According to Reichmann, 92% of amputees reported improved outlook after meeting with their peer visitor. An additional 50% requested an additional visit while in rehabilitation. This was of particular interest to bilateral amputees or amputees over the age of 60 years. Peer support yields positive psychosocial value that contributes to positive outcomes in a patient population already experiencing increased psychological distress [26].

Resources like the Amputee Coalition of America's Certified Peer Visitor (CPV) and Hanger Clinic's AMPOWER are two such mentorship programs that are currently available to help amputees connect. Goals include fostering a

community of inclusion, education, and mentorship in an effort to support amputees and their families throughout their recovery [27, 28].

Amputee Care Coordinator

A unique role implemented at the MGUH CWH to further synergize the coordinated care is the ACC. This position ensures continuity of patient care from initial pre-amputation consultation through receiving definitive prosthesis. Similar to a case manager, the ACC tracks each patient in the CWH documenting date of amputation. Based on date of amputation, prosthetist and peer support are scheduled. Discharge plans are monitored and patient status updates are relayed to the Wound Center for continued coordinated care. Healthcare costs rise as time to prosthetic delivery increases; therefore, it is essential to keep patients engaged through ambulation [29]. The follow-up provided by the ACC means patients at MGUH CWH experience a care pathway designed to improve outcomes, similar to other case manager platforms [30].

Traumatic Amputee

Much of the focus on amputee care in this chapter surrounds patients with diabetes and dysvascularity. The ability to initiate a care plan in advance of the amputation is always preferred. However, due to the inherent nature of traumatic amputations, this patient population unfortunately lacks the ability to have the pre-amputation consultation in its entirety as outlined above. Nevertheless, the traumatic amputee requires these resources and benefits from the same level of prosthetist, peer support, and ACC meetings. When a pre-amputation consultation is not an option, post-amputation peer support is proven along with the support of family, friends, and the workplace organization to play an integral role in developing confidence and motivation in these patients [22]. Fortunately for traumatic amputees, despite the inability to plan and prepare for amputation, they are often more successful with their prosthetic recovery when compared to their diabetic counterparts [31].

Immediate Post-operative Prosthetic Care

Recovery begins immediately post-surgery. The body initiates its regeneration process upon surgical trauma. The surgical team provides general medical and wound care dressings to tend to the sutures and the edematous limb. There are four common approaches in caring for a patient immediately following amputation: soft dressings, rigid dressings, immediate post-operative prosthesis (IPOP), and removable rigid dressings (RRD). The objectives in utilizing these modalities include mitigating pain and contractures, limb protection, and controlling edema to optimize limb volume and shape in preparation for prosthesis usage [11, 32].

Soft Dressings: Inclusive of wound dressings, ACE wrap, Tubigrip, or shrinkers. Soft dressings are cost-effective and readily available peri- and post-surgery and are an appropriate means to control edema. Care must be taken to ensure sutures are protected from friction during donning and doffing. ACE bandages require methodical donning to ensure appropriate pressure gradient and to mitigate excessive proximal compression which could create a tourniquet effect, resulting in a bulbous limb shape, thereby negating the intended purpose of the dressing.

Rigid Dressings: Proven over the past several decades to be the optimal clinical approach for post-operative care. Rigid dressings provide a level of compression needed to continue to shape the limb and reduce volume. The rigid design prevents the knee from flexing, protects the sutures from post-surgical strain, and prevents contracture formation while also providing a high level of protection against falls. Fall prevalence is high post-operatively with injuries resulting in extended hospital stays or revision surgeries [33]. Rigid dressings demonstrated significantly decreased healing time for transtibial amputation to initial casting for a prosthesis when compared to soft dressing [34–36]. Additionally, the use of removal rigid dressings (RRD) is shown to reduce acute care length of stay [35]. Reduced healing time and shorter time spent in acute care both benefit the amputee patient and potential pros-

thetic intervention. While utilization of RRDs did not reduce fall incidents, RRDs did reduce number and prevalence of injuries [37].

IPOP: A rigid dressing that is fitted with a prosthetic pylon and foot, suspended with a belt strap. IPOPs provide patients with a visual reference to assist in overcoming the psychological aspect of amputation. It also permits the patient to initiate weight bearing. However, care must be taken to ensure maintaining suture protection while developing skin tolerance. It can be difficult for patients to grasp toe-touch or light pressure, compared to full body weight. Although indicated for a traumatic amputee, IPOP is contraindicated for patients with at-risk dysvascular limbs due to poor blood flow and increased susceptibility of further skin breakdown. Utilizing an IPOP allows for low level function while healing from time of amputation, through wound closure and suture removal. Upon removal of the sutures, the patient's skin is typically no longer a limiting factor in providing a prosthesis.

RRD: Offer the same features and outcomes of the rigid dressing with the significant added benefit of being readily removable. Standard rigid dressings require the use of a cast saw for removal, which typically occurs every few days. In comparison, RRDs enable a caregiver to readily remove the dressing, provide the opportunity to monitor the skin, and change soft dressings easily or address other issues with limb recovery on a more frequent basis. According to a meta-analysis by Churilov, the RRD reduces the number of days it takes to fit the first prosthesis [36]. The RRD should be the new standard of care, combining the ability for frequent limb observation and protection to optimize recovery while expediting the time to initial ambulation.

Preparatory Prosthesis

A new amputee will undergo a multitude of changes during limb healing and maturation. Most notably, volume and shape are impacted. Regardless of cause, an amputation is a traumatic event to the body, with common side effects such as edema, redness, inflammation, and fluid retention. As outlined earlier, post-operative dressings are designed to assist the recovery by controlling edema and optimizing limb shape in preparation for a prosthesis. An IPOP might be initiated, while sutures remain and the wound is closing in an effort to begin weight bearing. Upon closure of the wound and suture removal, a preparatory prosthesis may be provided for total weight bearing. A preparatory prothesis is different than an IPOP in its material, suspension method, and when it is provided. The preparatory prosthesis is fabricated out of a durable polymer or carbon fiber and utilizes a gel liner with a pin or suspension sleeve rather than a waist belt. It is provided promptly after wound closure and suture removal rather than immediately post-operatively. The preparatory prosthesis is nearly identical to a definitive prosthesis; however, it is designed and fabricated with the understanding the limb will undergo significant changes in the early months and patient functionality is likely to change.

The first several months post-surgery are crucial to a patient's success [29, 38]. The provision of a preparatory prosthesis provides an avenue for the limb to mature. Perhaps more importantly, the preparatory prosthesis grants time for a patient to intrinsically evaluate themselves and re-evaluate their initial wants and needs. With an entry level prosthetic design, the patient will have a better sense of what they can and cannot accomplish while using this prosthesis and more accurately validate their Medicare defined K-Level (Table 25.1) [39]. Often starting with, but not restrictive to, K2 components, the majority of basic activities of daily living can be practiced. It allows physical therapy and gait training to broaden beyond pre-prosthetic training. While not typically providing the highest levels of functionality, the preparatory prosthesis enables early ambulation, serving as a diagnostic tool. If a patient cannot accomplish a more complex goal such as climbing stairs or running, the prosthetist will evaluate if the prosthesis is a limiting factor or work in collaboration with the patient care team to determine if there are other physiological or psychological considerations to be addressed.

Table 25.1 Medicare functional classification levels for amputees, updated January 2020 [39]

K-level	Description
K-0	Does not have the ability or potential to ambulate or transfer safely with or without assistance and a prosthesis does not enhance their quality of life or mobility
K-1	Has the ability or potential to use a prosthesis for transfers or ambulation on level surfaces at fixed cadence. Typical of the limited and unlimited household ambulator
K-2	Has the ability or potential for ambulation with the ability to traverse low level environmental barriers such as curbs, stairs, or uneven surfaces. Typical of the limited community ambulator
K-3	Has the ability or potential for ambulation with variable cadence. Typical of the community ambulator who has the ability to traverse most environmental barriers and may have vocational, therapeutic, or exercise activity that demands prosthetic utilization beyond simple locomotion
K-4	Has the ability or potential for prosthetic ambulation that exceeds basic ambulation skills, exhibiting high impact, stress, or energy levels. Typical of the prosthetic demands of the child, active adult, or athlete

The utilization of a preparatory prosthesis affords a patient the opportunity to assess their long-term desires and true functional goals. For example, a patient might exhibit a need for increased activity, ability to ambulate with variable cadence, and encountering uneven terrain—warranting an upgrade in componentry, thereby changing the K-Level from K2 to K3 (Table 25.1). Another patient might have an early goal of high activity, e.g., playing basketball on a dynamic foot. However, through the initial ambulatory timeframe, this primary goal might evolve into a desire to navigate inclined terrain, necessitating a different ankle design with increased range of motion through articulation. Further physical, occupational, or psychological therapy might be needed to improve strength, balance, and confidence. In conjunction with a more defined physiological outcome, early ambulation can aid the reduction of the $327 billion diabetic related annual health care costs [2, 29].

Definitive Prosthesis

Limb maturation occurs from 1 to 12 months post-operatively, at which point the limb volume has relatively stabilized [40, 41]. Skin tolerance toward bearing weight and pressure has improved. Functionality and long-term goals have been assessed. This period of time is ideal to provide a definitive prosthesis to the new amputee.

A definitive lower extremity prosthesis is designed for use over the next several months or years barring any substantial physiological or functional changes. It is inclusive of several components: suspension, socket, pylon, foot. For more proximal amputation levels, a knee or hip joint might be needed.

Suspension: A means to attach the prosthesis to the limb. Commonly used interfaces are gel liners. They create a high level of friction against the skin in order to suspend the prosthesis with a pin attachment or through a suction seal. The gel also creates a level of cushion around the limb, absorbing impact and assisting with pressure distribution. In addition, liners add a level of compression to the skin to contain shape and volume enhancing prosthetic control. Anatomical contours over boney prominences, skin fit, waist belts, or other strap mechanisms are also viable means of suspension.

Socket: The highly customized portion of the prosthesis that encompasses the limb. The socket is derived from an impression of the patient's limb and modified for an intimate fit. The goal is to optimize pressure distribution which enhances control of the prosthesis, reduces unnecessary energy consumption, and distributes floor reaction forces against the limb to mitigate skin breakdown. Typically fabricated out of polymers or carbon fiber to reduce weight and material thickness while maintaining integrity and durability.

Pylon: The segment of the prosthesis that connects the socket or knee to the foot made of a lightweight aluminum, titanium, or carbon material. A pylon enables adjustability for the prosthesis, ensuring the foot position relative to the socket, knee, and hip is in an inherently stable

orientation. It allows for rapid and precise changes to height and alignment based on patient presentation to optimize their gait pattern for efficiency, reducing energy consumption and fall risk. Contracture accommodation may be necessary to maintain balance, stability, and posture and is further accomplished with the modular nature and versatility of the pylon.

Foot: The most dynamic aspect of the prosthesis. The foot connects the prosthesis to the ground. There are a wide range of designs dependent on a patient's functional needs. Entry level SACH (solid ankle, cushion heel) feet provide basic needs for standing, transfers, and single cadence ambulation. Enhanced designs include energy storing feet with carbon springs that deflect and roll under pressure. Articulating ankles add hydraulic chambers to further control motion through dampening resistance. Microprocessor controlled articulating ankles are able to change dorsiflexion and plantarflexion hydraulic chambers independently and can have a marked improvement on balance and better mimic biological gait [42]. Self-powered ankles add motors to replace the missing gastrocnemius complex. This active design has been shown to reduce energy consumption, however, remains bulky and costly [43]. The overall goal of a foot is to provide a fluid motion to mimic the anatomical foot for balance, stability, and function.

The dynamic nature of the human body ensures that limb shape and volume are under constant change, even after reaching limb maturation. Volume changes occur through the day. External limb pressure from the socket during ambulation causes volume loss. Alleviating this pressure upon prosthesis removal results in limb volume increase. Compression is also utilized at night or when not using the prosthesis to mitigate the fluctuation, but a discrepancy will persist. Dietary choices can impact limb volume fluctuation. Patients on dialysis undergo extreme volume changes between dialysis appointments [41]. Long-term changes occur due to muscle atrophy, activity levels, and physiological aging. Socks provided to the amputee are a readily available solution for patients to accommodate these daily volumetric changes. Modifications to the socket might be necessary by heating and changing the shape, or addition/subtraction of padding. If a patient's limb has changed significantly, a socket replacement would be required to ensure optimal fit and function.

Patients' needs continually evolve. Functions change over time. It is imperative for the clinical team to have ongoing dialogue to ensure patient needs are met. One must not overlook the importance of including the patient within this dialogue. According to Valizadeh, there is a significant difference in what the clinical team deems essential when compared to what the patient perceives to be essential [22]. Continued discussions can ensure patient needs are met in conjunction with professional input, rather than based entirely on clinical assumptions. Surveys and outcome measures provide an additional avenue to enhance patient communication and success. The self-reported measure of the Prosthetic Limb Users Survey of Mobility (PLUS-M) provides a means for the patient to provide insight in order to assist with their clinical care [44].

Summary

A collaborative team provides patients with diverse clinical opinions in an effort to optimize patient function. Gait salvage is the goal in an effort to ultimately reduce mortality rates. This can be accomplished through limb salvage or amputation. Preventative measures are prioritized to save the at-risk, dysvascular limb. Orthotic intervention provides pressure distribution to prevent or treat ulcerative or contracted limbs to allow for healing. When healing is not likely, or would yield low function, amputation provides another means to improve gait. Peer support, ACC, and prosthetic consultations are resources available to the patient that can help overcome physical and mental obstacles associated with amputation. Post-operative care prepares the patient for prosthetic intervention and ambulation. A preparatory prosthesis allows for early ambulation along with setting realistic goals and expectations, assisting in designing the

first definitive prosthesis, intended for long-term use. Ongoing collaboration with the prosthetist, physical therapist, and limb salvage team provides each patient with a complete clinical plan designed to meet individual needs and optimize outcomes.

References

1. Jupiter DC, Thorud JC, Buckley CJ, Shibuya N. The impact of foot ulceration and amputation on mortality in diabetic patients. I: from ulceration to death, a systematic review. Int Wound J. 2016;13(5):892–903.
2. Prevention CfDCa. National diabetes statistics report, 2020. Atlanta, GA: Centers for Disease Control and Prevention, US Department of Health and Human Services; 2020. p. 12–5.
3. Ziegler-Graham K, MacKenzie EJ, Ephraim PL, Travison TG, Brookmeyer R. Estimating the prevalence of limb loss in the United States: 2005 to 2050. Arch Phys Med Rehabil. 2008;89(3):422–9.
4. Keast DH, Vair AH. Use of the Charcot restraint orthotic Walker in treatment of neuropathic foot ulcers: a case series. Adv Skin Wound Care. 2013;26(12):549–52.
5. Sen CK, Gordillo GM, Roy S, Kirsner R, Lambert L, Hunt TK, et al. Human skin wounds: a major and snowballing threat to public health and the economy. Wound Repair Regen. 2009;17(6):763–71.
6. Morbach S, Furchert H, Gröblinghoff U, Hoffmeier H, Kersten K, Klauke G-T, et al. Long-term prognosis of diabetic foot patients and their limbs: amputation and death over the course of a decade. Diabetes Care. 2012;35(10):2021–7.
7. Singh N, Armstrong DG, Lipsky BA. Preventing foot ulcers in patients with diabetes. JAMA. 2005;293(2):217–28.
8. LeMaster JW, Mueller MJ, Reiber GE, Mehr DR, Madsen RW, Conn VS. Effect of weight-bearing activity on foot ulcer incidence in people with diabetic peripheral neuropathy: feet first randomized controlled trial. Phys Ther. 2008;88(11):1385–98.
9. Crews RT, Schneider KL, Yalla SV, Reeves ND, Vileikyte L. Physiological and psychological challenges of increasing physical activity and exercise in patients at risk of diabetic foot ulcers: a critical review. Diabetes Metab Res Rev. 2016;32(8):791–804.
10. Cantanzariti AR, Haverstock BD, Grossman JP, Mendicino RW. Off-loading techniques in the treatment of diabetic plantar neuropathic foot ulceration. Adv Skin Wound Care. 1999;12(9):452.
11. Lusardi MM, Nielsen CC, Emery MJ, Bowers DM, Vaughan VG. Orthotics and prosthetics in rehabilitation. 2nd ed; 2007.
12. Lewis J, Lipp A. Pressure-relieving interventions for treating diabetic foot ulcers. Cochrane Database Syst Rev. 2013;1:CD002302.
13. Schaper N, Apelqvist J, Bakker K. Reducing lower leg amputations in diabetes: a challenge for patients, healthcare providers and the healthcare system. Diabetologia. 2012;55(7):1869–72.
14. Akhtar S, Schaper N, Apelqvist J, Jude E. A review of the Eurodiale studies: what lessons for diabetic foot care? Curr Diab Rep. 2011;11(4):302–9.
15. Lavery LA, Armstrong DG, Wunderlich RP, Mohler MJ, Wendel CS, Lipsky BA. Risk factors for foot infections in individuals with diabetes. Diabetes Care. 2006;29(6):1288–93.
16. Thomas E. Preventing amputation in adults with diabetes: identifying the risks. Nurs Stand. 2015;29(40):49.
17. Waaijman R, Keukenkamp R, de Haart M, Polomski WP, Nollet F, Bus SA. Adherence to wearing prescription custom-made footwear in patients with diabetes at high risk for plantar foot ulceration. Diabetes Care. 2013;36(6):1613–8.
18. Attinger CE, Brown BJ. Amputation and ambulation in diabetic patients: function is the goal. Diabetes Metab Res Rev. 2012;28:93–6.
19. Dillingham TR, Pezzin LE, MacKenzie EJ. Limb amputation and limb deficiency: epidemiology and recent trends in the United States. South Med J. 2002;95(8):875–84.
20. Bennett J. Limb loss: the unspoken psychological aspect. J Vasc Nurs. 2016;34(4):128–30.
21. Spiess KE, McLemore A, Zinyemba P, Ortiz N, Meyr AJ. Application of the five stages of grief to diabetic limb loss and amputation. J Foot Ankle Surg. 2014;53(6):735–9.
22. Valizadeh S, Dadkhah B, Mohammadi E, Hassankhani H. The perception of trauma patients from social support in adjustment to lower-limb amputation: a qualitative study. Indian J Palliat Care. 2014;20(3):229.
23. Coffey L, Gallagher P, Horgan O, Desmond D, MacLachlan M. Psychosocial adjustment to diabetes-related lower limb amputation. Diabet Med. 2009;26(10):1063–7.
24. Clinic H. General recovery time 2021.
25. Jain R, Jain S, Raison CL, Maletic V. Painful diabetic neuropathy is more than pain alone: examining the role of anxiety and depression as mediators and complicators. Curr Diab Rep. 2011;11(4):275–84.
26. Reichmann JP, Bartman KR. An integrative review of peer support for patients undergoing major limb amputation. J Vasc Nurs. 2018;36(1):34–9.
27. Coalition A. Certified peer visitor (CPV) program 2021. https://www.amputee-coalition.org/support-groups-peer-support/certified-peer-visitor-program/.
28. Clinic H. Emotional support 2021. https://hanger-clinic.com/patients/emotional-support/.
29. Miller TA, Paul R, Forthofer M, Wurdeman SR. Impact of time to receipt of prosthesis on total healthcare costs 12 months postamputation. Am J Phys Med Rehabil. 2020;99(11):1026–31.
30. Majumdar SR, Lier DA, Beaupre LA, Hanley DA, Maksymowych WP, Juby AG, et al. Osteoporosis case manager for patients with hip fractures: results of a

cost-effectiveness analysis conducted alongside a randomized trial. Arch Intern Med. 2009;169(1):25–31.
31. Hermodsson Y, Ekdahl C, Persson B, Roxendal G. Standing balance in trans-tibial amputees following vascular disease or trauma: a comparative study with healthy subjects. Prosthet Orthot Int. 1994;18(3):150–8.
32. Reichmann JP, Kritter Jr AE. Evidence-based postoperative care for transtibial amputees.
33. Jaime CY, Lam K, Nettel-Aguirre A, Donald M, Dukelow S. Incidence and risk factors of falling in the postoperative lower limb amputee while on the surgical ward. PM R. 2010;2(10):926–34.
34. Sumpio B, Shine SR, Mahler D, Sumpio BE. A comparison of immediate postoperative rigid and soft dressings for below-knee amputations. Ann Vasc Surg. 2013;27(6):774–80.
35. Taylor L, Cavenett S, Stepien JM, Crotty M. Removable rigid dressings: a retrospective case-note audit to determine the validity of post-amputation application. Prosthet Orthot Int. 2008;32(2):223–30.
36. Churilov I, Churilov L, Murphy D. Do rigid dressings reduce the time from amputation to prosthetic fitting? A systematic review and meta-analysis. Ann Vasc Surg. 2014;28(7):1801–8.
37. Gooday HM, Hunter J. Preventing falls and stump injuries in lower limb amputees during inpatient rehabilitation: completion of the audit cycle. Clin Rehabil. 2004;18(4):379–90.
38. Miller TA, Paul R, Forthofer M, Wurdeman SR. The role of earlier receipt of a lower limb prosthesis on emergency department utilization. PM R. 2020;13(8):819–26.
39. Medicare Cf, Services M. Local coverage determination: lower limb prostheses (L33787). Baltimore, MD: Centers for Medicare & Medicaid Services; 2016.
40. Koonalinthip N, Sukthongsa A, Janchai S. Comparison of removable rigid dressing and elastic bandage for residual limb maturation in transtibial amputees: a randomized controlled trial. Arch Phys Med Rehabil. 2020;101(10):1683–8.
41. Sanders JE, Fatone S. Residual limb volume change: systematic review of measurement and management. J Rehabil Res Dev. 2011;48(8):949.
42. Bai X, Ewins D, Crocombe AD, Xu W. A biomechanical assessment of hydraulic ankle-foot devices with and without micro-processor control during slope ambulation in trans-femoral amputees. PloS One. 2018;13(10):e0205093.
43. Montgomery JR, Grabowski AM. Use of a powered ankle–foot prosthesis reduces the metabolic cost of uphill walking and improves leg work symmetry in people with transtibial amputations. J R Soc Interface. 2018;15(145):20180442.
44. Hafner BJ, Gaunaurd IA, Morgan SJ, Amtmann D, Salem R, Gailey RS. Construct validity of the prosthetic limb users survey of mobility (PLUS-M) in adults with lower limb amputation. Arch Phys Med Rehabil. 2017;98(2):277–85.

26 Surgical Offloading, Tendon Balancing, and Prophylactic Surgery in Diabetic Limb Salvage

John S. Steinberg, Paul J. Carroll, Jayson N. Atves, and John D. Miller

Introduction

Surgical indications and techniques for limb salvage in the complex patient population are a constantly evolving field of medicine and surgery. Commonly, patients present with a biomechanically induced ulceration of the foot or ankle, peripheral neuropathy, and some degree of concomitant relative tissue ischemia. Beaulieu et al. reported the majority of these patients often have multiple conditions and comorbidities which challenge limb salvage efforts [1]. Further, Hobizal and Wukich noted several host factors including medical comorbidities, nutritional status, glycemic control, nonadherence to medical regimens, and socioeconomic status play a central role in patient outcomes [2].

J. S. Steinberg
Department of Plastic Surgery, Georgetown University School of Medicine and MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: John.Steinberg@medstar.net

P. J. Carroll
Department of Plastic and Reconstructive Surgery, MedStar Franklin Square Hospital, Baltimore, MD, USA
e-mail: Paul.J.Carroll@medstar.net

J. N. Atves (✉) · J. D. Miller
Department of Plastic and Reconstructive Surgery, MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: Jayson.Atves@Medstar.net

Following improvements in surgical technique and perioperative management, indications for surgery in the patients with diabetes have expanded. In 2003 Armstrong and Frykberg revised diabetic foot surgery classification into categories of indication based on risk [3] as seen in Table 26.1. Importantly, they established the concept of elective and prophylactic surgeries in the diabetic population shifting a paradigm of surgical intervention from "last-resort" to "early prevention." Using this system methods for surgical offloading range from prophylactic tendon lengthening and transfers to curative procedures with adjunctive surgical offloading techniques. In this chapter we review the guiding tenets for surgically based offloading pedal ulcerations utilizing ostectomies, osteotomies, tendon balancing, and other prophylactic surgery in the complex patient population.

In the complex and comorbid populations, especially in those patients with peripheral neuropathy, the formation and complication of deformity can create a perilous situation which precipitates wound formation, progression, and stagnation. As with deformity at any level of the lower extremity, this situation can not only impede one's ability to ambulate safely and effectively but also has major implications for quality of life. This lends to the major role and need for consideration of ground reactive forces throughout the lower extremity and the body's susceptibility to the formation of multi-level and

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_26

multi-tissue deformity, especially in the face of peripheral neuropathy. Although the full extent of lower extremity biomechanics lies well outside the scope of this discussion, ultimately, gait biomechanics in the complex wound patient are an especially important consideration due to the lower extremity's relationship with the weight-bearing surface, its interaction with ground reactive forces, and perhaps most importantly in a patient's ambulatory efforts and demands. Inherently, the extremity's contact with the ground in an ambulatory manner will repetitively undergo extreme multiplanar forces which may precipitate excessive force distribution resulting in and contributing to the formation of an assortment of pathologies which may also blunt the remaining tissues ability to heal or cause the formation of new areas of excessive force. This is nowhere more apparent than in the plantar aspect of the foot; however, anatomic areas surrounding joints with significant excursion like the ankle, midtarsal, tarsometatarsal, metatarsophalangeal, and interphalangeal joints are especially susceptible. This process is magnified in those patients where underlying deformity exists in the presence of peripheral neuropathy, where protective and corrective responses to ground reactive forces are blunted or grossly absent (Table 26.2).

Deformity of the foot and/or ankle may present in a variety of ways which may perpetuate wound formation and its correction may preclude the ultimate healing of a wound through undesirable and ultimately destructive force distribution within the extremity or the formation of altered mechanics which can irreparably alter gait. A deformity of the foot and/or ankle is truly of functional significance when the tissues do not permit sufficient mobility for the alignment and motions required during the normal gait cycle. Abnormal bone or joint alignment, ankylosis, and/or instability often occur in the foot and/or ankle but the onus of recognition of the exact anatomic level(s), plane(s), severity of deformity and especially the formulation of appropriate intervention(s) and/or consultations is ultimately placed upon the treating surgeon and team. The

Table 26.1 Risk-based classes of diabetic foot surgery. Adapted from: Armstrong, D.G. and Frykberg, R.G. (2003), Classifying diabetic foot surgery: toward a rational definition. Diabetic Medicine, 20: 329–331 [3]

Diabetic foot surgery class	Description	Potential risk for high-level amputation
Class I: elective	Procedure performed to alleviate pain or limitation of motion in a person without loss of protective sensation	Very low
Class II: prophylactic	Procedure performed to reduce risk of ulceration or re-ulceration in person with loss of protective sensation but without open wound	Low
Class III: curative	Procedure performed to assist in healing open wound	Moderate
Class IV: emergent	Procedure performed to limit progression of acute infection	High

Table 26.2 Excessive plantar pressures and causative ulcer factors

Intrinsic factors	Extrinsic factors	Behavioral factors	Iatrogenic factors
• Limited joint mobility	• Non-adapted footwear (too tight, prominent seams)	• Barefoot/ unprotected walking	• Unstable biomechanics
• Congenital, post-traumatic, other severe foot deformities (Charcot)	• Foreign body (pebbles, nails, etc.)	• Lack of daily foot surveillance	• Poorly performed debridement/amputation
		• Impossibility of foot care	• Resection of 1 or more metatarsal heads
		• Poor hygiene	• Escalating amputations

primary goal of foot and/or ankle reconstruction, whether prophylactic or therapeutic, should be to provide a structurally well-aligned and stable foot and ankle complex. Treatments should seek to achieve a plantigrade foot which provides dynamic alignment and stability during stance phase, clearance during swing phase, adequate step length and provides energy conservation throughout.

Goals of Surgical Intervention

Fundamental goals of limb salvage surgery include obtaining an infection-free, plantigrade, and stable extremity ideally maximizing ambulatory function within the patient's physical and medical capacity [4]. Also core to these tenets is the recognition and removal of high force areas where and when possible. Areas of callous formation with or without associated overlying erythema may indicate areas of osseous deformity predisposing to ulceration. Any foot or ankle deformity, be it hallux limitus, hammertoes, osteoarthritis, equinus, bony prominences, and/or Charcot neuroarthropathy, may play a causal role in force-induced ulcer development, stagnation, and chronicity. Raspovic et al. demonstrated that biomechanically induced ulcerations will inevitably lead to re-ulceration, increased amputation risk, and a decrease in quality of life unless corrected [5]; therefore, recognition of their presence and understanding of their potential progression warrant preemptive and proactive mentality in treatment.

Soft tissue changes may also contribute to lower extremity ulceration and should always be assessed. Plantarly prominent metatarsal heads have been attributed to developed weakness of the intrinsic pedal musculature, exacerbating plantarflexion toe deformities in the neuropathic foot. Adipose cushioning under the metatarsal heads is embedded within the flexor tendons and is believed to migrate distally with progressive hammering of the lesser digits, further reducing plantar cushioning of the metatarsal heads [6]. Additional nonenzymatic glycation of soft tissues resulting from long standing diabetes mellitus may also lead to thickening and reduced tissue flexibility of skin, tendon, ligaments, and joint capsules [7]. Although innocuous appearing, digital contractures in higher risk patients quickly progress to a preulcerative or ulcerative state. Therefore, early detection and minimization or removal of these excessive forces is critical in prevention or maintaining remission from ulceration.

Imaging and Diagnostics Studies

Radiographs

Plain film radiographs in multiple views are imperative for evaluating wound etiology particularly if the wound is located on a weight-bearing surface, as bony irritation on the foot or ankle can potentiate wound formation or support chronicity. Weight-bearing plain film radiography may confirm or better define osseous relationships and may display preliminary signs of underlying vascular disease such as calcifications. Transverse, frontal, and sagittal plane joint relationships may be evaluated and joint integrity can be investigated prior to clinical assessment. These parameters are essential when planning musculoskeletal balancing procedures.

Advanced Imaging

Advanced imaging techniques such as magnetic resonance imaging (MRI), computed tomography (CT), or radiolabeled scintigraphy/nuclear

scans may be appropriate for some patients in whom initial evaluations suggest osteomyelitis (OM). MRI may be useful to image the deeper layers of the foot and ankle. CT may be used to visualize changes in the cortical bone due to infection or for anatomical contour, position, and/or alignment. However thorough clinical evaluation and weight-bearing plain film radiographs are often all that is needed for assessment.

First Digit and Metatarsophalangeal Joint

First Metatarsophalangeal Joint Arthroplasty

Limitations in first metatarsophalangeal joint (MPJ) mobility are a common forefoot occurrence contributing to plantar hallux ulceration. While pressure reduction is usually attempted with external shoe modifications, this alone will not correct underlying osseous deformity and may result in an ulcer development despite best practices [8]. In 1886 Reidel described resection of the base of the proximal phalanx and exostectomy of the head of the first metatarsal as an alternative to unsatisfactory outcomes of first metatarsal head resection. This was later popularized by U.S. Army Captain William Keller in 1904, and more recently the efficacy of a Keller-type first MPJ arthroplasty procedure in diabetic patients with plantar first MPJ ulceration secondary to arthritic joint immobility has been well established [9] (Fig. 26.1). Patients who received surgical resection of the base of the proximal phalanx were noted to heal their plantar ulceration faster than the nonsurgical group without significant increase in complications and without prolonged recovery time [10].

Procedure

Patient is placed in the supine position. After administration of preferred anesthesia and intravenous antibiotics an Esmarch is applied and the ankle tourniquet inflated. A dorsomedial skin, deep, and capsular incision is made over the first metatarsophalangeal joint, protecting the dorsal medial cutaneous nerve and extensor hallucis longus tendon. If present, osteophytes are resected from the first metatarsal head surrounding the joint. Resection arthroplasty of the base of the proximal phalanx with oscillating sagittal saw typically involves a generous resection of the proximal phalanx, potentially up to one-third of the phalanx. Aggressive resection can include insertion of the flexor hallucis brevis, which may lead to toe shortening with transfer metatarsalgia and weakness in toe push-off.

Various modifications of soft tissue interpositional arthroplasty have been reported including autografts (extensor hallucis longus, extensor hallucis brevis, and extensor digitorum longus), allografts, and acellular tissue matrices. Commonly the remaining capsule is then transversely interposed into the joint and sutured to the lateral capsule with absorbable suture. Typically the joint is axially fixated with 0.062-mm Kirschner wire from ~5 degrees of valgus and ~10 to 15 degrees of extension. The foot is dressed in standard postoperative dressing and postop shoe. Sutures and Kirschner wire are removed in the clinic at 3 weeks, at which time the patient was allowed to bear full weight in a hard-soled shoe and begin range of motion. Regular shoes and activities were gradually advanced at that time.



Fig. 26.1 Clinical images (**a**, **c**) and radiographic images (**b**, **d**) multiple views—preoperative (**a**, **b**) and postoperative (**c**, **d**) status post-Keller style arthroplasty of the first metatarsophalangeal joint. This specific patient experienced increased postoperative mobilization of the dorsiflexion motion of the first metatarsophalangeal joint and decreased ground reaction force to the hallux with subsequent healing of the chronic recalcitrant plantar hallux wound

Lesser Digits and Metatarsophalangeal Joints

Lesser digital deformities such as hammer, claw, and mallet toes are frequent and known to increase pressure associated with neuropathic ulceration [11]. Lesser digit ulcerations are often the result of structural deformity and therefore are associated with high rates of recurrence [12]. Rigid digital contractures may cause preulcerative or ulcerative lesions to the dorsal aspect of contracted joints due to rubbing in shoe gear and also to distal digits. Contractures that are manually reducible may be corrected with soft tissue release alone; however, if the deformity is rigidly contracted and nonreducible it typically requires joint arthroplasty for correction.

Percutaneous Flexor Tenotomy

If the long flexor tendons overpower the intrinsic musculature, a flexion deformity of the DIPJ level is likely to occur. As a result, the distal tip of the digit will become plantarflexed with increasing pathologic pressures resulting in hyperkeratotic buildup and eventually ulceration in the neuropathic patient [12]. Flexor tenotomy can be performed for prevention of diabetic foot ulcers, in flexible lesser digits. Based on 6 published retrospective studies regarding flexor tenotomies for diabetic ulceration a total of 264 tenotomy procedures yielded a mean healing rate of 97% at a duration of 4 weeks [13]. While the lasting preventative effects of flexor tenotomy are not yet well described, current results demonstrate that flexor tenotomies are a simple, effective, and low-risk intervention for reducing non-rigid hammer and claw toes with a high healing percentage and a short mean time to heal. These procedures can also be done in an office setting with limited equipment costs and time constraints.

Procedure

Following completion of anesthesia per physician preference. The flexor digitorum longus of the selected digit is placed under tension ("bowstringing") by positioning the ankle joint in dorsiflexion, while at the same time positioning the affected toe in hyperextension. A stab-wound incision (around 3 mm) is made at the middle of the proximal phalanx by either blade or 18-gauge needle (author's preference), and the tendon is transected in a transverse swiping motion. The long extensor tendon should now hold the toe straight. All stab wounds should be irrigated and may or may not require suture. Typically a pressure bandage is applied for the first week. The foot remains offloaded for 24 h, after which the patient can bear weight again. The patient is examined at 1-week and subsequently followed-up at regular intervals.

Lesser Digital Arthroplasty

If contracture unrelieved by percutaneous flexor tenotomy or the deformity is precluded from soft tissue reduction by nature of being a rigid deformity, digital resection arthroplasty may allow for contracture reduction to facilitate wound healing and/or reduce the risk of wound recurrence [14]. Resection at the proximal interphalangeal joint permits shortening which allows for correction of deformity and relaxation of contracted soft tissues (Fig. 26.2). If reduction is still not possible following adequate resection, extensor tendon lengthenings or dorsal MPJ capsulotomies may be performed to augment reduction.

Procedure

Digital or ankle local anesthesia blocks are administered as needed. The affected proximal interphalangeal joint is surgically exposed by either dorsal longitudinal incision or transversely with the skin tension lines at the level of the joint. Dissection is carried out to expose the distal condyles of the proximal phalanx and a transverse supracondylar resection is made with bone-cutter or sagittal saw as desired. A 0.045″ Kirschner wire is then introduced at the proximal interphalangeal joint centrally and exited distally. The toe may then be digitally manipulated and the wire passed proximally to stabilize the digit in the corrected position. The wire may then be bent external to the digit to prevent



Fig. 26.2 Radiographic imaging AP foot views (**a**–**d**)—first metatarsophalangeal total joint arthroplasty with implantation of a long-term polymethylmethacrylate (PMMA) antibiotic spacer may be a useful means of long-term functional preservation

proximal migration. The incision is then closed and standard postoperative dressing applied with postoperative shoe. Incisions are then removed in the clinic in 2–3 weeks, and K-wire removed at 4 weeks.

Lesser Metatarsal Head Osteotomies

Ulcerations are also commonly encountered beneath the lesser metatarsal heads. In the event adequate offloading or soft tissue rebalancing is unable to resolve these high pressure areas surgical offloading of the metatarsal head whether through osteotomy or metatarsal head resection may be efficacious [15]. Isolated metatarsal head resections while effective at resolving plantar metatarsal ulcerations have been shown to have high rates of transfer lesion development to an adjacent metatarsal head and other complications such as floating toe [16]. Newer techniques adapted from elective surgery such as the Weil type osteotomy or floating type osteotomy allow for reduction in plantar pressures while retaining predictability and limiting dissection in the comorbid patient.

Distal metatarsal metaphyseal osteotomy (DMMO) is a percutaneous extra-articular lesser metatarsal neck osteotomy [17], which can be applied in a minimally invasive fashion to reduce the plantar pressure of the metatarsal head responsible for skin ulcerations in diabetic feet. Early studies demonstrate notable improvement in plantar pressures with reduction in the rate of transfer lesions as compared to historical rates with metatarsal head resections [18]. However, in these cases, the need to shorten the metatarsal bone must be weighed against the need to maintain a functional metatarsal parabola to prevent recurrent or transfer skin lesions.

Procedure

Patient remains in the supine position on the operative table and the local block is completed with the anesthetic agent of choice. The extremity is scrubbed and draped in routine aseptic fashion. A 3 mm incision is made dorsally at the planned osteotomy site after fluoroscopic identification of the surgical neck of the metatarsal. A perpendicular or short oblique osteotomy will be made at the neck or diaphysis of the affected lesser metatarsus [2–5]. The authors prefer to complete this with a 12 mm Shannon burr at a speed of 1600 rounds per minute and a torque of 80 N-m. Fluoroscopy and manual manipulation of the metatarsal head can be used again to confirm completion of the osteotomy. Following the osteotomy, the metatarsal head will freely displace dorsally. Fixation is not commonly utilized, however, can be used in the form of a K-wire to maintain corrected position. Skin closure will be achieved with a single suture. Full weight-bearing in a "postoperative" shoe will be permitted immediately and used until bone healing noted on radiographs.

Use of Functional Antibiotic Spacers

Elution of local antibiotics can yield high concentrations into target tissues and can be particularly effective in the setting of chronic osteomyelitis and poorly perfused tissues. Additionally, these antibiotics can be conjoined with structural filler or spacers such as non-absorbable polymethylmethacrylate impregnated cement, which can be particularly useful when needing to replace osseous structure lost during excision of infected tissue. Early randomized controlled trials demonstrate improved clinical cure rates when utilizing antibiotic impregnated bone cement as bone filler in the setting of diabetes related osteomyelitis [19]. Additionally, placement of antibiotic eluting cement spacers has been shown to have long-term stability, even in weight-bearing zones [20]. While these techniques are still in their infancy, newer devices and compositions will continue to expand their utilization and efficacy in this field (Fig. 26.3).



Fig. 26.3 Clinical images (**a**, **c**) and radiographic images (**b**, **d**) AP foot view—preoperative (**a**, **b**) and postoperative (**c**, **d**) of right third toe proximal interphalangeal joint arthroplasty for rigid hammertoe correction

Osseous Midfoot Deformity

Ulcerations of the midfoot can lead to devastating outcomes. Literature shows that 9% of diabetic neuropathic patients with midfoot ulcerations will go onto proximal amputation [21]. As with forefoot ulcers, midfoot ulcers are generally caused by increased plantar from a Charcot, subluxed midfoot joint(s), exostosis, poorly performed partial foot amputations [22–24]. First line treatment for midfoot ulcerations is external offloading with surgical shoes, custom shoes, total contact casting, or Charcot restraint orthotic walker (CROW) boot. When conservative treatment fails, surgical intervention is generally recommended.

Midfoot Exostectomy

Plantar foot exostoses can lead to increased plantar pressure resulting in ulcerations. In patients with stable midfoot joints, consolidated midfoot Charcot, or who are not in immediate risk of midfoot collapse, an exostectomy may be an acceptable surgical option.

Procedure

The patient is positioned on the operating table in the supine position with an ipsilateral hip bump. The author discourages the use of tourniquet to avoid incision healing complications. Incision placement is generally along either the medial or lateral glabrous function, depending on the laterality of the exostosis. This is recommended to allow for weight-bearing and prevent wound dehiscence. A 3 cm incision is made along the glabrous junction care taken to avoid unnecessary undermining. The muscle belly is retracted inferiorly and dissection is carried plantarly along the bones until the exostosis is encountered. After adequate dissection of the exostosis a sagittal saw is used to resect the prominence flush with the plantar border of the midfoot bones. The author recommends resection of an additional 3 mm of bone to ensure the exostosis is resected. Fluoroscopy is used to confirm resection of the exostosis. The incision is irrigated with copious amounts of saline. Hemostasis is achieved. Layer closure is performed, dry sterile dressing is applied.

Osseous Midfoot Reconstruction

When an exostectomy is not sufficient enough to surgically treat the deformity, a reconstruction may be necessary to stabilize the midfoot to prevent further joint collapse. If a reconstruction of the midfoot is required, generally a combination of osteotomies and fusions is needed as these are multiple planar deformities (Fig. 26.4). Extensive preoperative planning is of paramount importance when treating Charcot deformities as the goal of the reconstruction is to [25]:

- Maintain anatomic realignment
- Limit soft tissue dissection/use minimally invasive internal fixation
- Obtain joint fusion
- Fuse/fixate joint one level beyond Charcot affected midfoot
- Use rigid fixation
- Shorten foot to reduce soft tissue tension
- Use of external fixation if indicated

Procedure

The patient is positioned on the operating table in the supine position. Ipsilateral hip bump is recommended to prevent external rotation of the hip. A thigh tourniquet is recommended for patients without peripheral vascular disease. The equinus deformity is generally addressed first either by a percutaneous tendo-achilles lengthening or gastrocnemius recession. The authors also recommend fusing the subtalar joint to stress shield the midfoot correction. Incision placement is along the medial glabrous junction of the midfoot, over the base of the deformity. Dissection is carried down to bone. A subperiosteal dissection is performed superiorly and inferiorly across the midfoot laterally. A second incision is placed along the lateral glabrous and the subperiosteal dissection is then completed. After the dissection is completed, the placement of the midfoot osteotomy is based on the deformity. A section of bone in the midfoot is resected, to realign the foot in all



Fig. 26.4 Clinical images (**a**, **b**, **e**, **f**) and radiographic imaging (**c**, **d**, **g**, **h**) multiple views—preoperative (**a**–**d**) and postoperative (**e**–**h**) status post-single-stage multi-level, multi-plane, multi-tissue deformity Charcot reconstruction with TAL, corrective arthrodesis of the STJ, TNJ, and CCJ, and corrective midfoot osteotomy with internal fixation

three cardinal planes. It is also recommended to prepare and fuse adjacent midfoot joints to increase stability of the construct. After the midfoot is realigned and temporarily or provisionally neutralized, rigid fixation is placed. Options for fixation included plates and screws, intramedullary fixation or external fixation can be used. Intramedullary beaming is recommended when appropriate as it decreases soft tissue dissection compared to the use of plating. Beaming from the first metatarsal across the midfoot to the talus is performed to stabilize the medial column. Followed by additional medial column beaming from the second metatarsal into the talus and lastly lateral column beaming from either the fourth or fifth metatarsal into the calcaneus. In fixating the lateral column, it is important to address the calcaneal cuboid joint sag to prevent increased pressure plantar to the cuboid. Following internal fixation and external fixator may be placed to further protect and offload the reconstruction. Following the reconstruction patients are non-weight-bearing for several weeks with regular monitoring of plain film radiographs to observe bony consolidation at the surgical sites.

Osseous Rearfoot and Ankle Deformity

As is true with deformities within the remainder of the extremity, instances where accommodative treatment modalities are either insufficient or inappropriate to address the rearfoot and/or ankle deformity, corrective surgical treatments should then be considered. Numerous scenarios may contribute to a biomechanical deformity in the rearfoot and ankle; however, fortunately several treatment options exist in which to address these cases. Ultimately, the specific treatment modality should aim to correct the identified primary and secondary deformities in order to balance the deforming forces about the extremity and do so in an effective and definitive manner with the least potential for morbidity to the patient. Exact procedure selection for rearfoot and ankle reconstruction is largely based in the specific anatomic

level(s) and plane(s) of involvement which is often identifiable by a careful physical examination and with use of imaging modalities of plain film radiography and computed tomography. Those cases where deformity is either not sufficiently reducible manually, even after soft tissue release, or is severe in extent, are largely addressed with osseous reconstructive procedures.

Tibiotalocalcaneal Arthrodesis

Concomitant ankle and subtalar joint fusions, collectively a tibiotalocalcaneal (TTC) arthrodesis, is often considered as a limb salvage procedure in patients with complex pathologic conditions of the rearfoot and/or ankle that may otherwise warrant a below the knee amputation [26–28] (Fig. 26.5). The TTC fusion is defined by certain risk factors of patients undergoing the procedure and includes individuals with comorbidities associated with poor surgical healing or with local healing deficits that predispose to a high rate of delayed healing, nonunion, and malunion, among others. The TTC fusion can be a viable and functional option for those with significant deformity of the rearfoot and/or ankle including significant malalignment, bone loss, and/or instability. Perhaps the stereotypical example of such a surgical candidate is the Charcot's neuroarthropathy

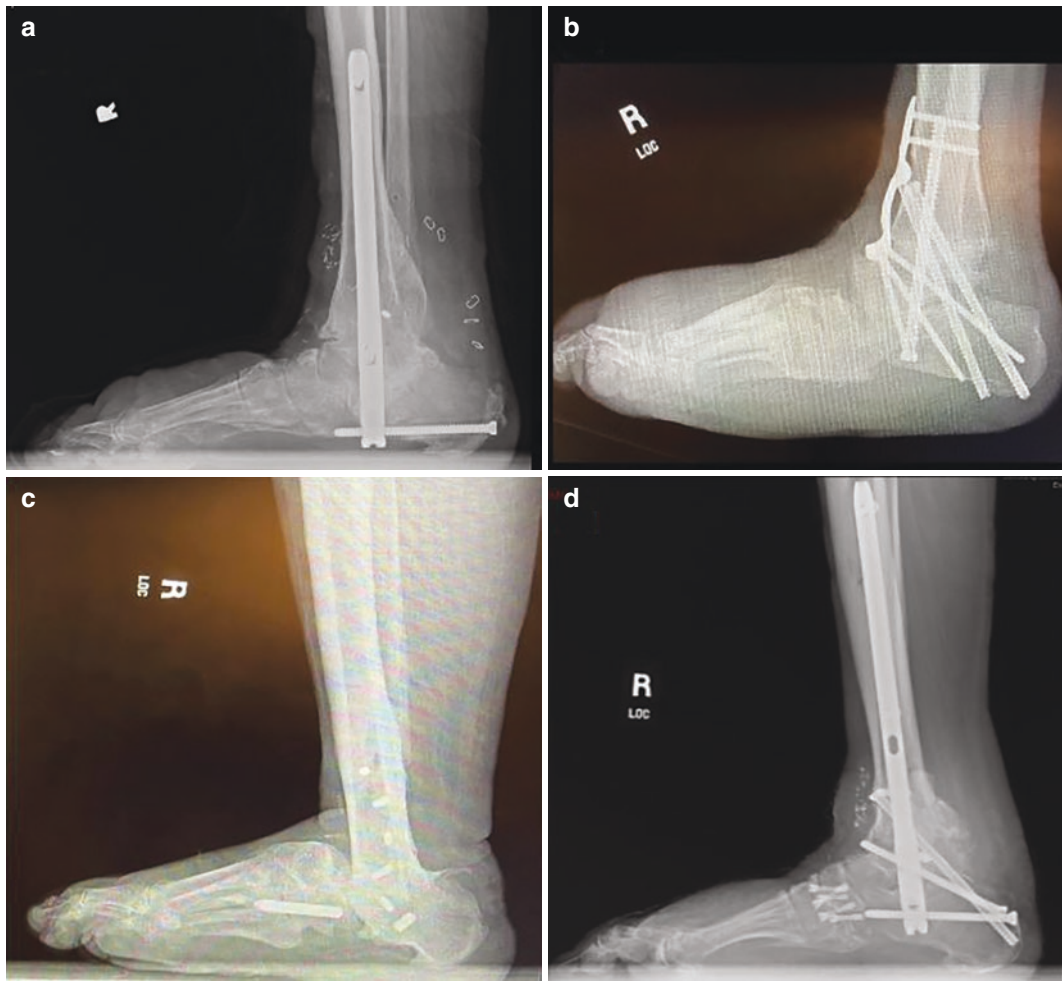


Fig. 26.5 Radiographic imaging lateral ankle view—postoperative (**a**–**d**) status post-tibiotalocalcaneal arthrodesis of four different patients with various fixation constructs

ankle and/or rearfoot; however, many other instances do occur. The greatest drawbacks to the TTC fusion are that it introduces a relatively large amount of indwelling hardware, increasing the risk of infectious processes, and requires major additional surgery and thus surgical dissection and rehabilitation. However, in the scenario where the alternative treatment is a more proximal amputation, a TTC may be considered as a useful option (Fig. 26.6).



Fig. 26.6 Clinical images and radiographic imaging multiple views—preoperative (**a**–**d**) and postoperative (**e**–**k**) status post-staged approach to multi-level, multi-plane, multi-tissue type deformity reconstruction in the face of inciting wound formation with infection to the plantar foot with eradication of infection, optimization of healing potential, soft tissue envelope closure, offloading circular external fixator, subsequent corrective lateral approach fibular "takedown" tibiotalocalcaneal arthrodesis with TAL and PT tendon transfer

Procedure

The patient is positioned supine on the operating table with the heel just distal to the edge of the bed. An ipsilateral hip bump is utilized as warranted to attain vertical orientation of the foot and avoid external rotation of the extremity. A platform fashioned from several folded blankets or operative foam is utilized to elevate the operative extremity above the level of the contralateral extremity for ease of operative performance, including for unobstructed use and views of intraoperative fluoroscopy. Alternatively, to remove the potential for obstruction the contralateral extremity may be placed into "frog leg" positioning or may be secured with foam padding off the bed entirely into a surgical stirrup or the like. A thigh tourniquet may be placed in patients without existing peripheral vascular disease and used in accordance with individual surgeon preference. The extremity is prepped and draped to at least the level of the tibial tuberosity in order to maintain accurate visualization for intraoperative alignment and orientation of the extremity as well as for access during concomitantly performed procedures. Soft tissue procedures are largely performed first in order to initiate, if not attain, appropriate reducibility of the existing rearfoot and/or ankle deformity. Equinus ankle deformity, for instance, may be addressed first either by a tendo-achilles lengthening or tenotomy or gastrocnemius recession. Incision placement for the tibiotalocalcaneal arthrodesis is largely dependent upon the preferred surgical approach and hardware construct in which the surgeon will gain access to the ankle and subtalar joints and place definitive internal fixation, respectively. An anterior, anteromedial, and anterolateral ankle incision will provide for direct access to the ankle joint alone. An Ollier's style dorsolateral foot incision will provide for direct access to the subtalar joint alone. A utilitarian lateral incision will provide for direct access to the ankle joint and subtalar joint concomitantly; however, a distal fibular "takedown" osteotomy may be required in order to appropriately gain surgical access to the ankle joint. This approach does provide for concomitant access to both the ankle and subtalar joints with the added benefit of direct access to the distal fibular bone which may be utilized for both structural and/or non-structural bone grafting as warranted. Additionally, minimally invasive surgical joint preparation may be utilized from standard arthroscopic port locations at the anterolateral, anteromedial, and posterolateral and posteromedial ankle, as well as the anterolateral and posterolateral subtalar joint. This approach has the benefit of minimizing surgical dissection; however, it requires greater surgical skill and precision than the standard open approach, requires additional equipment, and will ultimately restrict one's options for definitive fixation construct. Standard open approach surgical dissection is carried from skin, superficial fascia, deep fascia, and periosteum/capsule to the level of bone of the ankle and subtalar joints. A plethora of instrumentation are available in which the cartilage of the corresponding surfaces of both the ankle and subtalar joint is denuded to the level of healthy and bleeding subchondral bone. Care is taken in which to provide for a maintenance of bone stock so as not to create an excessive amount of bony resection which may add to a loss of length and integrity of the extremity while simultaneously achieving any additional bony angular or translational correction of the existing deformity(ies) which was not attained in soft tissue corrective procedures. Once the joints are sufficiently prepared, flushed, grafted as preferred, and reduction is attainable, the ankle and subtalar joints are neutralized into the reduced positions and preferred definitive fixation is placed. Given the extent and location of the procedures a surgical drain is placed and a layered closure is performed. The extremity is placed into a thick, well-padded, and compressive splint and the patient is maintained in a non-weight-bearing status for a minimum of 2 months with monitoring of appropriate clinical and radiographic healing.

Pantalar Arthrodesis

When significant deformity, represented by complex malalignment, bone loss, bone infection or necrosis, and/or instability occurs at both the level of the ankle and/or foot and within the foot, a pantalar arthrodesis may be considered as a functional means of limb preservation [29]. This option pro-



Fig. 26.7 Radiographic images (**a**–**f**) multiple views—preoperative (**a**–**c**) and postoperative (**d**–**f**) status post staged approach to multi-level, multiplanar, multi-tissue type deformity reconstruction in the face of inciting wound formation with infection to the plantar-lateral foot with subsequent acute Charcot neuroarthropathy of the ankle joint with eradication of infection, optimization of healing potential, soft tissue envelope closure, offloading circular external fixator with antibiotic spacer and, progression of ankle Charcot neuroarthropathy to consolidated state, and subsequent corrective combined lateral approach fibular "takedown" and medial approach Pantalar arthrodesis

duces rigid stability and, when performed correctly, adequate reduction of malalignment of the foot and ankle complexes for ambulation (Fig. 26.7). Numerous approaches and constructs are available to the surgeon and specific selection is largely driven by individual patient presentation, including but not limited to the exact anatomic location(s), plane(s), and severity of involvement of their pathology. As is the case with the tibiotalocalcaneal arthrodesis, the pantalar arthrodesis requires additional surgery and rehabilitation, including the ubiquitous placement of internal fixation. Additionally, with absolute stability and rigidity to the ankle and foot, patients require a rocker-bottom sole modification to their shoe gear in order to afford appropriate midstance rocker for more normal gait. However, the alternative, and perhaps quite viable and functional option in the face of failure of the pantalar arthrodesis, may well be a below the knee amputation. Herscovici et al. [30] saw acceptable outcomes including zero amputations in their 20 patients undergoing pantalar arthrodesis from either severe post-traumatic or neuropathic arthropathy with an average of 46 month follow-up. They concluded that pantalar arthrodesis is a reasonable limb salvage option regardless of the cause of disability or specific internal fixation device.

Procedure

Generally, for a combined medial and lateral approach the patient is positioned supine on the operating table with the heel just distal to the edge of the bed. An ipsilateral hip bump is utilized as warranted to attain vertical orientation of the foot and avoid external rotation of the extremity. A platform fashioned from several folded blankets or operative foam is utilized to elevate the operative extremity above the level of the contralateral extremity for ease of operative performance, including for unobstructed use of intraoperative fluoroscopy. Alternatively, to remove the potential for obstruction the contralateral extremity may be placed into "frog leg" positioning or may be

secured with foam padding off the bed entirely into a surgical stirrup or the like. A thigh tourniquet may be placed in patients without existing peripheral vascular disease and used according to surgeon preference. The extremity is prepped and draped to at least the level of the tibial tuberosity in order to maintain accurate visualization for intraoperative alignment and orientation of the extremity as well as for access during concomitantly performed procedures. Soft tissue procedures are largely performed first in order to initiate, if not attain, appropriate reducibility of the existing rearfoot and/or ankle deformity. Equinus ankle deformity, for instance, may be addressed first either by a tendo-achilles lengthening or tenotomy or gastrocnemius recession. Incision placement for the combined medial and lateral approach pantalar arthrodesis is dictated by access for appropriate performance of bony preparation and hardware placement in which the surgeon will gain access to the ankle and subtalar joints, as well as the talonavicular and calcaneocuboid joints. A curvilinear lateral incision will provide for direct access to the ankle, subtalar, and calcaneocuboid joints concomitantly; however, a distal fibular "takedown" osteotomy must be performed in order to appropriately gain surgical access to the ankle joint. As with the tibiotalocalcaneal arthrodesis, this approach provides for concomitant access to multiple joints with the added benefit of direct access to the distal fibular bone which may be utilized for both structural and/or non-structural bone grafting. A medial incision from the tip of the medial malleolus to the skin overlying the naviculocuneiform joint provides direct access to the talonavicular joint. Standard open approach surgical dissection at each incision is carried from skin, superficial fascia, deep fascia, and capsule to the level of bone of the ankle, subtalar, calcaneocuboid, and talonavicular joints. A plethora of instrumentation are available in which the cartilage of the corresponding surfaces of the joints of interest is denuded to the level of healthy and bleeding subchondral bone. Again, care is taken in which to provide for a maintenance of bone stock so as not to create an excessive amount of bony resection which may add to a loss of length and integrity of the extremity while simultaneously achieving any additional bony angular or translational correction of the existing deformity(ies) which was not attained in soft tissue corrective procedures. Once the joints are sufficiently prepared, flushed, grafted as preferred, and reduction is attainable, the ankle, subtalar, talonavicular, and calcaneocuboid joints are neutralized into their, respectively, reduced positions and preferred definitive fixation is placed. Given the extent and location of the procedures a surgical drain is placed and a layered closure is performed. The extremity is placed into a thick, well-padded, and compressive splint and the patient is maintained in a non-weight-bearing status for a minimum of 2 months with monitoring of appropriate clinical and radiographic healing.

Adjunctive Procedures

Outside of the auspices of this discussion, but rather important for considerations in osseous reconstruction of the rearfoot and ankle are adjunctive procedures often performed as a supplementary portion of the aforementioned tibiotalocalcaneal and pantalar fusions in the complex patient population. The talectomy and the supramalleolar osteotomy are extraordinarily useful adjuncts to the already advantageous osseous reconstruction procedure options and should be considered as viable adjuncts in the surgeons perioperative planning.

Talectomy

Surgical correction of severe osseous deformity and/or osteonecrosis and/or osteomyelitis using a talectomy procedure has previously been described in many lower extremity pathologies and remains a powerful adjunct within the reconstructive options in the limb salvage patient population. It appears that the mere removal of chronically infected and/or necrotic bone of the talus can provide the means in which to appropriately reduce existing malalignment and rid the body of potentially harmful and unstable tissues. In the complex patient population talectomy is combined as part of a reconstructive procedure in the form of tibiocalcaneal fusion or pantalar fusion (Fig. 26.8). Langan et al. saw limb salvage

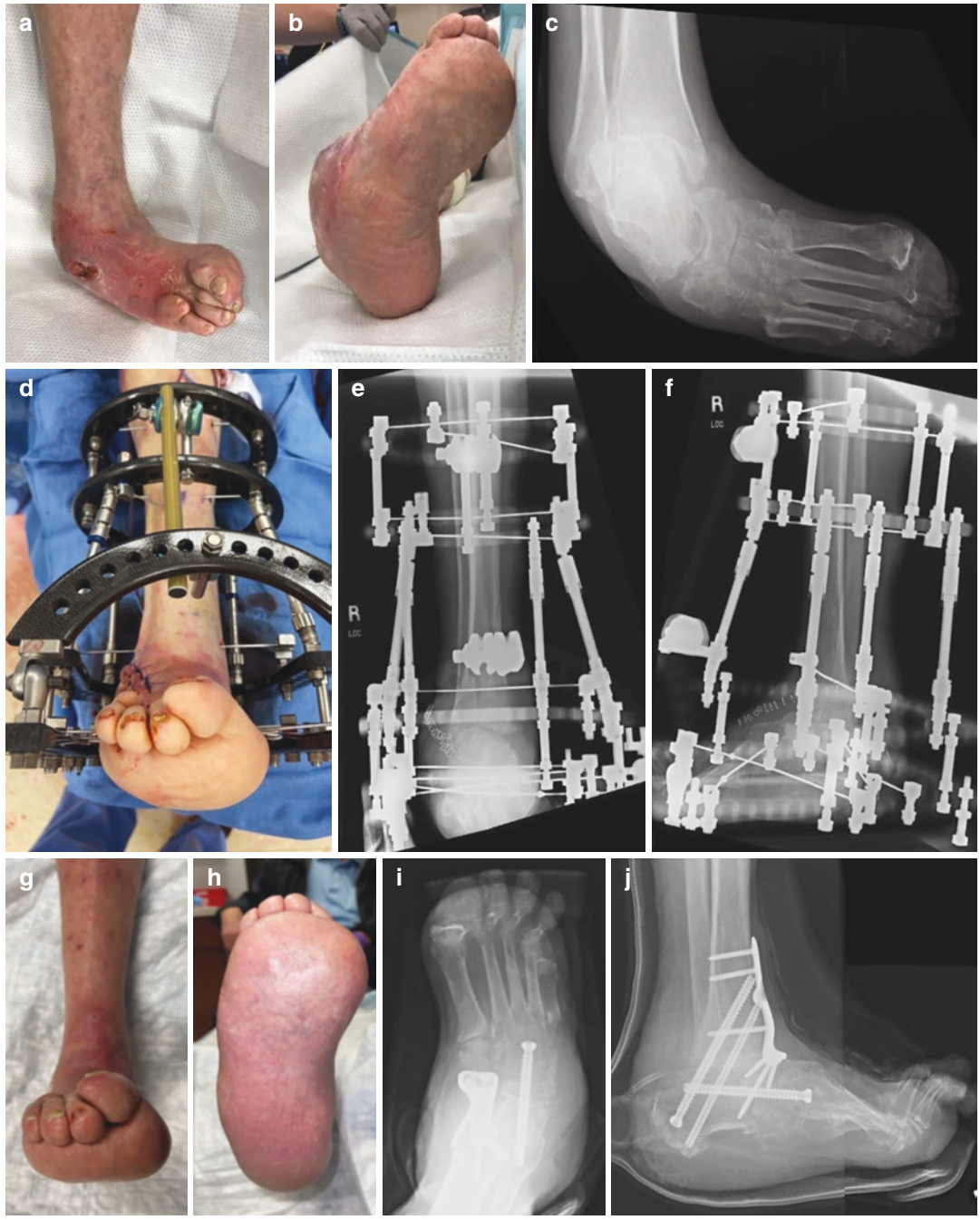


Fig. 26.8 Clinical and radiographic images multiple views—preoperative (**a**–**c**) and postoperative (**d**–**j**) status post-staged approach to multi-level, multiplanar, multi-tissue type deformity reconstruction in the face of inciting wound formation with infection to the dorsolateral foot with eradication of infection, optimization of healing potential, talectomy, midfoot osteotomy, extensive foot and ankle soft tissue releases, soft tissue envelope closure, offloading and compressive circular external fixator and subsequent exchange of external fixation for internal fixation with pantalar arthrodesis

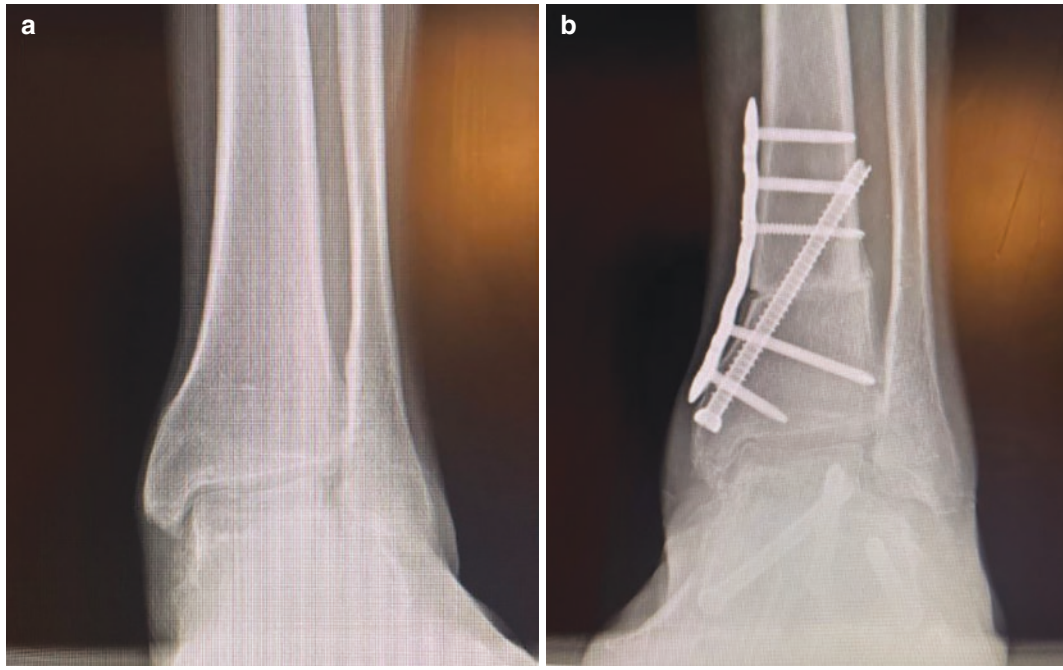


Fig. 26.9 Radiographic imaging AP ankle views (**a**, **b**)—preoperative (**a**) and postoperative (**b**) status post-medially based closing wedge type supramalleolar osteotomy for progressive valgus deformity of the tibia secondary to malunion triple arthrodesis. Note the significant lateral ankle "gutter" decompression achieved with this osteotomy. Of note, a corrective midfoot osteotomy was performed concomitantly to reduce the malunited triple arthrodesis and reposition the foot

occurred in 38 of 45 patients (84.4%) where talectomy was utilized with 6 of 7 patients (85.7%) who ultimately underwent amputation having a history of prior infection [31]. Ultimately, they concluded chronic lower extremity deformities can successfully be treated with a talectomy as a portion of the reconstructive procedures. Admittedly, the loss of height of the talus bone will precipitate structural limb length discrepancy; however, this may be remedied with shoe modification or with concomitant use of distraction osteogenesis limb lengthening procedures.

Supramalleolar Osteotomy

Outside of strictly isolated planar deformities of the ankle joint, the supramalleolar osteotomy may also be utilized as a useful adjunct in the reconstruction of complex rearfoot and ankle deformities [32–34]. An osteotomy through the tibia (and fibula where warranted) may provide single and multi-dimensional correction of the extremity in order to produce a more functionally ambulatory limb, especially important in the neuropathic population (Fig. 26.9). Horn et al. saw significant improvement in all postoperative radiographic angles in 22 patients with the use of a supramalleolar osteotomy and a dynamic six-axis external fixator [35]. They found this method particularly effective for correction with complex deformities, a compromised soft tissue envelope, or a prior history of infection. Additionally, the Siddiqui et al. also saw enhanced arthrodesis in 14 of 15 patients (93.3%) by combining distal tibial distraction osteogenesis with simultaneous tibiotalocalcaneal or tibiocalcaneal arthrodesis for the rearfoot and ankle in a limb salvage scenario. They concluded that the supramalleolar osteotomy with distraction osteogenesis supports enhanced vascularity to their rearfoot and ankle arthrodesis sites [36].

Soft Tissue and Tendon Balancing Procedures

Tendon Lengthening

Equinus deformity has classically been described as limitation of passive ankle joint dorsiflexion to less than a right angle of the foot on the leg. This limitation of joint mobility in dorsiflexion motion at the ankle has been implicated as a major deforming force in the development and chronicity of plantar wound formations as well as midfoot Charcot collapse, among many other pathologies. Glycation-induced collagen cross-linking secondary to diabetes mellitus sequelae causes general disorganization of the Achilles tendon, decreasing tensile strength and elasticity while increasing stiffness [14]. These changes in addition to the reduction in strength and flexibility common in increased sedentary lifestyle and advanced age result in pathologic reduction in ankle dorsiflexion during stance and swing phases of gait. This contracture creates profound increases in plantar pressures to the forefoot and midfoot, oftentimes precipitating plantar ulcerations in the neuropathic population [37]. Measuring the maximal passive dorsiflexion available at the ankle with the subtalar joint locked and the knee extended and then flexed accomplishes this task. Distinction between gastrocnemius or isolated equinus vs. gastrocnemius-soleus or combined equinus is significant when considering the correct procedure and level to perform surgical lengthening of the posterior group. The *Silfverskiold Test* is a common and reproducible way to determine the source of ankle contracture [38].

Tendo-Achilles Lengthening (TAL)

Tendo-achilles lengthening is a common procedure performed in an assortment of instances of foot and ankle pathology and in a number of ways in order to achieve restoration of the sufficient ankle dorsiflexion joint excursion required during normal gait. In the complex wound patient, the TAL is truly a utilitarian procedure for soft tissue ankle equinus. The authors often utilize the traditional Hoke [39] style percutaneous triple hemi-section of the distal excursion of the Achilles tendon for patients with either combined gastrocnemius-soleus equinus as well as those with isolated gastrocnemius equinus, due to its relatively minimally invasive approach, short procedure length, and profound effect on improving ambulatory ankle dorsiflexion range of motion (Figs. 26.10 and 26.11).

Procedure

With the foot held in maximal dorsiflexion and the Achilles tendon tensioned, vertical incisions are made posteriorly at the midline of the skin and fascia and into the Achilles tendon at 3, 6, and 9 cm proximal to the most superior aspect of the calcaneus. It is the author's preference to

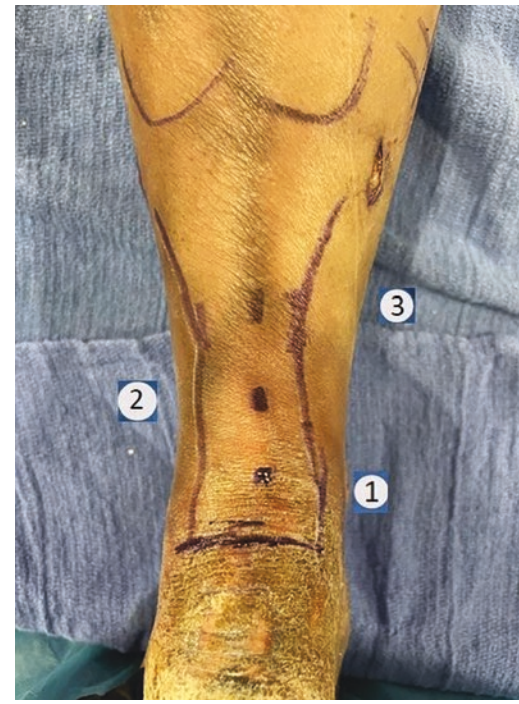


Fig. 26.10 Clinical image posterior view—incision placements for Hoke style triple hemi-section distally based tendo-achilles lengthening (TAL). Traditionally, the Hoke TAL is performed with two medially directed (distal and proximal) and one laterally directed (central) hemi-sections; however, surgeon preference dictates actual performance as long as the hemi-sections are performed in alternating directions



Fig. 26.11 Clinical images lateral view (**a**, **b**)—preoperative (**a**) and postoperative (**b**) status post-Hoke style tendo-achilles lengthening (TAL)

mark these intervals using a ruler and skin marker to ensure safe distance is maintained between incisions. At each marked interval the surgeon should palpate the medial and lateral borders of the Achilles tendon and a #15 blade is then inserted mid-substance within the tendon body with the blade facing in-line with the tendon fibers. The blade is then rotated 90° and exited the tendon in a sweeping motion alternating between medial and lateral exits at each interval. In effect this creates three separate partial hemi-sections of the Achilles tendon 50% from midline. Oftentimes a "release" of ankle contracture will be noted with forced dorsiflexion of the ankle, and additional partial swipes may be attempted at each tenotomy site to ensure complete hemi-section. This will provide for a correction for both combined gastrocnemius-soleus equinus and isolated gastrocnemius equinus until a sufficient intraoperative *Silfverskiold test* is confirmed.

Gastrocnemius Recession (GR) and Gastrocnemius-Soleus Recession (GSR)

Alternatively, if the *Silfverskiold test* determines equinus is visualized only with the knee extended but not with the knee flexed, patients may have isolated gastrocnemius equinus, and a gastrocnemius recession alone may be indicated (Fig. 26.12). The GR has several added benefits over a distally based TAL procedures, including direct visualization of surgical anatomy, more proximal calf location which may benefit from superior vascularity, avoidance of procedure in diseased tendon commonly seen in the comorbid population, and an anecdotally more "controlled" lengthening of the tissues. Additionally, access for a GR provides for the ability to also perform a lengthening of the soleus muscular fascia in what is termed a gastrocnemius-soleus recession, which may be preferable for patients with combined gastrocnemius-soleus equinus and may also be performed via an endoscopic approach (Fig. 26.13). The authors ascribe to a traditional Baumann [40] type approach to the GR and GSR when appropriate (Fig. 26.14).

Procedure

At 10 cm distal to the tibial tuberosity a 6 cm incision is centered at 50% of the posterior bulk of the calf between the medial tibial crest and the posterior aspect of the calf. With the ankle stressed passively into maximal dorsiflexion and moving from lateral to medial a long-handled scalpel with #15 blade is utilized to incise the anterior portion of the gastrocnemius intermuscular fascia, including the plantaris tendon, exposing the underlying gastrocnemius muscle



Fig. 26.12 Clinical images medial view (**a**–**f**)—preoperative (**a**–**d**) *Silfverskiold* test performed in a patient after a successful transmetatarsal amputation with free tissue flap for closure displaying formation of isolated gastrocnemius equinus. Postoperative (**e**, **f**) status post-Baumann style gastrocnemius recession (GR) shows a reduction of the passive ankle joint dorsiflexion range of motion



Fig. 26.13 Clinical image medial view—incision placement for endoscopic gastrocnemius-soleus recession

belly. This will provide for a correction of isolated gastrocnemius equinus. Additional releases to subsequent portions of the gastrocnemius intermuscular fascia may be performed until a sufficient intraoperative *Silfverskiold test* is confirmed. As mentioned, additional recession of the soleus intramuscular fascia is also easily accessible from this approach for instances of combined gastrocnemius-soleus equinus for GSR [41].

Tendon Transfers

Anterior Tibial Tendon Transfer

The anterior tibial tendon transfer (ATTT) was first described in 1940 for the correction of residual pediatric clubfoot [42, 43]. Since then, the indications for the ATTT) have expanded, where it is widely used to counter varus and supinatory forces while maintaining active dorsiflexion [43]. This is particularly useful in the treatment of acquired pathology such as dropfoot following stroke or acquired flexible forefoot equinovarus following partial foot amputation. Patients with plantar-lateral foot ulcerations, lateral column amputations with the loss of the peroneus brevis insertion or loss of peroneal tendon function often have increased supinatory motion and thus can benefit from the ATTT [43, 44] (Fig. 26.15). Transfer of the anterior tibial (AT) tendon to the lateral column can effectively balance the foot by increasing everting forces and decreasing lateral column pressures (Fig. 26.16). Traditionally, the distal insertion of the tendon is released from its medial attachment and transferred laterally to the lateral cuneiform. This aids to balance the powerful supinatory force of the posterior tibial tendon while maintaining active dorsiflexion of the foot. Additionally, lateralizing the transfer on the foot can increase its everting force, thus can be used to treated spastic rearfoot varus, spastic equniovarus, fixed equinovarus, and excessive supination.

Procedure

The patient is placed in the supine position. A thigh tourniquet and ipsilateral hip bump is generally used. As with most tendon transfers, general anesthesia with paralysis is recommended. The transfer of the anterior tibial tendon is generally performed through three incisions. When harvesting the tendon, the initial dorsal medial 3–4 cm incision is made over the medial cuneiform-metatarsal joint (directly over the insertion of the tendon). Expose and transect the tendon at its insertion and tag end of the tendon with a suture. The second incision is placed just lateral to the myotendinous junction in the distal lower leg. Palpate the course of the anterior tibial tendon to just below the muscle belly. A 3–4 cm incision is made just lateral to the tendon. This incision can be placed about 10–12 cm proximal to the ankle joint. Incise the tendon sheath and expose the AT tendon. Harvest the transected tendon proximally to its origin. Once harvested, a 2-0 prolene can be used) to whip stitch the distal portion of the tendon. The placement of the third incision is dependent on the desired function of the tendon. If pure dorsiflexion is desired, then the incision is placed over the lateral cuneiform

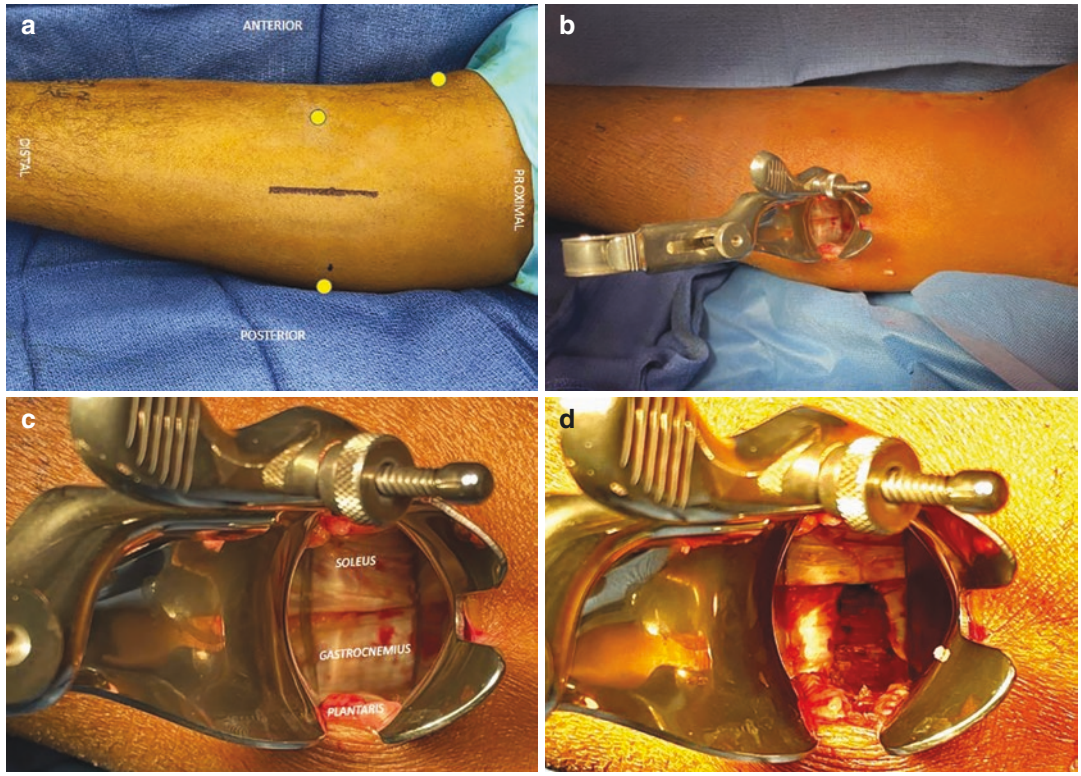


Fig. 26.14 Clinical images medial view (**a**–**d**)—intraoperative Baumann style gastrocnemius recession with (**a**) incision planning, (**b**) use of a vaginal speculum for appropriate visualization in the interval between the gastrocnemius and soleus intermuscular septum, (**c**) anatomic visualization of the soleus, gastrocnemius and plantaris, (**d**) status post-recession of the gastrocnemius intermuscular fascia, including the plantaris tendon, exposing the underlying gastrocnemius muscle belly

and the tendon is transferred into bone. If more of an eversion force is needed, a 3–4 cm can be placed over the base of either fourth or fifth metatarsal or distal cuboid. The tendon may be transferred into any of these bones. Next a tendon passer is tunneled subfascially from the third incision to the second incision. The tendon is pulled through to the lateral incision. Once the desired location of the transfer is exposed, a drill hole is made through the bone. The suture on a straight needle is fed through the bone tunnel out the plantar foot. The foot is then everted and dorsiflexed slightly beyond neutral and a biotenodesis screw is used to secure the tendon into the bone. The excessive suture is cut. The foot is placed through a gentle range of motion to determine if desired correction) is achieved. Incisions are irrigated and layer closure is performed. The patient is splinted and non-weight-bearing for 6 weeks.

When planning this transfer, the AT tendon muscle must have a minimal muscle strength of 4. Anything less will not have the desired result. Pitfalls to the complete AT tendon transfer include complete loss of function of the tendon at its native insertion, over tensioning can cause a severe pes planovalgus deformity and nerve irritation [43, 44]. It is all also recommended a tendo-achilles length be performed in conjugation with the transfer to address any equinus deformity.

Split Tibialis Anterior Tendon Transfer

The split tibialis anterior tendon transfer (STATT) procedure has gained some favor primarily as half of the transfer remains intact at its native



Fig. 26.15 Clinical images AP view (**a**, **b**)—preoperative (**a**) and postoperative (**b**) status post-anterior tibial tendon transfer (ATTT) for retained flexible forefoot varus following transmetatarsal amputation. Note the significant correction of the forefoot varus positioning and maintenance of balanced positioning postoperatively

insertion. The indications for the STATT are similar to the complete tendon transfer. The tendon can be transferred to the same locations as the complete transfer [45]. If the desired location is the base of the fifth metatarsal, the tendon may be tenodesed to the peroneus tertius.

Procedure

Patient positioning, anesthesia, incision, and harvest technique are the same for the STATT and AT tendon transfers with one minor difference. After the tendon is exposed in the lower leg, an osteotome or malleable retractor is placed under the tendon and tension is applied to the tendon. After the tendon) is held taut, using a # 15 blade a longitudinal full-thickness stab incision is made in the central aspect of the tendon. A 0–0 prolene or braided suture is fed through the split until equal length suture is on either end of the split. (The authors prefer to use fibertape to split the tendon longitudinally.) A tendon passer or suture loop passer is fed through the tendon sheath from the tendon's insertion at the medial cuneiform first metatarsal joint proximally up to the second incision. The suture is pulled through the tendon sheath distally. The foot is slightly plantarflexed and inverted to tension the tendon. In a back-and-forth sawing motion the suture is pulled distally toward the tendon insertion splitting the tendon in half. Care must be taken to pull the suture in the longitudinal direction of the tendon. If the suture deviates, it can cause premature transection of the tendon. This can cause loss of tendon length. Once the suture exits distally at the insertion, the lateral half of the tendon is identified) and transected. This portion is pulled proximally. A 2-0 prolene is whip stitched through the harvested tendon. The lateral portion of the tendon is then tunneled subcutaneously to the lateral foot and transferred into the base of the fourth, fifth metatarsal or distal cuboid. It may also be tenodesed to the peroneus brevis. As with the AT ten-

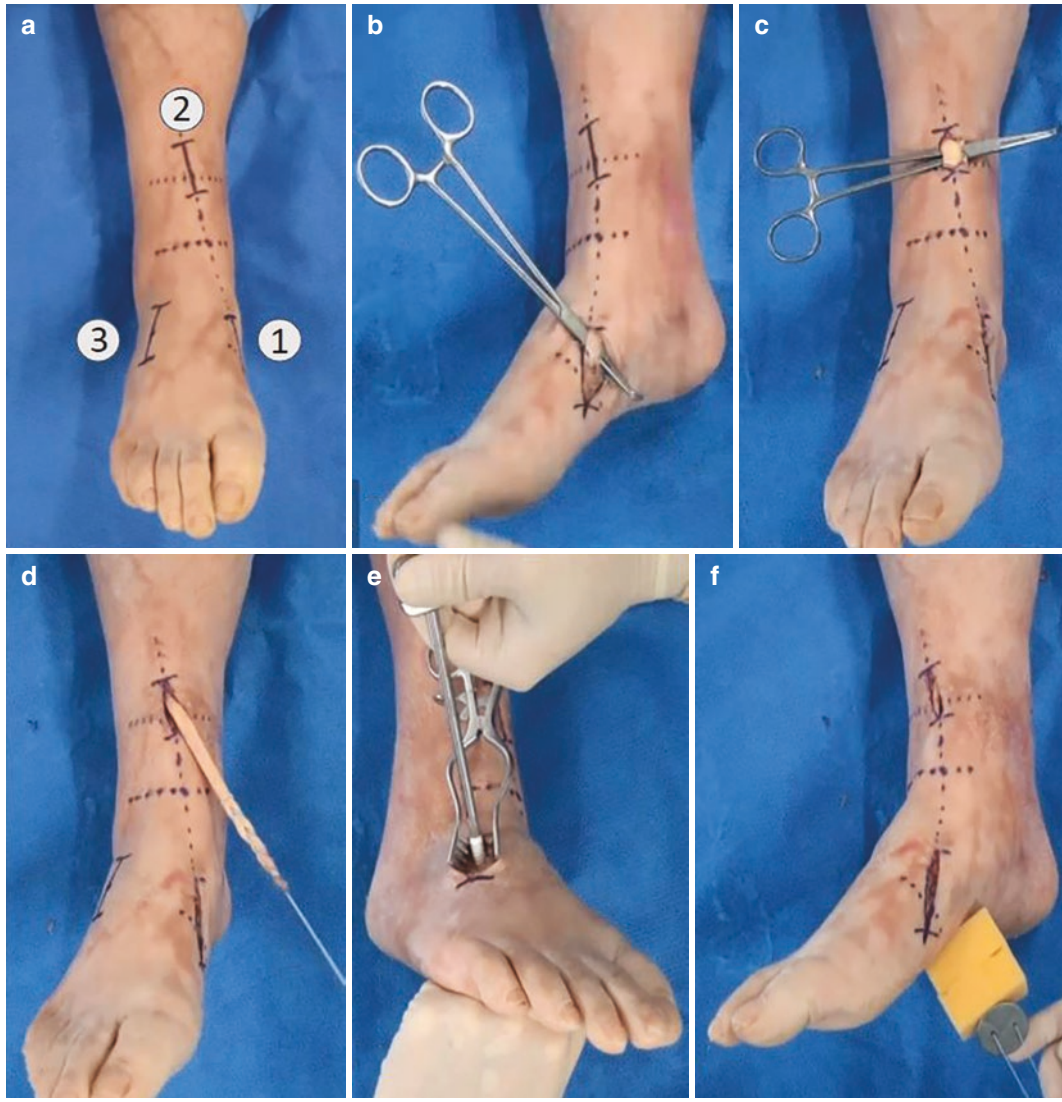


Fig. 26.16 Clinical images multiple views—sequential cadaveric performance of the AT tendon transfer into the lateral cuneiform bone via: (**a**) three-incision approach, (**b**) harvesting of the AT tendon at its insertion, (**c**) passing of the tendon to the anterior leg compartment, proximal to the extensor retinaculum, (**d**) placement of a passing suture in the form of a whip style stitch to the distal tendon, (**e**) final passing of the tendon to the dorsal foot with fixation via a biotenodesis screw, and (**f**) additional fixation with external button fashioned from the plunger of a 60 cc syringe and dry sterile sponge

don transfer the foot must be slightly everted and dorsiflexed beyond neutral before fixating. Postoperative course is the same as with the AT tendon transfer. Planning for the STATT is the same as with the AT tendon transfers. The STATT has advantages over the complete tendon transfer as it preserves native anterior tibial tendon function as well decreases risk of severe pes planovalgus deformity. Similarly, a tendo-achilles lengthening is recommended in conjunction with the transfer. Pitfalls to the STATT include under correction and tendon rupture.



Fig. 26.17 Clinical images AP view (**a**, **b**)—preoperative (**a**) and postoperative (**b**) status post-posterior tibial (PT) tendon transfer for combined equinovarus deformity following Lisfranc level amputation. Note the significant correction of the forefoot varus positioning and maintenance of balanced positioning postoperatively

Posterior Tibial Tendon Transfer

The anterior placed transfer of the posterior tibial (PT) Tendon was first described by Ober in 1933 [46]. Putti discussed transferring the tendon through the interosseous membrane in 1937, but this procedure was popularized by Watkins in 1955 [47]. Transfer of this tendon to the dorsum of the foot is mainly indicated for dorsiflexory weakness or paralysis such as is found in weak or paralyzed anterior muscle group, equinovarus, spastic equinovarus, recurrent clubfoot deformities, dropfoot, Charcot-Marie-Tooth disease, peroneal nerve palsy, and Duchenne muscular dystrophy. PT tendon transfers can also be used to reduce deforming supinatory forces and reduce varus recurrence such as in the setting of peroneal tendon weakness. This is commonly seen when osteomyelitis to the base of the fifth metatarsal requires loss of peroneus brevis insertion point (Fig. 26.17). A four-incision approach is preferred in order to harvest, prepare, pass, and subsequently secure the entirety of the PT tendon into a lateralized position relative to the axis of motion of both the subtalar joint and long axis of the midtarsal joint (Fig. 26.18). The authors prefer a complete PT tendon transfer utilizing a four-incision approach as it provides greater functional action of the tendon while also completely removing it from contributing as a deforming force. Additionally if the spring ligament and capsule of the talonavicular joint are intact they are likely not to permit midfoot progression to planus deformity.

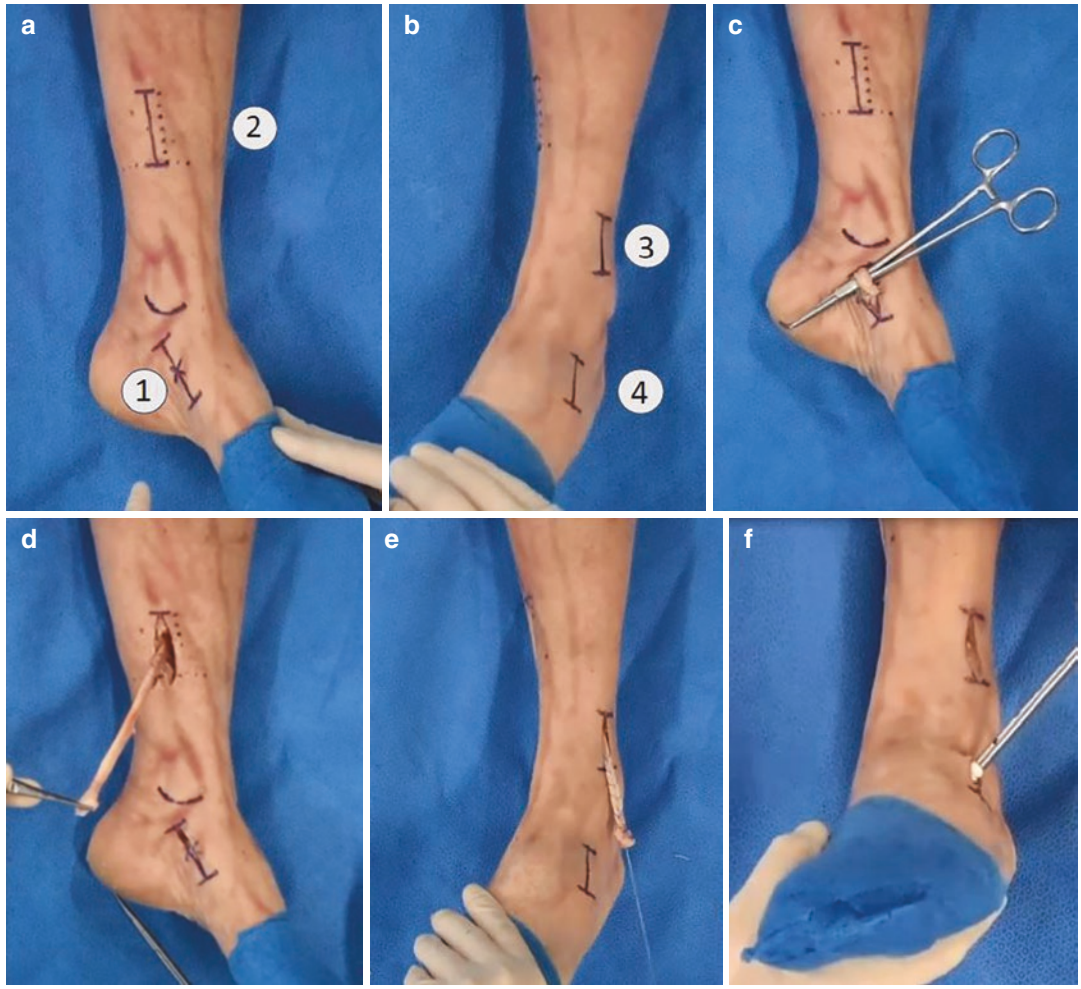


Fig. 26.18 Clinical images multiple views—sequential cadaveric performance of the PT tendon transfer into the cuboid bone via (**a**, **b**) four-incision approach, (**c**) with harvesting of the PT tendon at its insertion, (**d**) passing of the tendon to the deep posterior leg compartment, proximal to the flexor retinaculum with placement of a passing suture in the form of a whip style stitch to the distal tendon, (**e**) passing of the tendon to the anterior leg compartment via and interosseous membrane approach, (**f**) final passing of the tendon to the dorsal foot with fixation via a biotenodesis screw

Procedure

The patient is placed in the supine position. A thigh tourniquet and ipsilateral hip bump is generally used. As with most tendon transfers, general anesthesia with paralysis is recommended. The transfer of the posterior tibial tendon to the dorsum of the foot is generally performed through four incisions. The first incision made medial directly over the insertion of the tendon on the navicular tuberosity. This incision is generally 3–4 cm in length. Dissection is carried down to the tendon insertion, care is taken to preserve the flexor digitorum longus tendon. Preserving as much of the PT tendon as possible, the tendon is dissected off the navicular distally to proximally. Using a 2-0 prolene a whip stitch is placed through the distal tendon. A second 3 cm incision is made 13–15 cm proximal to the distal tip of the medial

malleolus on the medial calf just posterior to the medial aspect of the tibial crest. Dissection is carried down through the fascia, the first tendon encountered is the flexor digitorum longus which is retracted out of the way. Next the PT tendon is encountered. The distal tendon stump is then pulled proximally through the second incision. A hemostat may be used to assist with retrieval. Next using a large hemostat blunt, careful dissection is performed in distal and lateral direction on the posterior tibia. Care must be taken to avoid the neurovascular bundle as it resides in this area. Once the interosseous membrane is encountered, it is penetrated and the hemostat is advanced distally and laterally until the anterior skin is tented. A third, 3 cm incision is made over the tented skin. The hemostat is opened widely to enlarge the interosseous window. Leaving the hemostat open, a tendon passer is fed from the third incision to the second incision. The tendon is then fed through the membrane anteriorly out through the third incision. The fourth incision 3–4 cm can be placed over the lateral cuneiform or cuboid depending on desired tendon function and length (lateralizing the tendon insertion increased eversion force). The tendon is then passed deep to the extensor retinaculum and out the fourth incision. A drill hole is made through the bone and the suture on a free needle is fed through the bone tunnel and out the plantar foot. The foot is held at neutral in the sagittal plane and/or slight eversion when correcting for a varus deformity or lateral column ulcers. The tendon is tensioned and the biotenodesis screw is inserted. All incisions are irrigated, and a layered closure is performed. The patient is placed in a splint and non-weight-bearing for 6 weeks. The surgeon should be mindful of the length of the tendon when considering a PT tendon transfer. Care must be taken to preserve as much length as possible. The interosseous window should be wide enough to prevent any tethering of the tendon. It is also recommended to address any equinus deformity with an Achilles tendon lengthening or posterior ankle capsule release when performing the PT tendon transfer. If there is concern for medial column instability a flexor digitorum longus tendon transfer to the navicular can be considered.

External Fixation for Surgical Offloading

The use of external fixation is a viable alternative or even primary treatment to the aforementioned offloading strategies, especially when strict offloading or additional structural stability is absolutely necessary (Fig. 26.19). An external fixator may be applied either immediately following a definitive reconstructive closure attempt or during an interim period where an open surgical site requires offloading, structural support, or immobilization. Patients with tenuous or fragile grafts or flaps or other procedures like joint arthroplasty or fusion, osteotomy, and hardware removal/exchange may benefit from the weight-relief and/or structural support provided by an external fixator. A wire or pin hybrid "frame"



Fig. 26.19 Clinical image AP ankle view—ringed (circular) external fixator with hybridized skinny wire and half-pin construct design. The use of external fixation possesses a wide variety of constructs and uses in the complex wound population from static offloading, immobilization, osseous compression, and dynamic multiplanar deformity correction

may be applied in innumerable construct fashions and several manufacturers provide circular or "Ilizarov" frames, principally aimed at offloading or providing immobilization of a particular area about the foot and ankle. The primary shortcoming to this type of offloading is the morbidity associated with such a construct. Well-known potential complications associated with external fixation frames include pin or wire site irritation and/or infection, pin or wire failure, pin or wire associated fracture as well as external fixator associated psychosis or "cage rage." Certainly, not every patient is considered a candidate for this type of offloading and those under consideration should be properly counseled about the realistic expectations, the benefits of such a construct, and the potential for complication. Although not infallible, one may minimize the potentiation for the aforementioned and associated complications of external fixation by minimizing the patients collective time within the fixator, by providing as rigid and stable a construct as the tissues will tolerate, and by providing for inherent contingency of the internal component parts so that, should a pin or wire experience breakage or irritation/infection, a simple removal in office or bedside may be utilized, sparing the patient unneeded operative and anesthesia intervention for wire or pin exchanges. The authors prefer to plan utilization of external fixation for a maximum time period of 4–8 weeks, when possible, utilize a four-ring construct (two tibial rings, one talus ring, and one footplate ring), utilize a hybridized skinny wire and half-pin combination of fixation at the tibial rings, and utilize the narrowest ringed construct amenable to the patient's anatomy. In these ways, the possibility of many of the most common complications of external fixation can be minimized.

Prophylactic Surgery in Limb Salvage

In the high risk patient population, it may be beneficial to prophylactically correct a pedal deformity which has the potential to insite ulceration, prior to wound formation. Deformities such as hammertoes, bunions, hallux rigidus, tailor's bunions, pes planus, pes cavus, and ankle equinus are the most common pathologies that can lead to ulcerations in the neuropathic foot [48, 49]. When custom shoes or inserts fail to properly accommodate potential sites of ulcerations, surgical correction should be necessary.

When performing an elective surgical procedure on a high risk patient, the surgeon must understand the increased risk of wound healing complication and infection compared to a healthy individual. The authors recommend a thorough vascular work-up including arterial studies with vascular surgery consultation, glycosylated hemoglobin A1c of 7.9 or lower, fasting glucose level of less than 200 mL/dL on day of surgery, smoking/nicotine cessation greater than 6 weeks prior to surgery on any high risk surgical patient. It is also recommended to limit the amount of absorbable suture used and consider using antibiotic powder or biodegradable antibiotic delivery device on hardware and incisions. Following surgical correction of a pedal deformity, it is strongly encouraged patients receive custom inserts/shoes after they have completely healed. Patients should be followed routinely indefinitely after surgery for preventative care.

Summary

The diabetic foot and ankle is a complex structure with multiple intrinsic and extrinsic factors. Surgical offloading and prophylactic surgery performed at the appropriate time can be critical in preventing amputation. Identifying high pressure areas and selecting the appropriate surgical procedure is of paramount importance. Insufficient surgical offloading or unnecessary surgical procedures increase the risk of amputation. However, when performed appropriately, surgical offloading and prophylactic surgery can be a power tool in treating and preventing ulcers in the high risk diabetic foot.

References

1. Beaulieu RJ, Grimm JC, Lyu H, Abularrage CJ, Perler BA. Rates and predictors of readmission after minor lower extremity amputations. J Vasc Surg. 2015;62:101–5.
2. Hobizal KB, Wukich DK. Diabetic foot infections: current concept review. Diabet Foot Ankle. 2012;3(1):18409.
3. Armstrong DG, Frykberg RG. Classifying diabetic foot surgery: toward a rational definition. Diabet Med. 2003;20:329–31.
4. Edmonds ME, Sumpio BE. Limb salvage of the diabetic foot: an interdisciplinary approach. Berlin: Springer; 2019.
5. Raspovic KM, Hobizal KB, Rosario BL, Wukich DK. Midfoot Charcot Neuroarthropathy in patients with diabetes: the impact of foot ulceration on self-reported quality of life. Foot Ankle Spec. 2015;8:255–9.
6. van Schie CHM. A review of the biomechanics of the diabetic foot. Int J Low Extrem Wounds. 2005;4:160–70.
7. Besse J-L, Leemrijse T, Deleu P-A. Diabetic foot: the orthopedic surgery angle. Orthop Traumatol Surg Res. 2011;97:314–29.
8. Wu SC, Crews RT, Armstrong DG. The pivotal role of offloading in the management of neuropathic foot ulceration. Curr Diab Rep. 2005;5:423–9.
9. Finestone AS, Tamir E, Ron G, Wiser I, Agar G. Surgical offloading procedures for diabetic foot ulcers compared to best non-surgical treatment: a study protocol for a randomized controlled trial. J Foot Ankle Res. 2018;11:6.
10. Armstrong DG, Lavery LA, Vazquez JR, Short B, Kimbriel HR, Nixon BP, Boulton AJM. Clinical efficacy of the first metatarsophalangeal joint arthroplasty as a curative procedure for hallux interphalangeal joint wounds in patients with diabetes. Diabetes Care. 2003;26:3284–7.
11. Scott JE, Hendry GJ, Locke J. Effectiveness of percutaneous flexor tenotomies for the management and prevention of recurrence of diabetic toe ulcers: a systematic review. J Foot Ankle Res. 2016;9:25.
12. Fontaine JL, Crisologo PA, Lavery L. Current concepts in curative surgery for diabetic forefoot ulcers. Foot. 2019;39:37–44.
13. Bonanno DR, Gillies EJ. Flexor tenotomy improves healing and prevention of diabetes-related toe ulcers: a systematic review. J Foot Ankle Surg. 2017;56:600–4.
14. Frykberg RG, Bevilacqua NJ, Habershaw G. Surgical off-loading of the diabetic foot. J Am Podiatr Med Assoc. 2010;100:369–84.
15. Yammine K, Kheir N, Assi C. A meta-analysis of the outcomes of metatarsal head resection for the treatment of neuropathic diabetic foot ulcers. Adv Wound Care. 2021;10:81–90.
16. Molines-Barroso RJ, Lázaro-Martínez JL, Aragón-Sánchez J, García-Morales E, Beneit-Montesinos JV, Álvaro-Afonso FJ. Analysis of transfer lesions in patients who underwent surgery for diabetic foot ulcers located on the plantar aspect of the metatarsal heads. Diabet Med. 2013;30:973–6.
17. Henry J, Besse JL, Fessy MH, AFCP. Distal osteotomy of the lateral metatarsals: a series of 72 cases comparing the Weil osteotomy and the DMMO percutaneous osteotomy. Orthop Traumatol Surg Res. 2011;97:S57–65.
18. Tamir E, Tamar M, Ayalon M, Koren S, Shohat N, Finestone AS. Effect of mini-invasive floating metatarsal osteotomy on plantar pressure in patients with diabetic plantar metatarsal head ulcers. Foot Ankle Int. 2021;42:536–43.
19. Lipsky BA, Kuss M, Edmonds M, Reyzelman A, Sigal F. Topical application of a gentamicin-collagen sponge combined with systemic antibiotic therapy for the treatment of diabetic foot infections of moderate severity: a randomized, controlled, multicenter clinical trial. J Am Podiatr Med Assoc. 2012;102:223–32.
20. Elmarsafi T, Oliver NG, Steinberg JS, Evans KK, Attinger CE, Kim PJ. Long-term outcomes of permanent cement spacers in the infected foot. J Foot Ankle Surg. 2017;56:287–90.
21. Moon KC, Son JW, Han SK, Kim JY. Risk factors for major amputation for midfoot ulcer in hospitalized patients with diabetes. Foot Nail Care. 2021;48(2):163–8.
22. Lu Q, Wang J, Wei X, Wang G, Xu Y. Risk factors for major amputation in diabetic foot ulcer patients. Diabetes Metab Syndr Obes. 2021;14:2019–27.
23. Laborde J. Midfoot ulcers treated with gastrocnemius-soleus recession. Foot Ankle Int. 2009;30(9):842–6.
24. Wieman T, Griffiths G, Polk H. Management of diabetic midfoot ulcers. Ann Surg. 1992;215(6):627–32.
25. Siddiqui N, LaPorta G. Midfoot Charcot reconstruction. Clin Podiatr Med Surg. 2018;35:509–20.
26. Rammelt S, Pyrc J, Agren PH, Hartsock LA, Cronier P, Friscia DA, Hansen ST, Schaser K, Ljungqvist J, Sands AK. Tibiotalocalcaneal fusion using the hindfoot arthrodesis nail: a multicenter study. Foot Ankle Int. 2013;34(9):1245–55.
27. Burns PR, Dunse A. Tibiotalocalcaneal arthrodesis for foot and ankle deformities. Clin Podiatr Med Surg. 2017;34(3):357–80.
28. Lee BH, Fang C, Kunnasegaran R, Thevendran G. Tibiotalocalcaneal arthrodesis with the hindfoot arthrodesis nail: a prospective consecutive series from a single institution. J Foot Ankle Surg. 2018;57(1):23–30.
29. Wukich DK. Pantalar arthrodesis for post-traumatic arthritis and diabetic neuroarthropathy of the ankle and hindfoot. Foot Ankle Int. 2011;32(9):924.
30. Herscovici D, Sammarco GJ, Sammarco VJ, Scaduto JM. Pantalar arthrodesis for post-traumatic arthritis and diabetic neuroarthropathy of the ankle and hindfoot. Foot Ankle Int. 2011;32(6):581–8.
31. Langan T, Lalli TAJ, Smith CN, Wukich DK. Talectomy as part of chronic foot and ankle

deformity correction procedure: a retrospective study. J Foot Ankle Surg. 2020;59(1):16–20.
32. Hintermann B, Knupp M, Barg A. Supramalleolar osteotomies for the treatment of ankle arthritis. J Am Acad Orthop Surg. 2016;24(7):424–32.
33. Chopra V, Stone P, Ng A. Supramalleolar osteotomies. Clin Podiatr Med Surg. 2017;34(4):445–60.
34. Walcher MG, Fraissler L, Konrads C, Plumhoff P, Hoberg M, Rudert M. Distale tibiaosteotomien [osteotomies of the distal tibia]. Oper Orthop Traumatol. 2018;30(4):253–75.
35. Horn DM, Fragomen AT, Rozbruch SR. Supramalleolar osteotomy using circular external fixation with six-axis deformity correction of the distal tibia. Foot Ankle Int. 2011;32(10):986–93.
36. Siddiqui NA, Millonig KJ, Mayer BE, Fink JN, McClure PK, Bibbo C. Increased arthrodesis rates in Charcot neuroarthropathy utilizing distal tibial distraction osteogenesis principles. Foot Ankle Spec. 2022;15:394.
37. Lavery LA, Armstrong DG, Boulton AJM, Diabetes Research Group. Ankle equinus deformity and its relationship to high plantar pressure in a large population with diabetes mellitus. J Am Podiatr Med Assoc. 2002;92:479–82.
38. Silfverskiold N. Reduction of the uncrossed two-joints muscles of the leg to one-joint muscles in spastic conditions. Acta Chir Scand. 1924;56:315–30.
39. Hoke M. An operation for the correction of extremely relaxed flat feet. J Bone Joint Surg. 1931;13:773–83.
40. Firth GB, McMullan M, Chin T, Ma F, Selber P, Eizenberg N, Wolfe R, Graham HK. Lengthening of the gastrocnemius-soleus complex: an anatomical and biomechanical study in human cadavers. J Bone Joint Surg Am. 2013;95:1489–96.
41. Herzenberg JE, Lamm BM, Corwin C, Sekel J. Isolated recession of the gastrocnemius muscle: the Baumann procedure. Foot Ankle Int. 2007;28:1154–9.
42. Garceau GJ. Anterior tibial tendon transposition in recurrent congenital club-foot. J Bone Joint Surg Am. 1940;22:932–6.
43. Kuo K, Wu KW, Krzak J, Smith P. Tendon transfers around the foot: when and where. Foot Ankle Clin N Am. 2015;20:601–17.
44. Mulhern J, Protzman N, Brigido S. Tibialis anterior tendon transfer. Clin Podiatr Med Surg. 2016;33:41–53.
45. Cates NK, Bunka TJ, Kavanagh AM, Wynes J. Split anterior tibial tendon transfer to dorsal lateral foot for cavovarus deformities with neuropathic ulcerations: a case series. J Foot Ankle Surg. 2022;61:189–94.
46. Ober FR. Tendon transplantation in the lower extremity. N Engl J Med. 1933;209:52–9.
47. Watkins MB, Jones JB, Ryder CT, Brown TH. Transplantation of the posterior Tibial tendon. J Bone Jt Surg. 1954;36:1181–9.
48. Frykberg R, Bevilacqua N, Habershaw G. Surgical offloading of the diabetic foot. J Vasc Surg. 2010;52:44s–58s.
49. Smith D, Barnes B, Sands A, Boyko E, Ahroni J. Prevalence of radiographic foot abnormalities in patients with diabetes. Foot Ankle Int. 1997;18(6):342–6.

Negative Pressure Wound Therapy

27

Paul J. Kim

Introduction

Negative Pressure Wound Therapy (NPWT) has been utilized in wound care and limb salvage/limb function preservation for almost 30 years. This technology is considered an adjunctive standard of care treatment modality utilized in both the inpatient and outpatient settings. Imparting negative pressure onto the surface of wounds optimizes the wound bed by promoting the generation of granulation tissue, neovascularization, enhancing venous and lymphatic drainage, reduction of bacteria, and decreasing wound size. The device consists of a porous interface (foam or gauze material), drape, tubing, canister, and a pump. Further, NPWT is used over closed incisions to decrease incision-related complications. There have been many innovations in the original device design that include improvements in the software, hardware interface, the addition of instillation, foam and drape construct. Other innovations include increasing portability through smaller devices as well as mechanically and not electrically powered pumps (Fig. 27.1) (Table 27.1).

Author Disclosure: 3 M. Inc.

P. J. Kim (✉)
Department of Plastic Surgery, University of Texas Southwestern, Dallas, TX, USA

Department of Orthopedic Surgery, University of Texas Southwestern, Dallas, TX, USA
e-mail: Paul.Kim@UTSouthwestern.edu

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_27

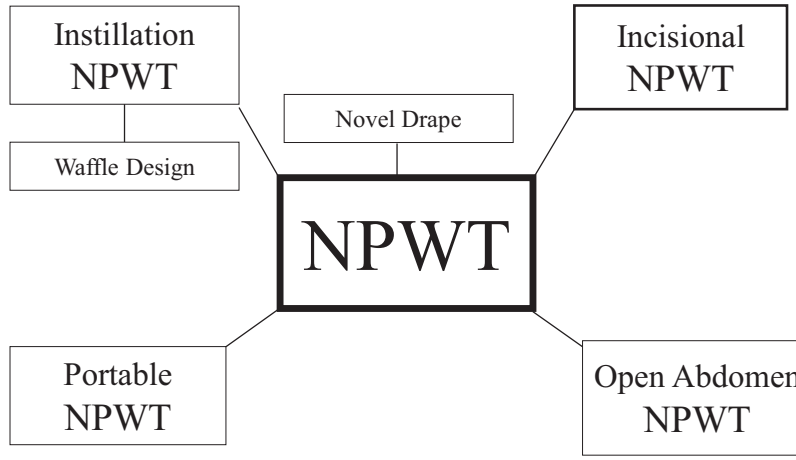


Fig. 27.1 There are a variety of innovations that have branched from the traditional NPWT device

Table 27.1 Advantages and disadvantages to NPWT systems

	Advantages	Disadvantages
Standard NPWT	Promotes wound bed conversion to a healthier state	Has battery backup but still needs electricity for recharge
Mechanically powered portable NPWT	Mobility	Limited for the use of smaller, minimally exudative wounds
Incisional NPWT	Decrease in incisional complications	No direct visualization of the incision Higher cost than traditional incision dressings
NPWT with instillation	Clearance of bacteria	Potential for leaks and maceration Can only be utilized in the acute setting or some long-term acute care settings

NPWT negative pressure wound therapy

Mechanism of Action

There are multiple proposed mechanisms of action for NPWT. The base device of NPWT provides multiple positive effects on the wound bed beyond that of decreasing overall wound dimensions and exudate removal (Fig. 27.2). Some believe that the primary clinical goal for the use of NPWT is to promote the growth of granulation tissue. Morykwas et al. in a porcine study examined the effect of different pressures on granulation tissue growth [1]. This study may have been erroneously extrapolated to suggest that granulation tissue growth is the goal of NPWT. However, it is important to understand that granulation tissue should be viewed simply as a sign of wound bed health and not necessarily the clinical end goal. The presence of granulation tissue indicates adequate perfusion and low bioburden (bacteria and nonviable tissue). Granulation tissue is essentially a bed of capillaries imbedded in a collagen matrix. This environment increases the likelihood of epithelization or provides a base to receive and incorporate a split-thickness skin graft, allograft, or xenograft.

NPWT can be programmed for continuous application of negative pressure or intermittent application of negative pressure. The evidence suggests that the intermittency (periods of lower or no negative pressure) is the preferred method in stimulating the wound bed. Morykwas et al. report that there is a 40% greater granulation tissue growth with intermittent negative pressure as compared with continuous negative pressure [2]. The intermittency appears to stimulate a greater response in cell proliferation and angiogenesis [3]. The engagement and disengagement of negative pressure provides the stimulus to the wound bed to react in response to tissue stress. The effect appears to be on small vessels in promoting a more organized, more dense vascular structure [4, 5]. Despite the evidence to suggest that intermittency is superior, many clinicians

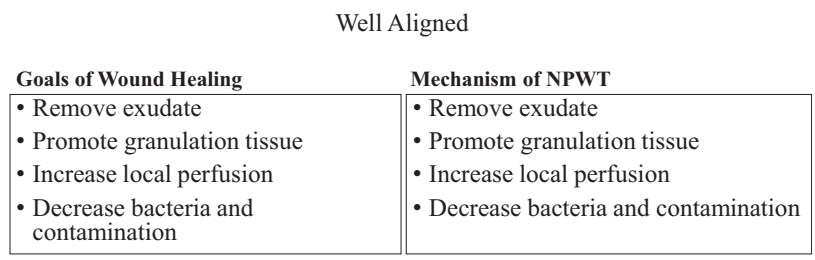


Fig. 27.2 There is good alignment between the goals of wound healing and the mechanism of NPWT

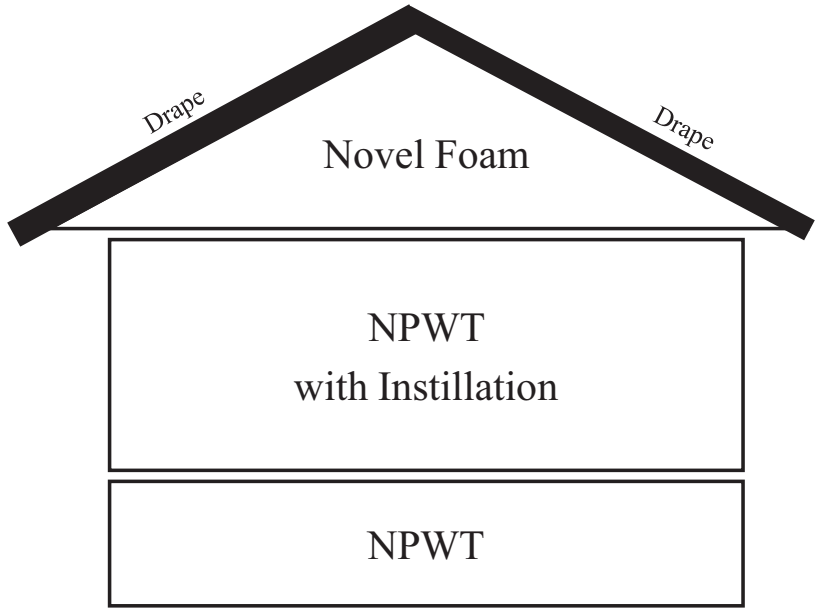


Fig. 27.3 This figure conceptualizes the combination of the innovations of NPWT. NPWT is the foundation of the house, while NPWT with instillation is its walls, the novel foam is the roof, and the novel drape is the shingles. The innovations build on the fundamental benefits of standard NPWT

utilize the continuous setting for pragmatic reasons including the reduced likelihood of leaks and alarms, and for greater patient comfort. A more recent porcine study by Lessing et al. reports no difference in granulation tissue thickness between continuous and intermittent negative pressure [6]. Further, they report that the use of NPWT with instillation promotes greater granulation thickness than either continuous or intermittent negative pressure.

The mechanical forces imparted by negative pressure provides for both macrodeformation and microdeformation [7]. Macrodeformation is essentially the centripetal forces that shrink the overall wound dimensions when negative pressure is applied. The decrease in overall wound dimensions decreases the strain across the wound bed and provides laxity in the tissue. Thus, the type of tissue or anatomical location of the wound dictates the degree of macrodeformation [8]. For example, indurated tissue will have less ability for macrodeformation. Microdeformation is imparted through the perforations in the porous foam. This type of force is responsible for protein activation and the cellular effects that promote cell migration and neovascularization [3]. The variants of NPWT including Negative Pressure Wound Therapy with Instillation (NPWTi) and incisional NPWT provide additional and different effects on tissue.

The most widely used NPWTi device utilizes a solution that is programmed to intermittently bathe the surface of the wound (Fig. 27.3). There

are other NPWTi devices that provide continuous flow of solution across the wound bed. Essentially, NPWTi combines the benefits of negative pressure and wound irrigation. The proposed mechanism of action of NPWTi is to provide a medium, through the instillate, to hydrate, solubilize, and evacuate the nonviable tissue as well as provide a medium for the bacteria to be removed and perhaps decrease the likelihood of reattachment. NPWTi has been demonstrated to not only reduce planktonic bacteria amounts but also destroy mature biofilm in in vivo and ex vivo porcine models [9, 10]. Yang et al. report in chronic human wounds a 48% reduction of bacterial amount utilizing NPWTi as compared with a 14% increase in bacterial amount with the use of standard NPWT [11]. Some have postulated that the reduction of bacteria may simply be the effect of an antimicrobial solution on the wound bed and has little to do with the NPWTi device itself. Kim et al. report in a randomized controlled trial of NPWTi in infected wounds; no difference in various surrogate clinical outcomes (e.g., length of hospitalization, number of surgeries) utilizing normal saline as compared with polyhexanide with betaine [12]. Kim et al. reported in a retrospective study on infected wounds a significant decrease in the number of operations, length of hospitalization, and shorter time to final surgical procedure utilizing NPWTi with normal saline as compared with standard NPWT [13]. This study suggests that there is an additive positive effect for the use of NPWTi beyond that of solely utilizing an antiseptic solution or standard NPWT.

A variety of solutions have been utilized with NPWTi. To date there is no robust data to suggest one type of solution is clearly superior to another. Antiseptics may have a role in highly infected or contaminated wounds. However, there may be cytotoxic effects on healthy tissue that prohibit its prolonged use. Normal saline is a viable alternative in many cases due to its wide availability and its tolerability. The instillate can also serve to moisturize the wound surface, thereby hydrating the underlying tissue and reduce desiccation. This is especially important for tissues such as ligament, tendon, and joint capsule. Another potential advantage is that NPWTi requires intermittency of negative pressure which the evidence suggests is superior to that of a continuous negative pressure setting as discussed above.

Incisional NPWT decreases the initial tensile forces experienced along the incision line by 50% by distributing the forces over a wider surface area [14]. Further, incisional NPWT has been reported to decrease edema through relieving venous congestion and enhancing lymphatic drainage [15–17]. This may have 2 consequences: (1) the decrease in edema decreases the tension along the incision, (2) expedite healing by more rapidly removing inflammatory factors. Incisional negative pressure is not designed to directly remove the underlying fluid in the incisional area. It is recommended that drains be used to serve this purpose. These drains should be placed at a distance from the foam/drape or gauze/drape construct to prevent interference with the device. Some have proposed that there are long-term benefits that include an increase in tensile strength across the incisional area and more organized scarring [17].

Indications

NPWT is utilized for soft tissue defects in all areas of the body. It is not indicated in areas such as inside the abdominal or thoracic cavities, spinal cord or brain, directly over identifiable vessels or nerves. NPWT can promote granulation tissue over less vascular structures such as bone, capsule, ligament, or tendon. However, the area must have adequate perfusion in order for this to occur. Thus, noninvasive or invasive vascular studies and/or intervention should be conducted prior to treatment onset. NPWT should be reserved for wounds that are not progressing, for complex wounds, or in compromised patients. Historically, NPWT was utilized to promote wound healing over time in a relatively clean wound bed. Armstrong et al. in the pivotal study in post-amputation foot wounds report a faster time to granulation with the use of NPWT compared with standard gauze dressing (42 vs. 84 days) [18]. The technology has evolved as an adjunctive therapy in wounds that are infected/

contaminated, and for closed surgical incisions in high-risk populations. Each NPWT platform has unique properties and characteristics that require proper application in order to maximize its benefits (Table 27.2).

Chronic Wounds

NPWT should be considered for wounds that are not healing as demonstrated by wound volume or surface area reduction. Further, the quality of the tissue in the wound bed may also benefit from NPWT by promoting the growth of granulation tissue over deeper exposed structures. In the lower extremity the fundamental principles of optimized perfusion, medical management and optimization of comorbidities, nutritional enhancement, serial sharp excisional debridement, and offloading/immobilization should be adhered to along with NPWT. There should be an ultimate treatment goal when utilizing NPWT. This includes: (1) terminal epithelialization, (2) creation of a wound bed that will support a split-thickness skin graft or other grafts, (3) as part of staged approach for a local flap or free tissue transfer. NPWT should not be used for a lengthy period without regular wound evaluation to assess that NPWT has had positive effects on the wound. If NPWT has demonstrated little or no change to the wound bed, other treatment options should be considered.

Table 27.2 Tips and pearls for the use of NPWT systems

	Tips and pearls
Standard NPWT	• Establish a definitive treatment goal (terminal epithelization, wound bed preparation for a graft) • Use bridging techniques away from weightbearing or boney prominences
Mechanically powered portable NPWT	• Use only on small, minimally exudative wounds • Should be reserved for outpatient to maximize its portability
Incisional NPWT	• Utilize drains as necessary away from the incision line • If utilizing the traditional black foam (not the prefabricated construct), cut the width that expands at least 2 cm on both sides of the incision line
NPWT with instillation	• Do not use large volumes of solution per dwell cycle • The volume of instillate may need to be adjusted at each dressing change with changing dimensions of the wound • Use of ostomy rings or paste may be helpful to maintain a seal utilizing the traditional polyvinyl drape, but do not use these products with the silicone composite drape • The novel foam should only be used with NPWT with instillation and not with traditional NPWT

NPWT negative pressure wound therapy

Traditional NPWT should not be used if there is an active infection or necrotic tissue in the wound bed. The infection should be treated and the necrotic tissue removed prior to application of NPWT. If the patient is not a surgical candidate or the patient refuses surgical intervention, NPWTi with the novel foam with the large perforation may be an option for wounds that have areas of necrotic and fibrotic tissue. This foam will be discussed in further detail below.

NPWT has also been utilized as a bolster for grafts [19, 20]. The foam or gauze is applied over an autologous graft, allograft, or xenograft and negative pressure is applied. The proposed benefit for this approach is to reduce seroma or hematoma formation that could otherwise lift the graft off the wound bed surface by evacuating fluid. The other proposed benefit is to affix the wound bed and the graft together to prevent graft drift or floating of the graft. There have been multiple reports of this technique in the literature; however these have been relegated to case studies/case series and underpowered comparative studies, thus the ultimate benefit remains unclear [21–25].

Closed Incisions

NPWT has been demonstrated to decrease complication in high-risk populations across all sur-



Fig. 27.4 (**a**) A photo of the posterior aspect of the heel after a partial calcanectomy and primary closure was performed to treat a chronic plantar heel ulcer with underlying osteomyelitis. This is a patient with type 2 diabetes and peripheral vascular disease. (**b**) An intraoperative photograph of an incisional negative pressure device applied over the incision. This device was applied for 10 days. (**c**) A clinical photograph 4 weeks after closure. Note the well-healed incision

gical specialties over closed incisions (Fig. 27.4). The device is placed over an incision at the time of surgical closure in the operating room. Surgical dehiscence can occur for a variety of reasons including host factors including age, comorbidities, and anatomical location. Incisional NPWT provides for local management of the incision. The literature is replete with publications supporting the use of incisional NPWT to decrease complications (dehiscence and infection) related to surgical incisions in a variety of anatomical locations. Stannard et al. were one of the first to report a significant decrease (1/5th less likely) in surgical site infections for open fracture management [26]. De Vries et al. report in a metanalysis of randomized controlled trials that there is a decrease in surgical site infections with the use of incisional NPWT as compared with customary dressings [27]. The potential cost saving in complication prevention is difficult to estimate. Karlakki et al. report in a randomized controlled trial a significant reduction of length of hospitalization for primary hip and knee arthroplasties but do not report a significant reduction in surgical wound complications although there was a strong trend ($p = 0.06$) with a fourfold reduction [28].

Prior to the introduction of the prefabricated dressings for incisional NPWT, traditional dressing kits were utilized. It is important that if utilizing the traditional dressing kits, the width of the contact foam/gauze span the incision with the material applied at least 2 cm on each side of the incision line. This allows for negative pressure to affect the tissue surrounding the incision line. The prefabricated dressing kits are specifically constructed for closed incisions and are constructed with these specific dimensions. There has been some speculation that lower negative pressure settings should be utilized over closed incisions. There is no robust evidence in either direction whether this should be conducted.

Infected/Contaminated Wounds

There is a growing acceptance for the use of NPWT with instillation (NPWTi) as an adjunct treatment for infected/contaminated wounds [29–34]. Typically, these wounds are excisionally

debrided and antibiotic therapy initiated prior to application of NPWTi. Kim et al. report in a prospective, multicenter, randomized trial a 3-log difference in the reduction of bacteria in favor of NPWTi as compared with conventional NPWT [35]. All wounds in this study were surgically debrided and managed in the acute care setting. It is important to explore all tunnels to prevent instillate fluid from being trapped in deeper tissue pockets. NPWTi can be used in the interval between staged excisional debridement. NPWTi is discontinued once the wound bed is ready for closure or coverage. However, NPWTi can also be utilized to prepare the wound bed prior to the single-staged closure or coverage or utilized after the initial excisional debridement with no immediate plan for coverage or closure [36].

A recent metanalysis suggests that NPWTi, as compared to NPWT and other wound therapies, has positive clinical and economic benefits by facilitating efficiency in wound bed conversion. Gabriel et al. report that NPWTi: (1) requires a fewer number of surgical debridements, (2) a quicker conversion of the wound bed for closure or coverage with a graft, (3) reduces bacteria amounts, (4) has a lower number of postoperative wound-related complications [37]. In the acute care setting. NPWTi may be the preferred negative pressure platform.

Innovation

Foam

A novel foam with larger perforations have more recently been introduced (Fig. 27.5). This construct involves the use of at least 2 stiffer foam pieces stacked on top of each other. The perforated foam dressing is placed in contact with the wound bed, then another foam dressing is placed on top of the perforated foam dressing. This foam construct is used in conjunction with NPWTi and not with standard NPWT. The probable mechanism of action is as follows: (1) the solution emulsifies the nonviable tissue (necrotic

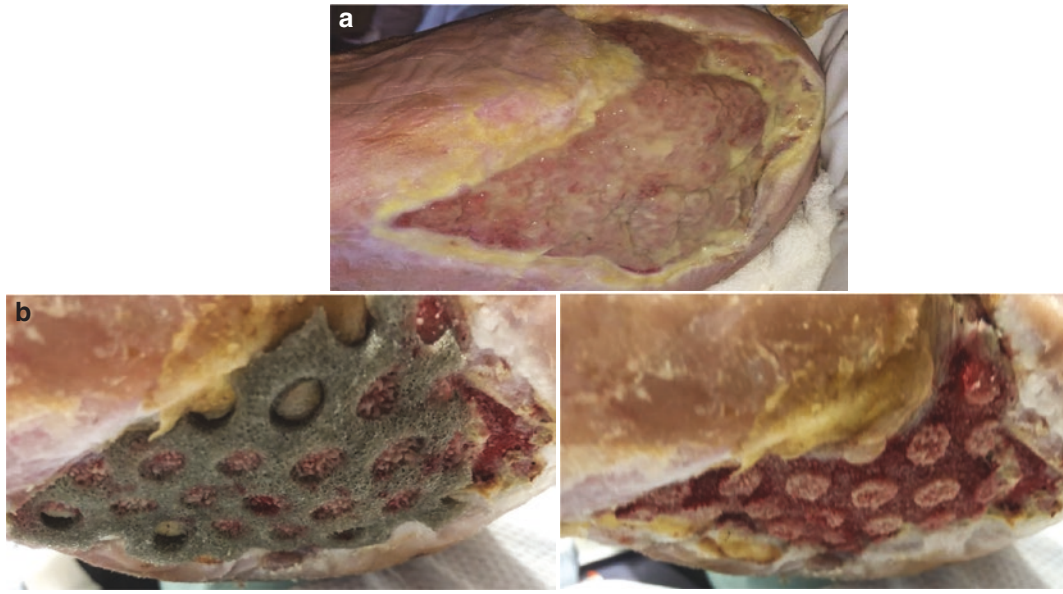


Fig. 27.5 (**a**) This photograph of a chronic plantar foot wound with significant amount of liquified, nonviable tissue. The patient had a prior surgical intervention that dehisced creating a chronic ulcer. This is a patient who refused surgical intervention for excisional debridement. (**b**) This photograph is at the first dressing change after application of NPWT with instillation (normal saline) and the novel foam. This was applied for 3 days. Note the conversion of the wound to a healthier state with a decrease in the amount of nonviable tissue as well as the growth of granulation tissue

and fibrotic tissue) during the dwell cycle, (2) as the negative pressure is applied, the larger perforations draws tissue through these holes, (3) the cycling of dwell and negative pressure against this novel foam construct mechanically breaks up the tissue, (4) the instillate provides an avenue for the nonviable tissue to be evacuated into the egress canister. This novel foam may be a good option for wounds that contain nonviable, necrotic, or sloughy tissue in patients who are not surgical candidates, refuse surgical intervention, there is no surgeon available for excisional debridement, or have had inadequate sharp debridement performed [38]. Although this innovation is promising, there is currently no robust studies with only a limited number of case studies/series reporting positive outcomes [39, 40].

Drape

Since the introduction of NPWT, the drape used to affix the foam dressing has been a polyurethane film coated with an acrylic adhesive on the contact side. The newest construct utilizes a polyurethane/acrylic/silicone composite. It has been suggested that the stiffness of the original polyurethane material can lead to leaks by breaking the contact with the surrounding skin with movement of the patient. This can result in maceration of the surrounding skin and the loss of suction. Therefore, ostomy rings and paste have been used to secure the drape onto the skin. Further, once the polyurethane drape is applied, the same drape cannot be removed and reapplied. Additional drapes are applied or bolster strips of the drape in order to create a better seal. This results in wasted material and time. Further, skin damage can occur with removal due to the tacky nature of the acrylic adhesive. The polyurethane/acrylic/silicone blend is more tolerant to stretch and can be applied and reapplied without the need for additional supplies. For this novel drape to be utilized effectively, the surrounding skin must be dry and if the skin is cold, it may take some time for the acrylic/silicone to activate to adhere to the skin surface. The silicone contact layer is also safe on fragile skin. This drape can be used for traditional NPWT or with NPWTi. This novel drape is yet to be widely available or adopted but it is a significant step forward.

Portability

Portability has allowed for NPWT to be more easily transferred from the acute setting to home or rehabilitation facility. Rechargeable battery powered NPWT devices allow for the patient to be more mobile. Other portable NPWT devices do not require electrically powered pumps but rather rely on potential energy stored in a coiled spring. These mechanically powered devices are small and extremely portable. However, this construct has no exudate container, thus is reserved for small, low exudative wounds. Armstrong et al. in a multicenter, randomized trial report no inferiority in wound size reduction or wound closure between a mechanically and an electrically powered NPWT devices [41]. The next leap in innovation for portability of NPWT should include the ability to provide instillation.

Remote Monitoring

As delivery of healthcare has evolved with a movement towards shorter hospital stays while maintaining quality of care provided to patients, monitoring of a NPWT device in the acute care setting is simpler than in an outpatient setting. Currently some NPWT devices have embedded sensors that provide information of NPWT use (device turned off) and malfunction (blockage, leaks, alarms) information. This information can be relayed to the patient, facility, visiting nurses, or wound center in real time. This allows for a quicker response to problems associated with the device. Newer software updates on some devices provide step-by-step troubleshooting animations to assist in NPWT management.

Conclusion

NPWT has emerged as an adjunctive frontline approach to complex/chronic wounds. NPWT is used globally in the continuum of care of a wound from the acute care setting to outpatient facility to home. The innovations have accelerated in the past decade and NPWT indications have expanded significantly. Data continues to be generated that report the effectiveness of this therapy as well as its impact on overall healthcare costs. Further, technological advances have improved its utility, reliability, and efficacy. It is important to maintain and practice fundamental principles of wound care and limb function preservation along with the use of NPWT and its derivatives.

References

1. Morykwas MJ, Faler BJ, Pearce DJ, Argenta LC. Effects of varying levels of subatmospheric pressure on the rate of granulation tissue formation in experimental wounds in swine. Ann Plast Surg. 2001;47(5):547–51.
2. Morykwas MJ, Argenta LC, Shelton-Brown EI, McGuirt W. Vacuum-assisted closure: a new method for wound control and treatment: animal studies and basic foundation. Ann Plast Surg. 1997;38(6):553–62.
3. Saxena V, Hwang CW, Huang S, Eichbaum Q, Ingber D, Orgill DP. Vacuum-assisted closure: microdeformations of wounds and cell proliferation. Plast Reconstr Surg. 2004;114(5):1086–96; discussion 97–8.
4. Erba P, Ogawa R, Ackermann M, Adini A, Miele LF, Dastouri P, et al. Angiogenesis in wounds treated by microdeformational wound therapy. Ann Surg. 2011;253(2):402–9.
5. Greene AK, Puder M, Roy R, Arsenault D, Kwei S, Moses MA, et al. Microdeformational wound therapy: effects on angiogenesis and matrix metalloproteinases in chronic wounds of 3 debilitated patients. Ann Plast Surg. 2006;56(4):418–22.
6. Lessing MC, James RB, Ingram SC. Comparison of the effects of different negative pressure wound therapy modes-continuous, noncontinuous, and with instillation-on porcine excisional wounds. Eplasty. 2013;13:e51.
7. Orgill DP, Manders EK, Sumpio BE, Lee RC, Attinger CE, Gurtner GC, et al. The mechanisms of action of vacuum assisted closure: more to learn. Surgery. 2009;146(1):40–51.
8. Huang C, Leavitt T, Bayer LR, Orgill DP. Effect of negative pressure wound therapy on wound healing. Curr Probl Surg. 2014;51(7):301–31.
9. Phillips PL, Yang Q, Schultz GS. The effect of negative pressure wound therapy with periodic instillation using antimicrobial solutions on pseudomonas aeruginosa biofilm on porcine skin explants. Int Wound J. 2013;10(Suppl 1):48–55.
10. Davis K, Bills J, Barker J, Kim P, Lavery L. Simultaneous irrigation and negative pressure wound therapy enhances wound healing and reduces wound bioburden in a porcine model. Wound Repair Regen. 2013;21(6):869–75.
11. Yang C, Goss SG, Alcantara S, Schultz G, Lantis Ii JC. Effect of negative pressure wound therapy with instillation on bioburden in chronically infected wounds. Wounds. 2017;29(8):240–6.
12. Kim PJ, Attinger CE, Oliver N, Garwood C, Evans KK, Steinberg JS, et al. Comparison of outcomes for normal saline and an antiseptic solution for negative-pressure wound therapy with instillation. Plast Reconstr Surg. 2015;136(5):657e–64e.
13. Kim PJ, Silverman R, Attinger CE, Griffin L. Comparison of negative pressure wound therapy with and without instillation of saline in the management of infected wounds. Cureus. 2020;12(7):e9047.
14. Wilkes RP, Kilpad DV, Zhao Y, Kazala R, McNulty A. Closed incision management with negative pressure wound therapy (CIM): biomechanics. Surg Innov. 2012;19(1):67–75.
15. Kamolz LP, Andel H, Haslik W, Winter W, Meissl G, Frey M. Use of subatmospheric pressure therapy to prevent burn wound progression in human: first experiences. Burns. 2004;30(3):253–8.
16. Kilpadi DV, Cunningham MR. Evaluation of closed incision management with negative pressure wound therapy (CIM): hematoma/seroma and involvement of the lymphatic system. Wound Repair Regen. 2011;19(5):588–96.
17. Kilpadi DV, Lessing C, Derrick K. Healed porcine incisions previously treated with a surgical incision management system: mechanical, histomorphometric, and gene expression properties. Aesthetic Plast Surg. 2014;38(4):767–78.
18. Armstrong DG, Lavery LA, Diabetic Foot Study C. Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial. Lancet. 2005;366(9498):1704–10.
19. Blackburn JH 2nd, Boemi L, Hall WW, Jeffords K, Hauck RM, Banducci DR, et al. Negative-pressure dressings as a bolster for skin grafts. Ann Plast Surg. 1998;40(5):453–7.
20. Gabriel A, Thimmappa B, Rubano C, Storm-Dickerson T. Evaluation of an ultra-lightweight, single-patient-use negative pressure wound therapy system over dermal regeneration template and skin grafts. Int Wound J. 2013;10(4):418–24.
21. Webster J, Scuffham P, Stankiewicz M, Chaboyer WP. Negative pressure wound therapy for skin grafts and surgical wounds healing by primary intention. Cochrane Database Syst Rev. 2014;10:CD009261.
22. Gkotsoulias E. Split thickness skin graft of the foot and ankle bolstered with negative pressure wound

therapy in a diabetic population: the results of a retrospective review and review of the literature. Foot Ankle Spec. 2020;13(5):383–91.
23. Petkar KS, Dhanraj P, Kingsly PM, Sreekar H, Lakshmanarao A, Lamba S, et al. A prospective randomized controlled trial comparing negative pressure dressing and conventional dressing methods on split-thickness skin grafts in burned patients. Burns. 2011;37(6):925–9.
24. Moisidis E, Heath T, Boorer C, Ho K, Deva AK. A prospective, blinded, randomized, controlled clinical trial of topical negative pressure use in skin grafting. Plast Reconstr Surg. 2004;114(4):917–22.
25. Nguyen TQ, Franczyk M, Lee JC, Greives MR, O'Connor A, Gottlieb LJ. Prospective randomized controlled trial comparing two methods of securing skin grafts using negative pressure wound therapy: vacuum-assisted closure and gauze suction. J Burn Care Res. 2015;36(2):324–8.
26. Stannard JP, Volgas DA, Stewart R, McGwin G Jr, Alonso JE. Negative pressure wound therapy after severe open fractures: a prospective randomized study. J Orthop Trauma. 2009;23(8):552–7.
27. De Vries FEE, Wallert ED, Solomkin JS, Allegranzi B, Egger M, Dellinger EP, et al. A systematic review and meta-analysis including GRADE qualification of the risk of surgical site infections after prophylactic negative pressure wound therapy compared with conventional dressings in clean and contaminated surgery. Medicine (Baltimore). 2016;95(36):e4673.
28. Karlakki SL, Hamad AK, Whittall C, Graham NM, Banerjee RD, Kuiper JH. Incisional negative pressure wound therapy dressings (iNPWTd) in routine primary hip and knee arthroplasties: a randomised controlled trial. Bone Joint Res. 2016;5(8):328–37.
29. Kim PJ, Attinger CE, Constantine T, Crist BD, Faust E, Hirche CR, et al. Negative pressure wound therapy with instillation: international consensus guidelines update. Int Wound J. 2020;17(1):174–86.
30. Brinkert D, Ali M, Naud M, Maire N, Trial C, Teot L. Negative pressure wound therapy with saline instillation: 131 patient case series. Int Wound J. 2013;10(Suppl 1):56–60.
31. Lehner B, Fleischmann W, Becker R, Jukema GN. First experiences with negative pressure wound therapy and instillation in the treatment of infected orthopaedic implants: a clinical observational study. Int Orthop. 2011;35(9):1415–20.
32. Kim PJ, Attinger CE, Steinberg JS, Evans KK, Powers KA, Hung RW, et al. The impact of negative-pressure wound therapy with instillation compared with standard negative-pressure wound therapy: a retrospective, historical, cohort, controlled study. Plast Reconstr Surg. 2014;133(3):709–16.
33. Gabriel A, Kahn K, Karmy-Jones R. Use of negative pressure wound therapy with automated, volumetric instillation for the treatment of extremity and trunk wounds: clinical outcomes and potential cost-effectiveness. Eplasty. 2014;14:e41.
34. Timmers MS, Graafland N, Bernards AT, Nelissen RG, van Dissel JT, Jukema GN. Negative pressure wound treatment with polyvinyl alcohol foam and polyhexanide antiseptic solution instillation in posttraumatic osteomyelitis. Wound Repair Regen. 2009;17(2):278–86.
35. Kim PJ, Lavery LA, Galiano RD, Salgado CJ, Orgill DP, Kovach SJ, et al. The impact of negative-pressure wound therapy with instillation on wounds requiring operative debridement: pilot randomised, controlled trial. Int Wound J. 2020;17(5):1194–208.
36. Kim PJ, Attinger CE. Negative-pressure wound therapy with instillation: a tool in the multidisciplinary approach to limb function preservation. Plast Reconstr Surg. 2021;147(1S-1):27S–33S.
37. Gabriel A, Camardo M, O'Rorke E, Gold R, Kim PJ. Effects of negative-pressure wound therapy with instillation versus standard of care in multiple wound types: systematic literature review and meta-analysis. Plast Reconstr Surg. 2021;147(1S-1):68S–76S.
38. Kim PJ, Applewhite A, Dardano AN, Fernandez L, Hall K, McElroy E, et al. Use of a novel foam dressing with negative pressure wound therapy and instillation: recommendations and clinical experience. Wounds. 2018;30(3 suppl):S1–S17.
39. Teot L, Boissiere F, Fluieraru S. Novel foam dressing using negative pressure wound therapy with instillation to remove thick exudate. Int Wound J. 2017;14(5):842–8.
40. Blalock L. Use of negative pressure wound therapy with instillation and a novel reticulated open-cell foam dressing with through holes at a level 2 trauma center. Wounds. 2019;31(2):55–8.
41. Armstrong DG, Marston WA, Reyzelman AM, Kirsner RS. Comparative effectiveness of mechanically and electrically powered negative pressure wound therapy devices: a multicenter randomized controlled trial. Wound Repair Regen. 2012;20(3):332–41.

Hyperbaric Oxygen Therapy in Functional Limb Salvage

28

Kelly Johnson-Arbor

Introduction

Hyperbaric oxygen therapy (HBO) is a treatment in which patients breathe 100% oxygen while pressurized in an enclosed treatment chamber to a depth greater than sea level. While HBO is often recognized as a treatment for decompression illness ("the bends") in SCUBA divers, there are multiple other applications of HBO in the medical community, including the adjunctive treatment of patients with complicated wounds who are referred for limb salvage attempts.

The use of hyperbaric pressurization as a treatment for medical conditions dates back to the 1600s, prior to the discovery of oxygen [1]. In 1664, an English physician, Dr. Henshaw, used organ bellows to compress air into an enclosed chamber; this was intended to "promote insensible respiration" and "to facilitate breathing" of his patients [2]. While the administration of compressed air was likely not associated with significant clinical improvements, the introduction of caisson construction 200 years later represented a monumental achievement in the current understanding of hyperbaric physiology. The use of caissons was pioneered in 1839 by the French engineer named Triger, who used a pressurized tube to facilitate the construction of bridge abutments and piers [3]. Bridge workers entered the caisson, which was then pressurized with air to expel water from the device; the workers could then excavate land and perform their construction duties while breathing the pressurized air. Unfortunately, after exiting the pressurized caisson at the end of their shift, many workers exhibited physical signs and symptoms that are now recognized as the classic manifestations of decompression illness. This painful syndrome was termed "caisson disease." Many bridge workers, including those who worked on construction of the Brooklyn Bridge in New York, were noted to assume a bent-over posture in an attempt to relieve the pain. This position was thought to resemble a stooped posture known as the "Grecian Bend" which was affected by fashionable women during this time period; the term "the bends" is derived from this nomenclature [4]. Despite the ongoing morbidity associated with caisson disease, bridge construction continued worldwide during the nineteenth century. In 1841, during excavation of the Loire River in France, caisson workers reported having severe extremity pain, after working for prolonged periods in the pressurized caisson [4]. During construction of the Hudson River tunnel in New York in 1879, up to 25% of all caisson workers died; after a medical lock was introduced to provide a slow decompression for the workers, the mortality rate dropped to 1% [5].

K. Johnson-Arbor (✉)
MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: Kelly.K.Johnson-Arbor@gunet.georgetown.edu

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_28

The physiology of hyperbaric oxygenation remained poorly understood in the 1920s, when a physician at the University of Kansas, Dr. Orval Cunningham, utilized HBO for medical conditions including influenza pneumonia [2]. A grateful patient donated one million dollars to allow Dr. Cunningham to construct the world's largest hyperbaric chamber in Cleveland, Ohio [6]. This chamber was 6 ft tall and contained 72 rooms, including one that held a grand piano [6]. Unfortunately, the facility was denounced by the American Medical Association as quackery, and the chamber was dismantled and sold for scrap metal during World War Two [2].

Modern HBOT facilities are largely located in outpatient wound centers, and serve as a primary or adjunctive treatment for selected medical conditions. Currently, HBO is used as a primary treatment for decompression sickness, air embolism, and carbon monoxide poisoning. It is also used as an adjunctive treatment for additional medical conditions including compromised grafts and flaps, chronic refractory osteomyelitis, and diabetic foot ulcerations (DFU). The Undersea and Hyperbaric Medical Society currently recommends the use of HBO as a treatment of the following conditions [7].

1. Air or gas embolism
2. Decompression illness
3. Acute carbon monoxide poisoning
4. Arterial insufficiencies, including enhancement of healing in selected problem wounds (including DFU)
5. Radiation-induced soft tissue and bone necrosis
6. Intracranial abscess
7. Clostridial myonecrosis
8. Necrotizing soft tissue infections
9. Compromised grafts and flaps
10. Crush injuries and compartment syndromes
11. Chronic refractory osteomyelitis
12. Thermal burns
13. Severe anemia where transfusion is impossible due to religious or medical concerns
14. Idiopathic sudden sensorineural hearing loss

While the above-mentioned conditions are the most commonly indicated diagnoses for the administration of HBO in the United States, other conditions such as traumatic brain injury and cerebral palsy are occasionally treated with HBO on an "off-label" or experimental basis. Although HBO is indicated for the enhancement of healing in patients with selected wounds, there is a lack of robust evidence to support the use of this treatment in the care of patients with wounds secondary to calcific uremic arteriolopathy, pyoderma gangrenosum, chronic peripheral vascular disease, and venous insufficiency; these conditions are considered to be "off-label" or experimental within the context of HBO administration. As the evidence supporting the use of HBO for these "off-label" conditions is minimal, and considering that the risks of the treatment may outweigh any recognized potential benefits, the use of HBO must be carefully considered for patients with these and other experimental diagnoses [8, 9]. In addition, in the United States, insurance reimbursement for the use of HBO for "off-label" diagnoses is limited, further complicating the ability to utilize HBO as a treatment for these conditions.

Hyperbaric Physiology

Hyperbaric oxygenation involves the systemic breathing of 100% oxygen under pressure. This process results in increased tissue oxygen delivery on a cellular level. The administration of systemic inhalation of hyperbaric oxygen results in the enhanced production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) [10]. When present in increased amounts, ROS and RNS stimulate the synthesis of cellular growth factors such as vascular endothelial growth factor (VEG-F) as well as mobilization of stem cells from the bone marrow [11]. Under hyperbaric conditions, endogenous production of VEG-F is significantly increased [12]. The heightened activity of both VEG-F and stem cell mobilization results in de novo blood vessel

growth (vasculogenesis) and new blood vessel growth by local endothelial cells (angiogenesis) [10]. These processes result in an increased efficiency in new blood vessel growth, especially in patients with diabetes and in areas of previous radiation therapy. For this reason, HBO is often utilized as a treatment for patients with DFU as well as skin and soft tissue necrosis due to previous radiation therapy.

Hyperbaric oxygenation also can mitigate the tissue necrosis and microcirculatory collapse that occurs after reperfusion of ischemic tissues [13]. Ischemia-reperfusion injury is characterized by neutrophil adhesion to the endothelium of injured tissue which occurs after the initial restoration of blood flow; this results in the production of free radicals and inflammatory mediators and leads to secondary tissue damage [14]. The administration of HBO reduces the adhesion of neutrophils to microvascular cell walls, reduces lipid peroxidation, and decreases the inflammatory response in ischemic tissue [13]. These mechanisms of action may account for some of the beneficial effects noted when HBO is used for the treatment of acutely compromised skin flaps and grafts, as well as necrotizing soft tissue infections and acute arterial ischemias.

Hyperbaric oxygenation has beneficial effects on infection control. The growth and proliferation of anaerobic bacteria is inhibited in the hyperbaric environment [15]. Administration of HBO can enhance the soft tissue penetration of selected antibiotics, including aminoglycosides, trimethoprim/sulfamethoxazole, and linezolid [16, 17]. HBO may also exert a synergistic effect against bacterial growth when used in conjunction with antibiotics, and also enhances the oxygen-dependent mechanisms ("oxidative burst") by which granulocytes kill microorganisms [17].

The systemic hyperoxygenation induced by HBO also has favorable effects on the management of anemia in patients who are unable to receive transfusion of blood products due to medical or religious concerns. In 1959, the Dutch surgeon Boerema published "Life without blood," a manuscript detailing the use of HBO for the treatment of anemia [18]. Boerema exsanguinated healthy piglets and replaced the blood volume with a plasma-like solution. The piglets' resulting hemoglobin concentration was 0.4 g/dL, a hemoglobin concentration which is incompatible with life. The piglets were then pressurized in a hyperbaric chamber to 3 absolute atmospheres (ATA) for 45 min. The animals survived this exposure, despite having essentially no hemoglobin present, and recovered uneventfully after they were re-infused with normal blood. Boerema noted that under hyperbaric conditions, the amount of oxygen dissolved in the plasma can greatly exceed the amount present while breathing air under normobaric conditions. This phenomenon is due to Henry's Law, which states that the amount of gas dissolved in a solution is directly proportional to the partial pressure of the gas. When partial pressures of a gas increase, such as under hyperbaric pressurization, more of that gas dissolves in solution. Breathing room air (21% oxygen) under normobaric conditions results in a PaO_2 of approximately 100 mmHg; breathing 100% oxygen under hyperbaric conditions results in a PaO_2 of greater than 1600 mmHg [19]. Under hyperbaric conditions, oxygen dissolved in the plasma can approximate or meet the body's metabolic demands of oxygen extraction [20]. This explains the rationale for the use of HBO as a treatment for anemia in patients who cannot receive blood transfusions, and also represents a mechanism of action of the use of HBO in patients with symptomatic SARS-CoV-2 (COVID-19) infection [21].

HBO and Limb Salvage

Hyperbaric oxygen chambers are commonly found within outpatient wound centers in the United States, and can serve as an integral part of the multidisciplinary limb salvage process. The use of HBO as an adjunctive treatment for limb salvage has been reported for many types of wounds including DFU and compromised skin

grafts or flaps, as well as vasculitis ulcers and wounds due to peripheral arterial disease [22]. While the beneficial effects of HBO are likely applicable to wounds of various etiologies, diabetic foot ulcerations and compromised skin grafts and flaps represent two of the better understood applications of HBO for limb salvage. The use of HBO for DFU and compromised skin grafts and flaps will be discussed in more detail in this chapter.

HBO and Diabetic Foot Ulcerations

Hyperbaric oxygenation has been used frequently as an adjunctive treatment of ischemic Wagner grade 3 or greater DFU (i.e., DFU extending to deeper structures and associated with abscess, osteomyelitis, or tendonitis). A majority of the evidence supporting the use of HBO encompasses the treatment of DFU [23]. Patients with DFU often exhibit impaired peripheral vascularity, lymphocytic function, and bacterial killing that inhibits wound healing potential [24]. The mechanisms of action of HBO, including neovascularization and enhanced bacterial killing ability, account for the beneficial effects noted in patients who receive HBO as a treatment for DFU. The neovascularization induced by HBO is not immediately identifiable; it takes approximately 8–10 treatments before this process is detectable, and up to 20–30 treatments before a plateau in neovascularization occurs [25]. Due to this, the hyperbaric treatment course for patients with DFU often involves 30–40 consecutive treatments.

Using GRADE (grading of recommendations, assessment, development, and evaluation) methodology, an analysis was performed in 2015 of published systematic reviews pertaining to HBO and diabetic foot ulcerations (DFU) [15]. The intent of this review was to rate the quality of evidence and general practice recommendations for the treatment of DFU with hyperbaric oxygen therapy. The study design included identification of a specific relevant population (patients with DFU), an intervention (HBO versus standard wound care), and identification of important outcomes. For the purposes of this investigation, standard wound care was defined as surgical debridement of devitalized tissue, use of mechanical offloading, infection control, and revascularization. Outcomes of interest for this review included major amputation and incomplete healing at 1 year. Questions investigated by the GRADE review committee included (1) for a patient with a DFU, is HBO with standard wound care more effective than standard wound care alone for the outcomes of interest; (2) for a patient with a Wagner Grade 2 or lower DFU that has not shown significant improvement after 30 days of treatment, is HBO with standard wound care more effective than standard wound care alone for the outcomes of interest; (3) for a patient with a Wagner Grade 3 or higher DFU that has not shown significant improvement after 30 days of treatment, is HBO with standard wound care more effective than standard wound care alone for the outcomes of interest; (4) for a patient with Wagner Grade 3 or higher DFU who has just had surgical debridement of the foot, is acute postoperative HBO with standard wound care more effective than standard wound care alone for the outcomes of interest. Thirty randomized controlled trials and observational studies involving HBO and DFU were included in this review; a majority of the initially identified studies were excluded from review as they did not report on outcomes of interest or include patients in the specific study populations. The analysis of the available evidence showed that HBO is beneficial in preventing amputation and promoting complete healing in patients with Wagner grade 3 or greater DFUs who have had recent surgical debridement of the foot, as well as patients with Wagner grade 3 or greater DFUs that have not shown significant improvement after at least 30 days of treatment. For patients with DFUs graded as Wagner 2 or lower, there was insufficient evidence found to justify the use of adjunctive HBO.

A series of additional articles have also investigated the effectiveness of HBO in treatment of patients with DFU. A cohort study of 6259 individuals with DFU associated with failed healing for at least 4 weeks despite adequate lower extremity arterial flow was performed to compare

the effectiveness of HBO versus standard therapy [26]. The primary outcomes evaluated in this study were wound healing and lower extremity amputation. The results of the study indicated that patients who received HBO were more likely to have an amputation and were less likely to achieve wound healing compared with the patients who received standard therapy. However, this study had significant limitations including a disparity in the baseline characteristics of the two cohorts. Forty-five percent of patients in the HBO cohort had a Wagner 3 or greater DFU, while only 18% of patients in the standard therapy cohort had a Wagner 3 or greater DFU; this significant difference in DFU severity between the two groups was a likely factor in the variance in primary outcome results between the two cohorts. Additionally, the study included patients with Wagner 2 DFU; in the United States, the presence of a Wagner 2 DFU is generally not an accepted indication for HBO.

A subsequent study investigating the utility of HBO in the prevention of amputation in patients with DFU was performed in 2016 [27]. In this double-blind, placebo-controlled study, adult patients with Wagner grade 2–4 DFU were randomized to receive sham pressurization (to 1.25 ATA) or standard HBO. The primary outcome was the subjective assessment by a single vascular surgeon of whether the patient met criteria for major or minor amputation after 12 weeks of treatment. The study investigators found no significant differences in the percent of patients meeting criteria for amputation between the two groups, and there was also no significant change in ulcer width of surface area noted between the groups. The investigators concluded that HBO does not appear to reduce the indications for amputation or facilitate wound healing in patients with chronic DFU. Similar to the previous study, this study did have significant limitations. Most notably, the patients included in the study were not required to be physically evaluated by the vascular surgeon who determined the indication for amputation; the surgeon was instead provided with clinical data and digital photographs obtained over the course of the study. Although that surgeon provided a determination of whether amputation was indicated based on this information, the actual amputation rates were not included in the manuscript. Additional limitations included a limited percentage of patients in the HBO group who completed a full course of HBO and the inclusion of patients with Wagner 2 DFU which is not consistent with accepted indications for HBO in the United States.

A third study, performed in 2018, investigated whether HBO could improve wound healing and reduce the rates of major amputation in patients with ischemic DFU [28]. This study evaluated 120 patients; subjects were administered standard wound care with or without a course of HBO. The primary outcomes analyzed were freedom from amputation above the ankle, and complete healing after 12 months of follow-up. There was no significant difference in complete wound healing or limb salvage noted between the two groups. As with the two previously described studies, this study also had significant limitations including the inclusion of patients with Wagner 2 DFU as well as a low percentage of patients in the HBO group who actually completed their HBO course as planned.

In conclusion, although recent literature surrounding the use of HBO for DFU has been limited by suboptimal study design, this treatment remains a viable adjunctive treatment for patients with DFU. HBO can be used as an adjunctive treatment for Wagner 3 or greater DFU and should be used in conjunction with other standard wound care treatment modalities including topical wound care, debridement, attention to glucose control, nutritional optimization, offloading, revascularization when indicated, and treatment of associated infection. For optimal neovascularization and wound improvement, DFU patients may require multiple weeks of treatment with HBO.

HBO and Compromised Skin Grafts and Flaps

While HBO is not indicated for the treatment of healthy tissue in skin grafts or flaps, it may be useful in the salvage of flaps or grafts that are

compromised by decreased tissue perfusion or local hypoxia [29]. When affected by prolonged ischemia, skin flaps experience irreversible damage to the microcirculation [30]. The hyperoxygenation which occurs during application of HBO may result in increased viability of compromised flap or graft tissue, reducing the need for additional surgical procedures and increasing the potential for limb salvage [31]. HBO has been used for the treatment of compromised skin grafts as well as ischemic random and free flaps [32].

The mechanisms of action affecting the utility of HBO in the treatment of compromised skin grafts and flaps include HBO-induced neovascularization, attenuation of inflammatory mediators, and hyperoxygenation of ischemic tissue [33]. Post-ischemic tissue reperfusion is associated with an increase in circulating neutrophils to vascular cell walls; the administration of HBO reduces this neutrophil adhesion and the ischemia-reperfusion injury associated with it [10]. The use of hyperbaric oxygenation may be optimized when the treatment is initiated within a short period of time (less than 1 week, and ideally less than 48 h) after identification of graft or flap compromise [34]. Delays in recognition of flap ischemia can result in irreversible tissue damage that will not be ameliorated by use of HBO [35]. As rapid identification of flap or graft ischemia is critical, use of intraoperative perfusion monitoring devices may be helpful in identifying early flap compromise so that HBO can be initiated in a timely fashion. Patients with acutely compromised skin grafts or flaps may benefit from twice-daily HBO sessions in order to optimize tissue oxygenation.

Although HBO is most often recognized as a treatment for arterial ischemia after skin flap or graft surgery, it can also be utilized as an adjunctive treatment for skin flaps complicated by venous occlusion. In an animal study, axial epigastric skin flaps were performed on rats; the flaps were then subjected to venous occlusion, while arterial inflow was left intact [36]. The animals were then randomized to receive HBO, leeching, or leeching and HBO. While the use of HBO alone was not effective in improving the venous outflow in this model, combined use of HBO and leeching resulted in a significant increase in flap survival compared with use of leeching as a sole treatment.

The use of HBO in the management of compromised grafts and flaps is most commonly limited to the postoperative period, but HBO preconditioning may also impact skin flap and graft survival. HBO preconditioning involves the initiation of HBO prior to a planned ischemic insult in order to potentially reduce the sequelae of subsequent hypoxia [37]. The mechanism of action of HBO preconditioning may involve induction of intracellular antioxidant enzyme systems [13]. HBO preconditioning may play a role in limiting the ischemic complications that occur after reconstructive surgical procedures; however, at this time, much of the evidence surrounding HBO preconditioning remains preclinical in nature [13].

To summarize, based on the available literature, HBO should be considered as an adjunctive treatment for skin grafts and flaps that exhibit compromise due to arterial inflow, venous occlusion, or both. When used to treat skin graft or flap compromise, HBO appears to be most effective if it is initiated soon after the ischemic insult. Although many HBO facilities are located within outpatient wound centers and do provide care to inpatients, the initiation of inpatient HBO treatments should be considered for patients with acutely compromised skin grafts or flaps in order to optimize the effectiveness of this treatment. If HBO is indicated for an acutely compromised skin graft or flap but only outpatient HBO care is available, the treating physicians may consider transfer of the patient to a facility that is able to accommodate the patient for inpatient hyperbaric treatments. Treatments may be administered once or twice daily as indicated, and treatments are discontinued when flap viability is achieved.

HBO in Clinical Practice

Systemic HBO is administered while a patient is enclosed within a hyperbaric chamber. These chambers, composed of steel and acrylic components, are commonly located within outpatient

wound centers in the United States and are utilized as an adjunctive wound healing modality. There are approximately 1300 hospital-based hyperbaric facilities present in the United States as of 2021 [38]. There are two main types of hyperbaric chambers: monoplace and multiplace. Monoplace hyperbaric chambers (Fig. 28.1) can accommodate one patient; multiplace hyperbaric chambers (Fig. 28.2) can accommodate multiple patients as well as caregivers, medical personnel, and equipment.

In the United States, monoplace chambers are the most commonly encountered hyperbaric treatment vessels in hospital settings. In the monoplace chamber, the patient remains enclosed in the chamber for the duration of the hyperbaric treatment; hands-on medical care is not possible in the majority of monoplace chambers, and due to this, patients must be clinically stable prior to being treated in the monoplace chamber. Advantages of monoplace chambers include enhanced patient privacy and reduced staffing requirements compared with multiplace chambers; in addition, monoplace chambers have a smaller physical footprint than many multiplace facilities, and some monoplace chambers are portable. The monoplace hyperbaric chamber is compressed with 100% oxygen; patients may be intermittently administered compressed air to breathe via face mask to reduce the risk of oxygen toxicity. The use of 100% oxygen enhances the risk of fire in the monoplace chamber; this risk is mitigated by careful patient preparation and meticulous oversight by the chamber operator.

In contrast, multiplace hyperbaric chambers are compressed with air. The use of compressed air instead of oxygen reduces, but does not completely eliminate, the risk of fire in the multiplace chamber. Patients treated in multiplace hyperbaric chambers receive 100% oxygen via the use of vinyl hoods that are attached to a silicon neck



Fig. 28.1 Monoplace hyperbaric chamber



Fig. 28.2 Multiplace hyperbaric chamber. (Photo credit: Wikipedia.com)

ring to make an airtight seal. The larger, more spacious nature of multiplace chambers is beneficial for many claustrophobic patients, as the risk of confinement anxiety is reduced in this setting. Additional advantages of multiplace chambers include the ability to treat multiple patients during each treatment session and the ability to perform hands-on patient care during the treatment. Critical care, including use of mechanical ventilatory support, can also be accomplished more easily in a multiplace chamber than in a monoplace chamber. Patients who are critically ill or hemodynamically unstable, including those with necrotizing soft tissue infections, crush injuries, and compartment syndromes, are best treated in a multiplace environment, as medical providers can accompany these patients into the chamber for the duration of the hyperbaric treatment to provide necessary care. Due to the increased costs associated with the staffing and operation of these chambers as well as the larger physical space requirements and increased relative complexity associated with their use, multiplace chambers are less frequently found than monoplace chambers in hospitals across the United States.

During hyperbaric treatments, patients sit or lie supine in the hyperbaric chamber and breathe 100% oxygen for the duration of the treatment. Due to fire safety standards, patients treated in the monoplace environment cannot bring books, magazines, cell phones, or other personal belongings into the chamber with them. Monoplace hyperbaric chambers commonly have a television monitor attached to the outside of the chamber; this allows the patient to watch television or a movie during each treatment, with sound available inside the chamber through a built-in speaker. Patients may be allowed to bring personal material into a multiplace chamber with them, but certain items (including many battery-operated devices, matches, and other highly combustible material) are never permitted in any hyperbaric environment due to the risk of fire. In the United States, the National Fire Protection Association (NFPA) sets fire safety codes for hyperbaric facilities that are adhered to by hospital-based hyperbaric programs [39]. The

NFPA code provides specific recommendations for hyperbaric facility construction as well as standards for patient safety and fire prevention. With proper adherence to the NFPA code and knowledge and application of the basic techniques used to reduce the risk of fire in the hyperbaric environment, the potential for fire in the hyperbaric environment is significantly reduced. Despite this, not all hyperbaric facilities follow NFPA regulations, and there have been fatal fires in the United States and abroad involving hyperbaric chambers.

The use of traditional medical equipment and implanted devices in the hyperbaric environment poses unique challenges related to the inability of many modern medical devices (including intravenous pumps and ventilators) to withstand the typical pressurization encountered in the hyperbaric chamber. Most monoplace chambers are unable to accommodate patients who are undergoing treatment with mechanical ventilation or continuous intravenous infusions. Some implanted medical devices are unsuitable for use in the hyperbaric environment, due to fire or other safety concerns; many newer medical devices have not been tested under pressure and may malfunction or experience structural failure when exposed to hyperbaric pressurization. Many pacemaker manufacturers have tested their devices under pressure, and thus permanent pacemakers are often not regarded as a contraindication to hyperbaric compression. Other medical devices, including insulin pumps and continuous glucose monitoring devices, have not been extensively tested under hyperbaric conditions; these devices are frequently not compatible for use in the hyperbaric environment.

Hyperbaric treatments are generally scheduled on a daily basis; most hyperbaric chambers in the United States operate during weekday business hours only, but some facilities may offer weekend or after-hours treatments for emergent conditions such as acute skin graft or flap compromise or necrotizing soft tissue infection. While a majority of hyperbaric patients receive daily treatments, patients with acute or emergent hyperbaric indications may benefit from twice daily treatment delivery, although availability may be limited due to logistical issues including facility staffing limitations. Each wound healing hyperbaric treatment is approximately 2 h in duration. Pressurization is maintained at a treatment depth ranging from 2.0 atmospheres absolute (ATA) to 2.5 ATA; the treatment regimens are derived from the United States Navy recompression tables and are generally not able to be significantly modified due to the potential for adverse events including systemic breathing gas toxicity. The HBO treatment course is typically tailored to each individual patient. The number of hyperbaric treatments required per patient varies based on the indication for treatment. Patients with acute or emergent treatment indications, such as necrotizing soft tissue infection or acute skin graft or flap compromise, may require ten or fewer HBO treatments to achieve clinical improvement. Patients who are treated with HBO for chronic conditions, such as DFU, may require 40–60 daily HBO treatments for maximum clinical effect. Some patients may end their treatment course earlier than expected based on a more rapid course of healing or symptom resolution. Interestingly, despite the lengthy time commitment and need to present to the hospital for daily treatments, HBO has not been associated with decrements in patient quality of life [40].

Adverse Effects of HBO

When administered by trained professionals with clinical oversight by a physician who specializes in Undersea and Hyperbaric Medicine, adverse effects of HBO are rarely encountered. Most adverse effects associated with HBO can be avoided or mitigated with careful patient preparation and attention to detail.

Middle ear barotrauma (MEBT) is the most common complication of HBO; MEBT occurs due to inadequate ear pressure equalization, often due to eustachian tube dysfunction. Preventive measures such as educating the patient on autoinsufflation techniques such as the Valsalva maneuver, are often used to reduce the risk of MEBT. Patients who are unable to equalize ear pressures despite adequate education may require

use of topical or systemic decongestant medications. In some cases, tympanostomy tube placement may be necessary.

Systemic oxygenation can also induce hyperactivity of the central nervous system (CNS) resulting in oxygen toxicity; the exact mechanism of this is not well understood, but may be related to the presence of ROS that result in alterations in enzyme inhibition or brain metabolism [41]. The risk of CNS oxygen toxicity is related to both the partial pressure of oxygen inspired and the exposure time; the clinical presentation involves tonic-clonic seizure activity that can occur with or without prodromal signs [42]. Seizures associated with CNS oxygen toxicity are rarely encountered in clinical practice; in a retrospective analysis of 2334 patients who received HBO, the incidence of seizures was 0.011% [42]. The risk of central nervous system oxygen toxicity may be reduced by the use of intermittent air breathing periods during each hyperbaric treatment.

In diabetic patients, HBO is associated with a significant decrease in blood sugar concentrations. The cause of this is not fully known; possible mechanisms include increased systemic glucose consumption or insulin production as well as increased tissue insulin sensitivity [43]. Pre-treatment glucose values may correlate with the presence of hypoglycemia during or after hyperbaric treatment; in one study, a pre-treatment blood glucose concentration of 150 mg/dL was predictive of subsequent hypoglycemia [44]. Due to the risk of hypoglycemia, diabetic patients who receive HBO are required to have blood glucose levels checked prior to each treatment, and treatments are generally withheld if the blood glucose value is below the hyperbaric facility's pre-defined threshold level.

Changes in visual acuity, most often affecting distance vision, may occur as a side effect of HBO. A myopic shift can be detected in almost 90% of patients who receive a standard course of 40 HBO treatments [45]. Patients may describe having difficulties with distance vision and nighttime driving. Fortunately, these visual changes are almost always temporary, and they resolve over the ensuing weeks to months after the treatment course is finished [46]. Due to the temporary nature of these visual changes, patients who experience myopia as a consequence of hyperbaric oxygenation are often counseled to not purchase new corrective lenses, as their vision will revert back to baseline after the treatments are completed. Nuclear cataract formation after HBO has rarely been reported to occur as a consequence of HBO, almost always in association with a prolonged course of treatment (greater than 150 HBO treatments) [47, 48].

Not all patients are acceptable candidates for treatment with HBO. Patients with underlying COPD or bullous lung disease are at increased risk for pulmonary barotrauma, including pneumothorax, which represents a potentially fatal complication of HBO. Fatal pulmonary edema has been reported to occur in patients with impaired cardiac function (ejection fraction less than 40%), as HBO administration results in an increase in pulmonary capillary wedge pressure [49]. As previously discussed, patients with implanted medical devices may be unable to safely receive HBO. The toxicities of some pharmacologic therapies may be exacerbated by exposure to hyperbaric oxygenation. Patients with severe anxiety, claustrophobia, or impaired cognitive function may benefit from treatment in a multiplace chamber instead of a monoplace, as medical personnel can accompany them into the former type of hyperbaric environment to provide assistance during the treatment process. Prior to starting a course of HBO, patients should be evaluated by a trained and experienced hyperbaric medicine physician and nurse in order to assess for these and other characteristics that could preclude them from safely receiving treatment in the hyperbaric environment.

Topical Oxygen Therapy

Discussions of oxygen therapy for wound care often include a mention of topical oxygenation. Topical oxygen therapy involves administration of oxygen via a bag, boot, or other device to a specific area of the body. This form of oxygen therapy involves regional application of oxygen

to an extremity and does not involve systemic oxygenation. The mechanism of action of topical oxygen therapy involves the direct application of oxygen to a wound; topical oxygen therapy does not share the same physiologic mechanisms as HBO. Topical oxygen therapy may be advantageous for certain patients, as its use does not require the patient to make daily visits to a hospital or outpatient treatment center; patients can receive topical oxygen therapy in out-of-hospital settings such as a private residence or nursing facility [19]. It is also associated with a lower treatment cost than traditional HBO. Although topical oxygen therapy is relatively simple and easy to use, it does require the patient to remain immobilized and attached to the external oxygen source during each treatment [50]. Unlike HBO, topical oxygen therapy is not associated with the potential for systemic oxygen toxicity. However, topical oxygen delivery systems generally do not achieve the high pressures found in hyperbaric chamber environments, and at this time there is not sufficient high-quality evidence to support the use of topical oxygen therapy as a medical treatment for wound healing and limb salvage [19, 20].

Conclusions

HBO is a valuable adjunctive treatment modality for patients with complicated wounds and represents a useful pillar of the comprehensive limb salvage process. The administration of hyperbaric oxygenation results in neovascularization, an improved inflammatory response, and enhancement of infection control; these clinical effects can have a favorable impact on patients with challenging wounds who are at risk for limb loss. When administered by trained professionals, HBO is a safe treatment modality that is associated with a limited number of adverse events. Systemic hyperbaric oxygenation should be considered as an integral adjunctive treatment for patients with complex wounds, especially DFU and compromised skin grafts or flaps, who are referred for attempts at limb salvage.

References

1. Edwards ML. Hyperbaric oxygen therapy. Part 1: history and principles. J Vet Emerg Crit Care (San Antonio). 2010;20(3):284–8.
2. Rendell-Baker L, Jacobson JH II. Hyperbaric oxygenation. Int Anesthesiol Clin. 1965;3:315–54.
3. Butler WP. Caisson disease during the construction of the Eads and Brooklyn bridges: a review. Undersea Hyperb Med. 2004;31(4):445–59.
4. Jacobson JH II, Morsch JH, Rendell-Baker L. Clinical experience and implications of hyperbaric oxygenation. THE historical perspective of hyperbaric therapy. Ann N Y Acad Sci. 1965;117:651–70.
5. McCallum RI. Decompression sickness: a review. Br J Ind Med. 1968;25(1):4–21.
6. Brecher ME. Transfusion medicine illustrated. The Timken Tank. Transfusion. 2011;51(7):1377–8.
7. Weaver LK, editor. Hyperbaric oxygen therapy indications. Florida: Best Publishing Company; 2014. p. iii.
8. Bell E, Wallace T, Chouinard I, Shevell M, Racine E. Responding to requests of families for unproven interventions in neurodevelopmental disorders: hyperbaric oxygen "treatment" and stem cell "therapy" in cerebral palsy. Dev Disabil Res Rev. 2011;17(1):19–26.
9. Bennett MH, Mitchell SJ. Emerging indications for hyperbaric oxygen. Curr Opin Anaesthesiol. 2019;32(6):792–8.
10. Thom SR. Hyperbaric oxygen: its mechanisms and efficacy. Plast Reconstr Surg. 2011;127 Suppl 1(Suppl 1):131S–41S.
11. Camporesi EM, Bosco G. Mechanisms of action of hyperbaric oxygen therapy. Undersea Hyperb Med. 2014;41(3):247–52, 259.
12. Sheikh AY, Gibson JJ, Rollins MD, Hopf HW, Hussain Z, Hunt TK. Effect of hyperoxia on vascular endothelial growth factor levels in a wound model. Arch Surg. 2000;135(11):1293–7.
13. Francis A, Baynosa R. Ischaemia-reperfusion injury and hyperbaric oxygen pathways: a review of cellular mechanisms. Diving Hyperb Med. 2017;47(2):110–7.
14. Buras J. Basic mechanisms of hyperbaric oxygen in the treatment of ischemia-reperfusion injury. Int Anesthesiol Clin. 2000;38(1):91–109.
15. Huang ET, Mansouri J, Murad MH, Joseph WS, Strauss MB, Tettelbach W, Worth ER, UHMS CPG Oversight Committee. A clinical practice guideline for the use of hyperbaric oxygen therapy in the treatment of diabetic foot ulcers. Undersea Hyperb Med. 2015;42(3):205–47.
16. Koomanachai P, Keel RA, Johnson-Arbor KK, Suecof LA, Nicolau DP, Kuti JL. Linezolid penetration into wound tissue of two diabetic patients before and after hyperbaric oxygen therapy. Undersea Hyperb Med. 2011;38(1):11–6.

17. Kaide CG, Khandelwal S. Hyperbaric oxygen: applications in infectious disease. Emerg Med Clin North Am. 2008;26(2):571–95, xi.
18. Boerema I, Meyne NG, Brummelkamp WK, et al. Life without blood (a study of the influence of high atmospheric pressure and hypothermia on dilution of the blood). J Cardiovasc Surg. 1959;13:133–46.
19. Mutluoglu M, Cakkalkurt A, Uzun G, et al. Topical oxygen for chronic wounds: a pro/con debate. J Am Coll Clin Wound Spec. 2015;5:61–5.
20. Anonymous. UHMS position statement: topical oxygen for chronic wounds. Undersea Hyperb Med. 2018;45(3):379–80.
21. Feldmeier JJ, Kirby JP, Buckey JC, Denham DW, Evangelista JS, Gelly HB, Harlan NP, Mirza ZK, Ray KL, Robins M, Savaser DJ, Wainwright S, Bird N, Huang ET, Moon RE, Thom SR, Weaver LK. Physiologic and biochemical rationale for treating COVID-19 patients with hyperbaric oxygen. Undersea Hyperb Med. 2021 First-Quarter;48(1):1–12.
22. Goldman RJ. Hyperbaric oxygen therapy for wound healing and limb salvage: a systematic review. PM R. 2009;1(5):471–89.
23. Huang E, Heyboer M III, Savaser DJ. Hyperbaric oxygen therapy for the management of chronic wounds: patient selection and perspectives. Chronic Wound Care Manag Res. 2019;6:27–37.
24. Gill AL, Bell CN. Hyperbaric oxygen: its uses, mechanisms of action and outcomes. QJM. 2004;97(7):385–95.
25. Marx RE, Johnson RP. Problems wounds in oral and maxillofacial surgery: the role of hyperbaric oxygen. In: Davis JC, Hunt KT, editors. Problem wounds: the role of oxygen. New York, NY: Elsevier; 1998. p. 71.
26. Margolis DJ, Gupta J, Hoffstad O, Papdopoulos M, Glick HA, Thom SR, Mitra N. Lack of effectiveness of hyperbaric oxygen therapy for the treatment of diabetic foot ulcer and the prevention of amputation: a cohort study. Diabetes Care. 2013;36(7):1961–6.
27. Fedorko L, Bowen JM, Jones W, Oreopoulos G, Goeree R, Hopkins RB, O'Reilly DJ. Hyperbaric oxygen therapy does not reduce indications for amputation in patients with diabetes with nonhealing ulcers of the lower limb: a prospective, double-blind, randomized controlled clinical trial. Diabetes Care. 2016;39(3):392–9.
28. Santema KTB, Stoekenbroek RM, Koelemay MJW, Reekers JA, van Dortmont LMC, Oomen A, Smeets L, Wever JJ, Legemate DA, Ubbink DT, DAMO2CLES Study Group. Hyperbaric oxygen therapy in the treatment of ischemic lower-extremity ulcers in patients with diabetes: results of the $DAMO_2CLES$ multicenter randomized clinical trial. Diabetes Care. 2018;41(1):112–9.
29. Kleban S, Baynosa RC. The effect of hyperbaric oxygen on compromised grafts and flaps. Undersea Hyperb Med. 2020 Fourth-Quarter;47(4):635–48.
30. Zamboni WA, Roth AC, Russell RC, Nemiroff PM, Casas L, Smoot EC. The effect of acute hyperbaric oxygen therapy on axial pattern skin flap survival when administered during and after total ischemia. J Reconstr Microsurg. 1989;5(4):343–7.
31. Baynosa RC, Zamboni WA. The effect of hyperbaric oxygen on compromised grafts and flaps. Undersea Hyperb Med. 2012;39(4):857–65.
32. Friedman HI, Fitzmaurice M, Lefaivre JF, Vecchiolla T, Clarke D. An evidence-based appraisal of the use of hyperbaric oxygen on flaps and grafts. Plast Reconstr Surg. 2006;117(7 Suppl):175S–90S.
33. Zhou YY, Liu W, Yang YJ, Lu GD. Use of hyperbaric oxygen on flaps and grafts in China: analysis of studies in the past 20 years. Undersea Hyperb Med. 2014;41(3):209–16.
34. Lotfi P, Dayan J, Chiu ES, Mehrara B, Nelson JA. Hyperbaric oxygen therapy and mastectomy flap ischemia following nipple-sparing mastectomy and immediate breast reconstruction. Plast Reconstr Surg. 2020;145(6):1114e–5e.
35. Harl MJ. Defining the role of hyperbaric oxygen therapy as an adjunct to reconstructive surgery. Surg Clin North Am. 2020;100(4):777–85.
36. Lozano DD, Stephenson LL, Zamboni WA. Effect of hyperbaric oxygen and medicinal leeching on survival of axial skin flaps subjected to total venous occlusion. Plast Reconstr Surg. 1999;104(4):1029–32.
37. Camporesi EM, Bosco G. Hyperbaric oxygen pretreatment and preconditioning. Undersea Hyperb Med. 2014;41(3):259–63.
38. Johnson-Arbor K, Verstraete R. No bad blood-surviving severe anemia without transfusion. JAMA Intern Med. 2021;181(1):7–8.
39. Hart JR, Rubadou CB. Chapter 14: Hyperbaric facilities. In: Hart JR, Rubadou CB, editors. NFPA 99 health care facilities code handbook. 11th ed. Quincy: National Fire Protection Association; 2017. p. 563–633.
40. Li G, Hopkins RB, Levine MAH, et al. Relationship between hyperbaric oxygen therapy and quality of life in participants with chronic diabetic foot ulcers: data from a randomized controlled trial. Acta Diabetol. 2017;54:823–31.
41. Hadanny A, Meir O, Bechor Y, Fishlev G, Bergan J, Efrati S. Seizures during hyperbaric oxygen therapy: retrospective analysis of 62,614 treatment sessions. Undersea Hyperb Med. 2016;43(1):21–8.
42. Manning EP. Central nervous system oxygen toxicity and hyperbaric oxygen seizures. Aerosp Med Hum Perform. 2016;87(5):477–86.
43. Heyboer Iii M, Wojcik SM, Swaby J, Boes T. Blood glucose levels in diabetic patients undergoing hyperbaric oxygen therapy. Undersea Hyperb Med. 2019 Third Quarter;46(4):437–45.
44. Stevens SL, Narr AJ, Claus PL, Millman MP, Steinkraus LW, Shields RC, Buchta WG, Haddon R, Wang Z, Murad MH. The incidence of hypoglycemia during HBO2 therapy: a retrospective review. Undersea Hyperb Med. 2015;42(3):191–6.
45. Riedl P, Škiljić D, Arnell P, Wannholt R, Zetterberg M, Andersson Grönlund M. Myopic shift and lens turbidity following hyperbaric oxygen therapy—a

prospective, longitudinal, observational cohort study. Acta Ophthalmol. 2019;97(6):596–602.
46. Churchill S, Deru K, Wilson G, Cable R, Bell JE, Weaver LK. Rates of visual acuity change in patients receiving hyperbaric oxygen in monoplace and multiplace chambers. Undersea Hyperb Med. 2016;43(3):217–23.
47. Palmquist BM, Philipson B, Barr PO. Nuclear cataract and myopia during hyperbaric oxygen therapy. Br J Ophthalmol. 1984;68(2):113–7.
48. Gesell LB, Trott A. De novo cataract development following a standard course of hyperbaric oxygen therapy. Undersea Hyperb Med. 2007;34(6):389–92.
49. Weaver LK, Churchill S. Pulmonary edema associated with hyperbaric oxygen therapy. Chest. 2001;120(4):1407–9.
50. Howard MA, Asmis R, Evans KK, Mustoe TA. Oxygen and wound care: a review of current therapeutic modalities and future direction. Wound Repair Regen. 2013;21(4):503–11.

Skin Grafting

29

IN: Functional Limb Salvage: The Multidisciplinary Team Approach

Adaah Sayyed, Paige K. Dekker, Caitlin S. Zarick, and Karen K. Evans

Introduction

Skin grafting is a surgical technique in which skin from one region of the body is harvested from its local blood supply and transplanted to another location. As a result of being separated from its vascular bed, the viability of a skin graft relies on the development of new blood supply from the regional bed in which it is placed [1]. This technique is thousands of years old, originating in 2500–3000 B.C. by surgeons of the Hindu Tilemaker Caste who used gluteal skin to recreate noses for those who suffered traumatic facial wounds. The focus of this chapter is *split-thickness skin grafting (STSG),* a technique first described in 1872 by Ollier and Thiersch [1]. Despite its initial use in facial reconstruction, skin grafting is commonly employed in soft tissue reconstruction of defects such as deep burns, sores, large wounds, cancer resections, and chronic ulcerations that are commonly encountered in diabetic populations. This chapter will discuss the techniques and outcomes of skin grafting, specifically STSG, in lower extremity wounds resulting from diabetes and peripheral artery disease. Timely closure and healing are critical in reducing the morbidity and cost associated with chronic lower extremity wounds.

A. Sayyed
Georgetown University School of Medicine, Washington, DC, USA
e-mail: as4425@georgetown.edu

P. K. Dekker
Department of Plastic and Reconstructive Surgery, MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: pkd15@georgetown.edu

C. S. Zarick (✉) · K. K. Evans
Department of Plastic and Reconstructive Surgery, MedStar Georgetown University Hospital, Washington, DC, USA

Center for Wound Healing and Hyperbaric Medicine, Washington, DC, USA
e-mail: caitlin.s.zarick@medstar.net; karen.k.evans@medstar.net

Categories of Skin Grafting

The two major classifications of skin grafts are autogenous and tissue-engineered skin grafts. *Autogenous skin grafts* are those transplanted from a donor site and grafted onto a different site on the same individual. Autogenous skin grafts can be further divided into split-thickness and full-thickness skin grafts. *Tissue-engineered skin grafts* are biologic cell-based dressings composed of live-cell constructs containing at minimum one layer of live allogeneic cells [2]. These are commonly used when traditional autogenous dressings have failed or are deemed inappropriate, such as in patients unable to undergo anesthesia for donor site harvesting. The take rate and healing rate of such grafts, however, are much

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_29

lower than of autologous STSGs [3]. Most tissue-engineered skin grafts do not provide complete definitive skin coverage after one usage, and they can also be more costly. A more complete discussion is presented in other chapters.

Split-Thickness Skin Grafts

Split-thickness skin grafts involve harvesting the epidermis and varying portions of the underlying dermis, allowing the donor site to heal from epidermal elements left behind. STSGs can be further divided into thin (0.008–0.012 in.), intermediate (0.012–0.018 in.), and thick (0.018–0.030 in.) [4]. Advantages of STSGs include the large surface area coverage they provide while using minimal donor skin that can be expanded via meshing techniques. Donor sites have the ability to heal completely in 10–15 days and can be reharvested at that time if necessary. Disadvantages of this technique include the limited pliability and elasticity afforded by STSGs, resulting in increased contracture upon healing. Additionally, STSGs are fragile, lack hair, heal with abnormal pigmentation, and lack a smooth texture.

STSGs are used in a variety of reconstructive procedures. Indications for STSG use include cases when simpler methods of wound closure such as healing by primary closure, secondary intention, or negative pressure wound therapy do not suffice or are not possible. In patients with large skin defects extending over the trunk or extremities (not including joints), the increased contractility of STSGs results in smaller areas of scarring. In addition, compared to large wounds treated with standard local wound care dressings, STSG provides more stable coverage than the scar created by secondary closure. STSG can also provide definitive coverage for wounds that closed partially in response to other therapies, or to improve healing of donor sites formed by other surgical procedures [4].

STSGs are also indicated in cases of acute skin loss (burns, infection, traumatic wounds) and chronic skin loss (leg ulcers). Utilization of thinner grafts is particularly beneficial in these cases as they have decreased metabolic needs. Intermediate-thickness STSGs provide the ideal graft for diabetic foot wounds, providing good quality repair and resultant skin with sufficient elasticity and reduced retraction [4]. The most common thickness used by the authors is 0.0012 in. The conservative approach to treating chronic wounds entails frequent debridement and dressing changes, along with topical solutions such as collagenase ointments, antimicrobial absorbent fiber sheets, saline, or iodine. The benefit of STSG, however, is the significantly shortened healing time achieved when compared to conservative treatment. One study reported an average healing time of 28 days with STSG versus 122 days in conservatively treated patients, as well as a decreased hospital length of stay and overall reduced cost of care [3, 5].

Full-Thickness Skin Grafts

Full-thickness skin grafts (FTSGs) require harvesting the entire layer of skin, including both the epidermis, dermis, and underlying adnexal structures such as sweat glands, hair follicles, and nerves [1]. Because FTSGs require full-thickness harvesting, the donor skin takes longer to revascularize relative to STSGs, and often requires closure by local advancement of the skin or by secondary local flap placement.

Benefits of FTSGs include their minimal wound contraction and ability to provide good color, texture, elasticity, and thickness to match the surrounding skin [1]. The aesthetic advantages provided by FTSGs make them a prime choice in the repair of hand and facial wounds, such as facial defects resulting from skin cancer resections. Patients have reported increased satisfaction with the matching of texture and color provided by FTSGs [6]. Their minimal contraction, pliable reconstructability, and improved capacity to provide sensation and temperature discrimination postoperatively also make FTSGs the preferred option in cases requiring grafting over mobile areas such as joints, palms, and fingertips [3]. They are used less frequently in complex lower extremity wounds due to the poor host

environment, weight-bearing surfaces of the foot, and often poor surrounding tissue quality.

Skin Graft Healing

Four main phases comprise skin graft healing:

1. The *plasmatic imbibition phase* occurs within the first 12–48 h. Fibrin attaches the graft to the recipient bed over the first 24 h. The graft gains up to 40% of its pregraft weight by absorbing the wound exudate, becoming edematous [1, 7]. This allows the graft to remain moist and receive nutrients, maintaining graft vessel patency until revascularization is possible. The fibrin located beneath the graft is progressively replaced with granulation tissue, resulting in the permanent attachment of the graft to its recipient bed [1]. The graft may appear pale or white during this ischemic phase. STSGs are able to survive up to 4 days of ischemia [8].
2. The *inosculation and capillary ingrowth phase* occurs within 48–72 h, once proper apposition of the graft has occurred. A fine vascular network is established within the fibrin layer created between the graft and recipient bed. Blood vessels within the recipient bed grow capillary buds, which anastomose with pre-existing graft vessels in the dermis, creating open channels. The establishment of blood flow results in the graft turning pink, a general sign of probable graft survival [7, 8].
3. The *revascularization phase* occurs within 5–7 days. The most commonly endorsed theory regarding graft revascularization proposes that after the inosculatory event, the definitive vasculature of the graft includes the blood vessels that were originally present within the graft. The process of *primary revascularization* occurs when graft healing progresses normally. The graft initially has inadequate reverse circulation, so the blood and fluids flowing into the graft become trapped, unable to return to the bed. Within 4–7 days postgraft, the newly established vascular connections begin to differentiate into afferent and efferent vessels. Once complete, full circulation is reestablished and blood flow is restored to the graft [7].
4. The graft goes through a final *maturation phase*, which can take over 1 year to complete. This phase involves changes in graft pigmentation, flattening, and softening [8].

Pathologies Treated

Many pathologies involving chronic skin loss in the lower extremities are able to be treated with the use of STSGs. This chapter will focus specifically on the use of skin grafts in the management of complex lower extremity wounds, most notably due to diabetes and/or peripheral arterial disease.

Diabetic Foot Ulcers

Due to the propensity for extensive polymicrobial infections in patients with diabetic foot ulcers, the need for a new skin barrier over these wounds is paramount. Skin grafting is a fast and efficient method for creating this barrier. It provides pliable soft tissue and results in minimal donor site morbidity while accelerating wound healing time. There is a common misconception that elevated hemoglobin A1c (HbA1c) levels in patients with poorly controlled diabetes is a contraindication for skin grafting. It has been found, however, that there is no difference in healed versus failed skin grafts in patients with elevated levels of HbA1c, some with levels greater than 9%. In diabetic patients with an average HbA1c of 8.7%, the mean time to heal was about 6.5 weeks [9]. It is still ideal to have blood sugars well controlled in the perioperative setting immediately before, during, and after surgery to ensure the best chance for healing. Ideally, random blood sugars around the day of surgery should be <180 mg/dL or lower.

Another common misconception regarding the use of STSG for diabetic foot ulcers involves perceived difficulties with graft healing on weight-bearing or plantar surfaces. Foot ulcers

resulting from neuropathy usually occur on the plantar surface of the foot. The challenges of reduced blood flow and difficulty offloading make chronic ulcers on plantar surfaces uniquely difficult to heal [5, 10]. There are low and comparable recurrence rates when STSGs are applied to the plantar foot compared to other locations [10]. One study found that of 20 patients with STSG application to plantar surfaces, only one patient required regrafting during a follow-up period of 2–8 years, and all patients resumed ambulation during their follow-up period [10]. In addition to providing a durable plantar surface, STSGs are also cost-effective, can be performed by most wound surgeons (relative to free tissue transfer, which requires a trained microsurgeon), and in some cases can be performed as an outpatient procedure [10].

Peripheral Arterial Disease

Peripheral arterial disease (PAD) and chronic total vascular occlusions have increased in prevalence as cases of diabetes and chronic kidney disease rise. Critical limb ischemia (CLI) with advanced wound presentation is a leading cause of nontraumatic lower extremity above- and below-the-knee amputations [11].

The goal in treating patients with PAD-induced ischemic wounds is to provide a durable protective barrier in order to prevent further infection and limb loss. Similar to the treatment algorithm for diabetic foot ulcers, wounds secondary to PAD can also be treated with conservative measures such as local wound care or STSG.

Adequate perfusion to the wound site plays a key role in healing wounds secondary to PAD. Literature discussing patients with CLI consistently reports that endovascular revascularization and surgical procedures to improve distal extremity perfusion are both superior to medical management alone. Research assessing time to healing in patients with PAD treated with STSG revealed that the most significant predictor of successful wound healing was a complete pedal arch, defined as a direct connection between a patent dorsalis pedis artery and at least one other patent plantar artery. Other patient factors, such as plantar wound location, various methods of wound bed preparation, or presence of bacteria at various culture time points, have not been shown to have a significant relationship with wound healing [11]. A discussion of the assessment of perfusion and revascularization methods is found in *Evaluation of Vascular Supply*.

Presurgical Evaluation

Numerous variables account for the success or failure of STSG therapy in comorbid patients with chronic wounds. Presurgical evaluation and optimization of these factors play a significant role in improving viability of skin graft therapy and resulting outcomes.

Evaluation of Vascular Supply

In patients evaluated for treatment of lower extremity ulcers, it is crucial to assess for peripheral vascular disease prior to skin graft application. Optimizing perfusion is the first step in preparation of the wound for therapy. If distal pulses of the posterior tibial artery, dorsalis pedis artery, or peroneal artery are not palpable, vascular status must be assessed further. Ideal methods for evaluation include noninvasive vascular testing, such as ankle brachial index (ABI), toe brachial index, doppler waveforms, and pulse volume recordings (PVR) [4, 5]. A handheld doppler can also help assess the vascular status but may not be accurate to diagnose peripheral arterial disease. For adequate wound healing, an evaluation by a vascular surgeon should be completed in order to ensure proper arterial flow and to perform any revascularization procedures needed.

Infection Control

Infection control and establishment of a clean, granulating wound bed are paramount for successful STSG application. The first step in wound bed preparation is the eradication of

infected, nonviable tissue via serial debridements while ensuring ample vascular supply to promote epithelial advancement. Pre- and post-debridement cultures should be obtained with each debridement in order to guide systemic antibiotic therapy as well as to confirm that negative or scant growth is achieved prior to undergoing closure with STSG. Parenteral antibiotics are often unable to penetrate and eradicate biofilms which are often present in diabetic foot wounds. Successful eradication of biofilms instead relies on aggressive, sharp surgical debridement, which should be performed until healthy bleeding tissue at the base of the wound is observed [4]. Sharp debridement also provides a 72-h window in which bacteria have increased susceptibility to antibiotics. Combination use of STSG and antibiotics during this therapeutic window has been suggested to improve wound healing [4].

It has been suggested that bacterial loads between 10^5 and 10^6 organisms per gram may negatively affect wound and skin graft healing [4, 5]. Conversely, some studies suggest that identification of more virulent organisms such as *Pseudomonas aeruginosa* or *Staphylococcus aureus* by preoperative wound culture swabs is more predictive of poor STSG outcomes than quantitative analysis of infection load [12]. Regardless of the method used to measure active infection, resolution of clinical infection is required prior to application of STSG [4].

After initial control of the infected wound, patients will often be discharged from the hospital setting and followed as an outpatient until their wound is ready for STSG application. Local wound care is important during this period to ensure the wound bed stays clean, healthy, and granular. Often, patients receive negative pressure wound therapy (NPWT) with dressing changes twice weekly. This ensures a clean and sterile dressing on the wound while building and increasing the granulation tissue in the wound bed. If NPWT is not being utilized, patients will commonly receive daily to weekly dressing changes in combination with offloading/immobilization and oral antibiotics if indicated.

Other Considerations

In addition to optimization of a patient's vascular supply and infection control, several other factors must be addressed in order to maximize STSG success. Smoking negatively impacts wound healing by reducing tissue oxygenation and subsequently decreasing collagen synthesis [4]. Smoking cessation should therefore be strongly encouraged in patients considering wound closure with STSG. Poor nutritional status can also contribute to initial ulcer formation and persistence; therefore, consultation with a dietician should be pursued in order to maximize nutritional status during the presurgical preparation period [5]. Lower extremity edema should be addressed with mechanical measures such as limb elevation and compressive dressings or by managing the underlying cause of peripheral edema in the patient [4]. In general, patients' medical comorbidities should be optimized to ensure the best chance for graft success. In some instances, however, wound closure may be needed prior to absolute optimization.

Operative Techniques

Once patient optimization is accomplished, the next steps in care include wound bed debridement, STSG harvesting, meshing, and STSG application (Table 29.1).

Wound Bed Debridement

As previously discussed, serial debridements are required to prepare the wound bed by eradicating infected, nonviable tissue while ensuring ample vascular supply to promote epithelial advancement. In order to ensure that adequate debridement and removal of the biofilm has been performed, the authors will often paint the entire wound with methylene blue before each debridement. Once the methylene blue is removed via sharp debridement, it can be ensured that every surface of the wound has been debrided (Fig. 29.1). Sharp debridement is frequently

performed with hydrosurgical instruments, curettes, rongeurs, and scalpels until healthy bleeding tissue is reached. The wound is then flushed with copious amounts of saline [4]. Patients undergo continued debridements until the wound bed is deemed ready for STSG, which is decided based on clinical evaluation of any infection. Serial debridements are often done in the in-patient setting if patients are to be brought to the operating room multiple times while receiving antibiotics [10, 11].

Table 29.1 Basic operative steps involved in split-thickness skin grafting (STSG) of a wound bed

Wound bed debridement
1. Paint the wound with methylene blue
2. Sharply debride the wound using hydrosurgical instruments, curettes, rongeurs, and scalpels removing all the methylene blue
3. Flush the wound with copious amounts of saline
STSG harvest
1. Mark the harvest site for appropriate size of graft to be taken
2. Inject tumescent solution into the harvest site
3. Lather the site with lubricant
4. Set power dermatome to the correct width and thickness and harvest the skin
Meshing
1. Select the appropriate mesher to the correct ratio (1.5:1 or 3:1) and mesh the skin graft. Dermis side should be facing up during meshing
STSG application
1. Carefully transfer the skin graft to the recipient bed, with the dermis side facing down
2. Secure the graft using skin staples or absorbable sutures

Thorough hemostasis at the recipient wound bed is imperative since hematoma formation beneath the skin graft can inhibit neoformed capillaries, thereby halting graft incorporation. Hemostasis can be achieved via meticulous handling of wound bed tissue as well as strategic electrocautery use throughout the procedure. Topical thrombin provides fast reduction of intraoperative bleeding and can also be applied as a hemostatic agent for especially large diabetic foot wounds [4].

Negative pressure wound therapy is often used as an adjunct to surgical debridement for wound bed preparation. In deep or unevenly contoured wound beds it can help to fill-in and even the surface [3, 5]. NPWT also helps to increase granulation tissue to the wound bed. In patients undergoing staged limb salvage procedures, the resulting wounds created can be managed with NPWT prior to definitive wound closure with STSG [4]. NPWT assists in stimulation of granulation tissue, removal of fibrotic tissue formation, and improved wound drainage [5].

STSG Harvesting

After the final debridement has been completed, the harvesting stage of the surgical procedure can

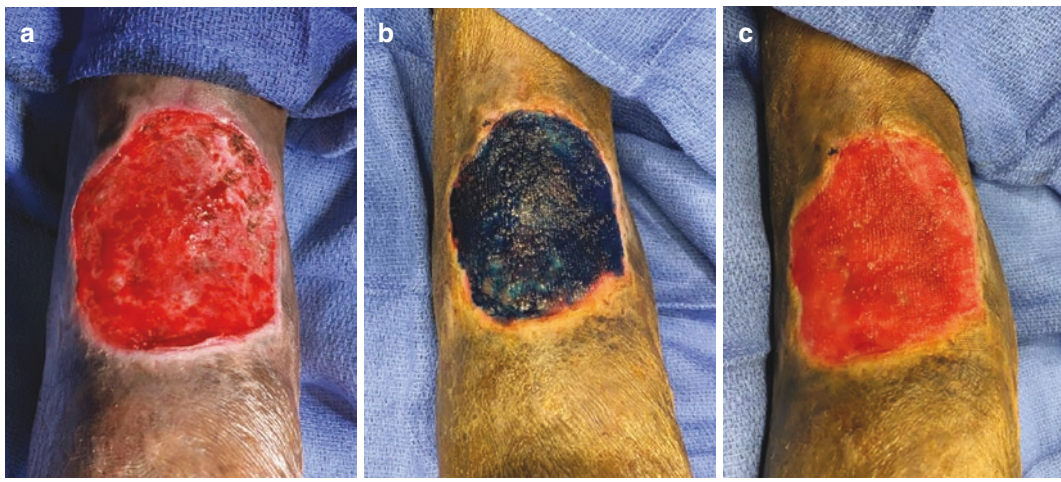


Fig. 29.1 The wound bed (**a**) is painted with methylene blue (**b**), which is removed using sharp debridements (**c**)

begin. A "classical" approach to harvesting the skin graft begins with donor site preparation [5]. The donor site is often the primary cause of distress and pain in patients recovering from STSG; therefore, care should be taken when deciding the ideal donor site for a given patient. Common STSG donor sites include anterolateral regions of the contralateral or ipsilateral thigh or leg [5]. The size of the wound should be measured in order to determine the size of the graft that needs to be harvested. One will also have to decide if the graft will be meshed or not. These factors will determine the location of harvest as well as the size of the dermatome to be used. Once the size of the graft is determined, the authors will typically mark the area out on the harvest site of the thigh (Fig. 29.2a). The donor site is further prepped by injection of tumescent solution into the harvest site in the subcutaneous layer (Fig. 29.2b). The benefits of tumescent solution injection include pain control, hemostasis, and a firm surface for graft harvest. The typical tumescent solution that the authors use includes 1 L of lactated ringers, one ampule of epinephrine, and 30 cc of 1% lidocaine plain. A large spinal needle can be used to inject the solution beneath the skin. The donor site should then be washed of any skin preparation solution, such as betadine, and generously lathered with a lubricant. The most common lubricant is mineral oil but other options could be surgical lubricating jelly, chlorhexidine scrub, or hibiclens solution (Fig. 29.3).

Various methods can be used to harvest STSG, including an oscillating Goulian knife, a surgical knife, or a powered dermatome. Challenges of manual harvesting involve irregularities in the donor site and skin graft. Due to this, power dermatomes are often the tool of choice due to their harvest consistency and the adjustability in graft thickness and width offered [8]. The power dermatome should be set to the appropriate width and thickness. In cases of chronic wounds, an intermediate-thickness STSG (0.012–0.018 in.) should be obtained [4]. Lubricant should be applied to the dermatome as well to ensure no skipping during harvest. The dermatome should be run at full speed during harvest with firm, even pressure to the skin surface. Assistants can apply traction to the donor site as well (Fig. 29.3). Following harvest, the donor site can be covered with an epinephrine- or thrombin-soaked sponge in order to minimize blood loss [8]. The authors will typically use a tumescent-soaked sponge.

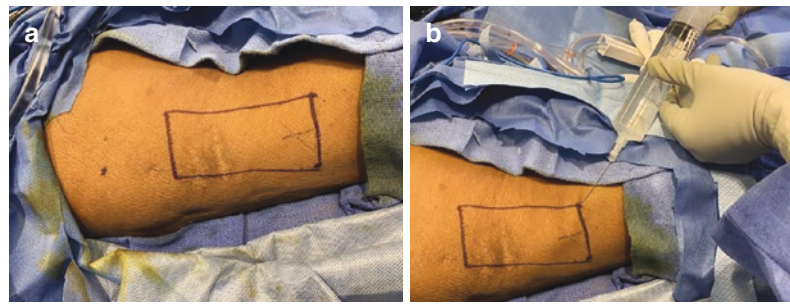


Fig. 29.2 (**a**) A marker is used to delineate the donor site, then (**b**) tumescent solution is injected into the subcutaneous layer of the donor site

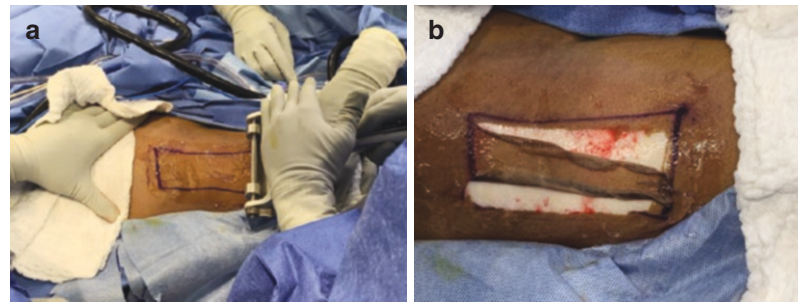


Fig. 29.3 Application of lubrication jelly at the donor site (**a**) and subsequent harvesting using a power dermatome (**b**)

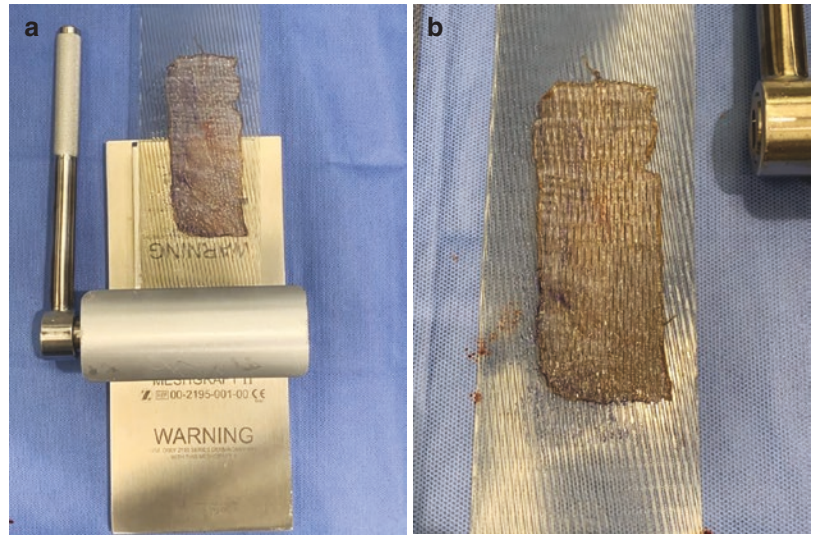


Fig. 29.4 Harvest skin placed in the hand-powered mesher (**a**) and the resultant meshed graft (**b**)

The next step involves skin graft preparation via meshing. This technique allows the graft to be stretched so that it can cover larger surface areas. Manual methods include using a scalpel to create fenestrations or "pie-crusting" the graft. A hand-powered meshing device (mesher) can also be used (Fig. 29.4). Meshers apply numerous slits at regular intervals in certain ratios. Higher ratios result in a larger degree of graft stretching, but also lead to longer healing times due to an increased area requiring epithelialization [8]. Commonly used ratios for chronic wound grafts using a mesher include 1.5:1 or 3:1. The holes created act as drainage sites to prevent blood, fluid, or seroma collection between the skin graft and its recipient bed, which can result in graft failure [4, 8]. When meshing the dermal side of the graft should be placed upwards for ease of application of the graft to the wound bed after meshing.

STSG Application

After meshing is complete, the skin graft is carefully transferred to the recipient bed, making sure to correctly orient the graft with the dermis side facing down (Fig. 29.5). If placed with the epidermis side down, the graft will fail. The graft is then secured to the recipient site with either skin staples or sutures, making sure to maintain minimal tension. Absorbable sutures like monocryl or chromic are typically utilized to secure the graft, since they do not require removal and dissolve close to the same time that the skin graft becomes adherent [8]. The authors will typically employ 4–0 monocryl in a running fashion around the wound edge.



Fig. 29.5 Placement of the skin graft on the debrided recipient site

Postoperative Healing

Various dressings and healing techniques can optimize outcomes during the postoperative period.

Donor Site Healing

Donor sites should be dressed with a nonadherent occlusive petrolatum gauze dressing covered by a transparent film dressing, such as Tegaderm [3, 5]. Some studies have also suggested the use of a polyurethane membrane over the donor wound. These donor site dressings can be removed after 2 days and should be kept dry [5]. The authors typically apply a nonadherent dressing, such as xeroform, covered with an abdominal (ABD) pad or gauze and tegaderm. Patients are instructed to leave the nonadherent layer in place until it falls off on its own. The outer dressing should be changed if saturated or soiled. The donor site will take longer to heal and continue to bleed if the nonadherent layer is frequently pulled off the donor site. Once the site is healed, patients can wash and moisturize the area regularly. Primary closure of donor sites was previously employed in instances where harvested grafts were thicker (for example 1:10,000) and thus healing times were longer. Today, the ability to harvest thinner grafts, injection of bupivacaine at the donor site, and biologic wound matrices have obviated the need for primary closure of donor sites in most cases.

While donor sites often heal successfully, patients should be counseled that donor site discomfort and pain are common [13]. Elderly patients and patients with underlying diabetes may experience a delayed or complete lack of healing at the STSG donor site. Regrafting the donor site has been proposed as a method to improve donor site healing while reducing associated pain and improving cosmesis. This can be achieved either by using a thin STSG from a separate site, or by recycling unused skin graft remnants from the original donor site rather than discarding them [13, 14]. Placement of any excess STSG at the donor site helps facilitate healing by providing scattered "islands" of tissue. Each island has its own reepithelialization potential and can improve overall epithelialization of the donor site [14]. The application of a thin STSG regraft on the donor site has been found to significantly shorten epithelialization time, reduce donor site pain, and prevent hyperplastic scar formation [13]. The secondary donor site providing the thin STSG was found to epithelialize within 5 days without any detrimental functional or cosmetic effects [13].

Recipient Site Healing

STSG dressings should provide maintenance of moisture to encourage graft viability, compression to prevent hematoma or seroma formation, reduction of shear forces to prevent movement of the graft, and overall protection from the environment. Common postoperative dressings for the recipient site include bolster dressings or NPWT [4]. The recommended polyurethane membrane for donor site coverage has utility for recipient sites as well; it can be used in place of NPWT and has been found to decrease operating room time due to the lack of suture attachment, and it can also assist with maintaining STSG hydration [5].

Bolster dressings firmly secure the graft in place with nonadherent petrolatum gauze and sterile plain sponges moistened with saline solution. They can remain on the wound for 3 weeks postoperatively [4]. Options for postoperative dressings to use with the bolster dressing include gauze, silicone splints, fibrin glue, foams, and other self-adherents [5]. A typical dressing for a STSG applied to the foot would include mepitel, an overlying sponge employed as a bolster, followed by a multilayer compressive dressing.

The alternative is the application of NPWT at the recipient site. A nonadherent dressing is placed over the graft, followed by NPWT with a wound VAC typically set between 75 mmHg and 125 mmHg of continuous pressure. The VAC should be left in place for 4–5 days postoperatively, after which it can be taken down. This is followed by the placement of a nonadherent dressing over the STSG to maintain moisture and prevent shearing [4, 5]. Studies have shown numerous benefits of using NPWT postoperatively including successful immobilization of the graft during the inosculation period in up to 97% of patients, improved graft take, reduced seroma

and hematoma formation, and improved epithelialization and STSG quality in patients treated with NPWT. Compared to conventional bolster dressings, NPWT post-skin grafts have been found to yield greater success rates for STSG, with approximately 80% less graft failure in NPWT patients compared to those treated with bolster dressings only [12]. These benefits have been attributed to increased oxygenation at the wound site, continuous removal of bacteria and exudate, maintenance of a moist wound environment, and uniform pressure application over the entire grafted area [3–5].

All patients should be non-weight-bearing to the extremity treated postoperatively. Immobilization of the graft is critical to allow for capillary ingrowth within the first 2–5 days of inosculation. In patients with isolated STSG for diabetic foot wounds, immobilization of the affected lower extremity can be achieved using a posterior splint or offloading boot to prevent movement during the healing phase [4, 5]. The STSG is expected to become engrafted within 2 weeks and fully healed in 4 weeks in nondiabetic patients [5]. In diabetic patients, studies have reported an average time to heal of 5 weeks with a range of 3–16 weeks [15]. Strict adherence to weight-bearing restrictions is crucial to STSG success and clear expectations regarding postoperative weight-bearing status should be communicated to the patient and his or her caretakers throughout the perioperative period. An example of a recipient graft on the tenth postoperative day can be seen in Fig. 29.6.



Fig. 29.6 Healing of the split-thickness skin graft on postoperative day 10

Complications and Revisions

While immense care is taken in preparing patients for lower extremity STSG procedures and caring for them postoperatively, there are still certain circumstances in which complications arise or skin grafts fail. Possible complications include infection, trauma, lack of wound bed/graft apposition, seroma or hematoma, noncompliance, and swelling, and each of these complications delays healing time by disrupting the graft and interfering with healing. Similarly, any patient requiring revisional surgery can also be expected to experience delayed healing times [15]. Studies of post-graft complication rates in diabetic patients have reported rates ranging from 2.6% to 38% [15]. Faster healing times have also been correlated with higher graft take percentage, with 100% graft take healing about 3 weeks sooner than patients with less than 95% graft take. Average time to healing is 5 weeks for non-complicated healing in diabetic patients but can increase to 10–16 weeks in patients with complications [15].

Factors Impairing Healing

Pre-existing comorbidities in diabetic patients have been found to delay healing time further by increasing postoperative infection risk and resulting in an increased need for revisional surgery when compared to nondiabetic patients. Graft failure in diabetic patients is also more common in actively smoking patients and those who experience wound infections postoperatively [3]. There is mixed evidence regarding the effect of wound size on time to healing. One study found that wound size had no effect on time to heal [15], but a separate study found that wounds >80 cm^2 were less likely to heal, with only a 52% success rate when compared to a 74% success rate in smaller wounds [3]. This finding may be due to wounds with greater cross-sectional areas having greater difficulty healing and requiring amputation more often [3].

Tissue ischemia and edema are common consequences of comorbidities such as PAD and congestive heart failure, and significantly impair

wound healing postoperatively. The inability of blood to reach the wound bed and skin graft results in inadequate supply of oxygen, nutrients, and angiogenic factors, resulting in improper healing and graft failure. Edema creates a larger barrier for oxygen diffusion and reduces the clearance of metabolites, resulting in further tissue damage and impaired graft take. Edema also reduces adherence of the skin graft by creating shearing forces and a poor environment for granulation tissue formation [12]. Congestive heart failure was found to result in a 2.55 times higher risk of STSG failure and is predictive of poor healing in both diabetic and nondiabetic patients [12].

The negative effects of fluid collection at the wound site further support the need for compressive dressings, NPWT, or bolster dressings postoperatively. If compromised oxygen delivery to wound tissues is of concern, hyperbaric oxygen has been found to increase levels of free oxygen available in capillaries, positively impacting healing through collagen synthesis and cross-linking, angiogenesis, and fibroblast proliferation. Hyperbaric oxygen therapy is indicated in patients requiring graft salvage secondary to skin graft failure [4].

Revisional Procedures

Impending graft failure may appear as an overly black eschar or a porcelain white graft—findings that are typically seen within 1–2 weeks of grafting. These findings may indicate only superficial necrosis with survival of the dermal portion of the graft. If this is the case, the patient should be educated that after several weeks they may notice superficial sloughing or necrosis, which will eventually be replaced by healthy tissue [16].

In cases of partial graft loss or graft failure, therapies are available to assist in promoting wound healing. Wet or moist saline-soaked gauze or dressing can be used to treat partial graft loss, allowing for secondary healing. In the case of complete graft loss, the wound bed should be reassessed for infection and vascularization status. If both are optimized, regrafting can be attempted once more. Alternatively, in certain circumstances the failed graft can be left in place to act as a biologic dressing over the wound to allow healing by secondary intention. Despite measures taken to preserve the limb, some patients may ultimately require free tissue transfer or major limb amputation [3].

Conclusion

The immense care and consideration that goes into preparing and treating patients with STSG is made possible in large part through a multidisciplinary team approach. A collaborative interprofessional team allows for streamlined and effective treatment of otherwise complex, comorbid patients. Numerous medical consultations should be requested as necessary to address patients' comorbidities preoperatively; these may include but are not limited to members from podiatric surgery, plastic surgery, vascular surgery, rheumatology, nephrology, cardiology, medicine, wound care, nutrition, orthopedic surgery, nursing, and physical therapy [4].

Postoperative coordinated care can be achieved by proper delineation of the donor site, recipient site, and date of the next dressing change by the surgical team, allowing the entire healthcare team to treat the patient appropriately. Nurses involved in patient care should be made fully aware of postoperative care management in STSG patients. Team roles should also include daily monitoring of the recipient site for bleeding, infection, and ischemia, with any change in the wound resulting in immediate notification of the surgeons involved. Wound dressing changes should occur according to surgeon preference and explicit instructions should be communicated to patients and caretakers prior to discharge [8].

Lower extremity chronic wounds treated with STSG are often delicate and complicated cases. Multidisciplinary care allows for the assembly of complex and adaptive plans of treatment, helping to ensure the best outcomes in terms of graft take and recovery.

Case Report

A 73-year-old female with a past medical history of type II diabetes mellitus, congestive heart failure, hypothyroidism, and necrobiosis lipoidica diabeticorum (NLD) presented to the wound care clinic for evaluation of a chronic left lower leg ulcer. The patient experienced moderate-to-severe "burning" pain with intermittent exacerbations associated with the wound. The ulcer occasionally drained significant amounts of fluid.

At the time the ulcer first appeared, the patient's legs were edematous, and her wound was assumed to be a venous ulcer secondary to venous stasis insufficiency. It was initially treated using compression (Unna boots, ACE wraps) and topical wound care, including silver alginate and zinc oxide. The patient also underwent venous ablation, which provided transient improvement, but the ulcer eventually grew in size despite the continued use of compression products. Of note, a previous venous ulcer of the right leg improved after the vein was removed. Due to her prior diagnosis of NLD and the presence of lesions bilaterally on her legs, the patient believed this wound was caused by her NLD as well. New lesions appeared when the patient experienced stress, but this was the first episode of wound ulceration. Topical steroids such as clobetasol and fluticonoid were applied as standard treatment for NLD but were discontinued since they did not improve healing of the wound and there was concern for inhibition of healing.

At the patient's first visit to the wound care clinic, notable vitals included hypertension and a BMI of 44. The patient's diabetes was relatively well controlled, with a HbA1c of 6.2%. The patient's HbA1c remained less than 6.5% throughout the course of her care. On physical exam, she had 2+ pulses bilaterally in her lower extremities and 2+ pitting edema at the dorsum of her left foot. She had normal range of motion in all four extremities. On her distal left lower extremity, there was a near circumferential and well-circumscribed ulcer measuring 22 × 10.2 cm with a clean base, areas of reepithelialization, and an erythematous rim. The wound had no odor, fluctuance, crepitus, warmth, or active drainage. On her right anterior lower leg, an erythematous to yellow-tinged atrophic, shiny plaque with overlying telangiectasias consistent with NLD was noted.

After establishing care, the patient was seen by the wound care clinic, dermatology, and rheumatology to provide care for her left lower extremity wound. A consensus was made that the etiology of the wound was likely multifactorial, resulting from a combination of venous stasis and early lipodermatosclerosis, recurrent wound colonization and infection, and diabetic components such as NLD and bullous diabeticorum that prevented the ulcer from healing. Treatment with oral and injectable steroids was begun, which for some time helped to reduce the size of the ulcer, support the creation of skin islands, and stabilize the wound. Approximately 9 months after the patient's initial presentation to the wound clinic, there was increased drainage and erythema of the ulcer, with the wound bed measuring 15 × 12 cm. In early 2019, the patient developed a malodorous, fibrogranular right heel ulcer as well, measuring 2.1 × 2 cm. Based on later biopsies of her wounds, dermatology ruled out pyoderma gangrenosum as the etiology and recommended against the use of steroids or other immunosuppressant therapies.

The patient underwent a total of 11 irrigation and debridement procedures of her bilateral lower extremity ulcers over the course of 2 years following her initial presentation to the wound clinic. She underwent her first STSG application nearly 2 years after her initial presentation. The STSG was harvested from the patient's left thigh and applied to her leg wounds bilaterally, with the left ulcer measuring 22 × 14 cm and the right ulcer measuring 4 × 2 cm at the time of application. The STSG was 1/10,000 in. thick and was meshed in a 3:1 ratio. The graft was secured to the ulcers using Dermabond. Three weeks following this application, the donor site appeared completely healed (Fig. 29.7a), and there was 95% flap take on the left lower extremity (Fig. 29.7b) and 90% graft take at her right lower extremity (Fig. 29.7c). Both grafts appeared healthy, clean, well adhered, and well perfused. Within 7 weeks, both grafts had fully healed.



Fig. 29.7 (**a**) Healing of the donor site on postoperative day 22, (**b**) healing of the left lower extremity ulcer by STSG, and (**c**) healing of the right lower extremity ulcer by STSG

Two months following STSG application, the patient began experiencing breakdown of her left lower extremity skin graft with the formation of a 3.5 × 1.5 cm ulcer. Graft breakdown was believed to be secondary to reduced ambulation, weight gain, and worsening lymphedema. Her right lower extremity STSG, however, remained intact. One year after the first STSG, the ulcerative wound bed that developed from the patient's left lower extremity graft enlarged to 11 × 6 cm. The patient underwent debridement of the left lateral leg compartment and peroneal tendon, followed by the application of a second STSG to the wound bed 4 days later. The same protocol, including donor site, graft thickness, and mesh ratio, was used for the repeat STSG. Within 1 week, there was 100% graft take on the patient's left leg. Despite proper postoperative care including leg elevation and the use of lymphedema pumps, the patient developed two ulcers in the graft within 4 months of repeat STSG application. The ulcers had a fibrogranular base and produced green drainage. Wound bed cultures grew *Pseudomonas aeruginosa* and at most recent follow-up (approximately 2 years after initial presentation) the patient is undergoing ongoing therapy with several topical and oral antibiotics. Despite the complex features of this patient's wound etiology, this case demonstrates the ability of STSG to serve as a reliable source of wound coverage, even in instances when repeat grafting is required.Disclosure StatementThere are no financial disclosures, commercial associations, or any other conditions posing a conflict of interest to report for any of the above authors.

References

1. Ratner D. Skin grafting. From here to there. Dermatol Clin. 1998;16(1):75–90. https://doi.org/10.1016/s0733-8635(05)70488-5.
2. Blok CS, Vink L, Boer EM, Montfrans CV, Hoogenband HM, Mooij MC, et al. Autologous skin substitute for hard-to-heal ulcers: retrospective analysis on safety, applicability, and efficacy in an outpatient and hospitalized setting. Wound Repair Regen. 2013;21(5):667–76. https://doi.org/10.1111/wrr.12082.
3. Rose JF, Giovinco N, Mills JL, Najafi B, Pappalardo J, Armstrong DG. Split-thickness skin grafting the high-risk diabetic foot. J Vasc Surg. 2014;59(6):1657–63. https://doi.org/10.1016/j.jvs.2013.12.046.
4. Ramanujam CL, Zgonis T. Stepwise surgical approach to diabetic partial foot amputations with autogenous split thickness skin grafting. Diabet Foot Ankle. 2016;7(1):27751. https://doi.org/10.3402/dfa.v7.27751.
5. Mccartan B, Dinh T. The use of split-thickness skin grafts on diabetic foot ulcerations: a literature review. Plast Surg Int. 2012;2012:1–6. https://doi.org/10.1155/2012/715273.
6. Iwuagwu FC, Wilson D, Bailie F. The use of skin grafts in postburn contracture release: a 10-year review. Plast Reconstr Surg. 1999;103(4):1198–204. https://doi.org/10.1097/00006534-199904040-00015.
7. Thornton JF, Gosman AA. Skin grafts and skin substitutes and principles of flaps. In: Selected readings

in plastic surgery, vol. 10. 1st ed. Dallas, TX: Selected Readings in Plastic Surgery; 2004. p. 1–6.
8. Braza ME, Fahrenkopf MP. Split-thickness skin grafts. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2020. https://www.ncbi.nlm.nih.gov/books/NBK551561/. Accessed 31 Jul 2020.
9. Sanniec K, Nguyen T, Asten SV, Fontaine JL, Lavery LA. Split-thickness skin grafts to the foot and ankle of diabetic patients. J Am Podiatr Med Assoc. 2017;107(5):365–8. https://doi.org/10.7547/15-200.
10. Walters ET, Pandya M, Rajpal N, Abboud MM, Elmarsafi T, Steinberg JS, et al. Long term outcomes of split-thickness skin grafting to the plantar foot. J Foot Ankle Surg. 2020;59(3):498–501. https://doi.org/10.1053/j.jfas.2019.09.027.
11. Naz I, Walters ET, Janhofer DE, Penzler MM, Tefera EA, Evans KK, Steinberg JS, Attinger CE, Akbari CM, Kim PJ. Outcomes of Split-thickness skin grafting for foot and ankle wounds in patients with peripheral arterial disease. Wounds. 2019;31(11):272–8.
12. Turissini JD, Elmarsafi T, Evans KK, Kim PJ. Major risk factors contributing to Split thickness skin graft failure. Georgetown Med Rev. 2019;3:1.
13. Bian Y, Sun C, Zhang X, Li Y, Li W, Lv X, et al. Wound-healing improvement by resurfacing split-thickness skin donor sites with thin split-thickness grafting. Burns. 2016;42(1):123–30. https://doi.org/10.1016/j.burns.2015.07.008.
14. Bradow BP, Hallock GG, Wilcock SP. Immediate Regrafting of the Split thickness skin graft donor site assists healing. Plast Reconstr Surg Glob Open. 2017;5(5):e1339. https://doi.org/10.1097/gox.0000000000001339.
15. Anderson JJ, Wallin KJ, Spencer L. Split thickness skin grafts for the treatment of non-healing foot and leg ulcers in patients with diabetes: a retrospective review. Diabet Foot Ankle. 2012;3(1):10204. https://doi.org/10.3402/dfa.v3i0.10204.
16. Prohaska J, Cook C. Skin grafting. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2020. https://www.ncbi.nlm.nih.gov/books/NBK532874/. Accessed 11 Sep 2020.

30 Local Flaps for Reconstruction and Limb Salvage of the Foot and Ankle

David Z. Martin and Gabriel Del-Corral

Introduction to Local Flap Reconstruction of the Foot

Despite the challenges posed by the diabetic foot, local flap reconstruction of the lower extremity can be performed with success rates greater than 90% in the appropriately selected patient. The success matches that of free flap reconstruction with lower overall reoperation rate [1].

In order for local flap reconstruction to succeed, the surgeon must adhere to the basic principles of reconstructive surgery. The foot is an unforgiving anatomic location. Ensuring a well-vascularized wound with respect to the angiosomes and performing serial debridements prior to reconstruction are crucial to success. Similarly, a respect for the underlying bony pathology or tendon imbalance will impact long-term success. Finally, flap selection will be impacted by vascular status, tissues requiring coverage, and location of wound. The value of good postoperative care cannot be overstated. Designing a postoperative protocol that patients can reasonably follow and involving them in the care plan is vital.

Ensuring a well-vascularized limb as early as possible during limb salvage can increase the chances of a good outcome. The surgeon must think beyond the ankle-brachial index as an indicator of adequate perfusion. Waveform analysis and determining whether the flow is antero or retrograde into each of the six angiosomes inform the surgeon about the vascularity of the wound and the availability of local reconstructive options. When the flow is inadequate, the surgeon must partner with the vascular interventionalist to ensure adequate perfusion. The six angiosomes of the foot include the calcaneal, medial, and plantar branches of the posterior tibial artery, the anterior perforating and calcaneal branches of the peroneal artery, and the dorsal pedis artery originating from the anterior tibial artery [2].

Prior to flap repair, the foot must be free of all devitalized tissue and infection. Debridement is fundamental and multiple debridements are typically required. Instituting a practice of debriding to negative post-debridement qualitative culture has been shown to improve success in local flap reconstruction of the foot at 90 days [3].

Bone pathology and tendon imbalance should be assessed as part of the reconstructive plan. Osteomyelitis is managed surgically with post-debridement cultures and pathologic margins directing decisions regarding length of antibiotic therapy. Major Charcot reconstructions or tendon rebalancing may be delayed until after successful wound reconstruction. However, planning for the management of these pathologies is important at

D. Z. Martin (✉) · G. Del-Corral
Department of Plastic and Reconstructive Surgery, Georgetown University Medical Center, Washington, DC, USA
e-mail: David.z.martin@medstar.net; Gabriel.A.DelCorral@medstar.net

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_30

the time of closure to improve the chances of long-term functional limb restoration.

Once the wound has been adequately prepared, the vascular status optimized, and structural pathology assessed, flap repair can proceed.

Flap selection is based upon the location and size of the wound, the involved structures (bone, tendon, nerve, or artery), and whether the tissue will be weight-bearing.

Local flap reconstruction is generally reserved for smaller defects. However, it can be combined with skin substitutes and autografting to achieve broader wound coverage if the vital structures can be covered with the local flap. Wound closure alone is not sufficient in functional limb restoration. Consideration must be given to the durability of the reconstruction over time.

Local foot flaps can be skin only, axial or perforator based, or include intrinsic muscles. It is often necessary to skin graft the donor site. Keeping the donor site on a non-weight-bearing surface will improve the durability of the repair.

Intrinsic muscles are good choices when available to cover bone. The choice is typically based upon the location of the wound. Commonly used intrinsic muscles of the foot include: Abductor digiti minimi (for lateral ankle and calcaneal coverage), abductor hallucis brevis (for medial midfoot, heel, and ankle coverage), extensor digitorum brevis (for anterior ankle coverage), and flexor digitorum brevis (for plantar heel coverage) [4].

When muscle is not needed or available, pedicled skin flaps can be useful. These include flaps based upon the following: first dorsal metatarsal artery, lateral calcaneal artery, medial plantar artery, and the reverse sural artery.

Finally, fillet toe flaps, random flaps, and tissue expansion can be utilized to round out the choices for local flap reconstruction of the foot.

Abductor Digiti Minimi Muscle Flap

The adductor digiti minimi (quinti) [ADM] muscle provides a small but reliable flap for reconstruction of the proximal to mid-plantar and lateral foot. It is a type II Mathes-Nahai flap and it is a straightforward elevation. The donor site is typically closed primarily. The muscle itself can be grafted or small defects left to heal secondarily.

Anatomy

The ADM muscle originates from the calcaneal tuberosity. It travels along the plantar lateral aspect of the foot to the base of the fifth metatarsal and then on to the lateral base of the fifth toe proximal phalanx. The dominant pedicle is a branch off the lateral plantar artery proximally. It is used as a proximally based flap.

Surgical Technique

Flap elevation is typically performed under regional anesthesia without tourniquet control. Loupe magnification and a handheld doppler can facilitate identification of minor and major pedicles. Surgical approach begins with a plantar lateral incision along the course of the muscle (Fig. 30.1). Existing wounds may be incorporated into the incision plan. The subcutaneous fat pad is easily separated from the muscle fascia on its superficial aspect. The tendon is released distally at the base of the fifth toe and dissection proceeds proximally. Suture tagging of the tendon can aid dissection. The muscle is separated from the flexor digitorum minimi brevis medially. The muscle easily separates from the metatarsal dorsally. Ligation of minor pedicles can be done with bipolar cautery or ligation clips. The pedicles are identified along the medial border of the muscle.



Fig. 30.1 Incision is planned along the lateral glabrous junction. Fifth metatarsal base is outlined

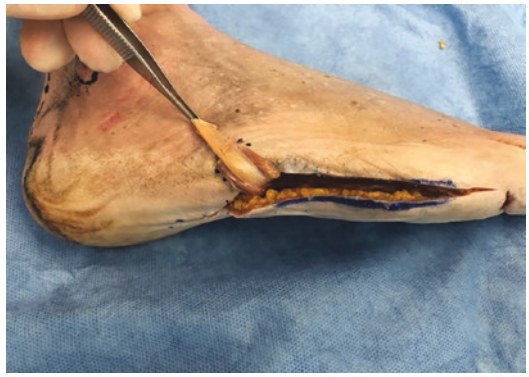


Fig. 30.2 ADM proximally transposed



Fig. 30.3 ADM extended by releasing attachments to metatarsal base while preserving vascular pedicle

Dissection proceeds proximally as needed for length depending on the location of the wound (Figs. 30.2, 30.3 and 30.4). The major pedicle is identified as a branch of the lateral plantar artery at approximately the level of the proximal cuboid [5] (Fig. 30.3). Care is taken at inset to prevent kinking of the pedicle. Doppler and physical assessment can assure safe transposition. The muscle can be inset with absorbable suture. Immediate skin grafting can be performed if needed.

Abductor Hallucis Muscle Flap

The abductor hallucis (ABH) muscle is usually used as a proximally based flap to cover defects at the medial aspect of the foot. It is classified as a Mathes-Nahai type II, supplied by one major proximal pedicle and minor distal pedicles. The flap is primarily useful for reconstructions of the calcaneus, medial malleolus, and medial midfoot. The muscle belly of the flap can be harvested with minimal morbidity and the scar is hidden in a non-weight-bearing area. The small muscle belly is ideal for closure of defects less than or equal to 3–6 cm. Structural stability and resistance to infection are the main advantages of muscle flaps in comparison to fasciocutaneous flaps when used for reconstruction of the sole of the foot [6].



Fig. 30.4 ADM proximally transposed after release from metatarsal base

Anatomy

The abductor hallucis muscle flap receives its blood supply from both the dorsal and ventral plantar system. The three main vessels are: the medial plantar artery, the deep branch of the medial plantar artery, and the superficial branches of medial plantar artery (Figs. 30.5, 30.6, 30.7 and 30.8). The lateral plantar artery is preserved during flap harvest, conserving the blood supply to the sole of the foot [7].

Surgical Technique

The procedure is started with the patient under general or spinal anesthesia. Tourniquet control can be used, but it is not necessary. A ventral incision is made along the medial aspect of the foot towards the axis of the first metatarsal. The plantar fascia is incised from the medial and lateral

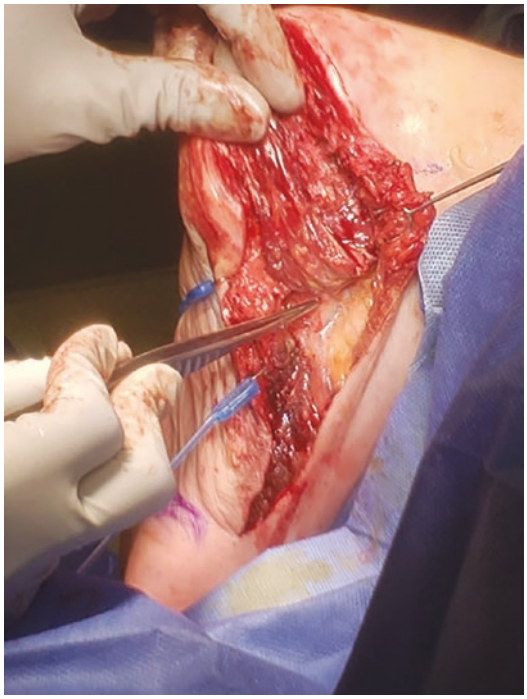


Fig. 30.5 Abductor hallucis muscle: elevation with perforator from the medial plantar artery

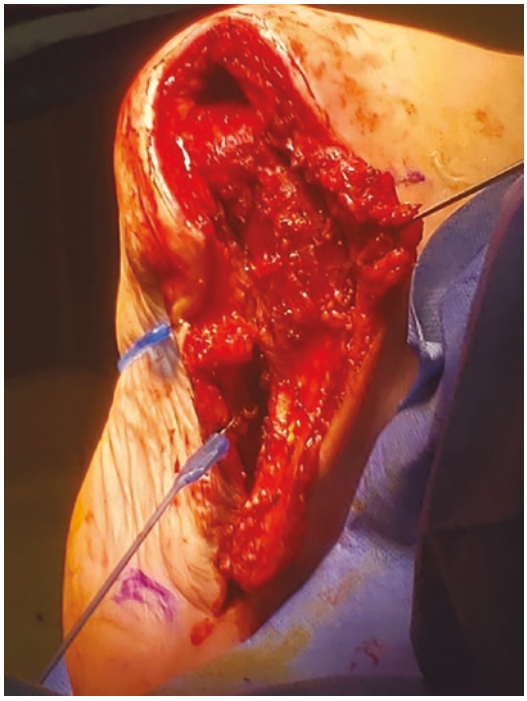


Fig. 30.6 Abductor hallucis muscle flap and calcaneal defect



Fig. 30.7 Flap inset and closure

border of the abductor hallucis. The insertion of the abductor hallucis is identified at the calcaneal tubercle. The muscle belly is dissected off the base of the proximal phalanx of the hallux. Supra-muscular dissection between the Abductor Hallucis muscle and the Flexor Hallucis Brevis tendon allows for complete exposure of the flap. Muscular branches from the medial plantar artery should be carefully preserved. The flap is then rotated proximally and inset into the calcaneal defect (Fig. 30.6). To prevent compression of the pedicle, the calcaneal attachments/plantar fascia can be released. If a greater arc of rotation is needed, the flap can be raised as an island flap allowing better rotation and more tissue bulk [8, 9].

The donor site can be covered with xenograft, and negative wound pressure therapy. A split thickness skin graft can be used 3 weeks later. The patient should remain on weight-bearing restrictions for 4 weeks until there is full incorporation of the graft (Fig. 30.7).

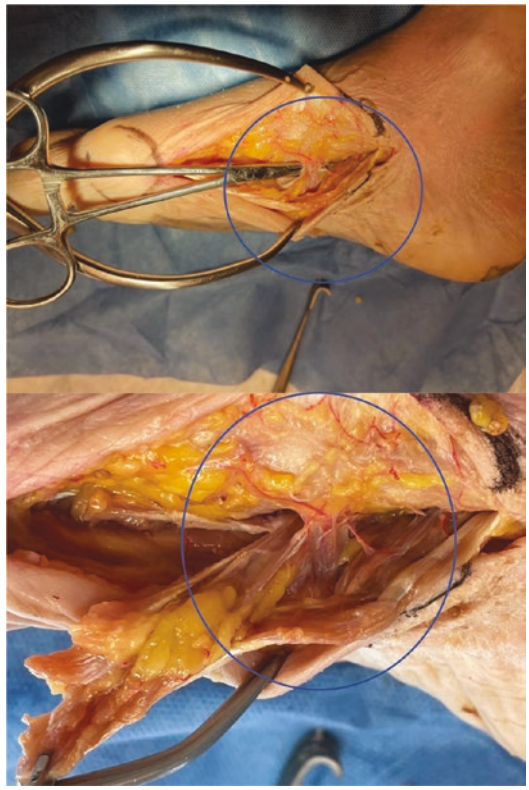


Fig. 30.8 Latex injection. Abductor hallucis muscle with muscular perforator from the medial plantar artery

Extensor Digitorum Brevis Muscle Flap

The extensor digitorum brevis [EDB] muscle flap provides muscle coverage for anterior and lateral ankle defects. Its donor site can be closed primarily. Its harvest, however, results in incisions within the dorsalis pedis [DP] angiosome which can result in wound healing complications. To extend the EDB distal ligation of the DP artery is required. Care should be taken with this flap to ensure adequate collateral circulation from the lateral plantar artery [4]. Its size makes it more appealing than other intrinsic muscle flaps for larger (5×7 cm) defects around the ankle and calcaneus [10].

Anatomy

The Extensor Brevis (EB) muscle originates from the tendocalcaneal ligament of the lateral foot. It

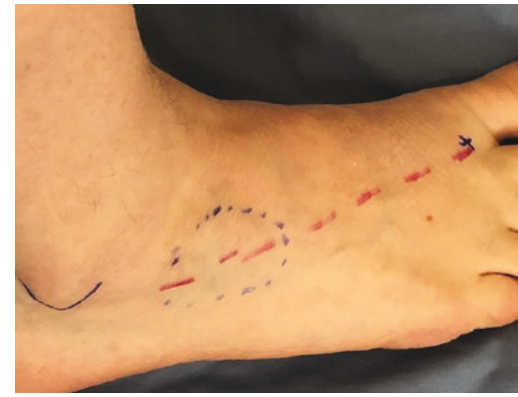


Fig. 30.9 A lazy S incision can be designed along the axis of a line from the lateral malleolus to the first web space

inserts into the extensor longus tendons of toes 2–4 and into the proximal phalanx of the hallux via the extensor hallucis brevis muscle. The lateral tarsal artery is the dominant pedicle entering proximally under the muscle belly [11] as a direct branch from the dorsalis pedis (DP) artery. It is a Mathes-Nahai type II vascular supply [12].

Surgical Technique

The operation is performed with the patient in the supine position under general or regional anesthesia. The EB muscle belly can be identified by having patients extend their toes preoperatively. A curvilinear incision is made along a line from the lateral malleolus to the first dorsal webspace (Fig. 30.9). The lateral tarsal branch of the DP is identified distal to the retinaculum along with the motor branch of the deep peroneal nerve.

Dissection is performed between the extensor hallucis longus and extensor digitorum longus [EDL] (Fig. 30.10). Creating a plane, dissection proceeds from medial to lateral elevating the EDL from the EB. Incising the extensor retinaculum facilitates this elevation. Once the plane is developed, the EB tendon are divided distally and the flap is elevated distally to proximally. The lesser vascular pedicles are ligated, preserving the lateral tarsal artery and deep peroneal nerve (Fig. 30.11). The arc of rotation can then be extended by ligating the DP distal to the pedicle (Fig. 30.12) [12]. The donor site is closed primarily. The ED muscle belly can be grafted.

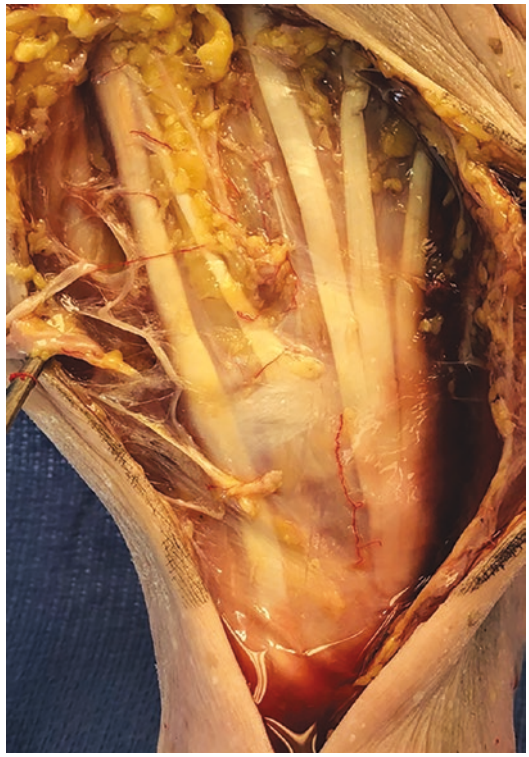


Fig. 30.10 A plane is developed between the EHL and EDL. Dissecting medially to laterally the EDL is dissected off the EB muscle

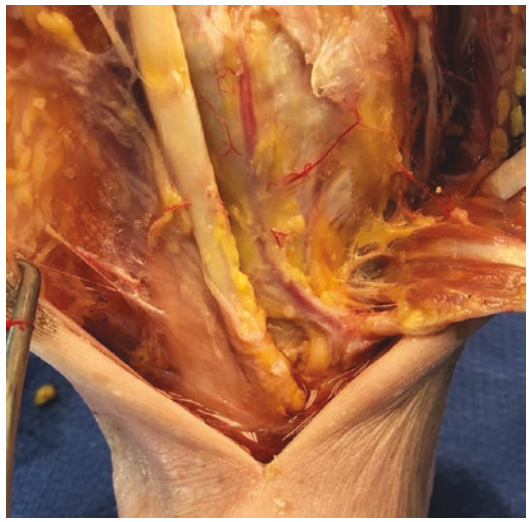


Fig. 30.11 The EB tendons are released distally and the flap is elevated, ligating the distal pedicles and preserving the lateral tarsal artery



Fig. 30.12 If more length is needed the DP artery is ligated distal to the pedicle and the arc of rotation is increased. Muscle is shown over the lateral malleolus

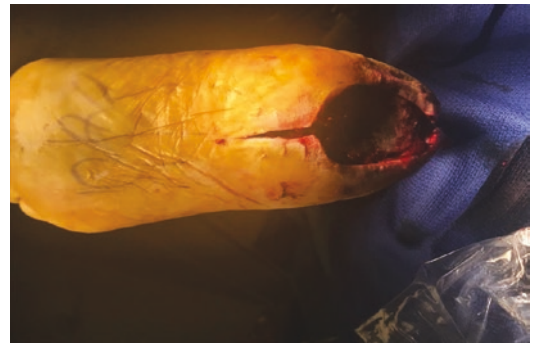


Fig. 30.13 Calcaneal wound with osteomyelitis. (*Courtesy Paul J Carroll, DPM)*

Although typically used as a proximally based flap, there are reports in the literature of using retrograde flow through the DP artery to provide muscle coverage to the forefoot [13].

Flexor Digitorum Brevis Muscle Flap

The flexor digitorum brevis [FDB] is a proximally based muscle flap. It is typically used to cover calcaneal defects. It is a Mathes-Nahai type II flap. Because it is a muscle flap, it is well suited for the management of osteomyelitis (Fig. 30.13). Although the donor site is closed primarily, skin grafting is typically used to cover the muscle after inset.

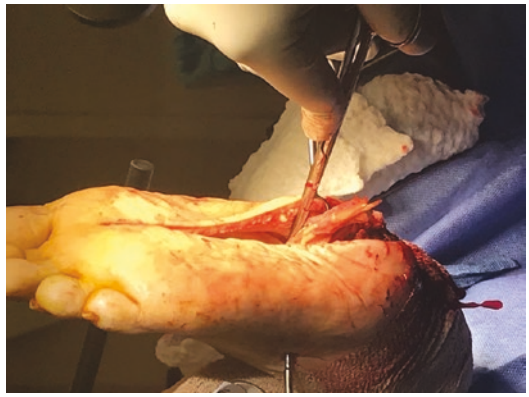


Fig. 30.14 Flap elevation through plantar midline with transposition. (*Courtesy Paul J Carroll, DPM)*



Fig. 30.15 Flap inset. (*Courtesy Paul J Carroll, DPM)*



Fig. 30.16 Primary closure of donor site with integra grafting of muscle. (*Courtesy Paul J Carroll, DPM)*

Anatomy

The flexor digitorum muscle originates from the medial process of the calcaneus and inserts into the middle phalanges of toe two, three, four, and five via tendons. The plantar fascia lies immediately superficial to it and the muscle is bordered medially by the abductor hallucis and laterally by the abductor digiti minimi. The lateral plantar artery is dominant. The artery enters within the proximal one third of the muscle [14].

Surgical Technique

Flap elevation is typically performed under regional anesthesia without tourniquet control. Loupe magnification and a handheld doppler can facilitate identification of minor and major pedicles. A midplantar incision is made with dissection performed to the plantar fascia (Fig. 30.14). The fascia is longitudinally incised and elevated medially and laterally exposing the muscle belly of the flexor digitorum brevis. The fascia can be included in the flap if additional bulk is needed. The muscle is exposed distally until the tendons are identified. The tendons are divided and the flap is dissected distally to proximally. The flap is dissected off the quadratus plantae which lies deep to the flap. Care is taken to preserve the perforators from the medial and lateral plantar arteries. The muscle is rotated into position (Fig. 30.15). The donor site is closed with permanent monofilament suture and muscle can then be grafted (Fig. 30.16). Disoriginating the muscle and elevating the lateral plantar artery are techniques that can extend the reach of this flap [15]. If the lateral plantar artery is included in the flap, care must be taken to ensure the dorsalis pedis pulse is preserved.

First Dorsal Metatarsal Artery Flap

The first dorsal metatarsal artery (FDMA) flap has been useful in the reconstruction of the defects on the dorsomedial side of the distal foot. The initial report of the FDMA flap was published by McCraw and Furlow in 1975 [16]. Ishikawa later described the distally based FDMA flap that was used to reconstruct the defects of the great toe, as well as the first ray

defects [17]. The vascular branching pattern allows for multiple variations of the flap including adipofascial and fasciocutaneous in reverse, propeller-type, and proximal transposition options (Fig. 30.17).

Anatomy

The first dorsal metatarsal artery originates from the dorsalis pedis or the deep plantar artery. The course of the first dorsal metatarsal artery (FDMA) has three variations relating to its orientation with respect to the first dorsal interosseous muscle belly. In 10% of cases it can course superficial to the muscle. In the majority of cases, the artery passes under the muscular arch formed by the tibial head of the first dorsal interosseous muscle and runs adjacent to the first metatarsal bone. The tibial head can be easily divided and the artery can be easily dissected in this space. No intramuscular dissection is needed. Multiple cutaneous perforators can be identified between the heads of the first and second metatarsals. The FDMA distal branch assumes a more superficial course after piercing the metatarsal ligament and frequently connects with the medial plantar artery [18].



Fig. 30.17 First dorsal metatarsal artery flap: latex injection flap outline

Surgical Technique

The operation begins with doppler ultrasound for identification of the first dorsal metatarsal artery and dorsalis pedis artery. A vein finder or a tourniquet without exsanguination can be used to delineate the venous network. Dissections proceed by incising a skin island directly over the audible perforator. The flap is then elevated in the subfascial plane until identification of the distal segment of the first dorsal metatarsal artery.

The dissection now proceeds, proximally, until identification of the proximal pedicle. Careful transection of all fascial attachments surrounding the pedicle follows to minimize the risk of venous congestion and flap failure. If a larger arc of rotation is needed, resection of the EHB muscle can be performed to allow for a tension-free flap inset [19]. The flap can be rotated up to 180°, making this flap useful to cover defects of the dorsum of the toe or webspace or defects exposing tendons on the distal dorsum of the foot [20] (Fig. 30.18).

The donor site can be closed primarily or with the assistance of a skin graft or skin substitute. Immobilization of the foot is recommended for 1 week with a posterior splint for support.

After this period, the patient can be transitioned into a walking boot until the incision is completely healed. Custom inserts and shoe gear can be useful in maintaining an even distribution of weight across the foot and decrease pressure over the flap site.

Lateral Calcaneal Artery Skin Flap

The lateral calcaneal artery (LCA) skin flap is a durable and reliable method of reconstructing the posterior heel and calcaneus of small and medium sized defects. Alternative methods of reconstruction in this area include free tissue transfer or skin grafting depending on the patient and wound conditions. This flap was described in detail in 1981 by William Grabb and Louis Argenta [21].

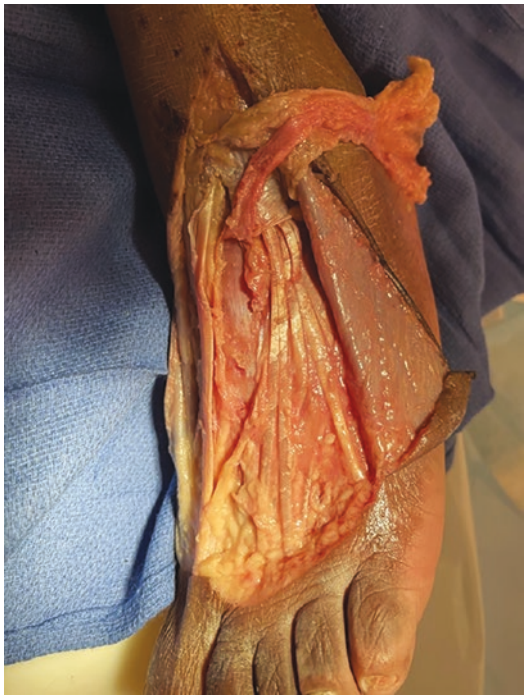


Fig. 30.18 First dorsal metatarsal artery flap: flap elevation at the level of the dorsalis pedis artery



Fig. 30.19 Lateral calcaneal artery flap after incision prior to dissection



Fig. 30.20 The proper plane for elevation is best found through the posterior incision at the periosteal level

Anatomy

The lateral calcaneal artery skin flap is a proximally based neurovascular skin flap that includes the lateral calcaneal artery, lesser saphenous vein, and sural nerve. The LCA is a branch of the peroneal artery. It arises at the level of the lateral malleolus between the Achilles and peroneal tendons. It travels distally into the foot giving rise to several smaller branches and terminating at the base of the fifth metatarsal (Fig. 30.21) [22].

Surgical Technique

The procedure is performed in the lateral decubitus or prone position. This can be done under regional or general anesthesia, with or without tourniquet control. The patency of the artery is assessed preoperatively with handheld doppler or angiography. After proper wound bed preparation, the flap can be designed. The base of the flap extends from the lateral border of the Achilles to the posterior border of the lateral malleolus. The base can start just proximal to the malleolus (Fig. 30.19). For posterior defects, the flap extends distally towards the plantar heel for a distance of approximately 8 cm. The distal posterior incision can be made down to the periosteum to identify the proper plane (Fig. 30.20). Once the flap is released distally, the dissection can proceed proximally. Care is taken along the anterior border where branches of the calcaneal artery and the sural nerve are continuing into the foot. The flap is elevated making sure to retain the LCA in the flap which runs deep to the subcutaneous tissue (Figs. 30.21 and 30.22). It is dissected proximally until an adequate arc of rotation is achieved to reach the defect in a tension-free manner (Figs. 30.23 and 30.24). The donor site typically requires skin grafting.



Fig. 30.21 In well-vascularized feet the flap can be extended by curving the flap design onto the foot and preserving the LCA and sural nerve as it curves distal to the lateral malleolus



Fig. 30.22 The flap is then elevated distal to proximal



Fig. 30.23 Anterior rotation of the flap



Fig. 30.24 Posterior rotation of the flap

Medial Plantar Artery

The medial plantar artery flap was first described by Shanahan et al. in 1979, as a rotational skin flap isolated on the medial plantar artery for coverage of plantar defect. The medial plantar flap is a fasciocutaneous flap (Mathes-Nahai Type B) that overlays the instep area between the first metatarsophalangeal joint (MTPJ) and the calcaneus (midline of heel). The midline and the navicular tuberosity are lateral and medial limits, respectively.

This flap is composed of glabrous skin that is ideally suited for reconstruction of weight-bearing portions of the foot, such as the heel. The flap can also be harvested as a neurotized flap of protective sensation of the heal or as a free flap for distant defects. Free flap reconstruction using the medial plantar artery has been described for sensate for finger pulp reconstruction [23, 24].

Anatomy

The skin flap is supplied by the medial plantar artery, a branch of the posterior tibial artery, which is one of the two terminal branches of the tibial–peroneal trunk. The medial plantar artery is the smaller of the two terminal branches of the posterior tibial artery, the other being the lateral plantar artery. The medial plantar nerve travels with the pedicle and it is a terminal branch of the posterior tibial nerve. The flap (12 × 6 cm maximum) can be islanded and pedicled on these vessels to cover defects on the heel. Another variation

is the distally based medial plantar artery flap which is supplied by retrograde blood flow through the medial plantar artery [25].

Surgical Technique

The procedure is performed under general or spinal anesthesia. A doppler ultrasound is used to map the perforator over the medial plantar artery and the posterior tibial artery behind the malleolus. A straight line connecting this point and the plantar aspect of the first metatarsal space denotes the midaxis of the flap (Fig. 30.25). This line is divided into three equal parts. The perforator usually emerges in between the middle and distal third and the flap is centered over the perforator. The distal border should be kept 2 cm behind the metatarsal heads in order to avoid the weight-bearing area [26].

The operation proceeds by making an incision along the medial border of the flap. Elevation of the flap now proceeds in the subfacial level and below the plantar aponeurosis. The neurovascular bundle now lies in between the flexor digitorum brevis (FDB) muscle laterally and abductor hallucis (AbH) muscle medially. Each muscle is retracted in the opposite direction to expose the pedicle and the medial plantar nerve. Sometimes, it is recommended to add a portion of the adductor hallucis and flexor digitorum brevis muscles along with the flap.

The pedicle can now be identified distally and divided to allow for proximal dissection. The dissection should remain in the subfacial level and continue to the level of the calcaneal tuberosity. The remaining of the lateral incisions can now be made after pedicle elevation and the flap is completely elevated (Fig. 30.26). The abductor hallucis muscle can be divided in order to increase the arc rotation of the flap (Fig. 30.27). Venous insufficiency can result as the venae comitantes are quite small. To lessen this possibility, a superficial vein (if encountered) can be harvested and preserved with the flap [27]. The main trunk of the medial plantar nerve should be preserved to avoid sensory loss over the distal foot (Fig. 30.28). Donor site closure proceeds with the use of a full

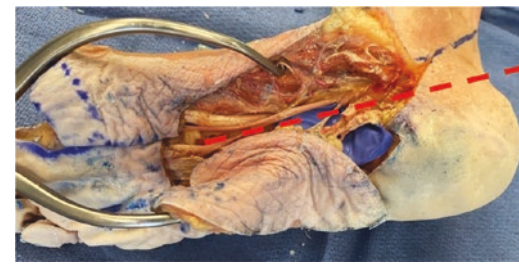


Fig. 30.26 Medial plantar flap: flap dissection



Fig. 30.27 Medial plantar artery flap pedicle dissection (red arrow). Medial plantar nerve dissected with flap for flap neurotization (black arrow)



Fig. 30.25 Medial plantar artery flap: skin markings (red line)



Fig. 30.28 Superficial dissection of the medial and lateral plantar nerves (arrows)

thickness skin graft or partial thickness graft. The patient remains non-weight-bearing for 14 days until the graft is completely healed [28].

Reverse Sural Artery Flap

The reverse sural artery flap is presented as an alternative flap for small to medium size defects when free flap procedures hold a higher risk. The reverse sural artery flap was first described by Masqualet in 1992 [29]. It was first depicted as a random flap based on the superficial flow of the sural artery. Traditionally, it has been used for sensate reconstruction of lateral malleolar and heal defects [30]. The distally based superficial sural artery flap is one of these neurocutaneous flaps, and its circulation depends on anastomosis of peri-sural vasculature with distal perforators of the peroneal artery near the lateral malleolus.

Anatomy

The proximally based sural artery flap is a fasciocutaneous, Mathes-Nahai type I flap (one dominant pedicle). The anatomic structures composing the flap are the sural artery, superficial and deep fascia, sural nerve, and saphenous vein. Both the sural artery and short saphenous vein originate from the popliteal artery and vein, respectively. The superficial sural artery arises from the popliteal artery in 65% of the cases, from the medial sural artery in 20%, and from the lateral sural artery in 8.3% [31]. In most cases, the artery descends into the lateral malleolus, and in less than 30% of the cases it fades distally into the distal third of the leg. It has a constant distal anastomosis with septocutaneous perforators from the peroneal artery and posterior tibial artery (5 cm above the lateral malleolus), which will supply a reverse-flow flap (Fig. 30.29). It is important to avoid raising the flap too far distally, as this could potentially affect the arterial and venous structures needed to preserve retrograde flow.



Fig. 30.29 Reverse sural artery superficial anastomosis through septocutaneous perforators from the peroneal artery

Surgical Technique

The procedure is performed under general or spinal anesthesia. Prone or lateral decubitus position with proper padding can be used for flap elevation. A vein finder can be used to mark the superficial saphenous vein network. The flap markings are as follows. A straight line is drawn connecting a point 1.5 cm posterior to the lateral malleolus and the cleft formed by the gastrocnemius muscle. This is the longitudinal



Fig. 30.30 Reverse sural artery flap: flap markings. The pivot point is marked 5 cm from the lateral malleolus. The vascular axis of the flap is between the midpoint of the malleolus and the lateral edge of the Achilles tendon



Fig. 30.31 Subfacial flap elevation. Medial sural vessels (blue arrow)

axis of the sural nerve and the vascular pedicle. The end of the distal dissection is marked with a transverse line 5 cm above the lateral malleolus. This is the pivot point of the flap, proximal to the most distal perforators from the peroneal artery. A doppler can be used to mark the course of the peroneal artery perforators at the lateral malleolus.

The flap is then outlined and centered over the pedicle. A tear drop configuration can be used to assist in later closure of the proximal defect (Fig. 30.30). An incision is made in the proximal border of the flap directly where the sural nerve and vessels can be identified at the midaxis of the flap. The dissection now proceeds from proximal to distal in the subfacial level (Fig. 30.31). Muscular perforators from the gastrocnemius are visualized and ligated. The incision in a lazy S fashion is then carried distally. The underlying pedicle is elevated with a width of approximately 2–3 cm, including the deep fascia [32]. The adipofascial cuff that remains around the pedicle should not be vio-



Fig. 30.32 Adipo-facial sleeve with preservation of the sural nerve, artery, and short saphenous vein

lated and the vascular structures should not be skeletonized (Fig. 30.32). The tourniquet is deflated, and the circulation in the flap is checked. The flap is then transposed distally and sutured to the receptor site. Our preference is to connect the defect and donor incisions and avoid a subcutaneous tunnel. The tear drop shape of the flap allows for easy inset and direct visualization of the pedicle [33]. Donor site closure proceeds in primary fashion if the defect is less than 4 cm. When closure is not possible, a skin graft is preferably used. Venous supercharging has also been found to be beneficial, as described by Herlin et al [34]. This is indicated especially for medial malleolus defects where it is easy to perform an anastomosis using the great saphenous axis, unlike the heel or Achilles' region which has a dearth of superficial veins. High-risk patients, such as the elderly, smokers, those with peripheral artery disease, diabetics, and those with signs of venous congestion, should undergo flap delaying in two stages to avoid postoperative vascular complications.



Fig. 30.33 Flap design based upon a first metatarsal head wound

Fillet Flap of Toe

The fillet flap of the toe is a versatile flap, easy to raise, and adheres to the "spare parts" principle of plastic surgery. It can be used to close distal dorsal, plantar, and forefoot wounds, as well as provide durable coverage for adjacent toes especially at the metatarsal phalangeal joint. It requires intact forefoot perfusion to be successful [35].

Anatomy

The fillet flap of toe is based upon the dual perfusion of the medial and lateral digital arteries. Depending on the perfusion of the foot it can be based upon one or both arteries. Typically, there are associated wounds involving the toe that dictate the design of the flap.

Surgical Technique

This procedure can be performed under local or regional anesthesia. Incision placement is based upon the intended destination of the flap. For dorsal foot wounds, the incision is placed dorsally and for plantar wounds, the incision is placed plantarly. The incision extends distally to the nail fold (Fig. 30.33). The nail fold, germinal, and sterile matrixes are excluded from the flap and left adherent to the distal phalanx. Depending on the length of flap needed, the incision can be carried medially and laterally around the nail and connected distally at the hyponych-



Fig. 30.34 Flap elevated with preservation of both digital arteries

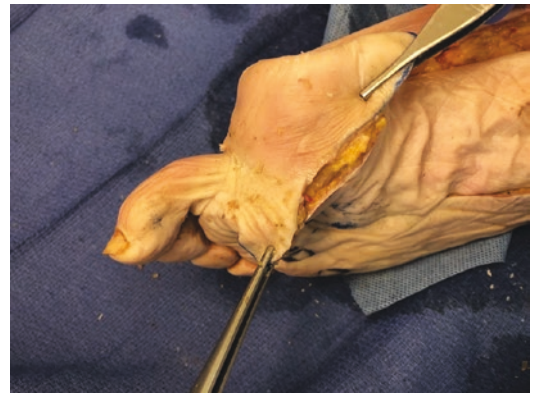


Fig. 30.36 Transposition of flap for coverage. Flap is trimmed and inset



Fig. 30.35 Degloved toe, discarded

ium. The incision is made full thickness to the periosteum and the toe bones are then degloved back to the metatarsal joint. Depending on the intended use, the flap can be elevated with double or single pedicles. The flap can be elevated with [36] or without tourniquet control. The tendons can either be included with the flap or proximally transected. Once the flap has been elevated and the phalanges degloved, the toe can be disarticulated with a scalpel (Figs. 30.34 and 30.35). The flap edges can be inspected for bleeding. Flap inset can then be performed typically with permanent suture (Fig. 30.36). The flap can be tailored during inset. Care should be taken to not skeletonize or disrupt the pedicle during this dissection. Flap dimensions of 4–5.5 cm have been described in literature [36]. Local wound care is usually sufficient to manage minor flap tip necrosis. The flap design is variable based upon the location of the wound and condition of the toe.

Random Skin Flaps

Local rotational and advancement flaps have been well described in the plastic surgery literature. There is a role for these flaps in limb salvage as well. Unlike other parts of the body where flap length: width ratios can exceed 3:1 and 4:1, in the foot, maintaining a 1:1 ratio is advised (Figs. 30.37, 30.38, 30.39, 30.40, 30.41, 30.42, 30.43 and 30.44). These flaps can be very sensitive to tension and atraumatic tissue handling is needed to decrease the risk of delayed wound healing.

Tissue Expansion

Internal tissue expansion of the lower extremity is known to carry a higher complication risk than expansion of other areas of the body [37]. It is generally not feasible in the foot and ankle. In certain circumstances the technique of external tissue expansion can be applied to achieve delayed primary closure of a wound. The successful application of external tissue expansion can result in full thickness coverage over tendon and bone leaving an incisional scar more durable



Fig. 30.37 V-Y advancement flap. (Courtesy John S. Steinberg, DPM)



Fig. 30.39 V-Y advancement flap. Place sutures to minimize distal flap tension. Notice focal blanching at suture locations. (Courtesy John S. Steinberg, DPM)



Fig. 30.38 V-Y advancement flap. After incising through the skin, cut down through fascia. Avoid any undermining. (Courtesy John S. Steinberg, DPM)

than a skin graft. Multiple techniques have been described in literature including stapling rubber bands in a crisscross pattern across a wound [38] and commercially available products that apply a constant 1.2 kg tension to skin anchors placed around a wound [39]. Given the relatively inelastic nature of the tissues in the foot, particularly in the presence of inflammation and edema, the role of tissue expansion in the authors' limb salvage practice is limited, but recurring. Generally, wounds that can almost be primarily approximated are best suited for this technique. External tissue expansion can be synergistically paired with negative pressure wound therapy. Larger defects with significant gaps between the wound edges are better served with alternative forms of reconstruction when available.



Fig. 30.40 V-Y advancement flap. Complete healing. (Courtesy John S. Steinberg, DPM)



Fig. 30.41 Rotational flap. When possible avoid incisions over high pressure areas like the metatarsal heads. (Courtesy John S. Steinberg, DPM)

When using the constant tensioning device on the foot, several principles should be followed. If the skin edges are adherent to the wound bed, they will need to be undermined to allow advancement of the expanded tissue. The skin needs to be protected from the monofilament band spanning between the skin anchors. Without this, linear areas of necrosis may occur along the course of the band. The stapled anchors and tension band can cause irritation and wounds themselves. Early removal (between 24 and 72 h) is preferred to limit additional wounding. When the device is removed it may be necessary to revise skin edges at the time of delayed primary repair. Despite these limitations, external tissue expansion can serve as a valuable instrument in the limb salvage surgeon's toolbox.



Fig. 30.42 Rotational flap. After incising along the arc of the flap, undermining is performed until the flap can freely rotate into position. (Courtesy John S. Steinberg, DPM)



Fig. 30.43 Rotational flap. Inset of the flap is performed taking care to make sure that the distal-most aspect of the flap is not under tension. (Courtesy John S. Steinberg, DPM)



Fig. 30.44 Rotational flap. Complete healing. (Courtesy John S. Steinberg, DPM)

Conclusion

Local flap reconstruction of the foot is an important component of any limb salvage service. The procedures tend to be straightforward and mostly can be done under ankle block anesthesia making it safer for the patient with multiple medical comorbidities than other more complex forms of reconstruction. It is critical that the surgeon take a holistic approach prior to entertaining any of these procedures. Medical management, vascular assessment, and wound bed preparation are prerequisites for any planned flap procedure in the lower limb.

Acknowledgment The authors wish to thank Zachary D. Martin BA (candidate) for his assistance in the cadaver lab.

References

1. Kozak GM, Hsu JY, Broach RB, Shakir S, Calvert C, Stranix JT, Messa C, Levin LS, Serletti JM, Kovach SJ, Fischer JP. Comparative effectiveness analysis of complex lower extremity reconstruction: out-

comes and costs for biologically based, local tissue rearrangement, and free flap reconstruction. Plast Reconstr Surg. 2020;145(3):608e–16e. https://doi.org/10.1097/PRS.0000000000006589.
2. Attinger Christopher E, Kim EK, Erwin B, Peter B, Paul C. Angiosomes of the foot and ankle and clinical implications for limb salvage: reconstruction, incisions, and revascularization. Plast Reconstr Surg. 2006;117(7S):261S–93S. https://doi.org/10.1097/01.prs.0000222582.84385.54.
3. Shuck J, Nolan J, Kanuri A, Evans KK, Attinger CE. The effect of positive post-debridement cultures on local muscle flap reconstruction of the lower extremity. Plast Reconstr Surg. 2015;136(4S):9–10. https://doi.org/10.1097/01.prs.0000472283.01460.a1.
4. Attinger CE, Ducic I, Cooper P, Zelen CM. The role of intrinsic muscle flaps of the foot for bone coverage in foot and ankle defects in diabetic and nondiabetic patients. Plast Reconstr Surg. 2002;110(4):1047–54.
5. Weinstein R, Larsen A. Orthoplastic foot and ankle reconstruction part 2. In: MacGlamry ED, Southerland JT, editors. McGlamry's comprehensive textbook of foot and ankle surgery. Philadelphia, PA: Wolters Kluwer Lippincott Williams & Wilkins; 2004. p. 204.
6. Ortak T, Ozdemir R, Ulusoy MG, Tiftikcioglu YO, Karaaslan O, Kocer U, Sensoz O. Reconstruction of heel defects with a proximally based abductor hallucis muscle flap. J Foot Ankle Surg. 2005;44(4):265–70. https://doi.org/10.1053/j.jfas.2005.04.001. PMID: 16012432.
7. Capobianco CM, Zgonis T. Abductor hallucis muscle flap and staged medial column arthrodesis for the chronic ulcerated Charcot foot with concomitant osteomyelitis. Foot Ankle Spec. 2010;3:269–73.
8. Craig GC. Intrinsic muscle flaps for coverage of small defects in the foot. Clin Podiatr Med Surg. 2020;37(4):789–802.
9. Wang JS, Gunsch C, Thompson C, Nigam M, Evans KK, Attinger CE. Proximally based split abductor hallucis turnover flap for medial hindfoot reconstruction: a case report. J Foot Ankle Surg. 2019;58(6):1072–6.
10. Landi A, Soragni O, Monteleone M. The extensor digitorum brevis muscle island flap for soft-tissue loss around the ankle. Plast Reconstr Surg. 1985;75(6):892–7.
11. Buntic R. "MICROSURGEON.ORG." Extensor digitorum brevis brevis flap. 2021. www.microsurgeon.org/extensorbrevis.
12. Abdelrahman I, et al. Versatility of the extensor digitorum brevis muscle flap in lower limb reconstruction. Plast Reconstr Surg Glob Open. 2018;6(12):e2071. https://doi.org/10.1097/GOX.0000000000002071.
13. Bakhach J, Demiri E, Chahidi N, Baudet J. Extensor digitorum brevis muscle flap: new refinements. Plast Reconstr Surg. 1998;102(1):103–10.
14. Hartrampf CR Jr, Scheflan M, Bostwick J III. The flexor digitorum brevis muscle island pedicle flap. Plast Reconstr Surg. 1980;66(2):264–70.
15. Vincenti R, Belczyk R. Can a flexor digitorum brevis muscle flap help manage a soft tissue defect after an open total calcanectomy? Podiatry Today. 2015;28:1.
16. McCraw JB, Furlow LT Jr. The dorsalis pedis arterialized flap: a clinical study. Plast Reconstr Surg. 1975;55(2):177–85.
17. Limthongthang R, Eamsobhana P. First dorsal metatarsal artery perforator flap to cover great toe defect. J Orthop Surg (Hong Kong). 2017;25(3):2309499017739497. https://doi.org/10.1177/2309499017739497. PMID: 29137568
18. Hou Z, Zou J, Wang Z, Zhong S. Anatomical classification of the first dorsal metatarsal artery and its clinical application. Plast Reconstr Surg. 2013;132(6):1028e–39e. https://doi.org/10.1097/PRS.0b013e3182a97de6. PMID: 24281608.
19. Serletti JM, Moran SL. Soft tissue coverage options for dorsal foot wounds. Foot Ankle Clin. 2001;6:839–51.
20. Vazales R, Masadeh S. First dorsal metatarsal artery flap for coverage of soft tissue defects of the distal foot: delayed technique, proximal and distally based Fasciocutaneous and Adipofascial variants. Clin Podiatr Med Surg. 2020;37(4):765–73. https://doi.org/10.1016/j.cpm.2020.07.001. PMID: 32919603.
21. Grabb WC, Argenta LC. The lateral calcaneal artery skin flap (the lateral calcaneal artery, lesser saphenous vein, and sural nerve skin flap). Plast Reconstr Surg. 1981;68(5):723–30.
22. Attinger CE, Evans KK, Bulan E, Blume P, Cooper P. Angiosomes of the foot and ankle and clinical implications for limb salvage: reconstruction, incisions, and revascularization. Plast Reconstr Surg. 2006;117(7S):261S–93S.
23. Koshima I, Urushibara K, Inagawa K, Hamasaki T, Moriguchi T. Free medial plantar perforator flaps for the resurfacing of finger and foot defects. Plast Reconstr Surg. 2001;107(7):1753–8.
24. Lee HB, Tark KC, Rah DK, Shin KS. Pulp reconstruction of fingers with very small sensate medial plantar free flap. Plast Reconstr Surg. 1998;101(4):999–1005.
25. Amarante J, Martins A, Reis J. A distally based median plantar flap. Ann Plast Surg. 1988;20(5):468–70.
26. Hanasono MM, et al. Handbook of reconstructive flaps. 1st ed. New York, NY: Thieme; 2021.
27. Gu JX, Huan AS, Zhang NC, Liu HJ, Xia SC, Regmi S, Yang L. Reconstruction of heel soft tissue defects using medial plantar artery island pedicle flap: clinical experience and outcomes analysis. J Foot Ankle Surg. 2017;56(2):226–9.
28. Baker GL, Newton ED, Franklin JD. Fasciocutaneous island flap based on the medial plantar artery: clinical applications for leg, ankle, and forefoot. Plast Reconstr Surg. 1990;85(1):47–58.
29. Masquelet AC, Romana MC, Wolf G. Skin island flaps supplied by the vascular axis of the sensitive superficial nerves: anatomic study and clinical experience in the leg. Plast Reconstr Surg. 1992;89(6):1115–21.
30. Coskunfirat OK, Velidedeoglu HV, Sahin U, Demir Z. Reverse neurofasciocutaneous flaps for soft-

tissue coverage of the lower leg. Ann Plast Surg. 1999;43(1):14–20.
31. Fachinelli A, Masquelet A, Restrepo J, Gilbert A. The vascularized sural nerve: anatomy and surgical approach. Int J Microsurg. 1981;3:57.
32. Mahmoud WH. Foot and ankle reconstruction using the distally based sural artery flap versus the medial plantar flap: a comparative study. J Foot Ankle Surg. 2017;56:514–8.
33. Cheema TA, Saleh ES, De Carvalho AF. The distally based sural artery flap for ankle and foot coverage. J Foot Ankle Surg. 2007;46(1):40–7.
34. Herlin C, Bekara F, Bertheuil N, Carloni R, Dast S, Sinna R, Chaput B. Venous supercharging reduces complications and improves outcomes of distally based sural flaps. J Reconstr Microsurg. 2017;33(05):343–51.
35. Kuntscher MV, Erdmann D, Homann H-H, Steinau H-U, Levin SL, Germann G. The concept of fillet flaps: classification, indications, and analysis of their clinical value. Plast Reconstr Surg. 2001;108(4):885–96.
36. Lin CH, Wei FC, Chen HC. Filleted toe flap for chronic forefoot ulcer reconstruction. Ann Plast Surg. 2000;44(4):412–6. https://doi.org/10.1097/00000637-200044040-00010. PMID: 10783098.
37. Huang X, Qu X, Li Q. Risk factors for complications of tissue expansion. Plast Reconstr Surg. 2011;128(3):787–97. https://doi.org/10.1097/PRS.0b013e3182221372.
38. Kenny EM, Egro FM, Russavage JM, Spiess AM, Acarturk TO. Primary closure of wide fasciotomy and surgical wounds using rubber band-assisted external tissue expansion: a simple, safe, and cost-effective technique. Ann Plast Surg. 2018;81(3):344–52. https://doi.org/10.1097/SAP.0000000000001506. PMID: 29905602.
39. Santiago GF, Bograd B, Basile PL, Howard RT, Fleming MDO, Valerio IL. Soft tissue injury management with a continuous external tissue expander. Ann Plast Surg. 2012;69(4):418–21. https://doi.org/10.1097/SAP.0b013e31824a4584.

31

Free Tissue Transfer in Diabetic Limb Salvage: Lessons Learned and Best Practices for Functional Salvage

Paige K. Dekker, Kevin G. Kim, Kenneth L. Fan, and Karen K. Evans

Introduction

Reconstruction of lower extremity defects using free tissue transfer (FTT) first occurred in 1973 when abdominal and groin flaps were used for coverage of distal lower extremity defects [1, 2]. Flap failure rates were initially as high as 40–50% [3] but continued advancements in microsurgery technique, surgical microscopes, and surgical instruments have led to success rates as high as 98–99% [4, 5], making FTT a highly reliable reconstructive modality in various clinical scenarios. FTT is now recognized as a mainstay reconstructive option for lower extremity reconstruction, yielding flap success rates up to 92% [6] and limb salvage rates of 83–84% [6, 7].

Contrary to previous beliefs, diabetes and peripheral vascular disease are not contraindications to microsurgical free flap reconstruction. Previous thinking held that hyperglycemia, neuropathy, and microvascular occlusive disease that developed secondary to diabetes resulted in impaired healing, compromising the viability of FTT and thereby making diabetic patients poor candidates for this reconstructive modality [7–9]. Various studies have since failed to demonstrate increased incidence of small vessel disease or endothelial proliferation in patients with diabetes [10–13]. Furthermore, our research and others' have maintained that free flap reconstruction can be performed with high success rates in the diabetic population [7, 9].

While FTT is not always a viable option, it offers several benefits over major limb amputation in appropriate patients. First, major amputation of one lower extremity increases the risk of contralateral amputation: nearly 50% of patients who undergo amputation will undergo a second amputation of the contralateral limb within two years [9, 14–16]. Second, major limb amputation has been shown to be associated with increased mortality. Patients with diabetes and chronic lower extremity wounds have a 5-year mortality of 43–55% [17–19] but mortality may increase to as high as 74–78% in patients who ultimately require amputation due to increased cardiovascular demand [17, 19, 20]. Oh et al. demonstrated a statistically significant increase in 5-year survival for diabetic patients undergoing FTT for lower extremity reconstruction relative to patients undergoing above-ankle amputation (86.8% versus 41.4%, respectively; $p < 0.001$) [7].

P. K. Dekker · K. G. Kim
Department of Plastic Surgery, MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: pkd15@georgetown.edu; kgk31@rwjms.rutgers.edu

K. L. Fan · K. K. Evans (✉)
Department of Plastic and Reconstructive Surgery, MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: Kenneth.l.fan@medstar.net; karen.k.evans@medstar.net

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_31

While FTT is a successful and reliable reconstructive modality for diabetic patients with lower extremity defects, several perioperative strategies can optimize success. Importantly, diabetic patients undergoing FTT generally require more debridements, have longer healing times, and have higher rates of re-exploration, flap failure, and local complications when compared to non-diabetic patients undergoing FTT [9, 21]. A carefully orchestrated multidisciplinary approach involving reconstructive, podiatric, orthopedic, and vascular surgeons as well as close collaboration with infectious disease, endocrinology, hematology, and nutrition colleagues is essential to optimizing free flap outcomes in this patient population [21]. This chapter will discuss the indications for FTT as well as strategies to optimize outcomes in the preoperative, intraoperative, and postoperative stages of care for patients with diabetes who are undergoing lower extremity reconstruction with FTT.

Indications

The reconstructive ladder is traditionally used to help guide the stepwise progression through reconstructive modalities. Free flap reconstruction was considered when primary closure, skin grafts, and local flap options were exhausted [22]. However, certain authors advocate for a reconstructive elevator rather than a reconstructive ladder [23, 24]. Primary closure is often precluded by the lack of soft tissue domain [9]. Robust soft tissue is required for ambulation, and skin grafting is precluded by exposed tendon and/or bone [9, 25, 26]. Local flaps have limited reach and may not always be a reliable reconstructive option, particularly in distal third defects with repetitive trauma [27, 28]. As surgeons seek to attain superior functional and aesthetic outcomes, FTT is often the first choice for reconstruction [21].

Keeping the aforementioned points in mind, indications for microsurgical free tissue transfer for reconstruction of lower extremity defects include those that (1) are large (>2–3 cm), (2) involve concurrent bone or muscle loss, and/or (3) exhibit exposed joint or neurovascular structures [9, 21]. Another primary indication for FTT is for reconstruction of areas of the foot or leg in ischemic angiosomes where there is minimal inline blood flow. In this regard, FTT acts as a vascular bypass adding vascularized tissue to ischemic wounds. Importantly, diabetes, peripheral vascular disease, and elderly age are not absolute contraindications for FTT; however, patients with these comorbidities do require special perioperative considerations as discussed further below [21]. Importantly, FTT is contraindicated in patients who lack a suitable recipient vessel and caution should be taken in diabetic patients receiving dialysis [9]. Patients with end-stage renal disease often have diffuse vessel calcification and impaired wound healing, while patients on dialysis are at increased risk of both thromboembolic events and hematoma formation [28–30].

Preoperative Evaluation and Optimization

The preoperative stage should focus on three tasks: (1) evaluating whether the patient is a good candidate for FTT, and if so, (2) early and aggressive optimization of underlying comorbidities as well as (3) preparation of the wound bed for FTT. Each of these steps requires multidisciplinary collaboration from both a surgery and medicine standpoint, which may include specialist expertise from podiatric and reconstructive surgery to cardiology, hematology, and hematology, among others. Our management algorithm is depicted in Fig. 31.1.

In addition to this multidisciplinary approach, patients must have a clear understanding of the reconstructive timeline as well as postoperative expectations and guidelines in order to maximize the chance of reconstructive success. To that end, counseling the patient and his or her caretakers should occur throughout the preoperative period. Ensuring a clear understanding of postoperative weight-bearing and ambulation progression are particularly important, as failure to comply with rehabilitation protocols can lead to flap failure.

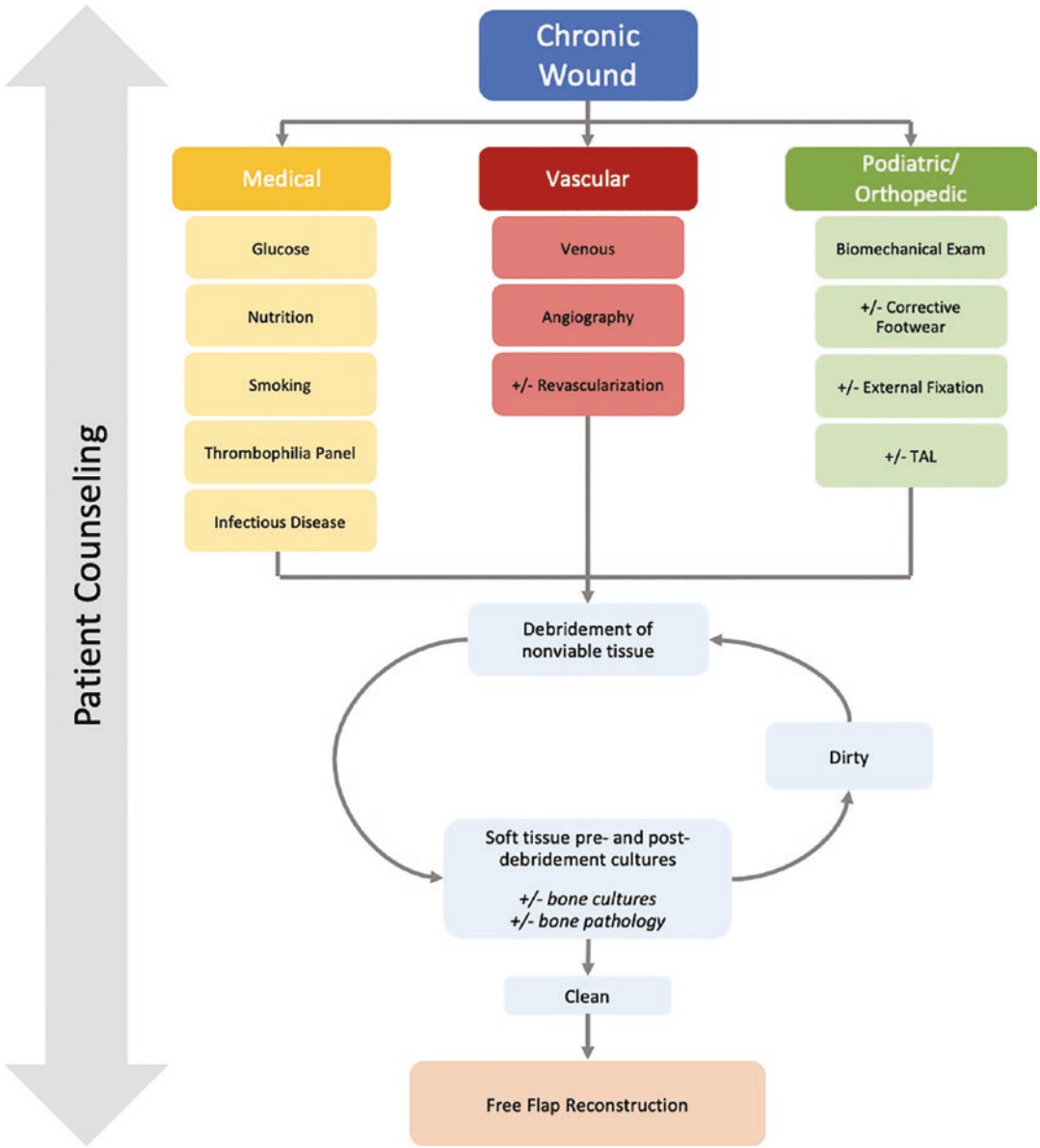


Fig. 31.1 Multidisciplinary approach to preoperative workup for free tissue transfer reconstruction

Medicine

Preoperative evaluation of the patient should include obtaining a thorough history that captures all pre-existing medical conditions in order to allow for early and aggressive optimization. In patients with diabetes, tight glycemic control in the perioperative period is essential: patients with blood glucose levels above 200 mg/dL are more than three times likely to experience wound dehiscence and patients with a hemoglobin A1c greater than 6.5% are more than three times as likely to undergo wound dehiscence and/or reoperation [31]. In addition to setting a target glucose level of less than 200 mg/dL, it is also important that glucose levels are maintained in a narrow range throughout the perioperative period, as patients who display wide variability in

glucose levels are at increased risk of reoperation [31]. Close collaboration with endocrine specialists and patient education regarding the importance of perioperative glucose control are essential to achieving these targets.

Surgical trauma induces a hypermetabolic state mediated by multiple endocrine pathways, which relies on adequate nutritional stores. Nutritional screening should therefore be included as a routine aspect of any preoperative workup [32]. Retrospective review of patients undergoing free flap reconstruction at our institution suggests that a preoperative albumin level above 2.7 g/dL within 30 days is a reasonable target for patients undergoing FTT, as levels below this value were associated with slower healing times and decreased overall flap healing rates (personal communication with Karen K. Evans, 2020).

Smoking cessation, or at the very least decreased use leading up to surgery, can reduce the risk of impaired wound healing, infection, partial flap loss, and need for revision surgery [33]. We typically encourage patients to quit or otherwise abstain from tobacco use for at least four to eight weeks prior to surgery.

Patients should also be screened for inherited or acquired traits that may predispose them to thrombosis. Patients with underlying hypercoagulability are at increased risk of microvascular thrombosis and subsequent flap failure with high rates of nonsalvageability [34–36]. In our institution, we employ a preoperative hypercoagulable workup for all patients undergoing FTT including a thrombophilia panel and thorough history taking to assess for any personal or family history of hypercoagulability [36]. As part of this history taking, patients should be asked about any personal or family history of clotting disorders, autoimmune disease, purpura fulminans, miscarriage, blood clots, or use of blood thinners [36]. Components of a thorough thrombophilia panel are outlined in Table 31.1 and include a complete blood count (CBC), prothrombin time (PT), partial thromboplastin time (PTT), homocysteine and factor VIII levels, testing for antiphospholipid antibodies, and measuring activity levels of protein C, protein S, and antithrombin III. Testing should also include genotypes for factor V Leiden *G1691A* and prothrombin *G20210A* as well as testing for the *A1298C* and *C677T* polymorphisms of the MTHFR gene and lastly for the 4G/5G polymorphism of the plasminogen activator inhibitor-1 (PAI-1) gene [36]. Implementation of this hypercoagulability testing protocol in our preoperative workup algorithm revealed that 61% of patients undergoing FTT for lower extremity reconstruction may have at least one thrombophilic trait and that 20% of patients were found to have three or more separate diagnoses [36].

Table 31.1 Components of a thorough thrombophilia screening panel

CBC
PT, PTT
Factor V Leiden *G1691A* genotype
Prothrombin *G20210A* genotype
Homocysteine level
Factor VIII level
Antiphospholipid antibody testing
Antithrombin III activity
Protein C activity
Protein S activity
MTHFR polymorphisms (*A1298C* and *C677T*)
PAI-1 4G/5G QST

CBC complete blood count, *MTHFR* methylenetetrahydrofolate reductase, *PAI-1* plasminogen activator inhibitor 1, *PT* prothrombin time, *PTT* partial thromboplastin time, *QST* quantitative sensory testing

Adapted from Defazio MV, Hung RWY, Han KD, Bunting HA, Evans KK. Lower Extremity Flap Salvage in Thrombophilic Patients: Managing Expectations in the Setting of Microvascular Thrombosis. *J Reconstr Microsurg*. 2016. doi:10.1055/s-0035-1571249

Patients with known or newly detected thrombophilia should receive a hematology consult in order to assist with preoperative risk stratification as well as have perioperative anticoagulation regimens optimized based on their level of thrombosis risk. We consider hematologic (hypercoagulable traits identified with thrombophilia panel), acquired (history of venous thromboembolism, myocardial infarction, cerebrovascular accident, malignancy, miscarriage(s), and/or use of blood thinners), and intraoperative (thrombosis, anastomotic revision, vascular calcifications) risk factors to stratify patients into low, moderate, and high-risk groups [34]. We use this risk stratification

to guide intraoperative and postoperative antithrombotic therapy as outlined in Fig. 31.2. Implementation of this risk-stratified anticoagulation algorithm at our institution resulted in significantly lower rates of total and partial flap loss in the risk-stratified group compared to non-stratified controls (total flap loss 3.0% versus 19.0%, $p = 0.06$; partial flap loss 10.0% versus 37.0%, $p = 0.025$) [34]. Several studies investigating patients undergoing free flap surgery have found 0% salvageability rates in the setting of postoperative thrombosis, regardless of anticoagulation protocol [34, 35]. Taken together, these findings reiterate the risk of non-salvageability in thrombophilic patients who develop thrombosis postoperatively and reinforce the potential benefits of a risk-stratified anticoagulation protocol.

Vascular

Flap success is highly reliant on adequate arterial supply and venous drainage of the transferred tissue, requiring thorough physical exam. The vascular supply defining the six foot and ankle angiosomes should guide the vascular exam, as this not only allows the surgeon to predict the viability of a newly placed free flap but it also allows the surgeon to plan for optimal placement of surgical incisions since adequate blood flow on either side of the incision is necessary for optimal healing. Furthermore, vascular exam and imaging assist in the coordination with a vascular surgeon for preoperative revascularization procedures, if necessary, to ensure that areas targeted for reconstruction have adequate blood supply. In patients with diabetes and/or peripheral vascular disease, using the six angiosomes as a framework to guide directional assessment of blood flow can ensure that (1) surgical incisions will not compromise blood flow to a given area of the foot and (2) that vascular bypass procedures will actually revascularize ischemic angiosome(s) [25, 37].

Arterial examination can be performed via palpation of pulses, ankle-brachial indices, handheld doppler, catheter arteriography, or computed tomographic (CT) angiography [38].

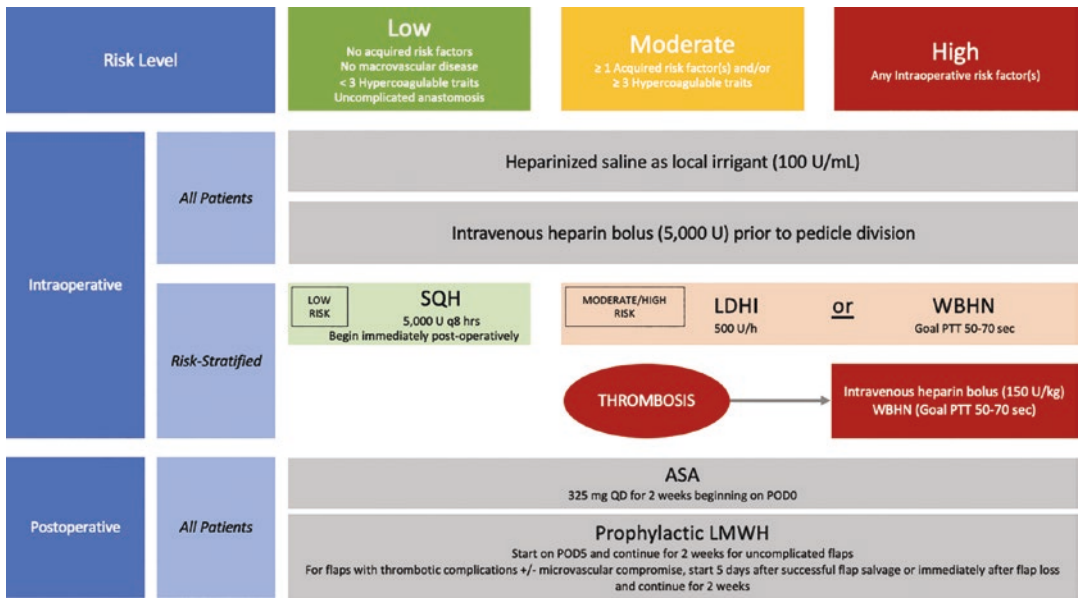


Fig. 31.2 Risk-stratified anticoagulation protocol for patients undergoing free tissue transfer. *ASA* acetylsalicylic acid, *LMWH* low molecular weight heparin, *POD* postoperative day, *PTT* partial thromboplastin time. (Adapted from DeFazio M, Economides J, Anghel E, Tefera E, Evans K. Lower Extremity Free Tissue Transfer in the Setting of Thrombophilia: Analysis of Perioperative Anticoagulation Protocols and Predictors of Flap Failure. J Reconstr Microsurg. 2019;35(04):270–286. doi:10.1055/s-0038-1675145)

We employ arteriography for all patients undergoing FTT. Conventional arteriography uses less intravenous contrast than CT angiography and provides more meaningful clinical data [38]. Routine use of this imaging modality in our institution identified arterial pathology in 67.8% of patients undergoing FTT for lower extremity reconstruction [38]. In the same series, diabetes was associated with the need for endovascular intervention as well as findings of stenosis or occlusion on angiography [38]. These findings highlight the utility of this imaging modality not only in diagnosing peripheral vascular disease but also in guiding recipient vessel selection and facilitating timely endovascular intervention [38].

Insufficient venous outflow resulting in flap congestion and delayed thrombosis is a leading cause of re-exploration and flap loss; thus, venous studies are also a key component of preoperative workup [4, 39]. Venous studies can identify venous insufficiency as well as venous anomalies that may predispose patients to venous congestion with subsequent thrombosis and flap failure. While there are many options for venous imaging, including CT venography, magnetic resonance (MR) venography, and catheter venography, we recommend venous duplex ultrasound because of its superior safety and efficacy profile relative to alternative imaging modalities. Importantly, duplex ultrasound is noninvasive and does not require contrast, which is particularly beneficial in diabetic patients who often have comorbid renal insufficiency. Utilization of venous duplex ultrasonography in patients undergoing lower extremity free flap reconstruction at our institution detected venous insufficiency in 39% of patients and deep vein thrombosis requiring anticoagulation in 6.78% of patients [40]. These findings highlight the utility of duplex ultrasound in detecting proximal deep venous thrombosis as well as venous reflux, making it a helpful tool in determining whether the deep venae commitantes versus the superficial saphenous system should be used as the recipient veins for a given patient's free flap reconstruction.

Podiatric and Orthopedic Surgery

All patients should undergo biomechanical examination in order to identify any mechanical factors that may be contributing to wound development and recurrence. This portion of the preoperative workup is particularly important for patients with diabetic neuropathy, as impaired protective sensation, proprioception, balance, and muscle strength in these patients can lead to increased plantar pressure, prolonged stance times, weakened dorsiflexion, and claw toes [41, 42]. Gait alterations in these patients may lead to changes in skeletal structure and muscle function, as well as loss of flexibility in the joint and Achilles tendon [42]. Reduced flexibility in the Achilles tendon impairs foot dorsiflexion, which can lead to Charcot development and subsequent plantar ulceration [43]. For this reason, we routinely address equinus gait with Achilles tendon lengthening, which has been shown to reduce wound recurrence by up to 94% in this population [44]. This procedure should be supplemented with additional measures to address other biomechanical abnormalities, including, but not limited to, external fixation for bony reconstruction in patients requiring Charcot reconstruction as well as appropriate corrective footwear [42].

Surgical

The next preparatory step entails achieving a clean wound bed via serial surgical debridement of all infected or devitalized tissue, senescent cells, and biofilm [25, 45]. Aerobic and anaerobic cultures should be obtained prior to and after debridement and should be collected deep to the wound surface [45]. Culture-driven antibiotic therapy should be given in conjunction with surgical debridements and should be maintained until negative cultures are achieved, at which point the patient is ready for further reconstruction from an infectious standpoint. Please refer to Chap. 13 of this text ("Debridement of the Diabetic Foot and Leg") for further information on this topic.

Intraoperative Optimization

Anesthesia

Close collaboration with the anesthesiologist is important, as they manage several factors capable of optimizing flap outcomes. Perioperative anticoagulation is of particular importance in free flap procedures because flap viability is so critically dependent on flap perfusion. As previously stated, hematology should be consulted to help devise an optimal anticoagulation regimen for any patient with underlying thrombophilia. In general, patients should be given aspirin or subcutaneous low-molecular-weight heparin for antithrombotic prophylaxis. We also typically administer 5000 U of heparin just prior to flap inset and vessel anastomosis.

Normothermia (average temperature > 37 °C) should be maintained throughout the surgery, as lower temperatures have been associated with increased risk of perioperative complications including recipient site infections [46]. Vasopressors can be administered as needed for hypotension as their use does not significantly increase the risk of complications, reoperation, or flap failure [46].

Flap Choice

One of four flap compositions can be utilized for the vast majority of lower extremity reconstructions: fasciocutaneous, muscle only, musculocutaneous, or chimeric. Fasciocutaneous flaps, which are harvested by elevating the skin along with its underlying deep fascia, offer several benefits including preservation of underlying musculature as well as being thin, pliable, and amenable to tissue expansion [47]. Large fasciocutaneous flaps (>8 cm) may require skin grafts at the donor site [47]. Typically, we avoid fasciocutaneous flaps if subcutaneous tissue is too thick. In these instances, we use a muscle flap with overlying skin graft. Revision procedures including debridement and repeat skin grafts for partial skin graft loss are not uncommon as blood supply may be altered in the vasculopathic population. Musculocutaneous flaps are harvested by elevating the skin and underlying muscle. These flaps are well vascularized and offer more bulk than fasciocutaneous flaps, making them more resistant to infection and more helpful for coverage of defects requiring obliteration of dead space [47]. Chimeric flaps can be helpful for patients with tendinous or bony defects. For example, a chimeric anterolateral thigh (ALT) with rolled fascia lata free flap can be used to reconstruct defects that require tendinous reconstruction [48]. Chimeric flaps that include vascularized bone can be helpful for reconstruction of defects with bony involvement [49].

In addition to flap composition, one must also consider the aesthetic and functional needs of the site that is being reconstructed. The subunit principle of the foot described by Hollenbeck et al. provides a helpful framework when determining which free flap best suits the unique needs of a particular area of the foot or ankle [50]. Heel ulcers (subunit 5) require reconstruction with a flap that will provide both bulk and durability, making either the vastus lateralis (VL) or ALT good options (Case 31.1) [25, 50]. The dorsum of the foot (subunits 3 and/or 4) requires a different reconstructive approach, as use of a bulky flap could prevent the patient from fitting into shoes. Instead, one must rely on flaps with thinner paddles such as the superficial circumflex iliac artery (SCIP) flap (Case 31.2), medial sural artery perforator (MSAP) flap, or fasciocutaneous ALT flap [25, 50]. Functional morbidity is also a key consideration in flap donor site, particularly in patients who may require future amputation. The free rectus flap and the latissimus dorsi flap are not preferable options as it is important to retain upper body and core strength for transfers should an amputation be required in the future.

Case 31.1 Vastus Lateralis Free Flap

A 45-year-old male with a past medical history significant for type I diabetes mellitus, peripheral artery disease, left below-knee amputation (BKA), right-sided weakness secondary to cerebrovascular accident, and right fifth ray partial

amputation initially presented with right foot wounds. On exam, the patient was afebrile (37.1) with stable vitals (HR 99, BP 128/72). Exam of the right foot revealed a wound with expressible purulence on the lateral aspect of the fifth metatarsal as well as a wound on the dorsomedial aspect of the first metatarsal shaft and head. Necrotic skin was noted on the plantar aspect of the foot, spanning across all metatarsal heads (Fig. 31.3). Labs were significant for a hemoglobin A1c of 8.8%. X-ray of the foot was negative for gas in the extremity but was concerning for cortical erosion of the talus and navicular bones. Purulence was expressed from the wound at the bedside and cultures were sent. Broad-spectrum intravenous antibiotics were initiated, and the patient was admitted for surgical management of his wounds.

The patient underwent two rounds of surgical debridement down to fascia in the operating room (Fig. 31.4). The patient also underwent arteriogram and subsequent percutaneous transluminal angioplasty of the right anterior tibial artery. The patient was discharged home on the tenth day of hospitalization with home health nursing and wound care instructions.

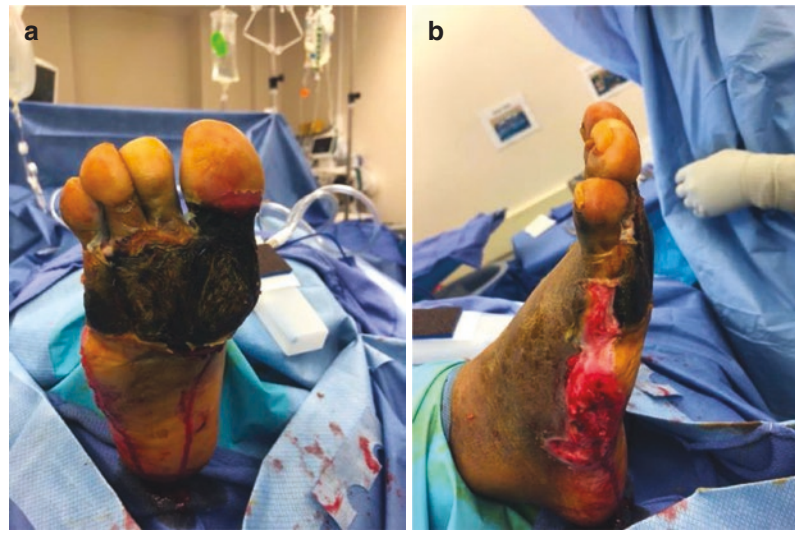


Fig. 31.3 Plantar (**a**) and lateral (**b**) surfaces of the right foot on initial presentation



Fig. 31.4 Plantar (**a**) and medial (**b**) surfaces of the right foot following two rounds of surgical debridement

Approximately one month later, the patient was re-admitted for debridement, length-preserving transmetatarsal amputation (which was especially important given the patient's contralateral BKA), tendon Achilles lengthening (TAL), and microsurgical free flap. We proceeded with our management algorithm as outlined in Fig. 31.1 prior to FTT:

- **Multiple debridements** were performed and cultures were obtained in order to achieve a clean wound bed prior to FTT. Cultures grew *Candida albicans* but this was ultimately attributed to secondary colonization. Targeted antimicrobial therapy was administered leading up to FTT.
- As described above, **vascular surgery** was consulted and arteriogram was performed during the patient's initial hospitalization. **Arteriogram** revealed multiple areas of stenosis and occlusion of the anterior tibial artery, which was treated with **endovascular revascularization**. The posterior tibial artery was also noted to have an occlusion without distal reconstitution.
- Vascular surgery was also consulted for **venous studies**. Venous duplex was performed twelve days prior to FTT and findings were significant for (1) no evidence of reflux, (2) no visualized perforators, and (3) no visualization of the small saphenous vein from the junction to the proximal calf.
- **Hypercoagulability studies** revealed that the patient was weakly positive for lupus anticoagulant and also had low protein S levels. These findings did not necessitate further workup with hematology or specialized intraoperative management.
- **Endocrinology** was consulted for **optimization of blood glucose levels**. At the time of the patient's initial admission, the patient's hemoglobin A1c was 8.8% and he had glucometer readings as high as 294 mg/dL the day before FTT. The patient was a non-smoker.

After TMA and percutaneous TAL were performed (Fig. 31.5), a **vastus lateralis** free flap was harvested from the right thigh (Fig. 31.6).



Fig. 31.5 Right foot after length-preserving transmetatarsal amputation and anterior tibial donor site preparation

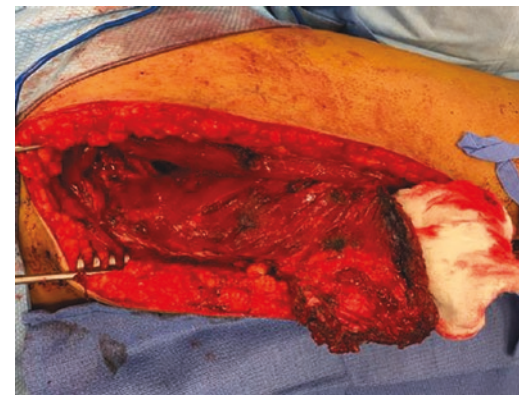


Fig. 31.6 Harvested vastus lateralis free flap

The descending branch of the lateral circumflex femoral artery was anastomosed to the recipient anterior tibial artery in an end-to-side fashion, followed by two venous anastomoses which were performed in an end-to-end fashion using a venous coupler. The patient was noted to have extensive calcifications in the recipient and donor site arteries; therefore, the arterial anasto-

mosis was performed in an inside-to-outside fashion. After flap inset, a split-thickness skin graft (STSG) was harvested, meshed, and affixed to the flap with staples (Fig. 31.7). The patient was discharged 17 days after FTT. At ten-month postoperative follow-up, the patient's flap donor and recipient sites were well healed and the patient was full weight-bearing with a custom molded orthosis (CMO)/ankle-foot orthosis (AFO) on the right lower extremity and a prosthetic device on the left lower extremity (Fig. 31.8).

Case 31.2 Superficial Circumflex Iliac Artery Perforator Free Flap

A 62-year-old female with a past medical history significant for right hallux rigidis presented approximately three weeks after undergoing right metatarsophalangeal joint fusion with 5/10 pain around the surgical site. The patient reported that she had completed a full 10-day course of antibiotics postoperatively. The patient was afebrile (36.6). Examination of the surgical site revealed intact sutures and erythema and skin sloughing around the incision. Incisional



Fig. 31.7 Medial (**a**) and dorsal (**b**) views of the flap immediately after microvascular anastomosis and skin grafting



Fig. 31.8 Final postoperative appearance

dehiscence probing to hardware was noted distally (Fig. 31.9). There was no purulence. X-ray of the foot showed generalized soft tissue swelling consistent with postoperative changes. Intravenous antibiotics were initiated and the patient was admitted for surgical management of her wound.



Fig. 31.9 Right foot wound prior to free flap closure

- **Vascular surgery** was consulted in order to evaluate blood flow to the distal extremity. This exam was particularly in this patient, who was a **current smoker**. **Arteriogram** revealed three-vessel runoff to the patient's foot and **venous duplex studies** revealed (1) no evidence of reflux, (2) no evidence of deep or superficial vein thrombosis, (3) no visualization of the distal small saphenous vein due to dressings/drainage, and (4) no visualization of perforators.
- The patient underwent **multiple debridements** and cultures were obtained in order to achieve a clean wound bed prior to proceeding with FTT. **Infectious disease** was consulted for management of targeted antimicrobial therapy.
- **Hypercoagulability studies** were all negative with the exception of minimally elevated anticardiolipin antibodies and minimally elevated protein C levels. No further hematology workup was required.

Once it was determined that the patient was ready for definitive closure, a SCIP flap was harvested from the patient's left thigh (Fig. 31.10). The right thigh was not used as a donor site due to the presence of intertrigo on this side. The superficial circumflex iliac artery perforator was anastomosed to a side branch of the dorsalis

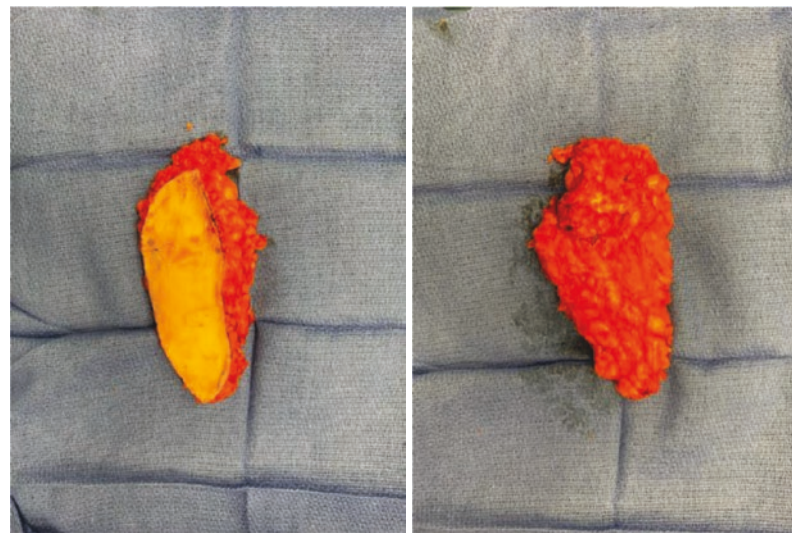


Fig. 31.10 Harvested superficial circumflex iliac artery perforator (SCIP) free flap

pedis artery in an end-to-end fashion, followed by two venous anastomoses: the superficial circumflex iliac vein was anastomosed to a deep vein of the anterior tibial artery and a superficial saphenous vein tributary was anastomosed to the saphenous vein. Both venous anastomoses were performed in an end-to-end fashion using a venous coupler. A small piece of bilaminar wound matrix was used for coverage at the proximal end of the flap-skin interface in order to minimize tension on the pedicle (Fig. 31.11). Five months after free flap reconstruction the patient underwent flap debulking with liposuction as well as a minor revision procedure to remove a portion of the flap that was growing pubic hair (Fig. 31.12). At six-month postoperative follow-up, the patient was healing well (Fig. 31.13).

In general, thigh-based flaps can be relied on as the workhorse flaps for lower extremity reconstruction. At our institution, the most commonly utilized flaps are the ipsilateral ALT flap or VL flap, both of which are based on the descending branch of the lateral femoral circumflex artery [25]. Both of these flaps offer the benefits of upper body and core strength preservation, low donor site morbidity, and long pedicles that are

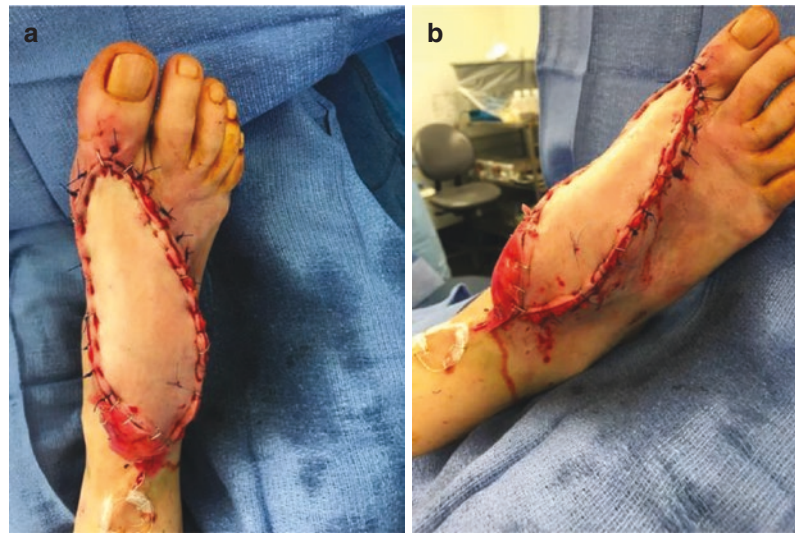


Fig. 31.11 Dorsal (**a**) and dorsolateral (**b**) views of the patient's right foot after free flap inset with bilaminar wound matrix to limit pedicle compression

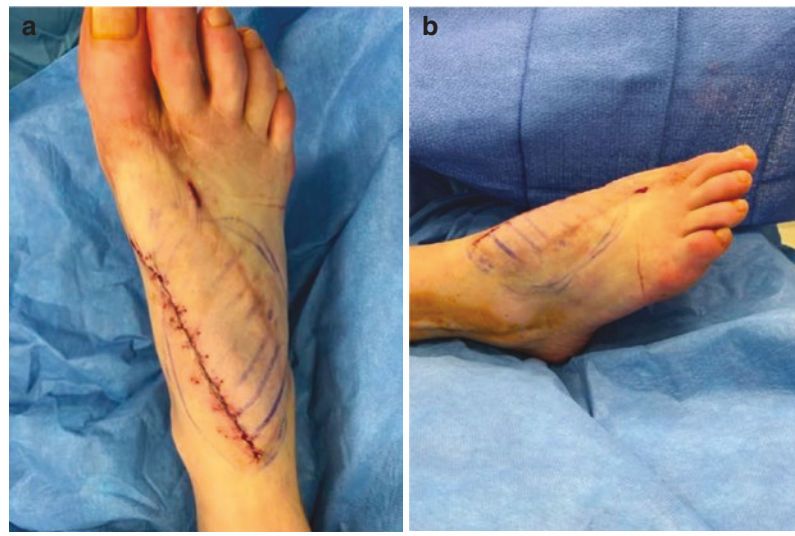


Fig. 31.12 Dorsal (**a**) and dorsolateral (**b**) views of free flap after debulking procedure



Fig. 31.13 Flap appearance at six-month follow-up

large in diameter [25, 51–53]. The ALT flap can be taken with or without underlying muscle, making it a good choice for defects requiring less bulk, while the VL is a useful option for defects requiring a thicker paddle. The SCIP and MSAP flaps are two other options that can be useful for reconstruction of defects that require thin paddles for coverage. Limitations of the SCIP flap include a short, small caliber pedicle while limitations of the MSAP flap include tedious muscle dissection and susceptibility to vein damage given the large caliber of tributaries [54, 55]. The gracilis flap is another thigh-based option but is often not used because of short pedicle length.

Vessel Anastomosis

Microvascular anastomosis can be particularly challenging in the diabetic patient population, as these patients often have comorbid peripheral vascular disease, atherosclerosis, and or diffuse calcifications which can cause recipient and donor vessels to become stiff, fibrotic, and fragile [25, 56]. These vessels are susceptible to traumatic injury and intimal damage during microsurgical anastomosis, increasing susceptibility to thrombosis and other surgical complications [25, 57, 58]. These patients also often have limited vascular supply to the lower extremity; therefore, the optimal anastomosis technique is one that allows for preservation of distal blood flow [25, 59]. End-to-end anastomosis is therefore not ideal in these patients as it requires a major recipient artery to be sacrificed in order to perfuse the flap. End-to-side anastomosis not only preserves distal blood flow to the limb but it also reduces the risk of recipient vessel vasospasm and allows the surgeon to compensate for vessel mismatch [60–62]. We prefer to use a longitudinal slit arteriotomy, as opposed to excising the vessel wall with scissors, as the former minimizes intimal trauma and allows for even further control of vessel size mismatch [61, 63]. Utilization of longitudinal slit arteriotomy with end-to-side anastomosis in highly comorbid patients undergoing free tissue transfer for lower extremity reconstruction at our institution has yielded excellent long-term limb salvage (83.5%) and flap success (93%) rates [63]. We generally gently palpate an area without calcium to make our incision. Two large Acland clamps are used to prop the vessel up. The donor vessel is cut at a 60-degree angle. A toe stitch is performed and tied down. The heel stitch is left untied with a micro clip on it to allow for visualization of each bite. The more difficult side is sutured first in a running interrupted fashion. Then the heel stitch is tied down. In patients who have diffusely calcified donor and recipient vessels, use of an end-to-side interpositional saphenous vein graft eliminates outside-to-inside suturing which can dislodge calcific plaques and increase the risk of anastomotic failure [25, 58, 63]. For severe calcifications, a cardiac needle on 7-0 Prolene can be used to perform the microsurgical anastomosis. Inside-to-outside suturing with a saphenous vein interposition graft tacks fragile intima up and minimizes disruption [25, 58, 63].

Flap Inset

After the microsurgical anastomosis and removal of all vessel clips, a Cook-Swartz implantable Doppler probe can be placed on the vein in order to allow for continuous monitoring of anastomotic patency. In the lower extremity, limited domain can cause venous compression during inset. Therefore, it is critical to use the implantable doppler to monitor the vein during inset. A ViOptix Tissue Oximeter can also be placed on skin-based flaps after closure to monitor postoperative flap perfusion. We have found that supplementation of clinical observation with these additional monitoring tools allows for more timely and accurate identification of possible flap compromise.

Postoperative Optimization

Flap Monitoring

The most common causes for flap re-exploration include pedicle (particularly venous) thrombosis and hematoma formation [4]. Not surprisingly, shorter time to re-exploration is associated with increased rates of flap salvage [4]. For this reason, postoperative flap monitoring is an essential component of flap success. The vast majority of flap complications necessitating urgent re-exploration will arise within the first 48 h after surgery; therefore, inpatient monitoring is typically recommended for 3–4 days postoperatively [4, 64]. Hourly flap checks are recommended for the first 24 h after surgery and then can be spaced to every four hours for the next 48 h [47, 65]. In addition to utilization of objective flap monitoring tools such as the Cook doppler and ViOptix, several visual and tactile cues obtained via physical exam are worrisome for flap compromise and warrant prompt investigation: changes in flap skin color, capillary refill, and tissue turgor; scant or brisk dermal bleeding; or a flap that is cool to the touch [47].

While the vast majority of reconstructive surgeons agree that a dangle protocol should be part of any postoperative plan following free tissue transfer, there is considerable variability with respect to the timing of initiation and frequency of such protocols. A recent systematic review found that the vast majority of studied protocols included 48 h of bedrest after surgery followed by initiation of a dangle protocol on postoperative day three [66]. Patients were typically allowed to start weight-bearing at the conclusion of the dangling protocol barring any concomitant orthopedic injuries that would preclude this [66]. The importance of patient counseling and education bears repeating at this stage, as failure to comply with weight-bearing and ambulation progression can lead to flap failure.

Conclusion

Preparing for free tissue transfer reconstruction requires coordinated care among various medical and surgical specialties. Free tissue transfer is a highly reliable reconstructive option for patients with diabetes, but optimization of blood sugar and other underlying comorbidities prior to surgery is essential to flap success. Thigh-based flaps can be used for the vast majority of lower extremity defects and end-to-side anastomosis allows for preservation of distal vascular supply. In the postoperative period, frequent flap checks and adherence to weight-bearing and ambulation protocols are key to flap success.

References

1. Rickard RF, Hudson DA. A history of vascular and microvascular surgery. Ann Plast Surg. 2014;73(4):465–72. https://doi.org/10.1097/SAP.0b013e3182710027.
2. Lineaweaver W. The first free flaps and the problems they addressed. Ann Plast Surg. 2014;73(6):623–4. https://doi.org/10.1097/SAP.0000000000000371.
3. Pattani KM, Byrne P, Boahene K, Richmon J. What makes a good flap go bad?: a critical analysis of the literature of intraoperative factors related to free flap failure. Laryngoscope. 2010;120(4):717–23. https://doi.org/10.1002/lary.20825.
4. Bui DT, Cordeiro PG, Hu QY, Disa JJ, Pusic A, Mehrara BJ. Free flap reexploration: indications, treatment, and outcomes in 1193 free flaps. Plast

Reconstr Surg. 2007;119(7):2092–100. https://doi.org/10.1097/01.prs.0000260598.24376.e1.
5. Yii NW, Evans GRD, Miller MJ, et al. Thrombolytic therapy: what is its role in free flap salvage? Ann Plast Surg. 2001;46(6):601–4. https://doi.org/10.1097/00000637-200106000-00005.
6. Fitzgerald Oconnor EJ, Vesely M, Holt PJ, Jones KG, Thompson MM, Hinchliffe RJ. A systematic review of free tissue transfer in the management of non-traumatic lower extremity wounds in patients with diabetes. Eur J Vasc Endovasc Surg. 2011;41(3):391–9. https://doi.org/10.1016/j.ejvs.2010.11.013.
7. Oh TS, Lee HS, Hong JP. Diabetic foot reconstruction using free flaps increases 5-year-survival rate. J Plast Reconstr Aesthetic Surg. 2013;66(2):243–50. https://doi.org/10.1016/j.bjps.2012.09.024.
8. Goldenberg S, Alex M, Joshi RA, Blumenthal HT. Nonatheromatous peripheral vascular disease of the lower extremity in diabetes mellitus. Diabetes. 1959;8(4):261–73. https://doi.org/10.2337/diab.8.4.261.
9. Ducic I, Attinger CE. Foot and ankle reconstruction: pedicled muscle flaps versus free flaps and the role of diabetes. Plast Reconstr Surg. 2011;128(1):173–80. https://doi.org/10.1097/PRS.0b013e3182173d3a.
10. Strandness DE, Priest RE, Gibbons GE. Combined clinical and pathologic study of diabetic and nondiabetic peripheral arterial disease. Diabetes. 1964;13:366–72. https://doi.org/10.2337/diab.13.4.366.
11. Barner HB, Kaiser GC, Willman VL. Blood flow in the diabetic leg. Circulation. 1971;43(3):391–4. https://doi.org/10.1161/01.CIR.43.3.391.
12. Conrad MC. Large and small artery occlusion in diabetics and nondiabetics with severe vascular disease. Circulation. 1967;36(1):83–91. https://doi.org/10.1161/01.CIR.36.1.83.
13. LoGerfo FW, Coffman JD. Vascular and microvascular disease of the foot in diabetes: implications for foot care. N Engl J Med. 1984;311(25):1615–9. https://doi.org/10.1056/NEJM198412203112506.
14. Kucan JO, Robson MC. Diabetic foot infections: fate of the contralateral foot. Plast Reconstr Surg. 1986;77(3):439–41. https://doi.org/10.1097/00006534-198603000-00018.
15. Goldner MG. The fate of the second leg in the diabetic amputee. Diabetes. 1960;9:100–3. https://doi.org/10.2337/diab.9.2.100.
16. Ecker ML, Jacobs BS. Lower extremity amputation in diabetic patients. Diabetes. 1970;19(3):189–95. https://doi.org/10.2337/diab.19.3.189.
17. Robbins JM, Strauss G, Aron D, Long J, Kuba J, Kaplan Y. Mortality rates and diabetic foot ulcers: is it time to communicate mortality risk to patients with diabetic foot ulceration? J Am Podiatr Med Assoc. 2008;98(6):489–93. https://doi.org/10.7547/0980489.
18. Moulik PK, Mtonga R, Gill GV. Amputation and mortality in new-onset diabetic foot ulcers stratified by etiology. Diabetes Care. 2003;26(2):491–4. https://doi.org/10.2337/diacare.26.2.491.
19. Faglia E, Favales F, Morabito A. New ulceration, new major amputation, and survival rates in diabetic subjects hospitalized for foot ulceration from 1990 to 1993: a 6.5-year follow-up. Diabetes Care. 2001;24(1):78–83. https://doi.org/10.2337/diacare.24.1.78.
20. Ikonen TS, Sund R, Venermo M, Winell K. Fewer major amputations among individuals with diabetes in Finland in 1997-2007: a population-based study. Diabetes Care. 2010;33(12):2598–603. https://doi.org/10.2337/dc10-0462.
21. Engel H, Lin CH, Wei FC. Role of microsurgery in lower extremity reconstruction. Plast Reconstr Surg. 2011;127(Suppl 1):228S–38S. https://doi.org/10.1097/PRS.0b013e3182008e12.
22. Mathes S, Nahai F. Reconstructive surgery: principles, anatomy, & technique. St Louis: Quality Medical Publishing; 1997.
23. Gottlieb LJ, Krieger LM. From the reconstructive ladder to the reconstructive elevator. Plast Reconstr Surg. 1994;93(7):1503–4. https://doi.org/10.1097/00006534-199406000-00027.
24. Bennett N, Choudhary S. Why climb a ladder when you can take the elevator? Plast Reconstr Surg. 2000;107(1):283. https://doi.org/10.1097/00006534-200005000-00062.
25. Black CK, Kotha VS, Fan KL, Ragothaman K, Attinger CE, Evans KK. Pedicled and free tissue transfers. Clin Podiatr Med Surg. 2019;36(3):441–55. https://doi.org/10.1016/j.cpm.2019.03.002.
26. Patzakis MJ, Wilkins J, Moore TM. Use of antibiotics in open tibial fractures. Clin Orthop Relat Res. 1983;178:31–5. https://doi.org/10.1097/00003086-198309000-00005.
27. Attinger C. Soft-tissue coverage for lower-extremity trauma. Orthop Clin North Am. 1995;26(2):295–334.
28. Endara M, Ducic I, Attinger C. Free tissue transfer for limb salvage in high-risk patients: worth the risk. Adv Wound Care. 2013;2(2):63–8. https://doi.org/10.1089/wound.2011.0309.
29. Yue DK, McLennan S, Marsh M, et al. Effects of experimental diabetes, uremia, and malnutrition on wound healing. Diabetes. 1987;36(3):295–9. https://doi.org/10.2337/diab.36.3.295.
30. Wattanakit K, Cushman M, Stehman-Breen C, Heckbert SR, Folsom AR. Chronic kidney disease increases risk for venous thromboembolism. J Am Soc Nephrol. 2008;19(1):135–40. https://doi.org/10.1681/ASN.2007030308.
31. Endara M, Masden D, Goldstein J, Gondek S, Steinberg J, Attinger C. The role of chronic and perioperative glucose management in high-risk surgical closures: a case for tighter glycemic control. Plast Reconstr Surg. 2013;132(4):996–1004. https://doi.org/10.1097/PRS.0b013e31829fe119.
32. Gillis C, Wischmeyer PE. Pre-operative nutrition and the elective surgical patient: why, how and what? Anaesthesia. 2019;74:27–35. https://doi.org/10.1111/anae.14506.

33. Ehrl D, Heidekrueger PI, Haas EM, et al. Does cigarette smoking harm microsurgical free flap reconstruction? J Reconstr Microsurg. 2018;34(7):492–8. https://doi.org/10.1055/s-0038-1639377.
34. DeFazio M, Economides J, Anghel E, Tefera E, Evans K. Lower extremity free tissue transfer in the setting of thrombophilia: analysis of perioperative anticoagulation protocols and predictors of flap failure. J Reconstr Microsurg. 2019;35(04):270–86. https://doi.org/10.1055/s-0038-1675145.
35. Wang TY, Serletti JM, Cuker A, et al. Free tissue transfer in the hypercoagulable patient: a review of 58 flaps. Plast Reconstr Surg. 2012;129(2):443–53. https://doi.org/10.1097/PRS.0b013e31823aec4d.
36. Defazio MV, Hung RWY, Han KD, Bunting HA, Evans KK. Lower extremity flap salvage in Thrombophilic patients: managing expectations in the setting of microvascular thrombosis. J Reconstr Microsurg. 2016;32(6):431–44. https://doi.org/10.1055/s-0035-1571249.
37. Attinger CE, Evans KK, Bulan E, Blume P, Cooper P. Angiosomes of the foot and ankle and clinical implications for limb salvage: reconstruction, incisions, and revascularization. Plast Reconstr Surg. 2006;117(7 Suppl):261–93. https://doi.org/10.1097/01.prs.0000222582.84385.54.
38. Janhofer DE, Lakhiani C, Kim PJ, et al. The utility of preoperative arteriography for free flap planning in patients with chronic lower extremity wounds. Plast Reconstr Surg. 2019;143(2):604–13. https://doi.org/10.1097/PRS.0000000000005265.
39. Fischer JP, Wink JD, Nelson JA, et al. A retrospective review of outcomes and flap selection in free tissue transfers for complex lower extremity reconstruction. J Reconstr Microsurg. 2013;29(6):407–16. https://doi.org/10.1055/s-0033-1343952.
40. Janhofer DE, Lakhiani C, Kim PJ, et al. The utility of preoperative venous testing for lower extremity flap planning in patients with lower extremity wounds. Plast Reconstr Surg. 2021;147(4):715e–6e. https://doi.org/10.1097/PRS.0000000000006384.
41. Fernando M, Crowther R, Lazzarini P, et al. Biomechanical characteristics of peripheral diabetic neuropathy: a systematic review and meta-analysis of findings from the gait cycle, muscle activity and dynamic barefoot plantar pressure. Clin Biomech. 2013;28(8):831–45. https://doi.org/10.1016/j.clinbiomech.2013.08.004.
42. Nishimoto GS, Attinger CE, Cooper PS. Lengthening the Achilles tendon for the treatment of diabetic plantar forefoot ulceration. Surg Clin North Am. 2003;83(3):707–26. https://doi.org/10.1016/S0039-6109(02)00191-3.
43. Nishimoto S, Sotsuka Y, Kawai K, Ishise H, Kakibuchi M. Personal computer-based cephalometric landmark detection with deep learning, using cephalograms on the internet. J Craniofac Surg. 2019;30(1):91–5. https://doi.org/10.1097/SCS.0000000000004901.
44. Colen LB, Kim CJ, Grant WP, Yeh JT, Hind B. Achilles tendon lengthening: friend or foe in the diabetic foot? Plast Reconstr Surg. 2013;131(1):37e–43e. https://doi.org/10.1097/PRS.0b013e3182729e0b.
45. Anghel EL, DeFazio MV, Barker JC, Janis JE, Attinger CE. Current concepts in debridement: science and strategies. Plast Reconstr Surg. 2016;138(3):82S–93S. https://doi.org/10.1097/PRS.0000000000002651.
46. Motakef S, Mountziaris PM, Ismail IK, Agag RL, Patel A. Emerging paradigms in perioperative management for microsurgical free tissue transfer: review of the literature and evidence-based guidelines. Plast Reconstr Surg. 2015;135(1):290–9. https://doi.org/10.1097/PRS.0000000000000839.
47. Basci D, Gosman A. Basics of flaps. In: Essentials of plastic surgery. 2nd ed. New York: Thieme; 2014. https://doi.org/10.1201/b16610-6.
48. Bekeny JC, Zolper EG, Fan KL, Evans KK. Composite cutaneous anterolateral thigh flap with rolled fascia Lata for tibialis anterior tendon reconstruction. Plast Reconstr Surg Glob Open. 2020;8(7):e2959. https://doi.org/10.1097/GOX.0000000000002959.
49. Azouz SM, Castel NA, Vijayasekaran A, Rebecca AM, Lettieri SC. Lower-limb reconstruction with chimeric flaps: the quad flap *. Microsurgery. 2019;39(2):182–7. https://doi.org/10.1002/micr.30335.
50. Hollenbeck ST, Woo S, Komatsu I, Erdmann D, Zenn MR, Levin LS. Longitudinal outcomes and application of the subunit principle to 165 foot and ankle free tissue transfers. Plast Reconstr Surg. 2010;125(3):924–34. https://doi.org/10.1097/PRS.0b013e3181cc9630.
51. Tayfur V, Magden O, Edizer M, Atabey A. Anatomy of vastus lateralis muscle flap. J Craniofac Surg. 2010;21(6):1951–3. https://doi.org/10.1097/SCS.0b013e3181f4ee7f.
52. Cavadas PC, Sanz-Jiménez-Rico JR. Use of the extended-pedicle vastus lateralis free flap for lower extremity reconstruction. Plast Reconstr Surg. 2005;115(4):1070–6. https://doi.org/10.1097/01.PRS.0000156154.23630.7A.
53. Hanasono MM, Skoracki RJ, Yu P. A prospective study of donor-site morbidity after anterolateral thigh fasciocutaneous and myocutaneous free flap harvest in 220 patients. Plast Reconstr Surg. 2010;125(1):209–14. https://doi.org/10.1097/PRS.0b013e3181c495ed.
54. Al-Himdani S, Din A, Wright TC, Wheble G, Chapman TWL, Khan U. The medial sural artery perforator (MSAP) flap: a versatile flap for lower extremity reconstruction. Injury. 2020;51(4):1077–85. https://doi.org/10.1016/j.injury.2020.02.060.
55. Koshima I, Nanba Y, Tsutsui T, et al. Superficial circumflex iliac artery perforator flap for reconstruction of limb defects. Plast Reconstr Surg. 2004;113(1):233–40. https://doi.org/10.1097/01.PRS.0000095948.03605.20.
56. Lee YK, Park KY, Koo YT, et al. Analysis of multiple risk factors affecting the result of free flap transfer for necrotising soft tissue defects of the lower extremities in patients with type 2 diabetes mellitus. J Plast Reconstr Aesthetic Surg. 2014;67(5):624–8. https://doi.org/10.1016/j.bjps.2014.01.047.

57. Chen HC, Coskunfirat OK, Özkan Ö, et al. Guidelines for the optimization of microsurgery in atherosclerotic patients. Microsurgery. 2006;26(5):356–62. https://doi.org/10.1002/micr.20252.
58. DeFazio MV, Fan KL, Evans KK. Greater saphenous vein-patch interposition to facilitate flow-sparing microanastomosis of calcified arteries in the distal lower extremity. Plast Reconstr Surg. 2019;144(2):340e–1e. https://doi.org/10.1097/PRS.0000000000005851.
59. Verhelle NAC, Heymans O. How to deal with difficult microsurgical end-to-side anastomoses. Microsurgery. 2005;25(3):203–8. https://doi.org/10.1002/micr.20100.
60. Godina M. Preferential use of end-to-side arterial anastomoses in free flap transfers. Plast Reconstr Surg. 1979;65(6):849. https://doi.org/10.1097/00006534-197964050-00013.
61. Tan BK, Wong CH, Chew W, Hong SW. Use of the slit arteriotomy for end-to-side arterial anastomosis in free-tissue transfers to the extremities. J Plast Reconstr Aesthetic Surg. 2009;62(11):1519–23. https://doi.org/10.1016/j.bjps.2008.05.016.
62. Samaha FJ, Oliva A, Buncke GM, Buncke HJ, Siko PP. A clinical study of end-to-end versus end-to-side techniques for microvascular anastomosis. Plast Reconstr Surg. 1997;99(4):1109–11. https://doi.org/10.1097/00006534-199704000-00029.
63. Black C, Fan KL, Defazio MV, et al. Limb salvage rates and functional outcomes using a longitudinal slit arteriotomy end to side anastomosis for limb threatening defects in a high-risk patient population. Plast Reconstr Surg. 2020;145(5):1302–12. https://doi.org/10.1097/prs.0000000000006791.
64. Kroll SS, Schusterman MA, Reece GP, et al. Timing of pedicle thrombosis and flap loss after free-tissue transfer. Plast Reconstr Surg. 1996;98(7):1230–3. https://doi.org/10.1097/00006534-199612000-00017.
65. Brown JS, Devine JC, Magennis P, Sillifant P, Rogers SN, Vaughan ED. Factors that influence the outcome of salvage in free tissue transfer. Br J Oral Maxillofac Surg. 2003;41(1):16–20. https://doi.org/10.1016/S0266-4356(02)00260-7.
66. Soteropulos CE, Chen JT, Poore SO, Garland CB. Postoperative management of lower extremity free tissue transfer: a systematic review. J Reconstr Microsurg. 2019;35(1):1–7. https://doi.org/10.1055/s-0038-1667049.

32

Advanced Plastic Surgical Reconstruction Options in the Lower Extremity

John M. Felder and Joon Pio Hong

Introduction

For microsurgeons, diabetic foot reconstruction represents an opportunity to provide substantial quality of life and mortality benefits to an often neglected patient population. However, free tissue transfer in diabetics is among the most challenging for a variety of reasons, with a higher risk of failure than in many types of microsurgery. The multifactorial nature of the disease and the inevitable presence of multiple significant medical comorbidities mandate that reconstruction be approached in the context of a multidisciplinary team. Even with a team approach, questions as basic as indications for salvage may be difficult to answer, and much of the literature surrounding microsurgical reconstruction focuses on flap success rates rather than the more complex questions of proper patient selection and meaningful outcomes. Presenting scenarios vary widely in regard to wound types, underlying bony and vascular abnormalities, functional abilities and demands of the patient, complicating medical diseases, social resources, and availability of infrastructure to support complex reconstructive efforts.

This chapter is geared toward the surgeon who already has a strong grasp of these complex issues. *Advanced reconstructive* techniques provide microsurgeons additional tools to tackle challenging and complex cases, as well as tools to reduce the morbidity of reconstruction. A broad palette of options allows the surgeon to be flexible and create elegant solutions that are best suited to the unique circumstance of the patient. Examples of advanced techniques include "supermicrosurgery" (anastomosis involving vessels <0.8 mm in luminal diameter), perforator to perforator anastomoses, superthin flaps, flow-through flaps, and other techniques. Advanced reconstruction requires the surgeon to be able to shift perspectives away from classic dogma when needed to choose the actual best option for the given scenario. Unfamiliar principles such as working with small vessels near the zone of injury may actually provide the simplest, quickest, and least morbid reconstruction to the patient without jeopardizing outcomes. However, judicious use of both old and new principles will be required to obtain consistently excellent outcomes across the spectrum of problems encountered in this challenging field.

J. M. Felder
Division of Plastic Surgery, Department of Surgery, Washington University in St. Louis School of Medicine, St. Louis, MO, USA

J. P. Hong (✉)
Department of Plastic Surgery, Asan Medical Center, University of Ulsan, Seoul, South Korea
e-mail: joonphong@amc.seoul.kr

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_32

Patient Population and Selection

Ninety percent of diabetic foot reconstructions can be accomplished by simple techniques, and only roughly 10% require complex flap reconstruction [1]. Patients needing *microsurgical* reconstruction are often those that have failed traditional wound care or reconstruction and therefore are at high risk for amputation.

Presenting patients are typically middle-aged to elderly, although younger patients with severe diabetes are becoming more common as the global epidemic mounts. Obesity, neuropathy, poor glucose control, peripheral vascular disease, osteomyelitis, cardiovascular disease, kidney disease, and visual and mobility impairment are common. Thus, patient selection typically begins within a pool of patients that are traditionally considered poor candidates for complex or lengthy surgeries. Because of this, proper patient selection is paramount. Unfortunately, because the comorbidities listed above (and the critical details of each—e.g., where exactly is the osteomyelitis or PVD) may occur in a countless number of individual combinations, useful algorithms to guide patient selection do not exist.

The surgeon therefore must consider the pertinent contributions of each of these complicating factors to create a plan with any likelihood of success. This ability can only be gained through experience and multidisciplinary collaboration. It is also advisable that the surgeon be familiar with the principles and practice of amputation surgery, so that the role of properly performed amputations can be included in the decision-making process.

The foremost consideration in patient selection is the current and anticipated level of function of the patient. While some scenarios are clear-cut, such as coverage of a limited area of bone exposure in a younger and active patient, most require careful evaluation to determine if an attempt at salvage will be in the best interest of the patient. For instance, younger and highly active patients with extensive osteomyelitis or arthropathy in which salvage would require sacrifice of the critical bony architecture of the foot will have better function with a transtibial amputation. However, elderly diabetic patients have difficulties putting on a prosthesis without support. In many cases their neuropathy has already limited their hand and finger coordination. In addition, they suffer from diabetic retinopathy. Thus, counterintuitively, salvage to maintain limb length for independent transfers and minimal weight bearing is of benefit to preserve independence (Fig. 32.1). Unfortunately, patients who are much older but very active and who are highly motivated to pursue salvage may at times be too frail to withstand complex surgery, hospitalization, and a prolonged period of healing and rehabilitation. The variations are endless, such that seasoned judgment is required.

Obesity is problematic in terms of limiting flap selection to mostly muscle flaps and increasing the difficulty of surgical dissection. It also tends to increase donor site complications such as seroma, dehiscence, and fat necrosis. Finally, increasing obesity tends to be associated with poorer rehabilitation and ambulation potential.

Poor glucose control has been independently associated with dehiscence in lower extremity diabetic wound closures; thus, involvement of internists and/or endocrinologists is critical [2]. Sensory neuropathy does not affect surgical success rate and is not a contraindication to salvage, but increases the risk of ulcer recurrence [3] and late reconstructive failure. Motor neuropathy is of increasing significance for rehabilitation as involvement moves proximally from the foot into the leg.

Osteomyelitis is a frequent indication for microsurgical coverage but presents a wide spectrum of considerations depending upon the location of the involved bone(s). Skeletal deformities of the foot (e.g., Charcot arthropathy)



Fig. 32.1 Determining candidacy for salvage may be complex. Counterintuitively, less functional patients may be indicated for salvage. A 78-year-old wheelchair-bound diabetic female with ESRD presented with osteomyelitis after failed attempts at partial calcanectomy and closure. Although extensive calcaneal osteomyelitis with a large soft tissue should prompt consideration for amputation in ambulatory patients, in this elderly, debilitated patient, salvage was indicated to preserve length for independent transfers. (**a**) Wound at presentation with desiccated calcaneal bone at base. The patient had undergone a failed attempt at partial calcanectomy with primary closure. (**b**) Radiographs demonstrate a fractured residual calcaneus with osteomyelitis. (**c**) Wound following debridement, antibiotic therapy, and negative pressure wound therapy. Note the granulation from the calcaneal bone, which is an indicator of good blow flow. (**d**, **e**) Stable result at 2 years post-op after coverage with a free vastus lateralis flap and glabrous skin graft from the instep. Anastomosis was end-to-side (ETS) to the posterior tibial vessels

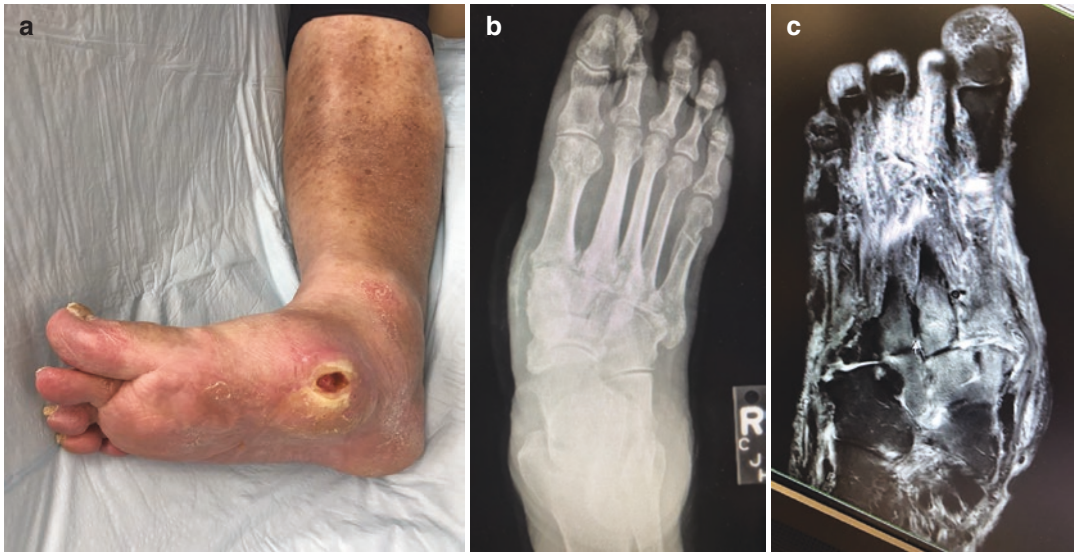


Fig. 32.2 Underlying biomechanical abnormalities and extent of infection must be considered before proceeding with salvage. (**a**) A small wound of the midfoot appears favorable for salvage. (**b**) X-ray demonstrating Charcot arthropathy. (**c**) Magnetic resonance imaging (MRI) demonstrating extensive osteomyelitis of the midfoot. In this case, salvage would not have been appropriate despite the small wound. Below knee amputation was undertaken and the patient returned to ambulation in 8 weeks

may further complicate the feasibility or advisability of salvage (Fig. 32.2). It is useful to consider the foot in thirds, with osteomyelitis and deformities of the forefoot, midfoot, and hindfoot being progressively less feasible for salvage, as destruction of bony architecture (either by infection/debridement or bony collapse) in critical weight bearing joints will lead to a nonfunctional foot. For these reasons, it is important to have a collaborative relationship with orthopedic surgeons, who may be able to extend the indications for salvage with antibiotic spacers, fusions, tendon transfers, and external fixation.

Associated peripheral vascular disease (PVD) is more the rule than the exception for cases requiring microsurgical reconstruction. Classically, in diabetics, this is at the level of the leg trifurcation vessels and is relatively amenable to vascular intervention (Fig. 32.3). However, the high prevalence of associated physical, medical, and social comorbidities such as age, renal failure, and tobacco abuse mean that in reality, vascular disease can be diffuse and very problematic distally in the leg and foot. Milder PVD may be simply an obstacle in recipient vessel selection, but severe PVD associated with tissue loss represents a stage of disease that is much more difficult to treat and associated with high limb loss rates independent of flap success. A close collaborative relationship with vascular surgery is critical.

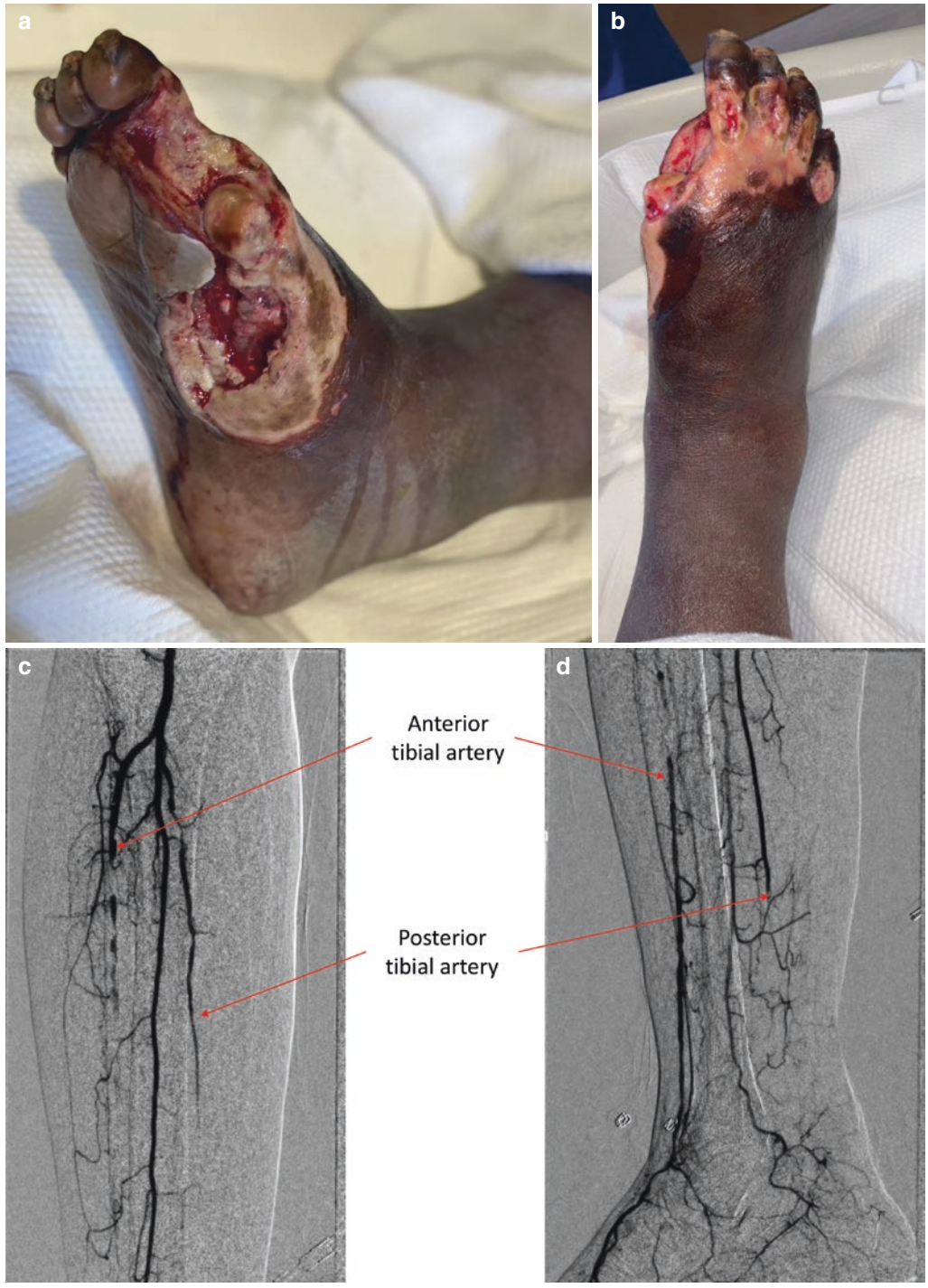


Fig. 32.3 Peripheral vascular disease is a complicating factor in diabetic foot reconstruction that is at play more often than not. Diabetics typically present with trifurcation level (infrapopliteal) disease. (**a**, **b**) A 54-year-old diabetic woman presented with a plantar forefoot ulceration leading to first metatarsophalangeal joint infection and underwent incision and drainage with hallux amputation. (**c**, **d**) Angiography demonstrated chronic total occlusions of the anterior and posterior tibial arteries in the mid-leg. (**e**, **f**) The occlusions of the anterior tibial and posterior tibial arteries were treated with balloon angioplasty, resulting in 3 vessel runoff

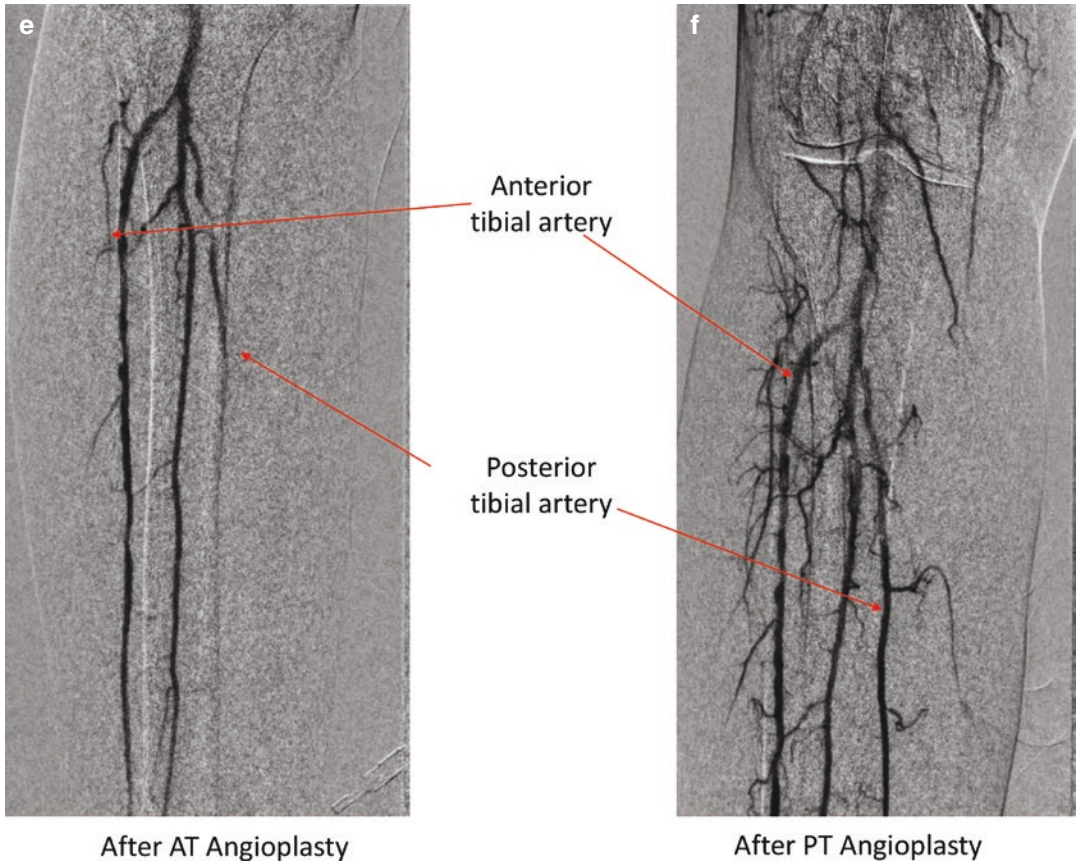


Fig. 32.3 (continued)

Pre-operative Surgical Evaluation

Preoperative Counseling

Patients requiring microsurgical reconstruction are often those that have failed traditional wound care or reconstruction and therefore are at high risk for amputation. In most cases, patients should be frankly counseled that they may be at the point of facing amputation if salvage is unsuccessful, and that diabetic foot infections themselves are a marker for increased risk of mortality. Patients should understand that the wound is a serious warning bell, and that even successful reconstruction is not to be taken lightly. Patients should be realistically counseled about the surgeon's success rate in challenging cases such as in the presence of advanced peripheral vascular disease. The realistic success rate of microsurgical diabetic foot reconstruction is markedly lower than in most other applications of microsurgery. Even in successful cases, it is the rule rather than the exception that minor complications such as areas of delayed wound healing will occur.

Because of the frequent presence of advanced medical comorbidities, the surgeon must consider patient safety to a greater degree than in most other applications of microsurgery. Safety requires a thorough medical workup, as detailed below.

Finally, the surgeon must keep in mind that healing from microsurgical reconstruction of the diabetic foot generally means a 6–12 week period of non-weightbearing on the foot. Therefore, patients should be evaluated for willingness to undergo a lengthy period of non-

weightbearing, as well as for *noncompliance*. Patients expected to be noncompliant with postoperative activity restrictions are not candidates for reconstruction.

Preoperative History

A history of any prior wound or surgery (including amputations) of either lower extremity should be sought. A history of prior vascular intervention is critical to obtain. *Specific attention should be paid to determining the patient's level of ambulatory function*. Previous history of thrombophilia, stroke, unexplained miscarriages, or venous diseases should be sought. Specific attention must be paid to use of anticoagulants and recommendations obtained for perioperative anticoagulant therapy. Many patients will be anticoagulated either for cardiac reasons or owing to lower extremity vascular surgery.

Preoperative Examination

The wound is assessed carefully by measuring its size and depth and is then photographed. A metallic probe is used to assist in the evaluation of the depth of the wound. If the probe touches bone, there is an 85% chance that osteomyelitis is present. If tendon is involved, the infection is very likely to have tracked proximally or distally. Note the presence and extent of cellulitis and differentiate from dependent rubor. Antibiotic therapy should be initiated after deep cultures are performed [1].

A critical error to avoid is to simply consider the wound itself. Instead, the surgeon must consider the *extent* of the underlying disease processes at play (vascular, bony, neuropathic, osteomyelitis). Plastic surgeons are often called upon to treat wounds. However, plastic surgeons may not be used to the idea that a fundamental, progressive, underlying change of the foot is going on and must be evaluated and treated as a whole in order to obtain meaningful success.

Assessment for peripheral vascular disease is paramount. Femoral, popliteal, and pedal pulses should be palpated. Pencil Doppler examination of blood flow to the foot is the cornerstone of vascular examination and should be performed in all cases, even when a pulse is palpable. Specific effort should be made to determine whether flow is antegrade or retrograde in both the dorsal and plantar systems, via selective occlusion of arteries [4].

Preoperative Studies

X-ray examination of the foot should be performed in all cases to assess for osteomyelitis or biomechanical deformities such as Charcot neuroarthropathy that may impact reconstruction. MRI may be useful when the presence of osteomyelitis is uncertain, or when `the exact extent of osteomyelitis will have implications for salvage (Fig. 32.2). X-ray images often will also reveal valuable information regarding the extent of arterial calcification within the foot and ankle (Fig. 32.4).

When free flap reconstruction is being planned, and unless there are multiple palpable pulses, traditional angiography should be obtained rather than computed tomography or magnetic resonance imaging. Traditional angiography provides superior visualization for recipient vessel planning and avoids artifacts caused by vessel calcification, which is frequent in this population (Fig. 32.4). When pulses are palpable and there is low concern for significant arterial calcification, such as in younger diabetic patients, CT angiogram is an adequate screening examination that has the added benefit of being able to visualize perforators (e.g., anterolateral thigh, circumflex iliac) and assist with planning the flap harvest. If abnormalities are noted on the CT angiogram, then formal angiography should be pursued.

Ultrasound to exclude the presence of active deep venous thromboses is advisable [5]. Duplex ultrasound should be used to map recipient vessels for perforator to perforator type anastomoses [6].



Fig. 32.4 Arterial calcification is a common complication factor in diabetic foot reconstruction and can lead to technical difficulties with anastomosis, as well as signal a more advanced state of disease. Plain radiographs should be assessed for the presence and extent of vascular calcifications. (**a**) Calcification of the first dorsal metatarsal and digital arteries can be seen. (**b**) Extensive calcifications of the anterior tibial, posterior tibial, dorsalis pedis, and lateral plantar arteries can be seen

In addition to standard preoperative laboratory testing, nutrition labs (albumin, prealbumin) are important to obtain. Hemoglobin A1C may help define whether the patient is likely to be compliant. In the setting of osteomyelitis, baseline and subsequent ESR/CRP are useful to help tailor the length of antibiotic therapy and determine suitability for delayed bony procedures such as fusion or arthroplasty. Microbial cultures are mandatory prior to reconstruction.

Anemia is common, due to chronic disease, kidney disease, and other comorbidities. Transfusion may be needed when Hgb < 10 for cardiac reasons or if blood loss is anticipated (e.g., in anticoagulated patients).

Preoperative Consultations

Appropriate interdisciplinary consultations are essential for patient safety. Safety profiles for lengthy surgery should be determined by colleagues in internal medicine, cardiology, or anesthesia. Internal medicine or endocrinology should be involved preoperatively for tight perioperative glycemic control. Nephrology may be needed for co-existing kidney disease, dialysis, and adrenal insufficiency. Operative planning may need to account for hemodialysis schedules, which can also affect administration of blood products and antibiotics. Infectious diseases consultation is recommended for all patients, given the frequent need to consider drug interactions, extended courses of intravenous antibiotics, and microbial antibiotic resistance. Vascular surgery should be consulted for angiography and, frequently, for preoperative vascular intervention.

Preparation for Reconstruction

Before consideration of reconstruction, it is imperative to achieve adequate debridement. All necrotic material, foreign material, and microorganisms must be removed while delicately spar-

ing intact tissue to maintain substrate for healing. Cultures should be taken before and after debridement and used to guide antibiotic therapy. Flap reconstruction should be delayed until negative post-debridement cultures are obtained. Negative pressure wound therapy, with or without fluid instillation, can be helpful in managing the wound between debridements [1].

In cases where vascular disease has impeded healing, vascular intervention should be pursued before debridement and reconstruction. The periwound tissues must be capable of tolerating debridement and healing to the flap. If vascular intervention is required, the patient should be referred to a vascular surgeon who *specializes* in distal revascularizations, as bypass surgery is clinically still superior to endovascular revascularization. Ideally, this is the same person who performed the preoperative arteriography. Angiosome-specific reperfusion is preferable when possible because this generally provides better options for flap recipient vessels adjacent to the wound. When impossible, then revascularization should target the best outflow available [7].

After successful bypass surgery, it then takes 4–10 days to maximize the periwound tissue oxygen level. If angioplasty is performed, then it may take up to 30 days for tissue oxygen saturation to reach maximal levels. Definitive debridement and aggressive wound care should follow as soon as signs of revascularization occur, such as new granulation and so forth. Wet gangrene, ascending cellulitis, and necrotizing fasciitis demand immediate debridement.

Timing of reconstruction in relation to revascularization is critical when pursuing the supermicrosurgery or perforator to perforator approach. Use of smaller recipient vessels near to the wound may be dependent upon the continued patency of a recent angioplasty. Because up to 60% of angioplasties may be occluded within 2–3 months, capitalizing on the window of reperfusion shortly following an angioplasty is important.

Another factor to consider is the healing potential of the surrounding tissues in the setting of PVD. Even with a healthy flap, failure may occur if the surrounding tissues are inadequately perfused. In this scenario, two adjuncts may be helpful. The first is preoperative hyperbaric oxygen therapy (HBOT). HBOT may be begun immediately following reperfusion surgery while awaiting demarcation of viable tissues. The goal is to reach a $TCP0_2$ of 40 mmHg, which has been shown in multiple studies to promote angiogenesis from the surrounding tissues into the flap.

The second option is to employ aggressive debridement according to angiosomes. This is not necessary in well-perfused limbs. However, in the setting of severe PVD manifesting as a wound within a defined angiosome, the entire ischemic angiosome surrounding the wound should be resected, such that the remaining surrounding angiosomes are all adequately perfused for healing. This requires judgment and confidence on the part of the surgeon, as the wound may be significantly enlarged as a result. Failure to completely debride the ischemic angiosome can result in tissue edges that will not heal to the flap or result in marginally perfused tissue that is susceptible to infection, which can also be a source of late flap failure.

Partial foot amputation should be considered when approaching more extensive cases of tissue loss or osteomyelitis. This is because good biomechanical function is the goal of reconstruction. This is a frequent scenario in the forefoot, and flaps can often be combined with partial foot amputations (such as the transmetatarsal amputation) for meaningful salvage (Fig. 32.5).



Fig. 32.5 Forefoot wounds with involvement of the toes in patients with peripheral vascular disease (PVD) should be considered for conversion to a transmetatarsal amputation (TMA), with flap coverage if needed. This provides a stable, definitive level of amputation that is functional for ambulation and does not risk the formation of future toe wounds with progression of PVD. (**a**–**c**) The patient from Fig. 32.3 after revascularization and debridement with first ray resection. Although perfused, the toes have significant wounds with tendon exposure that would require complex coverage. They are at significant risk of wound recurrence. (**d**) Conversion to a TMA was performed, and the first ray amputation defect covered with a gracilis flap anastomosed end-to-end to the first dorsal metatarsal artery and subcutaneous vein. The gracilis muscle flap was chosen rather than a skin flap because the patient required angioplasty for reperfusion of the foot. Muscle flaps provide a larger capillary bed and lower outflow resistance, which may assist with maintaining patency of vascular interventions. (**e**, **f**) Stable, healed TMA at 1 year post-op. The patient returned to ambulation without assistive devices and had no recurrence of wounds

Algorithmic Approach to Reconstruction

Although diabetic foot wounds can be complex with many reconstructive considerations, a simple 3-step algorithm is a good starting point for the advanced microsurgical approach. The algorithm assumes the operator is comfortable with any flap type and focuses on choosing the best reconstruction for the particular defect based on three factors:

1. Consider the wound and the reconstructive requirements.
2. Review angiography or other vascular imaging (e.g., ultrasound) and *commit to a choice of recipient vessels*, using the best-available vessels.
   (a) If there is no significant PVD and high-quality vessels are available *adjacent to the wound*, these should be chosen preferentially, regardless of their size, to decrease operative morbidity.
   (b) If severe PVD is present or no suitable small vessels are adjacent to the wound, major recipient vessels should be chosen regardless of their distance from the wound.
3. Choose the flap based on:
   (a) The *appropriate pedicle length* from the chosen recipient vessels to the wound and
   (b) The reconstructive requirements of the wound (e.g., thick/thin skin, weight bearing or not, dead space, outflow resistance, etc.)

The following sections deal with each of these considerations in turn. The presented cases will also emphasize this algorithm.

Types of Wounds and Defect-Specific Considerations

The foot is a specialized weight bearing structure and enough of its critical components must be intact if functional ambulation is the goal. This includes the bony architecture, specialized glabrous skin, protective sensation, vascular perfusion, and thin contour that allows footwear.

Diabetic foot wounds can present with an endless variety of involvement of each of these components [8]. This chapter will focus on common examples, organized by forefoot, midfoot, hindfoot, ankle, and massive wounds. The examples considered will be exclusively those that require microsurgical reconstruction. It should be recognized by the reader that local flap alternatives may exist and be preferable in some of the scenarios discussed, but their inclusion is beyond the scope of this chapter [9, 10].

Forefoot Wounds

The forefoot is a relatively privileged area in that significant bony sacrifice can be made while preserving good function. This is important, as many forefoot wounds that reach the point of requiring free tissue transfer for salvage will involve osteomyelitis. However, the forefoot also has the significant downside of being the area most affected by peripheral vascular disease. Thus, patients with good blood flow are often high priority candidates for salvage despite osteomyelitis and soft tissue loss. Conversely, patients with the same wound and significant PVD are generally poor candidates for salvage.

Generally, acral forefoot wounds such as toe infections or osteomyelitis of the toes can be treated with limited amputation of the involved digits, or fillet flaps. We have reported reconstruction of toe or webspace defects with superthin flaps (e.g., superficial circumflex iliac artery perforator—SCIP, posterior interosseous artery perforator—PIA) connected to the digital vessels (Figs. 32.6 and 32.7) [11, 12]. Use of these techniques must be carefully considered against the more traditional options of toe amputation or fillet flap due to the reliability of these traditional procedures for resolution and prevention of recurrence. However, the goal of "advanced reconstruction" is to be able to provide new solutions that are function-sparing and more

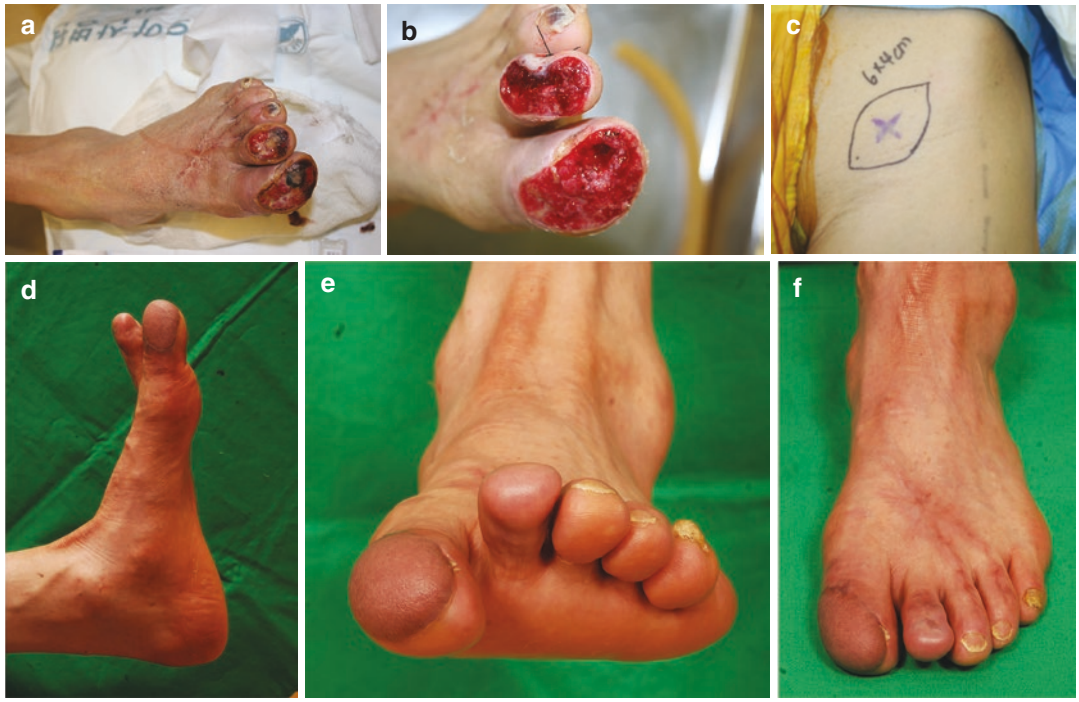


Fig. 32.6 An example of "advanced reconstruction" is to utilize low-morbidity free flaps to prevent even minor levels of amputation, such as toe amputations. Flaps can be used in combination with simpler methods such as local flaps when appropriate. (**a**) A 65-year-old diabetic male presented with chronic osteomyelitis of the first toe and small defects of the first and second toes. After debridement, a SCIP flap was used to reconstruct the first toe. second toe, fillet flap was used. Free flap used Digital artery end-to-side and superficial vein. Let me know your thoughts. (**b**) The wounds after debridement. (**c**, **d**) A superficial circumflex iliac artery perforator (SCIP) flap was used to reconstruct the great toe defect, with end-to-side arterial anastomosis to the digital artery and end-to-end venous anastomosis to a superficial vein. A fillet flap was used to close the second toe defect. (**e**, **f**) Final appearance

elegant than ablative techniques. And so, if the surgeon is capable of performing such reconstructions with minimal morbidity, we advocate their use.

Dorsal forefoot wounds, such as those with exposed tendon or bone, generally result from infection or unintentional injury and subsequent debridement. Dorsal or medial/lateral foot wounds are the most favorable for reconstruction, as many options exist for flap coverage, and soft tissue coverage alone generally suffices, without the need for any specialized considerations. The anterior tibial vascular system is easily accessible throughout the dorsum of the foot, for use as convenient recipient vessels. The SCIP flap excels in providing dorsal foot reconstruction and is a workhorse in this regard (Fig. 32.8). Other fasciocutaneous flaps elevated at the suprascarpal plan (e.g., ALT) also work well (Fig. 32.9).

Combined wounds of the toes and dorsal foot should be strongly considered for transmetatarsal amputation (TMA). An excellent indication for a flap is for dorsal foot coverage to allow salvage of a transmetatarsal amputation with intact plantar skin (Figs. 32.5 and 32.10).

Plantar wounds of the forefoot are either simple or highly problematic. These tend to occur as pressure ulcers related to altered weight bearing patterns in the diabetic foot. Biomechanical changes such as tendon contracture or arthropa-



Fig. 32.7 This case demonstrates use of supermicrosurgery for toe salvage as well as superthin flap for achieving thin contour at the ankle. (**a**, **b**) A 62-year-old male with a history of diabetes and smoking presented after a chemical burn involving the distal leg, medial ankle, dorsal forefoot, and medial first MTP joint. (**c**, **d**) Initial attempts to manage the burns with excision and grafting failed, due to a failure to consider the vascular status of the limb. The wounds converted to wet gangrene. (**e**) Angiography demonstrated a short segment chronic total occlusion of the proximal popliteal artery, which responded to angioplasty. The patient was placed on aspirin, clopidogrel, and heparin by vascular surgery following the angioplasty. (**f**) The wounds following revascularization and debridement with exposure of toe extensor tendons, ankle extensor tendons, and tibial bone. (**g**) The toe wounds were reconstructed with a posterior interosseous artery (PIA) free flap anastomosed end-to-side to the second toe digital vessel, with venous anastomosis to a superficial vein. (**h**) A suprascarpal ALT flap was used to cover the ankle and leg defect. (**i**) In cases where anticoagulation cannot be held, it can be beneficial to loosely inset the free flap so that bleeding can drain from beneath the flap as seen here. The patient is then returned to the operating room on postoperative day 5–7 for definitive closure when bleeding risk has passed. (**j**, **k**) Healed flaps at 3 months post-op with good contour for footwear



Fig. 32.7 (continued)



Fig. 32.8 The SCIP flap is a workhorse in diabetic foot reconstruction and excels at providing thin coverage for the dorsal foot. A 55-year-old female presented with bilateral diabetic foot wounds, including (**a**) a dorsal foot wound with dry gangrene of the toes on the right and (**b**) a posterior ankle wound on the left with exposure of the Achilles tendon and an equinus contracture. Again the cases you shared with me were beautifully done using a superthin ALT. Here is a case for the chapter if you decide to use them. A 55-year-old female patient with bilateral DM foot. Right foot with exposed tendon and necrosis of the toes. Covered with SCIP flap by end to side on the dorsalis pedis artery. Left foot with chronic ulcer that ended in tightening of the Achilles and tendon exposure. One stage Achilles lengthening and ALT free flap end to side on the posterior tibial artery. Both wounds were reconstructed on the same day all at once. This case shows the importance of orthoplastic thinking and approach. The follow-up at 3 years shows good function and coverage. (**c**) The right foot wound was treated with first and second toe amputation, followed by debridement of the dorsal foot wound and coverage with a SCIP flap. (**d**, **e**) the left ankle wound was treated with open lengthening of the Achilles tendon to treat the contracture and immediate coverage with an ALT flap. (**f**, **g**) Healed result at 3 years demonstrating good function and coverage. This case shows the importance of the orthoplastic thinking and approach, respecting biomechanical abnormalities as well as soft tissue coverage



Fig. 32.8 (continued)

thy combine with loss of protective sensation and susceptibility to tissue injury caused by peripheral vascular disease. The result is a callous or ulcer that then becomes infected, frequently leading to osteomyelitis of the metatarsophalangeal joints. It is critical to seek the underlying *biomechanical* mechanism for these wounds and correct it. Most commonly, this is an *equinus contracture* of the Achilles tendon, and Achilles tendon lengthening must be performed along with reconstruction, or else early recurrence is certain [13, 14]. Metatarsophalangeal joint resection, metatarsal head resection, or even in situ metatarsal neck osteotomy may be required to remove infection or pressure points and are well-tolerated biomechanically. Those wounds that can heal with biomechanical correction and traditional wound care are considered simple. Wounds that are severe enough to threaten the foot even with biomechanical correction (e.g., extensive osteomyelitis, extensive soft tissue loss, and particularly those associated with PVD) require advanced reconstruction.

Reconstruction of plantar forefoot wounds is indicated because, if successfully reconstructed, normal ambulation can be restored. Unfortunately, they are also highly challenging to reconstruct with free tissue transfer. This is because they are the furthest from accessible large vessels at the ankle, and management of recipient vessels and pedicle length become challenging. "Workhorse" flaps must have a very long pedicle (12+ cm) to reach from the posterior tibial vessels at the ankle to the plantar ball of the foot (Figs. 32.11, 32.12 and 32.13). Conversely, the use of short-pedicle flaps such as the SCIP can be limited by absence



Fig. 32.9 The suprascarpal ALT is an alternative option to provide thin dorsal foot coverage for larger wounds. A 41-year-old diabetic man presented with wet gangrene stemming from a plantar ulcer beneath the fifth MTP joint. (**a**) He underwent amputation of the second-fifth toes and extensive dorsal foot debridement, removing much of the dorsalis pedis angiosome. (**b**) Diagnostic angiogram demonstrated 3 vessel runoff to the foot. (**c**) A suprascarpal ALT flap was used for reconstruction, with end-to-end anastomosis to the distal anterior tibial artery. End-to-end anastomosis to major vessels of the leg and foot should rarely be performed in patients with diabetes. However, in cases where the wound encompasses the entire distal angiosome, it may be appropriate. (**d**) The use of drains is critical when reconstruction with superthin skin flaps is performed. The thin flaps are very vulnerable to injury by pressure from underlying fluid collections. In this case, despite the use of closed-suction drainage, a seroma formed that threatened to compromise the proximal flap integrity. The flap recovered with prompt drainage. (**e–g**) Healed and stable result at 1 year post-op. The contour was appropriate for normal diabetic shoes without any revision surgery



Fig. 32.9 (continued)



Fig. 32.10 Dorsal foot coverage with a thin flap to allow TMA closure is a strong indication for a free flap, because the TMA level of amputation is highly functional for ambulation. The SCIP flap excels in this context. This flap has the advantage of thin, pliable coverage, with minimal pedicle dissection. (**a**) A 55-year-old active diabetic man presented with a necrotic dehiscence of a TMA site, with adequate plantar skin for weight bearing, but inadequate dorsal skin for bone coverage. (**b**) Result at 6 months post-op following coverage with SCIP flap. Terminal distal vessels were used as recipients: the flap artery was anastomosed to the first dorsal metatarsal artery (FDMA) and the superficial circumflex iliac vein (SCIV) to the medial marginal vein, within 1 cm of the wound edge. The patient returned to ambulation at 6 weeks post-op

of suitable recipients immediately adjacent to the wound, particularly in the presence of concomitant PVD. Further, thin flaps such as the SCIP have lower capacity for dead space obliteration and weight bearing durability. Partial resection of metatarsals and phalanges is commonly necessary in the setting of osteomyelitis and creates significant dead space within the wound that must be addressed.

Strategies to combat these challenges include use of flaps with very long pedicles, components that adequately address dead space, and components such as thick skin or fascia to add durability for weight bearing. Flaps such as the partial medial rectus (Fig. 32.11), TDAP (thoracodorsal artery perforator) (Fig. 32.12), and radial forearm (Fig. 32.13) can be harvested with very long pedicles to provide reliable long-term inflow from



Fig. 32.11 Reconstruction of plantar forefoot wounds is the most challenging scenario in diabetic foot reconstruction but is indicated because of the possibility of restoring a foot with normal function. (**a**) An ischemic neuropathic diabetic plantar forefoot ulcer caused by equinus contracture and severe PVD. The patient was status post remote popliteal to posterior tibial artery bypass but developed stenosis of the bypass origin and progression of intrapedal disease. Angioplasty of the bypass origin was performed to restore inflow. (**b**) In the setting of ischemia, robust flow from the ankle is desirable. A flap with a very long pedicle is needed, and the surgeon must manage the intervening tissue without tunneling. In this case, the partial medial rectus flap was chosen to allow length extension of the inferior epigastric pedicle by dissection into the muscle. Rectus fascia was included to add durability to the weight bearing surface of the foot. The flap was anastomosed end to side to the distal extent of the bypass graft. A trough was created along the medial glabrous junction of the foot for the pedicle to lay in. (**c**) Options for coverage of the exposed pedicle include skin grafting directly onto the pedicle. Skin undermining to allow closure should not be performed in the setting of PVD. (**d**, **e**) Outcome at 3 years post-op

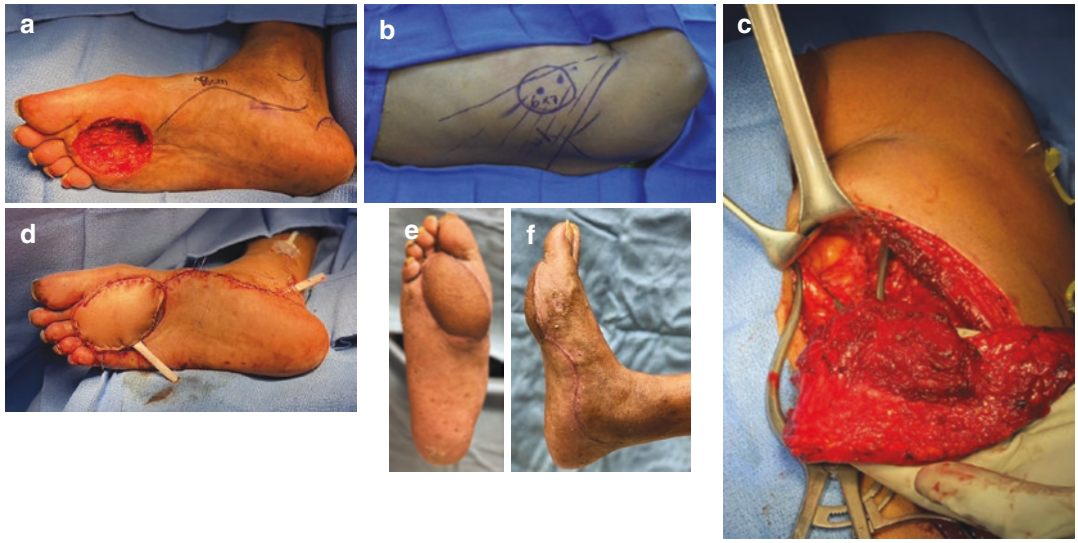


Fig. 32.12 The thoracodorsal artery perforator (TDAP) flap provides another option for plantar forefoot coverage. The TDAP flap has the advantages of thick skin and a long pedicle for reach to the forefoot. (**a**) This defect resulted from squamous cell carcinoma excision in a diabetic man without PVD and resulted in exposure of the second-fourth metatarsal heads in a critical area of weight bearing. An incision is designed along the glabrous junction to allow inset of the pedicle between the recipient vessels at the ankle and the wound in the distant plantar forefoot. (**b**) The TDAP flap is designed centered preferentially around the most distal perforator in order to achieve maximal pedicle length. (**c**) Although not necessary for perfusion, a small portion of the muscle can be included around the perforator to assist in dead space obliteration while still maintaining a thin flap at the skin level. (**d**) The flap was anastomosed end-to-end to the medial plantar vessels beneath the abductor hallucis. The medial plantar vessels can be considered minor vessels in patients without PVD and are appropriate for end-to-end anastomosis. The subcutaneous tissue and fascia beneath the glabrous junction incision are removed in a 1 cm swath to create room for the pedicle. An implantable Doppler probe is placed around the recipient vein. The glabrous junction incision is carefully and loosely closed unless or until the venous signal is lost. In this case, sutures in areas that were too tight to close were placed loosely and then tied at the bedside on postoperative day 7. (**e**, **f**) Healed flap at 6 months

the posterior tibial vessels at the ankle. Generally speaking, the pedicle cannot be completely covered by the flap, and it is necessary to create a trough between the anastomosis and wound and cover the flap vessels with skin graft, biologic matrices, or carefully planned chimeric components of the flap (Fig. 32.11). In patients with normal blood supply and good tissue quality, the skin edges of the trough can occasionally be undermined enough to close over the pedicle without tension, although this must be done carefully while listening for loss of venous Doppler signal. More often, we place sutures loosely and delay closure to 1 week post-op at the bedside, once the pedicle has had time to fibrose and develop resistance to compression (Fig. 32.12). Skin edges should never be undermined in patients with PVD. Tunneling of flap pedicles on the dorsal and lateral foot is possible, although risky from the point of view of venous compression. Tunneling of flap pedicles on the plantar foot is not generally possible.

Severe plantar forefoot wounds also present a challenge for salvage of the partial foot with a transmetatarsal amputation. This is because integrity of the distal plantar skin is necessary to close a traditional TMA that will withstand the weight bearing demands of the foot. Because the TMA is a highly functional level of amputation, attempts to salvage a TMA with distal plantar reconstruction are warranted (Fig. 32.14) [15].



Fig. 32.13 Reconstruction of plantar forefoot wound with long-pedicle free flaps—radial forearm flap. (**a**, **b**) A diabetic man with neuropathy and severe PVD presented with a lateral plantar forefoot ulcer and dorsal toe wounds. (**c**) After revascularization, a radial forearm flap was designed to cover the plantar and critical dorsal defect at the first metatarsophalangeal joint capsule. (**d**) The flap was harvested with a very long pedicle to reach the plantar forefoot through a trough cut into the medial glabrous junction. Anastomosis was performed end to side to the posterior tibial artery at the ankle. Anastomosis to major vessels at the ankle was performed because of the severity of the PVD. The distal venous arch of the foot was arterialized end to side to the radial artery to improve flow to the ischemic toes. (**e**, **f**) Healed flap at 2 months. The patient initially dehisced his flap due to inattention in the early postoperative period. A total contact cast was then used to allow delayed healing. (**g**) Upon resumption of ambulation, the ulcer began to recur due to uncorrected prominence of the third and fourth metatarsal heads. Attention to biomechanics with adequate bony resection before reconstruction would have prevented this complication. The ulcer resolved with Achilles tendon lengthening



Fig. 32.14 Use of flaps with long pedicles for plantar forefoot reconstruction: when plantar coverage is needed to salvage a TMA, the TDAP is a good choice because of its thick skin and long pedicle. (**a**) Salvage of a TMA defect with significant plantar tissue loss. (**b**) Initially, reconstruction was performed with a SCIP flap to the distal FDMA vessels. (**c**) The flap covered the distal bone stumps, but provided inadequate coverage of the plantar surface, with a need for skin grafting that broke down with weight bearing. (**d**) Distal recipient vessels in the plantar forefoot (e.g., for another SCIP flap) are relatively poor, and therefore a TDAP flap was chosen with a long pedicle created by intramuscular dissection. The pedicle had adequate reach for anastomosis to the PTA vessels. The patient did not have ischemic disease, and so the incision to accommodate the pedicle could be undermined and closed gently over the pedicle without creating compression. (**e**, **f**) Healed SCIP/TDAP on left allowed return to normal ambulation without assistive devices (the patient also had reconstruction of a complex TMA defect on the right with a latissimus myocutaneous flap)

Midfoot Wounds

Dorsal wounds of the midfoot, as with the forefoot, are favorable for reconstruction, with few functional implications. Coverage should be thin, so as to allow for fitting into footwear. The SCIP, PIA, and suprascarpal ALT flaps (Figs. 32.8 and 32.9) are excellent options here.

Plantar midfoot wounds frequently result from biomechanical abnormalities such as Charcot arthropathy and must be carefully evaluated for underlying cause before considering reconstruction (Fig. 32.2). Uncorrectable Charcot (or similar biomechanical abnormality) will create a high likelihood for recurrence of the ulcer. Infected Charcot arthropathy (osteomyelitis) should prompt strong consideration for amputation, as removal of bones of the midfoot generally leads to worsening biomechanical abnormalities that affect ambulation negatively. Scenarios where salvage is most indicated for the plantar midfoot are defects limited to soft tissue that result from infection or trauma, with the underlying skeletal structure intact. Instances of underlying skeletal abnormality that can be corrected to preserve ambulation (e.g., treatment of Charcot arthropathy with triple arthrodesis) are also good indications for soft tissue reconstruction [16–18]. Finally, occasionally, salvage in the setting of biomechanical abnormalities and infection may be reasonable if the goal is not ambulation, but length preservation for transfer (Fig. 32.15).

Hindfoot Wounds

Hindfoot generally refers to the plantar heel, as dorsal and lateral defects at this level will be of the ankle. Defects are commonly the result of neuropathic ulceration and infection. Plantar heel reconstruction has the opposite positive and negative considerations as forefoot reconstruction.

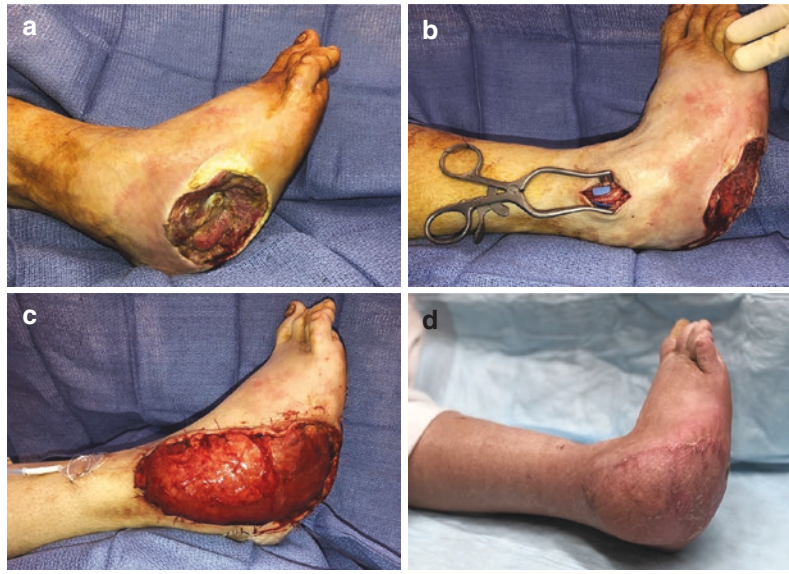


Fig. 32.15 Reconstruction of severe midfoot defect. (**a**) A nonambulatory, wheelchair-bound, morbidly obese diabetic female with leukemia, a contralateral BKA, and ankle varus deformity resulting from chemotherapy-induced peroneal neuropathy presented with a complex lateral midfoot wound resulting from osteomyelitis of the fifth metatarsal. Reconstruction was indicated only in an attempt to preserve limb length for independent transfers. For an ambulatory or healthier patient, amputation would have been a more functional result. (**b**) Anastomosis was to the terminal perforating branch of the peroneal vessels, with resection of the remaining intervening angiosome of the wound. (**c**) The gracilis flap was chosen due to the need for obliteration of extensive dead space, and an ETE anastomosis was performed given the terminal position of the vessels with respect to the wound angiosome. (**d**) With a healed wound and a brace, the patient was able to use the leg for transfer in and out of a wheelchair

Blood supply is most likely to be preserved or accessible, while bone sacrifice is of high functional consequence. Thus, osteomyelitis of the calcaneus requiring significant bony resection, regardless of vascular status, should prompt strong consideration for amputation, as ambulatory function will be compromised (Fig. 32.16). Exceptions, again, are patients who are minimally or nonambulatory and require maximal limb length preservation for independent transfer (Fig. 32.1). In ambulatory patients where the extent of calcaneal osteomyelitis is limited and a limited partial calcanectomy can be performed that will preserve functional ambulation, salvage is indicated.

Isolated wounds of the medial, lateral, and posterior heel without osteomyelitis are generally excellent indications for reconstruction (Fig. 32.17). For wounds of the plantar heel, consideration should be given to using a flap with thicker skin, such as gluteal and thoracodorsal artery perforator flaps, or flaps from the circumflex scapular system. Muscle can be used to cover the heel, and conforms well, but has the propensity to atrophy, allowing the calcaneal tuberosity to erode through the flap with time. A useful technique is to resect the tuberosity of the calcaneus when approaching plantar heel reconstruction in order to prevent this delayed erosion [19].

Reconstruction of heel wounds in the ischemic foot is a challenging scenario with a higher failure rate than elsewhere in the foot. The heel is a watershed area, which normally has a dual supply from the posterior tibial and peroneal arteries. However, in advanced PVD, the anterior tibial artery may be the only supply to the foot. Therefore, when debriding according to the angiosome concept, two angiosomes may need to be debrided, resulting in a very large defect. The success rates of heel reconstruction are markedly higher when at least one of the native vessels (PT or peroneal) is intact. When only the AT artery is intact, reconstruction has a high chance of failure. Surgeons must examine the preoperative angiogram with these considerations in mind before deciding on reconstruction [20].

Ankle Wounds

Generally, an attempt at reconstruction should always be made for ankle wounds. Good options for bony fusion procedures or long-term antibiotic spacer placement make even infected arthropathy of the ankle relatively salvageable compared to the midfoot or plantar heel. Easy access to three distinct recipient vessel systems provides a hospitable environment for free tissue transfer. Thin skin coverage is the ideal reconstruction at the ankle, and flaps such as the SCIP, suprascarpal ALT (Figs. 32.7, 32.8), suprascarpal SIEA (Fig. 32.18), PIA, distal lateral arm (Figs. 32.19 and 32.20), and radial forearm (Fig. 32.21) fit the defect requirements nicely. Muscle flaps are an alternative that provide thin coverage by atrophy.

Common scenarios requiring coverage at the ankle are posterior defects involving the Achilles tendon (Figs. 32.8, 32.17, 32.18 and 32.20), anterior defects related to failed arthroplasty or fusion procedures (Fig. 32.21), and lateral ankle defects related to vascular (frequently venous) disease or prior surgery (Fig. 32.19).

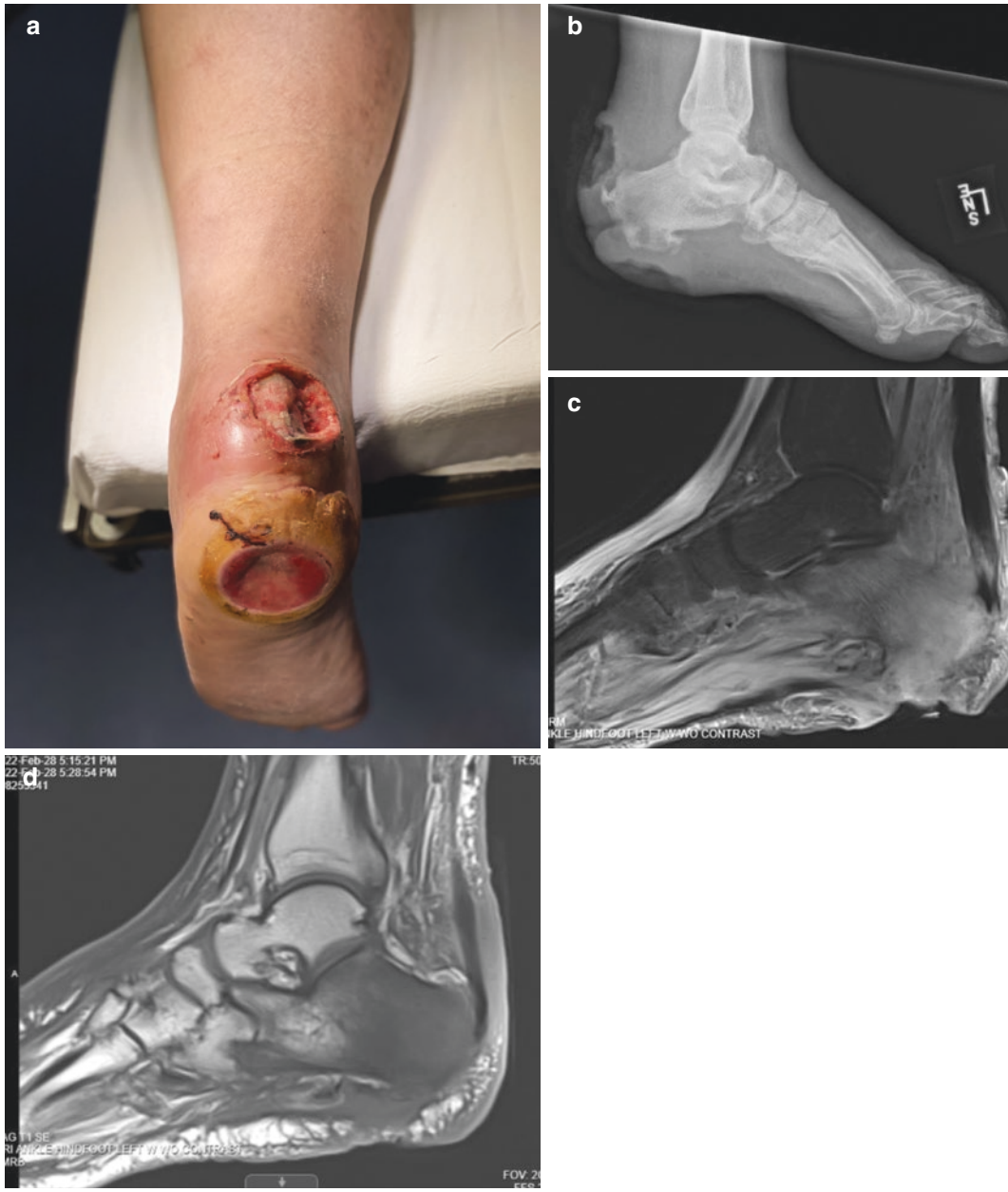


Fig. 32.16 Patients who are strong ambulators but have extensive osteomyelitis of the calcaneus should be strongly considered for below knee amputation, regardless of the wound size or vascular status. (**a**) A 46-year-old diabetic man with a 2 year history of a chronic plantar heel ulcer with osteomyelitis developed extension of the infection to the Achilles tendon with acute abscess formation. The wounds are shown after incision and drainage. Many options exist for flap coverage. (**b**) Plain radiographs of the foot demonstrate advanced osteomyelitis of the calcaneus, with cortical disruption and multiple areas of cystic degeneration of the calcaneus. (**c**) MRI T1 images show avascular necrosis of the majority of the calcaneus. (**d**) MRI T2 images show osteomyelitis of the entire calcaneus that is confluent with the plantar heel wound. The patient went on to have an Ertl BKA and regained the ability to run using a prosthetic within 3 months



Fig. 32.17 Defects of the non-weightbearing hindfoot are very favorable for salvage, as only skin coverage is required. (**a**) A 74-year-old ambulatory diabetic man with history of prior TMA presented with acute infection of a chronic posterior heel wound. (**b**) Defect following debridement. (**c**, **d**) Stable coverage with ALT flap with ETS anastomosis to PTA



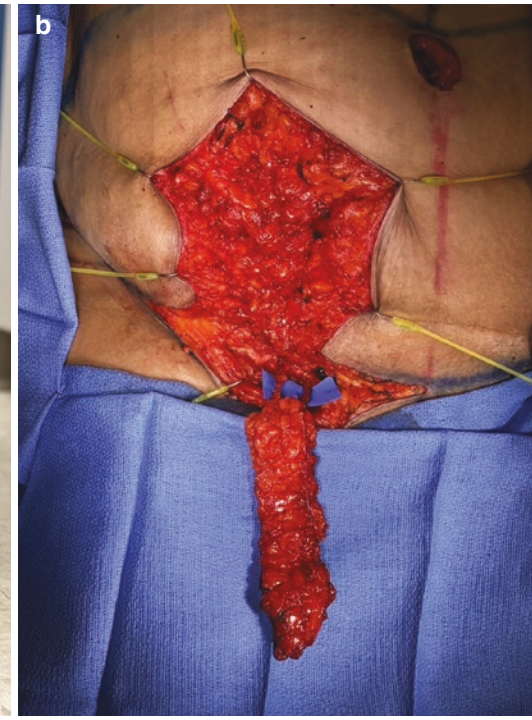




Fig. 32.18 Coverage of the ankle with ultrathin skin flaps. (**a**) A 61-year-old obese female with a history of diabetes and smoking presented with a chronic would of 18 months duration after surgical repair of a ruptured Achilles tendon. (**b**) Because obesity made other skin flap donor sites unfavorable, an ultrathin superficial inferior epigastric artery (SIEA) flap was chosen and raised in the subdermal plane just deep to the SIEV. (**c**) Healed flap at 3 months with satisfactory contour match to the thin skin of the ankle



Fig. 32.19 Thin skin coverage options for ankle defects. Lateral ankle wound resulting from chronic venous dermatitis. In chronic cases, the zone of scar tissue surrounding the wound may encompass the local perforating vessels, making perforator-to-perforator anastomosis undesirable. The distal lateral arm/forearm flap is a useful very thin alternative to the SCIP, with a long pedicle to reach outside the zone of scarring. The peroneal vessels can be easily accessed behind the fibula for lateral ankle wounds. (**a**) Chronic venous stasis wound with surrounding zone of scarring. (**b**) Design of distal lateral arm flap using very thin skin overlying lateral epicondyle. (**c**) Flap pedicle in situ adjacent to radial nerve, demonstrating generous length of pedicle. (**d**) Exposure of the peroneal vessels behind the fibula. (**e**) Completed end-to-side anastomosis to the peroneal vessels. (**f**, **g**) Healed flap with satisfactory contour to lateral ankle

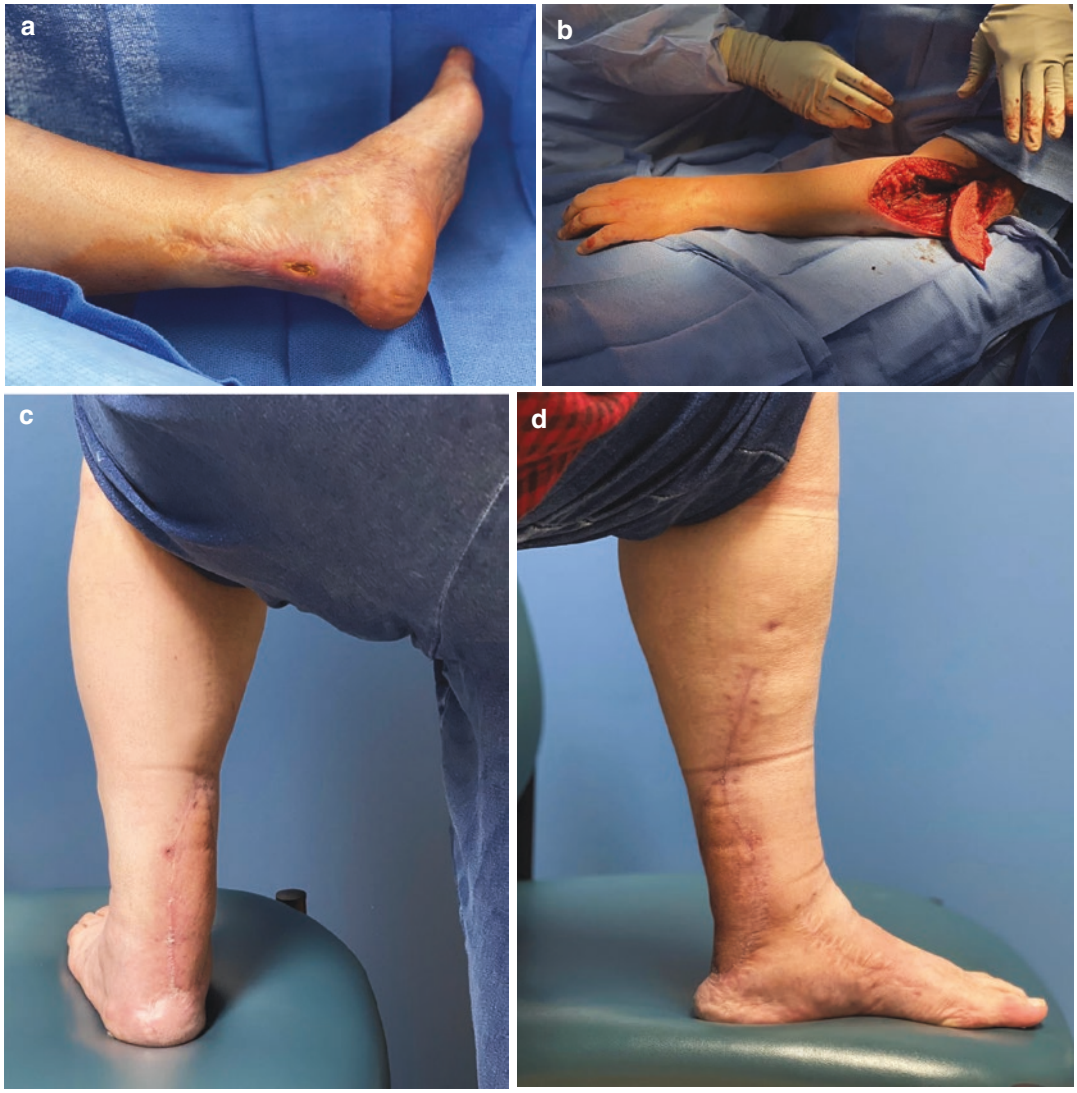


Fig. 32.20 The lateral arm flap can provide thin coverage for the ankle in morbidly obese patients. (**a**) A 53-year-old morbidly obese diabetic female with a BMI of 56 presented with a chronic Achilles wound of 7 years duration. (**b**) The forearm was the only anatomical area with a reasonable skin thickness match to the posterior ankle. A distal lateral arm flap is elevated. (**c**, **d**) Healed flap at 3 months post-op with appropriate contour to the ankle



Fig. 32.21 Anterior ankle wounds are often favorable for reconstruction because bony fusion or arthroplasty procedures can address osteomyelitis. (**a**) A morbidly obese diabetic man presented with a chronic, draining anterior ankle wound with osteomyelitis following failed arthroplasty and multiple attempts at closure with biologic matrices and skin grafting. (**b**) Defect following debridement and placement of antibiotic cement spacer. (**c**) Stable coverage with radial forearm flap. The radial forearm flap was chosen rather than the SCIP because of the multiply reoperative field, with heavy scarring, which made anastomosis well outside the zone of injury preferable. The patient returned to ambulation in a brace with the antibiotic spacer left in place

Massive Wounds

Massive wounds generally result from necrotizing infection or abscess and may cross anatomical areas, for instance, from the plantar foot up to the proximal leg. These wounds often occur in the setting of poorly controlled diabetes and noncompliance. Candidacy and methods for reconstruction must be selected on an individual basis considering the extent of pathology, functional status of the patient, and likelihood of compliance with a complex reconstructive effort that may take months to heal. At times, necrotizing soft tissue infection leaves a mostly skin-level defect that is amenable to salvage even if massive. In the setting of massive wounds, large muscle flaps such as the latissimus may be the best option to provide coverage (Fig. 32.22). If skin flaps are used, then several flaps may be necessary, and these can be performed to separate recipient vessels, or "stacked" as flow-through flaps (Fig. 32.23). However, our experience has been that in the case of circumferential wounds of the lower leg with circumferential disruption of the lymphatic system, skin flap reconstructions are more prone to chronic edema than muscle flap reconstructions (Figs. 32.23 and 32.24).

All of these factors should be considered when approaching Step 1 of our algorithm above:

- "Consider the wound and the reconstructive requirements."

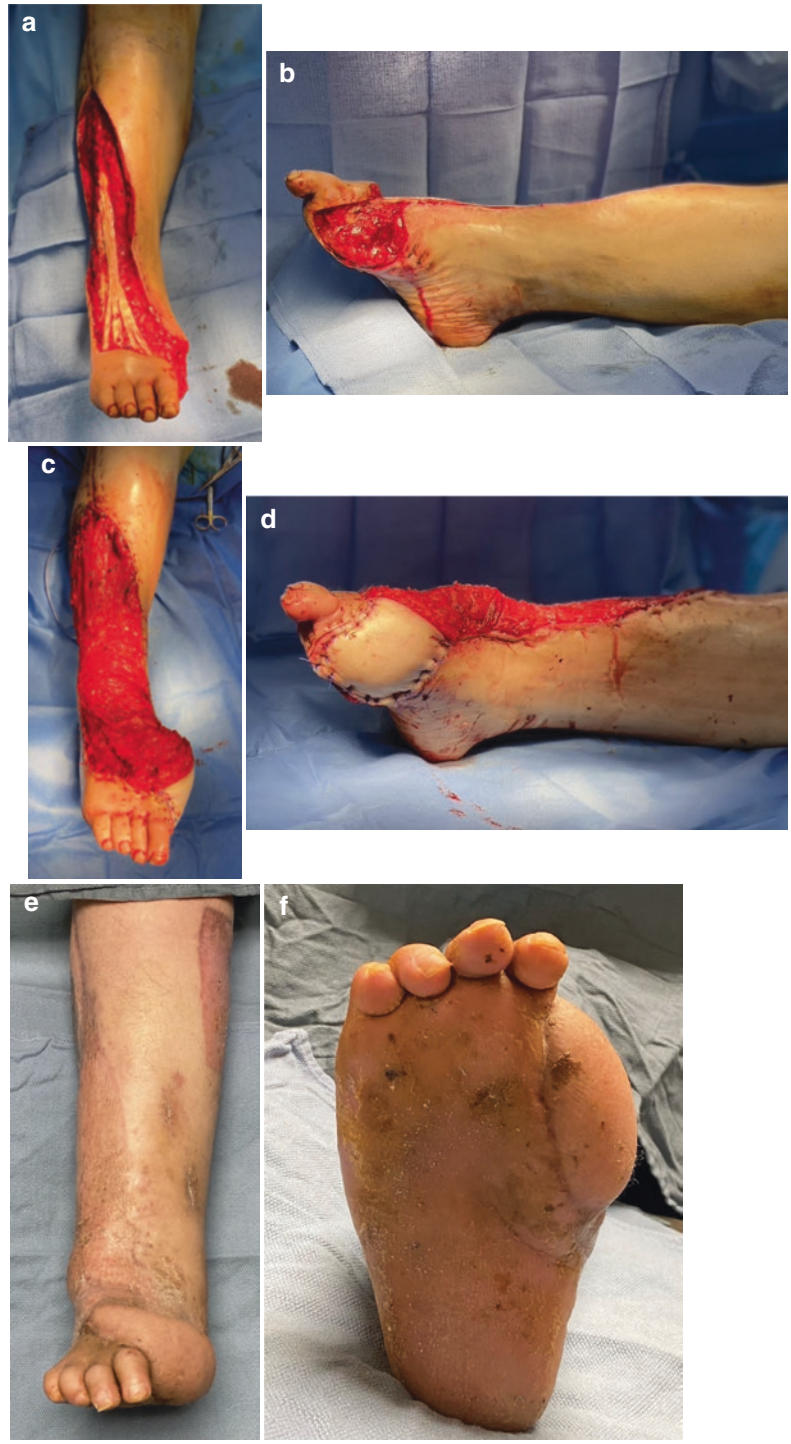


Fig. 32.22 Massive wounds often result from gas gangrene or necrotizing fasciitis. (**a**, **b**) A 37-year-old man with Prader-Willi syndrome and type II diabetes developed gas gangrene resulting from an infected hallux ulcer. The resulting defect included exposure of the anterior compartment tendons in the distal leg, ankle, and dorsal foot, as well as a first metatarsal ray amputation defect of the medial forefoot. (**c**, **d**) Coverage was achieved with a split-latissimus dorsi muscle with a distal skin paddle. The transverse branch of the muscle covered the proximal leg wound. The descending branch of the muscle covered the ankle and dorsal foot. (**e**, **f**) 8 months postoperative demonstrating stable coverage with satisfactory contour for shoe wear



Fig. 32.23 Massive wounds and the choice of fasciocutaneous versus muscle flaps for coverage of infected tendons. An undiagnosed diabetic man presented with a necrotizing infection due to mucormycosis. (**a**, **b**) Radical debridement resulted in circumferential wounds with extensively exposed tibia and tendons. (**c**) The wound was reconstructed with "stacked" ALT flaps and skin grafting. The first flap was anastomosed end-to-side to the anterior tibial artery, and the second flap end-to-end to a flow-through vessel of the first flap. There was initially satisfactory contour. The patient developed an abscess beneath the flaps several weeks out from surgery, due to persistent mucor infection and potentially due to nonadherence of the fasciocutaneous flap to the underlying infected tendons. A muscle flap might have had better adherence to the tendons for eradication of infection. (**d**, **e**) The patient was lost to follow-up and returned several months later with healed but very swollen flaps. These photos are after 1 week of compression therapy. Early and sustained postoperative compression therapy might have prevented the edema seen here, especially in the context of a circumferential wound with loss of the superficial venous drainage system. A muscle flap would likely have been less prone to develop edema and would have been a better option



Fig. 32.24 Coverage of massive wounds and the choice between fasciocutaneous and muscle flaps for large wounds with infected tendons. (**a**, **b**) A 64-year-old diabetic man presented with a severe, circumferential venous stasis ulcer with exposure and infection of multiple tendons. (**c**, **d**) Following radical debridement with preservation of longitudinal structures, the wound was covered with a latissimus dorsi muscle flap anastomosed end-to-side to the posterior tibial vessels. (**e**) By 8 weeks post-op, the flap and skin graft had excellent contour. There was no occurrence of infection beneath the flap, which had good adherence to the infected tendons. There was no notable edema despite the known presence of venous stasis disease. This contrasts favorably to the outcome with fasciocutaneous flap for a similar situation in Fig. 32.23

Recipient Vessel Selection

Recipient vessels in the ankle and foot include the anterior tibial, posterior tibial, and peroneal vascular systems. Detailed knowledge of the anatomy of each is critical to successful operative planning, particularly in the presence of vascular disease where anatomy is abnormal. Readers are referred to the excellent article by Attinger on angiosomes of the foot and ankle for a detailed review of vascular anatomy and its assessment [4].

Selection is straightforward in diabetics with minimal or no vascular disease, such as very young patients. However, in the more common scenario of concomitant peripheral vascular disease, recipient vessel selection is often the most challenging and critical facet of reconstructive planning.

Recipient vessels of the foot and ankle can be broken down into "major" and "minor" vessels, which anatomically roughly correspond to "proximal" and "distal." Major systems include the tibial vessels at the ankle, and the peroneal vessels in the leg behind the fibula (the peroneal vessels are infrequently used). Minor systems include perforators of major vessels, distal branches of the major systems, such as the first dorsal metatarsal artery (FDMA) (Fig. 32.25), medial and lateral plantar systems, digital vessels (Figs. 32.6 and 32.7), intrinsic muscle pedicles, peroneal vessels at the ankle (Fig. 32.15), and intact collateral vessels in the setting of PVD. It is strongly recommended to obtain formal angiography for recipient vessel planning in all cases [21]. In addition to anatomical information, angiography gives information on the consequences of potential vessel sacrifice—for instance, even if a palpable pulse of the dorsalis pedis is present, end-to-end anastomosis to this vessel may be devastating to a foot with an occult occlusion of the posterior tibial artery, where the plantar pedal circulation is dependent on retrograde flow from the dorsal system. Formal angiography suffices for vessel selection if one of the major systems is to be used. However, for the minor vessels, angiography alone may not give the spatial information needed to accurately locate suitable recipients, particularly in the setting of PVD. Duplex ultrasound has lately become a frequently employed and useful technique for assessment of minor vessels as recipients for e.g., "supermicrosurgery" using flaps such as the SCIP that have small caliber and short pedicles. The ultrasound generally should be performed by the surgeon him/herself, who must be an experienced operator of the equipment.

In general, for any critical defect, major vessels are a preferred solution due to their reliability, anatomic consistency, and long-term patency. "Traditional" workhorse type flaps require large caliber vessels for anastomosis. Major vessels should never be used when in-line flow to the vessel is absent or cannot be reestablished by vascular surgery. The downside of using major vessels comes into play in the distal foot, where intervening tissue between the major vessels at the ankle and the distal defect becomes a problem with respect to pedicle placement. This may require sacrifice of intervening skin (making the wound worse in the case of flap failure), or unconventional treatment of the pedicle, such as skin grafting the pedicle itself (Fig. 32.11). As well, closure over the anastomosis to major vessels often produces compression of the veins, which creates other considerations for flap inset.

Minor vessels are generally useful when attempting to minimize the morbidity of reconstruction with the "supermicrosurgical" approach. Minor vessels are an excellent option in the setting of normal vascular anatomy, or mild to moderate PVD. Minor vessels, for those experienced with supermicrosurgery, are best used for forefoot/toe defects, dorsal foot defects, ankle defects, or salvage of partial foot amputations. Minor vessel anastomosis is generally with end-to-end technique. The most common example is use of the SCIP flap with anastomosis to distal vessels (Figs. 32.10 and 32.25). This approach has benefits in that small vessels are present within or immediately adjacent to the wound, and their preparation requires minimal or no dissection of the foot outside of the wound (Figs. 32.5, 32.6, 32.7 and 32.8). This minimizes surgical trauma to the foot. It also potentially shortens operative time, as both flap pedicle dissection are

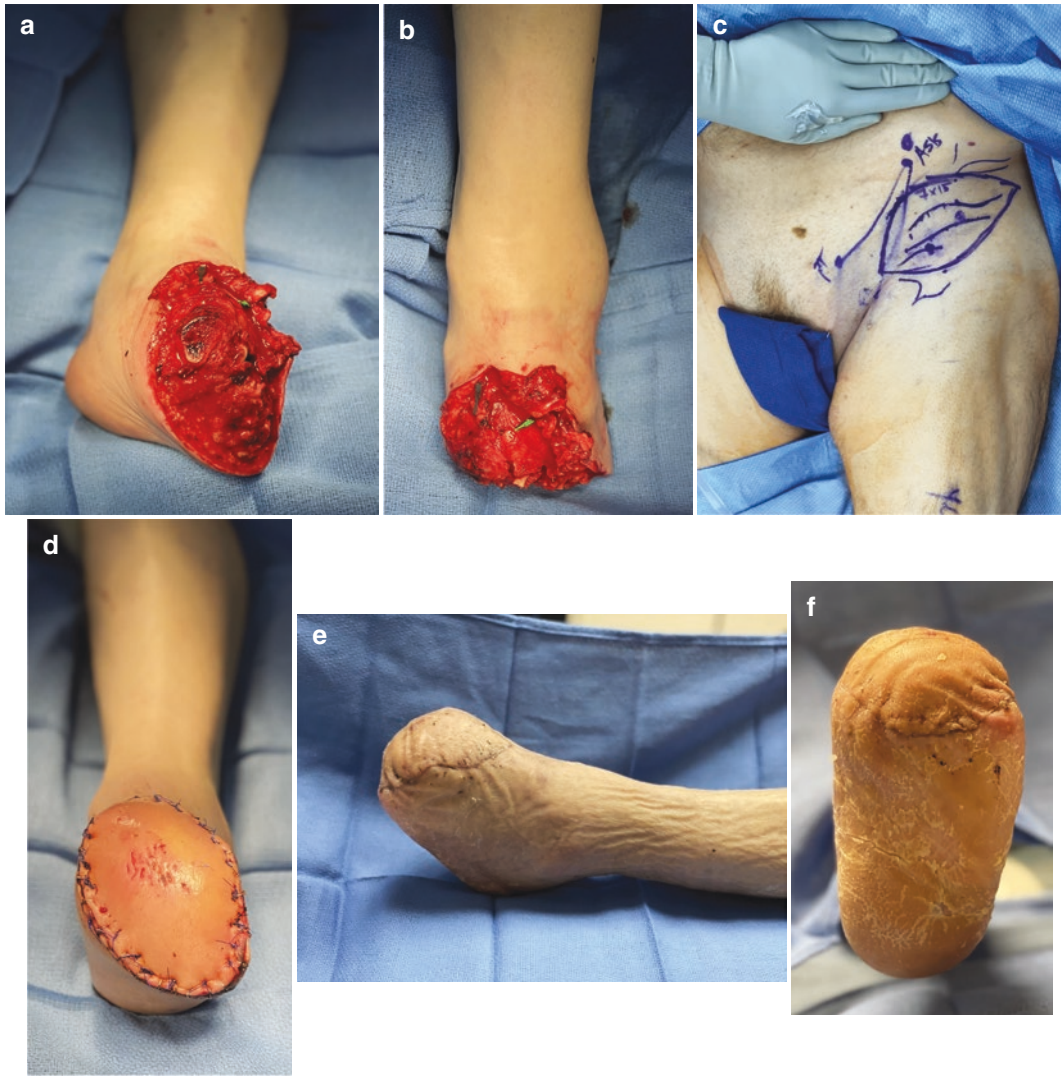


Fig. 32.25 Use of the first dorsal metatarsal artery (FDMA) system as recipient vessels. These vessels are ideal recipients for reconstruction of open TMA defects. (**a**, **b**) A diabetic man underwent guillotine TMA for necrotizing infection. The green Acland clamp is on the FDMA. (**c**) A SCIP flap was used for reconstruction, with end-to-end anastomosis to the first dorsal metatarsal artery and subcutaneous vein. (**d**) The flap was monitored using the "scratch test" to look for bright red bleeding. At 1 week post-op, the flap is viable. However, one can see that nursing staff mistakenly made repeated scratches. Only one scratch is necessary, and it can be encouraged to bleed repeatedly with mechanical agitation. (**e**, **f**) Demonstrating healed flap at 8 weeks post-op. The wrinkled skin is due to the use of compression wrapping, which facilitates rapid healing

more rapid (using flaps with short pedicles), and recipient vessel preparation is rapid, as only a short length of small vessels needs to be isolated. In contradistinction to major vessels, minor vessels can be used when in-line flow is absent; e.g., when supplied via collaterals, so long as there is strong pulsatile outflow from the vessel. The downside of using minor vessels is their anatomic inconsistency *in the setting of PVD*, and the anatomical limits imposed by finding appropriate vessels near enough to the wound when using flaps with very short pedicles. *It is essentially mandatory* to use preoperative duplex ultrasound to confirm the presence and exact location of usable vessels when taking this approach, as traditional pencil Doppler examination with surgical exploration can be very misleading [22]. The anatomy of blood supply to minor vessels in the setting of PVD may be markedly distorted, with abnormal collateral channels taking unpredictable courses.

In the setting of significant PVD, we consider the use of major vessels the safest option. Salvage in these cases is a difficult prospect, and vessels with the most reliable and robust flow should be used, to add substantial tissue and vascularity to the foot and to simplify the already challenging variable of recipient vessel selection. Optimization of major vessels should always be performed by vascular surgery prior to the flap. Pulsatile vessels are ideal, but anastomosis to severely atherosclerotic vessels is a common scenario and does not affect success rates provided that in-line flow is present and technique is meticulous. We always employ end-to-side anastomotic technique when utilizing major recipient vessels, as all diabetics can be expected to have progression of peripheral vascular disease over time; maintaining multivessel inflow is therefore critical. When major vessels are not available adjacent to the wound, such as in the case of a dorsolateral foot defect in a single-vessel leg fed by the posterior tibial artery, then vein grafting to the intact major system may be necessary and is preferable to the use of minor collateral vessels for substantial defects. Alternatively, when possible, a distal vascular bypass can be performed by vascular surgery and anastomosis can be to either the bypass vessel or the distal reconstitution of, e.g., the posterior tibial artery that the bypass targets (Fig. 32.26). Muscle flaps provide the lowest outflow resistance, and so should be used preferentially when using highly diseased major recipient vessels that required significant angioplasty or bypass to serve as targets. Skin flaps with limited vascular beds create resistance to outflow, which may contribute to thrombosis of vessels that are already tenuous and have been freshly injured by angioplasty or bypass anastomosis.

With all of the above in mind, the second step of our algorithm should be considered as follows:

Review angiography or other vascular imaging (e.g., ultrasound) and *commit to a choice of recipient vessels*, using the best-available vessels.

- If there is no significant PVD and high-quality vessels are available adjacent to the wound, these should be chosen preferentially, regardless of their size.

  The supermicrosurgery approach with small adjacent recipient vessels and thin skin flaps with short pedicles minimizes operative length and morbidity.
- If severe PVD is present or no suitable small vessels are adjacent to the wound, major recipient vessels should be chosen regardless of their distance from the wound.

  Flaps with long pedicles or vein grafting may be necessary.
- Critical or "high stakes" defects may shift the decision in favor of major recipient vessels and highly reliable workhorse flaps.



Fig. 32.26 Flaps may be used in conjunction with a distal vascular bypass when no other options for salvage are available. In this case, muscle flaps should be used to provide additional outflow for the bypass and assist with maintaining patency. (**a**, **b**) A diabetic man with severe PVD and long-segment chronic total occlusions of the anterior tibial, posterior tibial, and peroneal arteries underwent guillotine TMA for a gangrenous forefoot wound. The remaining foot was poorly vascularized and the plantar flap was insufficient for closure of the TMA. (**c**) A popliteal to posterior tibial artery bypass was performed to restore flow to the foot. (**d**) The distal bypass vessel was then the only available recipient option for a free flap. (**e**) Flap anastomosis is performed end-to-side to the distal bypass vessel. Access to the forefoot from the medial ankle is via a trough along the glabrous junction. The implantable doppler is placed on the recipient vein, proximal to the venous anastomosis (proximal to coupler in picture). (**f**) The serratus muscle flap was chosen because it has a long pedicle for reach from the ankle to the forefoot and because the muscle provides a large outflow bed (with low resistance) for the bypass. (**g**) Closure over the 3 anastomoses was not possible at the conclusion of the case, and so the anastomoses were covered temporarily with a biologic matrix (Integra Bilayer matrix), and then later with a full thickness skin graft. (**h**, **i**) Stable result at 3 months

Flap Selection

A wide variety of flaps are applicable to diabetic foot reconstruction, and their selection and application is limited only by the surgeon's imagination and the constraints imposed by vascular disease.

A review of every flap is beyond the scope of this chapter, and multiple examples are provided in the included case presentations. However, pearls and pitfalls relating to flap selection are presented below. Flaps are considered as "workhorse" and "supermicrosurgical." Workhorse flaps are all muscle flaps, and skin flaps such as the anterolateral thigh (ALT), TDAP, or radial forearm that are based on larger vascular systems; generally with 2 mm or greater caliber vessels. Supermicrosurgical flaps are those with vessel calibers of 1 mm or less and include flaps such as the SCIP or PIA.

We typically begin the process of flap selection by first committing to a choice of recipient vessels and then choosing a flap based on its pedicle. This is because recipient vessels are often not normal or even absent in diabetics with PVD and so the particular anatomy of remaining vessels is a constraining factor in planning the reconstruction. A flap with an appropriate pedicle length to allow a straight/unkinked lie of the pedicle and appropriate vessel size for anastomosis to the intended recipient vessels should be chosen. The particular flap (there are usually multiple possibilities depending on the reconstructive requirements of the wound) is then chosen based on the combination of its pedicle characteristics and tissue characteristics. In the era of supermicrosurgery, the mantra of "bigger vessels and longer pedicle length are better" is therefore no longer always true. A flap with a short pedicle and smaller vessels may very well be the most advantageous if appropriate recipient vessels are available next to or within the wound, whereas a longer pedicle with larger diameter vessels is favorable for distant recipient vessels and severe PVD.

In some perforator flaps, such as the ALT and TDAP, pedicle length can sometimes be adjusted by choosing more proximal or more distal perforators to supply the skin island, to achieve either a shorter or longer pedicle length. The surgeon should also not be afraid to shorten the pedicle of a flap if doing so allows a better inset. It is better to have a smaller vessel caliber with an unkinked pedicle inset, then to have a longer pedicle with redundancy. Smaller vessel caliber does not affect flap success rate in our experience.

After choosing a flap with the appropriate pedicle, other characteristics of the flap can be considered to match the wound requirements and vascular situation. Among the workhorse flaps, it is important to realize that atherosclerosis differentially affects certain flap pedicles. Generally, flaps harvested from the lower extremity are the first to be affected, and the ALT pedicle is the most prone to atherosclerosis among workhorse flaps (the same applies to the vastus lateralis muscle flap). The flap can be used despite the presence of atherosclerosis in the pedicle, but considerable anastomotic technical difficulty may be encountered if both the flap and the recipient vessel are atherosclerotic. In this situation, some authors advocate the use of an interposition vein graft at the anastomosis [23]. Among lower extremity workhorse flaps, the gracilis pedicle, based on the medial femoral circumflex, tends to be relatively spared from vascular disease. The gracilis is a highly useful flap in the foot, being highly reliable in its perfusion, having good caliber vessels for anastomosis to either major or minor recipients, and also a short enough pedicle length to allow direct coverage of the anastomosis with the muscle flap itself (Fig. 32.5). The sural arteries also tend to be spared in diabetic PVD, which makes the medial sural artery perforator (MSAP) flap a tempting choice. However, the use of this flap must be considered carefully, as its donor site is the basis for the posterior flap of the below knee amputation (BKA) which is a very realistic eventual prospect for many in this patient population. Additionally, closure of the donor site of this flap creates compression or tightness of the leg, which may be problematic

for venous drainage of the flap. For these reasons, we do not employ the MSAP in diabetic foot reconstruction.

The chest vessels are typically the last to be affected by atherosclerosis and for this reason the latissimus, serratus, and other derivatives of the thoracodorsal system are particularly useful in the setting of PVD. This system offers the ability to cover large areas and use chimeric components including muscle, skin, and bone. Downsides of the latissimus flap are the potential to create weakness of the shoulder girdle that may be relevant in transfers (or crutch walking) for temporarily or permanently nonambulatory patients. This has not been proven, but is worth considering. This can be avoided by using the transverse partial latissimus flap [24], which sacrifices some of the area of the flap but preserves function and maintains the advantage of healthy flap vessels. Specific pitfalls of the latissimus and its derivatives are the need to consider pedicle coverage. The usable segment of the thoracodorsal pedicle extends well proximal to the proximal border of the muscle, so that the muscle does not overlap the anastomosis. This is particularly relevant in the foot and ankle, as opposed to the leg. There is little soft tissue laxity in the foot to close over an anastomosis, and the length of the pedicle is such that the muscle itself cannot be positioned over the anastomosis without creating redundancy and a risk for kinking. Thus, when using the latissimus on the foot or ankle, the surgeon should make preparations for pedicle coverage. This can at times be done by including a propeller-type island of skin in the proximal muscle [25]; however, this is inadvisable in obese patients. Other options include harvest of serratus muscle for pedicle coverage, skin grafting of the pedicle, or use of a biologic matrix for temporary pedicle coverage followed by delayed skin grafting.

The SCIP flap is currently enjoying a surge of popularity for diabetic foot reconstruction. The flap can be harvested and completed very quickly, which is an important consideration for minimizing operative time in sick patients [26, 27]. The minimal recipient vessel dissection minimizes surgical injury to the remaining foot. The SCIP contours very well to convex defects and provides rapid skin-to-skin healing (Figs. 32.6, 32.8, 32.10, 32.25 and 32.27). However, as previously discussed, the flap does have some limitations, including: the necessity of appropriate recipient vessels adjacent to or within the wound, the thin nature of the skin that may be less durable for weight bearing surfaces, and its minimal ability to treat dead space. The pedicle of the SCIP flap can also be calcified in the setting of severe PVD such as that seen in ESRD. In the setting of PVD, when the flap is anastomosed to abnormal collateral or other distal vessels, the viability of inflow from these vessels may be uncertain in the long term, particularly if angioplasty is used to achieve adequate inflow prior to surgery. When using the SCIP flap, it is important to include the superficial circumflex iliac vein (SCIV) or superficial inferior epigastric vein (SIEV) as the venous drainage for the flap, rather than solely on the vena comitante of the flap. Isolated use of the perforator vena comitante has been associated with partial flap necrosis in our experience, whereas use of the superficial subcutaneous venous system provides consistent venous drainage. The SCIV is directly subdermal in the lateral portion of the SCIP flap, and then penetrates the Scarpa's fascia medially. Most of the flap drainage comes from the lateral association of the vein with the skin. To maintain a thin flap, it is necessary to keep the vein with the flap laterally (where it is in the subcutaneous layer) and then separately dissect the vein from the medial portion of the flap (where the vein changes to the subscarpal layer). The posterior interosseous artery (PIA) flap is an alternative to the SCIP flap. It is also very thin, with an even shorter pedicle, which may be desirable in certain scenarios (Fig. 32.7). As compared to the SCIP, the venous drainage is more straightforward, being reliably drained by the perforator vena comitante. Donor site morbidity is minimal, although esthetically less desirable than the SCIP donor site.

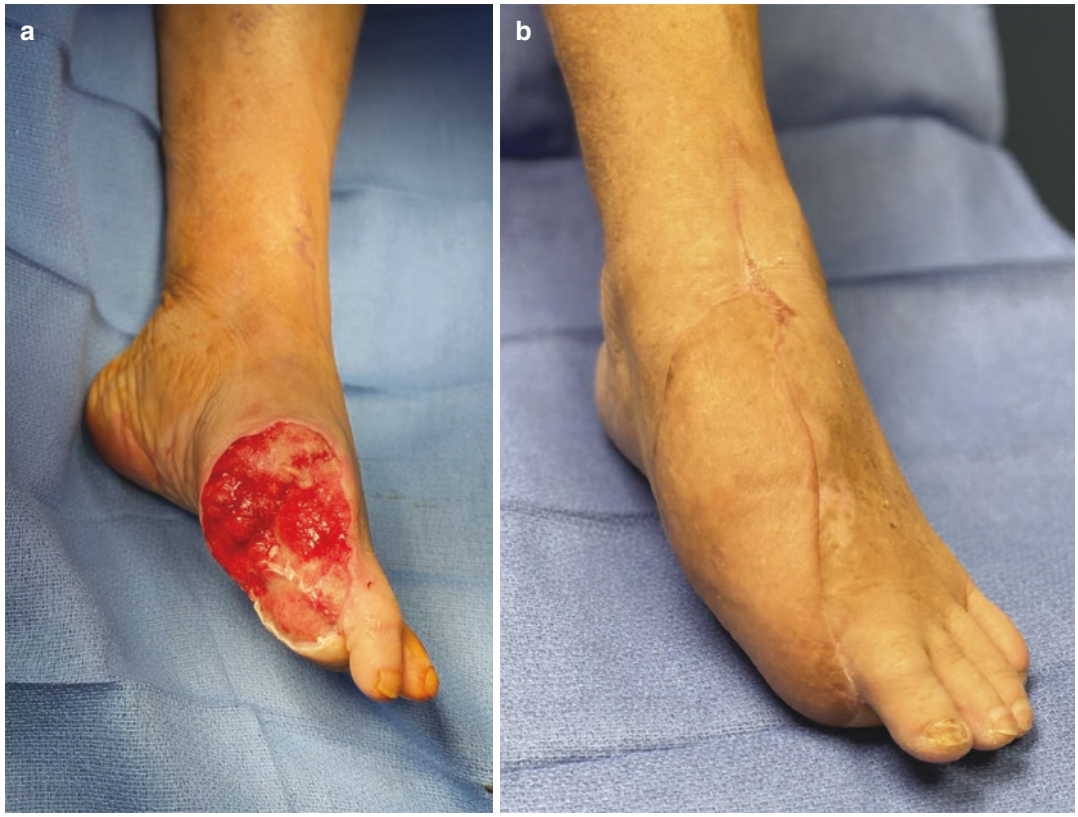


Fig. 32.27 The SCIP flap is popular in diabetic foot reconstruction because it is thin and contours well to convex defects. Its short pedicle with small-caliber vessels allows use of minor recipient vessels near the wound. (**a**) First ray amputation defect resulting from diabetic foot infection. (**b**) 10 weeks following reconstruction with SCIP flap. The patient had a congenitally absent dorsalis pedis, and the flap was anastomosed to a dorsal foot small perforator artery and subcutaneous vein

Our general advice on use of the SCIP flap in the diabetic foot is that it is an excellent option for diabetics without severe PVD, in which only skin coverage is required without significant need for dead space obliteration. In this setting, it provides a rapid and simple solution with minimal reconstructive morbidity. Use of the SCIP flap in patients with severe PVD should be approached *more carefully*. In this setting, recipient vessel mapping with ultrasound and flow velocity measurements is critical, as normal small-vessel vascular anatomy is inherently abnormal. Published literature from authors experienced with SCIP reconstruction has identified concomitant PVD and history of prior amputation as the only two significant predictive factors for flap failure [28]. Use of essentially the terminal portion of a diseased vascular system for inflow has the twin disadvantages of unpredictable inflow and skin healing to potentially diseased surrounding tissues. Many surgeons who use SCIP flaps in the setting of PVD

routinely utilize hyperbaric oxygen therapy (HBOT) as an adjunct. In many health systems, this is a difficult proposition with regard to logistics and insurance coverage.

The SCIP *can* be used in cases of PVD and is used by the authors. However, attention to the details noted above is critical. Ultrasound mapping of recipient vessels with flow velocity measurements, consideration for pre- and postoperative use of HBOT, and enough experience with supermicrosurgery to allow flexibility in decision-making. The chosen minor recipient vessel *must have strong pulsatile flow*, not impaired flow, in order for the flap to be successful; this is where ultrasound mapping with flow velocity becomes useful. Additionally, the surgeon must respect the angiosomes of the foot and ankle and realize that in the setting of PVD, the wound may be a declaration of failure of the entire angiosome. Thus, the entire angiosome may need to be resected to properly prepare the defect, such that the defect edges will have sufficient perfusion to heal to the flap [28].

With regard to the longstanding question of whether muscle or fasciocutaneous flaps are preferable, this remains subject to debate. We suggest not viewing this question as binary—it has subtleties that need to be considered. However, it is the authors' recommendation that muscle flaps still be frequently employed as an option, even in the setting of "advanced reconstruction." Diabetic foot reconstruction is complex, and efforts to improve outcomes should be utilitarian. Simplifying flap factors can remove one more element of difficulty from the equation. Several other factors make muscle flaps very useful. Muscle is the best substrate for conforming to irregular contours and filling dead space, which is often a concern in more grave wounds (which frequently are those requiring free tissue transfer). Muscle adheres more rapidly to the underlying tissue bed, reducing the risk of seroma or abscess formation. Although the efficacy of particular flap types for coverage of osteomyelitis as a global issue probably has more to do with adequate bony debridement and host factors than with flap choice, it has been our experience nonetheless that muscle is very effective for adhering to bone and providing rapid tissue healing, which seems to be helpful in the setting of infection. When extensive tendon coverage is necessary, flaps lined with fascia on their undersurface, such as the fasciocutaneous ALT, are more prone than muscle to have delayed adherence to the underlying tendons and allow fluid collections to form. This is because the undersurface of fascia is poorly vascularized and because muscular fascia is, by design, relatively inflexible. Whereas this may be desirable in areas where tendon excursion is critical such as hand reconstruction, it represents a considerable risk in the diabetic foot population where rapid resolution of wound and infection is the paramount consideration (Figs. 32.22, 32.23 and 32.24). Muscle also has the advantage of thin coverage after atrophy has taken place, which allows return to normal footwear. Finally, muscle flaps also have a larger-volume vascular bed which equates to greater outflow and lower outflow resistance. This is an important consideration in situations where the risk of arterial thrombosis is high (such as in the case of severely calcified recipient vessels without normal intima or when vein grafts are used), or in instances where the flap is critical to maintain the patency of a vascular bypass or angioplasty. A larger outflow bed and lower outflow resistance may add to the durability of vascular interventions such as angioplasty or bypass, as compared to smaller skin flaps or the native diseased microvasculature which have a high resistance to flow (Figs. 32.26 and 32.28).

In contrast, fasciocutaneous flaps of the foot are more likely to require revisions for contour issues [29], particularly in the setting of obesity,



Fig. 32.28 The benefits of muscle flaps for contour and in vasculopathy. (**a**) A diabetic gentleman presented with a severe dysvascular foot wound stemming from a plantar fifth MTP joint ulceration with septic arthritis and dorsal foot extension. Tissue perfusion is visibly compromised, with impending necrosis of several toes. His X-rays are shown in Fig. 32.4 and demonstrate diffuse, severe calcifications of the pedal arteries. Severely calcified distal arteries on X-ray suggest that finding useable recipient vessels near the wound will be unlikely. (**b**) Angiogram demonstrated single-vessel runoff via the anterior tibial artery, with severe disease of the plantar circulation. Because of the severity of the PVD and vascular calcification, major vessels (the anterior tibial at the ankle) were chosen as recipient vessels. For the same reason, a muscle flap was chosen to provide lower resistance to outflow through the anastomosis and minimize the risk of arterial thrombosis at the anastomosis to a heavily calcified vessel. (**c**, **d**) Threatened toes should be amputated because calcific changes of small vessels on X-ray suggest microcirculatory impairment that will result in new wounds with minor trauma to tenuously perfused toes. The serratus flap was chosen because of its long vascular pedicle that allows reach from the ankle to the forefoot, and its relative thinness. The pedicle can be partially closed over and the remainder skin grafted. The serratus was also chosen because flaps from the chest tend to have less calcification of their pedicles than flaps from the lower extremity or abdomen. When the recipient vessel in the foot is known to be severely calcified, it is preferable to choose a flap with a vessel that will not be calcified in order to avoid anastomosing calcified vessel to calcified vessel. (**e**, **f**) Healed result at 3 months. The muscle flap already has satisfactory contour and will continue to undergo atrophy

which is frequent in the diabetic population. Skin-to-skin inset of fasciocutaneous flaps can be tight when covering convex contours, unless the flap is very thin to match the thinness of the foot skin. This can create a compressive environment beneath the flap. When postoperative swelling takes effect, both venous compression and skin edge necrosis may result. The surgeon must therefore carefully take into account the thickness of the flap and the effect of postoperative edema.

Use of thinner skin flaps without deep fat and fascia components obviates some of these problems. Common examples include the SCIP and suprascarpal ALT or SIEA flaps (Figs. 32.6, 32.7, 32.8, 32.9, 32.10, 32.18, 32.25 and 32.27). Use of the suprascarpal plane for skin flap elevation has greatly improved the applicability of these flaps to diabetic foot reconstruction. Flaps harvested above the Scarpa's fascia are thinner and much more pliable than those harvested with deep fat and fascia, enhancing their ability to conform to the foot and allow appropriate footwear without the need for revision surgeries (Fig. 32.9). The prospect of even minor revision surgeries on diabetic foot flaps is a significant consideration, as it creates other opportunities for wound breakdown or infection, and often means another period of non-weight bearing which is significant in frail patients. Multiple methods exist for harvesting these flaps and have been described by the authors [30, 31]. Generally, as long as the chosen perforator has a strongly audible venous Doppler signal, we have found no difference in the reliability of the skin paddle with suprascarpal flaps versus traditional fasciocutaneous flaps and the suprascarpal plane is therefore our preferred plane of elevation in all but the thinnest of patients.

Fasciocutaneous flaps have the advantage of native skin healing and the potential for a more natural appearance. They may be preferable when reoperation is planned, such as a delayed orthopedic joint surgery that takes place after successful skin coverage and resolution of infection. Fasciocutaneous flaps such as the TDAP, parascapular, gluteal artery perforator, and medial plantar flaps also have the ability to provide thicker, more durable skin for plantar surfaces (Fig. 32.12). Theoretically, this is an advantage for weight bearing areas. Muscle flaps in comparison will demonstrate atrophy, and purposeful bony contouring such as partial calcanectomy should be utilized to prevent ulceration through the flap in weight bearing areas [19]. Muscle flaps can be augmented by inclusion of fascia or by fat grafting to improve their suitability for weight bearing. However, in our experience, in the neuropathic diabetic population, thicker skin flaps do not prevent recurrence of ulceration; the same underlying neuropathy and behavioral inattention that encouraged initial wound formation will put any flap at high risk for reulceration (Fig. 32.29). Finally, the advantages of both flap types can be had by including a small muscle component to a fasciocutaneous flap, which allows the advantages of fasciocutaneous flaps along with the capacity for dead space obliteration (Fig. 32.12).

With all of the above in mind, the third step of our algorithm should be considered as follows:

Choose the flap based on:

- The *appropriate pedicle length* from the chosen recipient vessels to the wound.
  Longer is not always better.
- The reconstructive requirements of the wound (e.g., thick/thin skin, weight bearing or not, dead space, outflow resistance, etc.).



Fig. 32.29 Both skin and muscle flaps can be equally prone to reulceration if the underlying etiologies or behaviors leading to wound formation are not reversed. In this patient, even a "like with like" reconstruction with glabrous skin re-ulcerated due to noncompliance with positioning. (**a**) A morbidly obese, wheelchair-bound diabetic female with end stage renal disease, PVD, bilateral lower leg lymphedema and bilateral leg venous stasis changes presented with gangrenous decubiti and osteomyelitis of both heels from inattentive positioning on her wheelchair foot plates. The wounds are shown after debridement. Salvage was indicated to avoid bilateral above knee amputations and preserve independence for transfers in and out of the wheelchair. (**b**) Antibiotic-impregnated calcium sulfate beads were used to fill the cavitary defects in the osteomyelitic calcanei. (**c**, **d**) After vascular intervention, the right foot was salvaged with a medial plantar flap and the left with a free transverse partial latissimus flap. (**e**, **f**) Despite exhortations to use padded foot protectors and avoid prolonged pressure on her wheelchair foot plates, the patient re-presented 6 months later with erosions through both flaps

Technical Considerations and Adjuncts to Improve Outcomes

Key technical considerations and adjuncts for each phase of surgery are considered below.

Wound Preparation

Formal angiography should always be obtained prior to microsurgical reconstruction. The wound should be serially debrided to negative post-debridement cultures before reconstruction. Debridements should be planned as much as possible according to the angiosome affected by the wound [28]. If significant PVD is contributing to wound formation, at times it may be advisable to resect the entire affected angiosome, to ensure that the margins of the wound (perfused by adjacent angiosomes) have adequate perfusion for healing to the flap. Negative pressure wound therapy with fluid instillation is a very effective way of staging and preparing a wound between debridements. Preoperative HBOT with a goal TCP02 of 40 mmHg is an excellent adjunct for reconstruction of the ischemic foot, when it is logistically feasible within a health system.

Recipient Vessel Selection

Recipient vessels should always be determined before flap planning. When PVD is mild or absent, minor recipient vessels near the wound edge are the preferred option for the supermicrosurgical approach because this decreases both donor and recipient site morbidity. When minor vessels are used, e.g., in the context of supermicrosurgery, preoperative use of duplex ultrasonography has become an indispensable part of planning and significantly simplifies the recipient vessel selection. This is critical when using flaps with short pedicles, such as the SCIP flap, where it is mandatory to have recipient vessels adjacent to the wound. Intra-operatively, the surgeon must evaluate the recipient vessels to ensure that there is good pulsatile flow. Supermicrosurgery can still be used with major vessels, with a small "poke hole" in the recipient vessel used for end-to-side anastomosis of a < 1 mm flap vessel.

When using major vessels, formal angiography is obtained. Although recipient vessel choice is often limited by the pattern of PVD, generally speaking, the PT and AT vessels are the most robust and the best choice, with the peroneal vessels at the ankle being a distant third choice. If the peroneal vessels are to be used, it is preferable to perform the anastomosis proximally behind the fibula in the mid-leg and choose a flap with a long pedicle (Fig. 32.19). Frequently when accessing the peroneal vessels in this fashion, there are large muscular branches to the soleus that can be used for end-to-end anastomosis without disrupting the major vessel, obviating the need for an ETS. The muscular branches are also typically less calcified than the main peroneal vessel. When the extent of PVD is severe, only a single major vascular system is available, and the vascular system is remote from the wound (e.g., dorsal forefoot wound in a single-vessel leg with only posterior tibial artery, vein grafting from the best-available major vessel is safer than attempting minor vessel use). When vein grafting from heavily diseased vessels is employed, consideration should be given to therapeutic anticoagulation during the early post-op period.

Flap Planning

The flap should be chosen *after* the recipient vessels are chosen, and the flap should be selected by considering the ideal pedicle size and length to reach from the wound to the targeted recipient vessels. Once the pedicle characteristics are decided upon, then the proper flap is chosen by considering the reconstructive requirements of the wound.

As with recipient vessel selection, duplex ultrasonography has proven highly useful in visualizing and selecting perforators prior to flap harvest. In flaps such as the SCIP, identifying the dominant perforators before dissection reduces the need for exploration and decision-making during surgery, saving both time and effort.

Incision Planning

Incisions on the foot should be made along glabrous junctions or in watershed areas between the angiosomes of different arterial systems. An excellent review of this topic with specific advice for incision planning can be found in Attinger's "Angiosomes of the Foot and Ankle" article [4], and this is recommended reading for any surgeon planning to approach complex foot and ankle reconstruction.

When it is necessary to sacrifice intervening tissue between the flap and recipient site, the tissue should be resected in a pattern consistent with the intervening angiosome of the foot supplied by the recipient vessels [28]; this is particularly true if the anastomosis was performed in an end-to-end fashion, which devascularizes the distal angiosome.

Incision planning should take into account the expected orientation of the flap pedicle after inset. If there is a long distance between the recipient site and wound, the flap should either cover the pedicle, or a "trough" can be made between the recipient vessels and wound, which should follow the watershed between angiosomes (often the glabrous junction) (Figs. 32.11, 32.12, 32.13 and 32.14).

Use of the Tourniquet

The surgeon should take into account before the case whether it will be possible to use the tourniquet. It is highly desirable to use the tourniquet for recipient vessel dissection, as many patients will have woody, fibrotic tissues, with dense adhesions of vessels to surrounding tissue that impede dissection and create a risk for inadvertent rupture of deep venae comitantes. They may also be anticoagulated. However, there are frequent contraindications to the use of a tourniquet in patients with diabetes and PVD. These include a recent angioplasty, stenting, or bypass. Frequently, even when no strict contraindications exist, attempted use of tourniquet in patients with PVD will also create a venous tourniquet due to calcifications of the arteries of the thigh. This situation actually increases bleeding and impedes vessel dissection.

Anastomosis

When possible, the supermicrosurgical approach with end-to-end (ETE) anastomosis to minor vessels within or around the wound is our preferred technique. As stated above, this is most appropriate when the surrounding vascular tree is not severely affected by PVD. A high-quality operating room microscope is needed, and fine supermicro or lymphatic surgery instruments that allow dilation and manipulation of vessels <1 mm in diameter. Suture size is usually between 9–0 and 11–0 and an average of 6–7 sutures are placed.

When using workhorse flaps or in the setting of severe PVD, we recommend anastomosis to a major vessel of the ankle, using an end-to-side (ETS) technique. This provides robust and durable inflow. The vessels at the ankle are large enough that 8–0 nylon can be used, which is much easier to work with than 9–0 or smaller sutures, particularly with calcified vessels where decreased vessel pliability leads to more resistance to knot tightening, which may rupture weaker sutures. Highly calcified vessels, such as those seen in end stage renal disease (ESRD) patients, may need to be sutured using 7–0 prolene on cardiac CC needles to penetrate the dense calcific plaque.

ETS technique should be exclusively with the "slit arteriotomy" method in the diabetic foot [32]. This is in contradistinction to cutting out a patch of the artery. The reason for this is that the recipient vessels often contain calcified plaque that will fracture in an irregular fashion when cutting out a patch of the vessel, leading to unstable intimal edges with a tendency to dislodge. Making a straight, clean arteriotomy does not disrupt the plaque and provides clean edges to sew to. The arteriotomy should be made using an anterior chamber ophthalmic knife to create a slit equal in length to the diameter of the flap artery, or slightly smaller. The surgeon and the assistant should each grab and lift up the adventitia of the

recipient vessel on either side of the planned arteriotomy to prevent the tip of the ophthalmic knife from injuring the intima on the deep surface of the vessel. In extremely calcified vessels, such as those seen in ESRD, a micro Potts scissor may be required to complete the arteriotomy. The flap artery should be cut at an angle so that it branches from the source vessel with a distal orientation, for a favorable lie. When suturing the anastomosis, the surgeon must be very careful to puncture the calcified plaque from inside to outside in such a way as to "tack" the intima to the vessel wall and avoid pulling it away from the wall and into the lumen. The intimal plaque is very easily dislodged in such cases, and it is critical to respect this fact to avoid technical failure with anastomosis. We find it useful to take relatively uneven bites of the flap vessel and recipient vessel. The flap vessel can be sutured in the traditional fashion, taking small bites at the edge. Bites of the recipient vessel should be taken from deep within the lumen, much further from the vessel edge, to avoid disrupting plaque at the edge of the arteriotomy. Although counterintuitive, this discrepancy in the size of the bites does not cause an issue and is safe.

When end-to-end anastomosis is necessary, the surgeon must ensure that the dorsal and plantar systems of the foot adequately perfuse one another (e.g., "complete arch"); otherwise, sacrifice of one of these systems may lead to severe vascular embarrassment of the foot. When end-to-end anastomosis is chosen, the flap may need to replace the angiosome of the disrupted recipient vessel. When sensible to do so, the anastomosis should be performed at the level of terminal patent branches of the arterial system. This is most often utilized when the wound encompasses the majority of the distal angiosome of the recipient vessels (Figs. 32.9 and 32.15).

Use of Flow-Through Flaps or "T-Shaped Anastomoses"

T-shaped or flow through anastomosis also plays an important role to preserve or to reconstruct distal flow [33, 34]. In our experience, use of a flow through anastomosis to reconstruct an injured major artery has demonstrated a positive effect in combating infected wounds, such as in cases of chronic osteomyelitis or diffuse gangrenous infection [35]. Thus, if a gap of an axial artery is noted, flow through anastomosis or bypass for the artery defect should be considered to have the best possible reconstruction [36, 37]. Consideration should be given to use of a flow through anastomosis whenever end-to-end anastomosis of a major vessel is planned. An additional use of the T-shaped anastomosis is to overcome positioning limitations that sometimes occur when performing end-to-side anastomosis in an unfavorable exposure/anatomical constraint. In this setting, converting the plan from end-to-side anastomosis to T-shaped anastomosis can facilitate the technical ease of the microsurgery without sacrificing important blood flow.

Bony Contouring and Biomechanical Correction

Bony contouring should always be given consideration when reconstructing the weight bearing surface. Often, biomechanical deformities are the initial cause of ulceration and infection. Flap coverage over a displaced metatarsal head will result in immediate recurrence of the ulcer after healing, unless the bony displacement is addressed. Whenever the plantar heel is covered, the calcaneal tuberosity should be resected to prevent focal pressure ulceration through the flap [19].

When reconstructing the plantar forefoot or reconstructing a partial foot amputation, a percutaneous Achilles tendon lengthening should be performed to treat or prevent equinovarus contracture (Achilles tendon contracture) that is either the cause of the initial ulcer or will contribute to reulceration after reconstruction (Fig. 32.13).

When multiple toes are involved in the wound, a transmetatarsal amputation should be considered. When metatarsals are resected, they must be beveled inferiorly to avoid sharp edges, and the normal parabola should be recreated in terms of bony length.

Use of Antibiotic Cements and Bone Void Fillers

Dead space management in the setting of osteomyelitis is a critical element of successful treatment and may prompt consideration for antibiotic-impregnated cement or bone void fillers. The choice of bone void filler is up to the individual surgeon, and multiple different substrates are effective (Fig. 32.29).

Drains

Drains should be routinely utilized beneath flaps in diabetic foot reconstruction, as essentially all diabetic foot wounds are infected. As well, even very small fluid collections can mean flap death in the tight soft tissue envelope of the foot (Fig. 32.9). Either small (e.g., 10 French or smaller) closed suction drains or penrose type drains are acceptable. For very small flaps such as a small SCIP, a vessel loop can be used as a small drain. Closed suction drains should be placed with attention to avoid creating suction near anastomoses or delicate perforator vessels. Drains are kept for 2–5 days when using muscle flaps, when the output is very low, when there is minimal dead space, or when there is very low suspicion for residual infection after debridement. When the risk of infection beneath the flap is felt to be high, or when less adherent tissues such as fascia or fat are used over poorly adherent recipient surfaces (such as bone or tendon), drains may be kept in place for longer. Frequently, diabetic patients are anticoagulated in the perioperative period; in this case, penrose drains and loose suturing allow better egress of potential blood. Any fluid collection or hematoma noted beneath the flap in the early post-op period should be dealt with by prompt return to the OR for drainage.

Flap Inset

The primary consideration during flap inset should be achieving a totally straight lie of the veins, without any venous compression. Even if this means using skin graft or a temporary biologic matrix dressing (e.g., Integra Bilayered Matrix, Integra Lifesciences, Plainsboro, New Jersey, USA) over the pedicle or anastomosis, this point is non-negotiable. The surgeon must also account for the effects of postoperative edema on the flap pedicle. Diabetic patients are frequently anticoagulated in the post-op period and at high risk for hematoma formation beneath the flap. Even a small hematoma will invariably produce flap failure or partial necrosis and may be initially difficult to distinguish from expected postoperative edema. At times (in the setting of anticoagulation) it is advisable to loosely inset the flap, placing but not tying sutures, and to tie the sutures down 3–5 days after surgery when edema and risk for hematoma have begun to subside (alternatively, the flap can be tacked in placed and then the patient returned to the operating room 5–7 days postoperatively for definitive inset (Fig. 32.7)). This seems to be particularly true for superthin skin flaps, which are very susceptible to skin edge necrosis with any amount of tension and which have delayed adherence to the underlying wound bed, making fluid collections more likely. Mattress sutures are recommended for flap inset, particularly when sewing to glabrous skin, which is prone to rapidly epithelialize suture lines with any amount of inversion, delaying wound healing. Vertical mattress sutures create less local ischemia than horizontal mattresses and so are our suture of choice.

Anticoagulation

For anastomoses involving healthy vessels, we typically give aspirin, or no anticoagulants at all. For cases of severe PVD, with completely calcified vessels and no normal tunica intima, we recommend anticoagulation with a heparin drip (goal PTT 50–60), along with aspirin, and sometimes clopidogrel as well depending on the difficulty of the anastomosis. When a vein graft is used in the setting of severely diseased vessels, therapeutic anticoagulation should also be administered. When therapeutic anticoagulation is planned, we recommend only loosely insetting

the flap at the time of index surgery in order to allow bleeding to occur without creating a hematoma (Fig. 32.7). Delayed inset can be performed at 5–7 days post-op once the flap has demonstrated viability and the risk of hematoma formation has passed.

Postoperative Monitoring

For traditional workhorse flaps with anastomosis to major vessels, use of the Cook implantable Doppler (Doppler Blood Flow Monitor, Cook Medical LLC, Bloomington, Indiana, USA) is recommended when possible, particularly when using muscle flaps. The silicone cuff and doppler crystal should be placed on the recipient vein, just proximal to the venous anastomosis. The utility of the Cook Doppler has to do with continuous venous monitoring that gives immediate feedback on vein compression during inset of the flap and closure. At times, a single suture placed during closure (particularly over the anastomosis) can produce acute venous compression or occlusion, and the implantable venous Doppler is the best way to detect this (Fig. 32.26). Reconstruction of the foot uniquely involves a tight tissue envelope and accommodation of sometimes complex contours, with minimal native tissue available for coverage of the anastomosis. A straight inset of the pedicle may be challenging, depending on flap choice and the specific situation. There is also usually significant intraoperative and postoperative swelling that may contribute to venous compression. Venous occlusion is by far the most common cause of flap failure and can be quickly detected with the Cook system. Muscle flaps in particular may not have a detectable venous signal in the substance of the flap using pencil doppler. The flap is usually covered with skin graft, which makes color assessment difficult. Muscle flaps may continue to have an arterial signal even days following venous thrombosis. Skin flaps can be more reliably monitored with traditional assessment, although the Cook is still very useful for the reasons listed above [38].

For supermicrosurgical flaps such as the SCIP and PIA, pencil Doppler exam can be misleading, as underlying Doppler signals from the wound bed will easily transmit through the very thin flap. For these flaps, monitoring is performed by making a partial thickness scratch into the dermis to cause a small area of bleeding. The bleeding should be bright red. The flap is checked by irrigating the scratch with heparinized saline at bedside, and mechanically agitating it with either wet gauze or a blunt tipped needle (Fig. 32.25). Duplex ultrasonography can also be employed at bedside if desired.

Patients are kept in the hospital for up to 10 days to detect and prevent subacute complications that may result in delayed (non-anastomotic) flap failure.

The white blood cell count (WBC) and C-reactive protein (CRP) should be checked daily, as unrecognized postoperative infection can lead to delayed flap failure.

If an angioplasty was required to provide sufficient blood flow for reconstruction, then postoperative monitoring must be frequent until the wound has fully healed. This is because unexpected reocclusion of the post-angioplasty segment may lead to delayed flap failure. Emergency return to the OR for repeat angioplasty may be indicated for flap salvage.

Positioning

The surgeon must maintain careful control over postoperative positioning. Patients are kept on bedrest for 5 days following surgery. The foot must be constantly elevated above the level of the heart. Any amount of pressure with dependency can lead to either venous occlusion (particularly when the PT vessels are used, or vein grafting is needed) or neuropathic decubitus ulceration. A splinted dressing that is very well padded with Jones cotton is most often used to protect the flap. The heel must be carefully padded to prevent decubitus ulceration. The surgeon should clearly mark areas vulnerable to pressure on the dressing with tape and a marker. Alternatively, an Ilizarov frame is the surest method to avoid flap complications related to postoperative positioning, but comes with significant potential downsides.

Compression

The use of early compression therapy over lower extremity free flaps has been a major recent advance that hastens healing and reduces complications associated with edema. It also reduces reliance on arcane and unsubstantiated "dangling protocols." In our institutions, we routinely apply an early compression protocol (from postoperative day 3–5) to all flaps when applicable. Flaps that are used for resurfacing can be candidates for compression with the exception of flaps that are used for ischemic limbs, where arterial supply may be very sensitive to any degree of external compression (especially in the setting of concurrent vascular bypass).

In health systems where custom compression garments are available, these can be fabricated prior to the reconstruction and are designed based on the mirror measurements of the contralateral limb with the aim of generating a compression pressure of 30–40 mmHg. When a mirror image is not possible, the compression garment is tailored after manual measurement then fitted accordingly to reach the target pressure. As the flap swelling is reduced and molded into contour, the garment can be adjusted accordingly. The area covered by the compression garment includes the micro-anastomosis site and the flap pedicle.

In institutions where compression garments are not available, we have found that a multilayer compression wrap functions adequately as the "poor man's compression garment." The wrap is made of readily available supplies and includes a cotton gauze wrap from the toes to the knee, followed by an ACE bandage, followed by 3 in. Coban elastic bandage. A total contact cast can then be applied atop the compression wrap (Fig. 32.30).

Compression helps to stabilize the soft tissues against shearing and allows for earlier ambulation with less risk of dehiscence. For lower extremity reconstruction in non-weightbearing areas, the patients are allowed to ambulate at day 5 under compression. For non-weightbearing flaps, full weight bearing is commenced at 7–14 days if tolerable. If there was skeletal instability, initiation of ambulation must be adjusted accordingly. For weight bearing flaps, compression is applied on day 5 along with short leg splints and partial-weight bearing begun with the aid of walkers, gradually reaching full weight bearing at 3–6 weeks when the splints are removed. Usually the patient is discharged at day 7–10, educated with the protocol, and visits the outpatient clinic every week for follow-up.

The weaning of the compression garment usually ensues after several months. If the flap does not swell without applying the garment after a full day of activity, then the patient can stop using compression. As for weight bearing flaps, the compression is recommended whenever the patient ambulates for more than a short distance, to minimize any shearing of the tissue related to weight bearing [39].

External Fixation

The use of Ilizarov-type external fixation for offloading, flap protection, and tissue immobilization is a powerful tool [40]. It can also control biomechanical deformities, such as the equinovarus contracture of the Achilles tendon that may occur during the prolonged period of healing. The frame can be fitted with a foot plate to allow some weight bearing for transfers. However, complications such as pin tract infections with osteomyelitis are known to occur. Additionally, the Ilizarov frame makes edema control difficult, as contiguous wrapping of the extremity cannot be performed. The presence of the protective foot plate that allows weight bearing may wrongly encourage the patient to allow prolonged dependent positioning of the operated foot.

Total contact casting is an alternative option for flap protection. Total contact casting in the acute postoperative setting carries a risk of secondary pressure injuries from the cast, as well as being laborious for the clinic staff. However, it is highly effective in protecting the reconstruction and allowing earlier ambulation. Commercially



Fig. 32.30 Use of compression wrapping and total contact casting. Compression wrapping eliminates the need for "dangling" and provides a significant reduction in early and late flap edema. It also seems to expediate healing. Custom compression garments can be fabricated or effective compression wrapping can be performed with readily available materials. (**a**) A layer of soft cotton or rolled gauze is first applied from the metatarsal heads to the knee. (**b**) This is then over-wrapped with an ACE bandage, with very gentle pressure. (**c**) The wrap is completed with an elastic crepe bandage. The multiple layers provide gentle but effective compression. (**d**) Finally, if desired, a total contact cast can be applied to immobilize and protect the flap. The total contact cast is advantageous versus an Ilizarov frame because compression wrapping can be used beneath the cast. It is difficult or impossible to apply a compression wrap when an Ilizarov frame is in place. This fact, along with the weight of the frame creating a tendency to keep the foot dependent, can lead to significant and prolonged edema. If the flap is in a weight bearing area, the cast is not initially fitted with a cast shoe, and the patient remains non-weightbearing. Once the sutures have been removed, ambulation in a cast shoe is allowed. The cast is no longer needed once the incisions are felt to have regained full tensile strength (6–12 weeks)

available casting systems can be applied in minutes and fitted with a cast shoe to allow for weight bearing without direct pressure on the surgical site. Additionally, a compression wrap can be applied beneath the total contact cast. This combination seems to do an excellent job of controlling edema, facilitating healing, and protecting the flap from injury.

Hyperbaric Oxygen Therapy (HBOT)

It is very useful to have access to HBOT services when attempting reconstruction of the diabetic foot. HBOT can support flap viability but, more commonly, is used to improve the surrounding tissue bed and optimize healing to the flap. Ideally, in very high risk cases (such as with

severe concomitant PVD and osteomyelitis), HBOT should be started before reconstruction and continued after reconstruction. 30 dives before surgery and 30 after are ideal. Preoperative transcutaneous oxygen measurements (TCOMs) should be taken of the surrounding skin to determine whether HBOT will be of benefit. TCOM values should be 40 mmHg or greater to support healing.

Conclusions

The advent of supermicrosurgery and the other advanced techniques described herein have expanded the possibilities for reconstruction and decreased the morbidity associated with traditional flap surgery. These tools have allowed us to shift our goals from "obtaining coverage" to creating individualized and elegant reconstructions that seek to provide the best functional outcomes for the patient. However, reconstruction of the diabetic foot remains challenging. It requires considerable knowledge of underlying pathophysiology, disease progression, and functional consequences of salvage versus amputation. It is at times highly technically demanding, and there is no room for error in any of the variables. Successful outcomes can only be obtained in a multidisciplinary setting, and by careful planning in concert with flawless technical execution. It is an excellent area for surgeons who enjoy a challenge and who enjoy teamwork. However, the surgeon and patient must also be prepared to accept early and late reconstructive failures. It is a field with great room for innovation that creative surgeons will enjoy.

References

1. Clemens M, Attinger C. Functional reconstruction of the diabetic foot. Semin Plast Surg. 2010;24(01):043–56. https://doi.org/10.1055/s-0030-1253239.
2. Endara M, Masden D, Goldstein J, Gondek S, Steinberg J, Attinger C. The role of chronic and perioperative glucose management in high-risk surgical closures. Plast Reconstr Surg. 2013;132(4):996–1004. https://doi.org/10.1097/prs.0b013e31829fe119.
3. Armstrong DG, Boulton AJ, Bus SA. Diabetic foot ulcers and their recurrence. N Engl J Med. 2017;376(24):2367–75.
4. Attinger CE, Evans KK, Bulan E, Blume P, Cooper P. Angiosomes of the foot and ankle and clinical implications for limb salvage: reconstruction, incisions, and revascularization. Plast Reconstr Surg. 2006;117(7S):261S–93S. https://doi.org/10.1097/01.prs.0000222582.84385.54.
5. Janhofer DE, Lakhiani C, Kim PJ, et al. The utility of preoperative venous testing for lower extremity flap planning in patients with lower extremity wounds. Plast Reconstr Surg. 2020;145(1):164e–71e. https://doi.org/10.1097/prs.0000000000006384.
6. Cho MJ, Kwon J, Pak C, Suh H, Hong J. The role of duplex ultrasound in microsurgical reconstruction: review and technical considerations. J Reconstr Microsurg. 2020;36(07):514–21. https://doi.org/10.1055/s-0040-1709479.
7. Neville RF, Attinger CE, Bulan EJ, Ducic I, Thomassen M, Sidawy AN. Revascularization of a specific angiosome for limb salvage: does the target artery matter? Ann Vasc Surg. 2009;23(3):367–73. https://doi.org/10.1016/j.avsg.2008.08.022.
8. Hong JP, Oh TS. An algorithm for limb salvage for diabetic foot ulcers. Clin Plast Surg. 2012;39(3):341–52. https://doi.org/10.1016/j.cps.2012.05.004.
9. Attinger CE, Ducic I, Cooper P, Zelen CM. The role of intrinsic muscle flaps of the foot for bone coverage in foot and ankle defects in diabetic and nondiabetic patients. Plast Reconstr Surg. 2002;110(4):1047–54. https://journals.lww.com/plasreconsurg/Fulltext/2002/09150/The_Role_of_Intrinsic_Muscle_Flaps_of_the_Foot_for.7.aspx.
10. Attinger CE, Ducic I, Zelen C. The use of local muscle flaps in foot and ankle reconstruction. Clin Podiatr Med Surg. 2000;17(4):681–711.
11. Suh HS, Oh TS, Hong JP. Innovations in diabetic foot reconstruction using supermicrosurgery. Diabetes Metab Res Rev. 2016;32(Suppl 1):275–80. https://doi.org/10.1002/dmrr.2755.
12. Yoon CS, Noh HJ, Malzone G, Suh HS, Choi DH, Hong JP. Posterior interosseous artery perforator-free flap: treating intermediate-size hand and foot defects. J Plast Reconstr Aesthet Surg. 2014;67(6):808–14. https://doi.org/10.1016/j.bjps.2014.03.007.
13. Chen L, Greisberg J. Achilles lengthening procedures. Foot Ankle Clin. 2009;14(4):627–37. https://doi.org/10.1016/j.fcl.2009.08.002.
14. Holstein P, Lohmann M, Bitsch M, Jørgensen B. Achilles tendon lengthening, the panacea for plantar forefoot ulceration? Diabetes Metab Res Rev. 2004;20(S1):S37–40. https://doi.org/10.1002/dmrr.452.
15. Lumley E, Kwon J, Kushida-Conteras BH, et al. Free tissue transfer after open transmetatarsal amputation in diabetic patients. J Reconstr Microsurg. 2021;37(9):728–34. https://doi.org/10.1055/s-0041-1726394.

16. Ramanujam CL, Stapleton JJ, Zgonis T. Diabetic Charcot neuroarthropathy of the foot and ankle with osteomyelitis. Clin Podiatr Med Surg. 2014;31(4):487–92. https://doi.org/10.1016/j.cpm.2013.12.001.
17. Short DJ, Zgonis T. Management of osteomyelitis and bone loss in the diabetic Charcot foot and ankle. Clin Podiatr Med Surg. 2017;34(3):381–7. https://doi.org/10.1016/j.cpm.2017.02.008.
18. Sinkin JC, Reilly M, Cralley A, et al. Multidisciplinary approach to soft-tissue reconstruction of the diabetic Charcot foot. Plast Reconstr Surg. 2015;135(2):611–6. https://doi.org/10.1097/prs.0000000000000861.
19. Kuwae MY, Costa EN, da Silva RP, Albieri AD, de Moraes FB. Resection osteotomy for calcaneus flattening after micro-surgical flap: technical note. Rev Bras Ortop. 2017;52(1):119–22. https://doi.org/10.1016/j.rboe.2016.11.003.
20. Kim H, Altiparmak M, Pak C, Suh H, Hong J. Reconstruction using free flaps for diabetic heel defects: outcomes and risk factor analysis. J Reconstr Microsurg. 2020;36(07):494–500. https://doi.org/10.1055/s-0040-1709477.
21. Janhofer DE, Lakhiani C, Kim PJ, et al. The utility of preoperative arteriography for free flap planning in patients with chronic lower extremity wounds. Plast Reconstr Surg. 2019;143(2):604–13. https://doi.org/10.1097/prs.0000000000005265.
22. Tashiro K, Harima M, Kato M, et al. Preoperative color Doppler ultrasound assessment in planning of SCIP flaps. J Plast Reconstr Aesthet Surg. 2015;68(7):979–83. https://doi.org/10.1016/j.bjps.2015.03.004.
23. DeFazio MV, Fan KL, Evans KK. Greater saphenous vein-patch interposition to facilitate flow-sparing microanastomosis of calcified arteries in the distal lower extremity. Plast Reconstr Surg. 2019;144(2):340e–1e. https://doi.org/10.1097/prs.0000000000005851.
24. Buntic RF, Horton KM, Brooks D, Lee CK. The free partial superior latissimus muscle flap: preservation of donor-site form and function. Plast Reconstr Surg. 2008;121(5):1659–63. https://doi.org/10.1097/prs.0b013e31816a9fa3.
25. Rainer C, Meirer R, Gardetto A, Schwabegger AH, Ninkovic MM. Perforator-pedicled skin island flap for coverage of microvascular anastomoses in myocutaneous flaps in the lower extremity. Plast Reconstr Surg. 2003;112(5):1362–7. https://doi.org/10.1097/01.prs.0000081468.12246.38.
26. Abdelfattah U, Power HA, Song S, Min K, Suh HP, Hong JP. Algorithm for free perforator flap selection in lower extremity reconstruction based on 563 cases. Plast Reconstr Surg. 2019;144(5):1202–13. https://doi.org/10.1097/prs.0000000000006167.
27. Goh TLH, Park SW, Cho JY, Choi JW, Hong JP. The search for the ideal thin skin flap. Plast Reconstr Surg. 2015;135(2):592–601. https://doi.org/10.1097/prs.0000000000000951.
28. Suh HS, Oh TS, Lee HS, et al. A new approach for reconstruction of diabetic foot wounds using the angiosome and supermicrosurgery concept. Plast Reconstr Surg. 2016;138(4):702e–9e. https://doi.org/10.1097/prs.0000000000002401.
29. Nelson J, Fischer J, Haddock N, et al. Striving for normalcy after lower extremity reconstruction with free tissue: the role of secondary esthetic refinements. J Reconstr Microsurg. 2015;32(02):101–8. https://doi.org/10.1055/s-0035-1558986.
30. Felder JM, Willborg BE, Zhu WY. The SIEA SHRIMP flap: an ultrathin axial pattern free flap useable in obese patients. Plast Reconstr Surg Glob Open. 2022;10(4):e4274. https://doi.org/10.1097/gox.0000000000004274.
31. Hong J, Choi D, Suh H, et al. A new plane of elevation: the superficial fascial plane for perforator flap elevation. J Reconstr Microsurg. 2014;30(07):491–6. https://doi.org/10.1055/s-0034-1369807.
32. Black C, Fan KL, Defazio MV, et al. Limb salvage rates and functional outcomes using a longitudinal slit arteriotomy end-to-side anastomosis for limb-threatening defects in a high-risk patient population. Plast Reconstr Surg. 2020;145(5):1302–12. https://doi.org/10.1097/prs.0000000000006791.
33. Kim JT, Kim CY, Kim YH. T-Anastomosis in microsurgical free flap reconstruction: an overview of clinical applications. J Plast Reconstr Aesthet Surg. 2008;61(10):1157–63. https://doi.org/10.1016/j.bjps.2008.03.048.
34. Verhelle NAC, Heymans O. How to deal with difficult microsurgical end-to-side anastomoses. Microsurgery. 2005;25(3):203–8. https://doi.org/10.1002/micr.20100.
35. Hong JP, TLH G, Choi DH, Kim JJ, Suh HS. The efficacy of perforator flaps in the treatment of chronic osteomyelitis. Plast Reconstr Surg. 2017;140(1):179–88. https://doi.org/10.1097/prs.0000000000003460.
36. Fernandez-Garrido M, Penha TL, Qiu S. Flow-through flaps in the absence of an arterial gap for extremity defect reconstruction: minimizing the donor-site morbidity. J Reconstr Microsurg. 2018;35(05):329–34. https://doi.org/10.1055/s-0038-1676497.
37. Toia F, Zabbia G, Roggio T, Pirrello R, D'Arpa S, Cordova A. Vascular grafts and flow-through flaps for microsurgical lower extremity reconstruction. J Reconstr Microsurg. 2017;33(S 01):S14–9. https://doi.org/10.1055/s-0037-1606560.
38. Abdou SA, Sharif-Askary B, Zolper EG, Evans KK. Intraoperative utility of the implantable Doppler in lower extremity reconstruction: a matched case-control study. Plast Reconstr Surg Glob Open. 2020;8(11):e3229. https://doi.org/10.1097/gox.0000000000003229.
39. Suh H, Jeong HH, Hong JP. Is early compression therapy after perforator flap safe and reliable? J Reconstr Microsurg. 2018;35(05):354–61. https://doi.org/10.1055/s-0038-1676604.
40. Clemens MW, Parikh P, Hall MM, Attinger CE. External fixators as an adjunct to wound healing. Foot Ankle Clin. 2008;13(1):145–56.

Partial Foot Amputations: Technique and Outcomes

33

Jayson N. Atves, Ali Rahnama, and Tiffany K. Hoh

Introduction

Partial foot amputations are frequently performed procedures where the most common impetus are trauma, infection, and ischemia [1, 2]. Less commonly seen indications include thermal injury, malignancy, deformity, and intractable pain. Centuries of historical review cite many examples of limb amputation as a means of ameliorating inciting infection, traumatic injury, or concerns for "deadening" of tissues. Instances of wartime use of extremity amputation illustrate the quite literal life-saving benefits of lower extremity amputations. Despite its storied history, surgeons continue to develop and refine surgical techniques in lower extremity amputations and partial amputations of the foot are no exception to this tact. Recent innovations in vascular intervention and wound management techniques and considerations have improved patient outcomes and in turn have allowed for partial foot amputations to gain increased popularity and success. However, perhaps the greatest advancements have been born out of the emphasis on the multidisciplinary approach to lower extremity amputations. The collaborative efforts of multiple specialties, including but not limited to, podiatric surgery, plastic surgery, vascular surgery, infectious disease, and orthotics and prosthetics have transformed and invigorated the paradigm of partial foot amputations. In this chapter we review the guiding tenets of partial foot amputations and offer an assortment of strategies and techniques aimed at their appropriate selection, successful performance, and ultimately continued endurance.

Indications

General

The overarching purpose of any amputation is to excise the tissues which would otherwise impart patient harm if not removed. In many cases the overwhelming indication for partial foot amputation is either ischemia and/or infection, although others exist.

Weledji and Fokam noted in the limb which presents with pure ischemia, vascular optimization and prevention of superimposed infection may result in favorable outcomes [3]. The degree of tissue loss, however, is highly dependent on the time of discovery and time to vascular intervention. The anatomic location, distribution, and degree of the vascular involvement are important

J. N. Atves (✉) · A. Rahnama · T. K. Hoh
Department of Plastic Surgery, Georgetown University School of Medicine and MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: jayson.atves@medstar.net; ali.RahnamaVaghef@medstar.net; tiffany.k.hoh@medstar.net

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_33

parameters which can influence the precise level of amputation.

Any patient with an open skin lesion is predisposed to lower extremity infection, particularly in the comorbid population, especially the immunocompromised and diabetic populations for example. Infections can be either acute or chronic and include soft tissue and/or bone infections. As shown by Altemeier and Fullen, fulminant infections such as necrotizing infections, gas gangrene, and infections that cause hemodynamic instability all require urgent surgical intervention [4]. In such cases, the postoperative soft tissue deficit, bone loss, and the predicted functional outcome often dictate the level of final amputation. Price demonstrated that chronic infections have a dramatic impact on patient quality of life, increase the risk of osteomyelitis, and have major implications in overall amputation risk [5].

Another major factor that may contribute to ultimate partial foot amputation is deformity. While deformity alone is not typically a primary indication for amputation, in patients with failed osseous reconstructions or those who are at high risk for complex surgical correction of lower extremity deformities, such as those seen in Charcot neuroarthropathy, amputation may be considered the treatment of choice primarily, especially if functional status and quality of life cannot be predictably improved with reconstructive surgery. More common, acquired skeletal deformities predispose the neuropathic patient population to ulcer development and increased fall risk. Raspovic et al. demonstrated that when ulcers develop secondary to biomechanical aberration, healing the ulcer without addressing the underlying osseous structural alignment and/or stability will inevitably lead to recurrent ulceration, increased amputation risk, and a decrease in quality of life [6].

All too often patients have a combination of the aforementioned cardinal pathologies. They present with a biomechanically induced ulcer, have peripheral neuropathy, have some degree of ischemia, and are typically infected or at minimum chronically harbored with bacteria. Beaulieu et al. reported that these patients often have multiple conditions and comorbidities which increase the risks for amputation [7] and challenge limb salvage efforts. Hobizal and Wukich illustrated that several host factors such as medical comorbidities, nutritional status, glycemic control, nonadherence to medical regimens, and socioeconomic status clearly play a role in these patient outcomes [8].

Without question, the compromised patient host presents clinical and socioeconomic complexity to the discussion of amputation. Partial foot amputations must be understood as a single component of a larger process within the continuum of a patient's diseased state. Many patients have a subset of known and unknown medical conditions each of which may not be well controlled, have associated risks, and have particular and even predictable patterns of evolution. Though each patient presents with unique and distinct challenges, the overall sequence of events can be somewhat predictable if these parameters are properly identified, stratified, and mitigated in a timely, continuous, and conscientious manner.

Yazdanpanah et al. demonstrated how optimization of disease-modifiable factors such as glycemic control, blood pressure, and vascular insufficiency may allow patients to have more favorable long-term health outcomes [9]. However, once ulceration, deformity, neuropathy, or infection occurs, the risk for amputation remains undeniably high. Every effort must be taken to slow the rate of progression and prevent the onset of disease-related complications. Fernandez et al. reported how healthcare disparities, food insecurity, and cultural, ethnic, and language barriers all carry socioeconomic implications which impact the overall quality of care in the

at-risk population [10]. Ultimately, partial foot amputations are largely cumulatively based on patient-specific risk factors and may be simply unavoidable.

The surgical indications for amputations must not be made in isolation of the patient's ambulatory status and must include a realistic assessment of the patient's overall capacity to ambulate following amputation. The level of amputation must be carefully taken into account during sur-

gical planning and must align with the patient's wishes. Regardless of the exact level of amputation, disease progression, advancing age, and worsening vascular pathology almost guarantee the need for revisional surgery and perhaps more proximal amputation. Furthermore, Glaser et al. elucidated how the contralateral extremity becomes a high-risk limb due to the increased load subsequent to an amputation and peripheral arterial disease [11]. In truth, bilateral foot pathologies leading to amputations are commonplace.

Wound

Wounds about the foot most commonly occur due to underlying vascular or biomechanical processes which must be addressed in order to both heal the wound itself and to avoid further progression or complication. In some instances this may be a matter of offloading management, obtaining appropriate shoe gear and having the patient perform daily foot checks in addition to glycemic control to prevent recurrence. Unfortunately, in many instances the prevention of recurrence or further complication such as chronic osteomyelitis may require surgical intervention. Therefore, determining the etiology of the wound is an imperative first step to prevent further complications. Once the etiology is/are identified and addressed, the hard work of meticulous wound care can begin to help achieve wound healing. The key goal of wound care is debridement of nonviable tissues within the wound bed and periphery to the level of healthy bleeding and noninfected tissue margins. This not only decreases the bacterial burden of the wound when performed in the appropriate setting, but also helps create an environment within the wound that is conducive to healing [12]. That is, one where foreign, nonviable, necrotic tissue is removed from the wound and what remains is healthy, vascularized tissue that can allow the body to heal. Although outside the scope of this chapter, a dedicated wound care team, ideally a multidisciplinary collection of specialists in podiatric surgery, plastic surgery, vascular surgery, and infectious disease, is paramount to any limb salvage and vital to the performance and endurance of any partial foot amputation.

Infection

Foot infections are among the most common reasons for hospital admission for the diabetic patient [13] (Fig. 33.1). While there are many factors that must be considered to achieve successful outcomes in any partial foot amputation, there are four major factors which can greatly help predict the likelihood of success. Those factors are the presence and extent of infection or bacterial bioburden, the vascular supply to the involved anatomy, ability to provide appropriate soft tissue coverage, and biomechanical functionality of the considered amputation. Infection can play an important part in determining the level of successful amputation. Both soft tissue and bony (osteomyelitis) infections can play roles in choosing the level of amputation. It is important to note that there may be scenarios where there is soft tissue infection that does not involve the osseous anatomy, those where there is acute or chronic osteomyelitis but the overlying soft tissues are largely viable and can be used for a salvage attempt and finally those where there is involvement of both the soft tissue envelope and underlying osseous structures. Each of these scenarios, while unique, has similarity in their requirement to eradicate the infection, regardless of the level of localization, in order to insure the best chance for a successful outcome and decrease the need for subsequent surgical intervention [14]. While much is yet to be determined, such as the ideal number of debridements to achieve adequate eradication of infection, there is consensus in trying to achieve an environment in which the wound is clean and as close to culture-negative as possible prior to the performance of definitive closure [15]. A close relationship between the surgical and infectious disease teams is paramount in determining which organisms to tailor antibiotic coverage to and how to manage antibiotic coverage postoperatively. At our institution, we routinely obtain pre-debridement tissue cul-



Fig. 33.1 Clinical images multiple views: (**a**, **b**, **c**, **d**, **e**, and **f**) Infection of the foot and ankle is appreciated at varying levels of involvement. Infection may present in a number of ways and may range from the subtle to the frankly obvious. Many times, patients with infection present with concomitant relative ischemia (**f**)

tures and post-debridement tissue cultures taking care to separate our clean instruments from the dirty instruments via two separate surgical tables and strictly avoiding cross contamination between the two. While surgical debridement cases are often not technically challenging to perform, any cross contamination, especially in obtaining tissue cultures can lead to false positives and unnecessary or incorrect antibiotics and every precaution must be taken to avoid such a scenario. Additionally, a false positive culture may result in unnecessary further trips to the operating room in order to achieve a clean environment in the wound prior to closure.



Fig. 33.2 Clinical images multiple views: (**a**, **b**, **c**, **d**, **e**, and **f**) Ischemia of the foot and ankle secondary to insufficient arterial perfusion is appreciated at varying levels of involvement

Ischemia

Arterial perfusion to the foot, the degree of ischemia, and the potential to restore adequate blood flow all play arguably the largest role in determining the healing potential of any level of amputation (Fig. 33.2). Indeed, if there is significantly decreased blood flow to the foot and the patient lacks adequate intervention candidacy or revascularization options, major amputation is indicated at the most distal level that has adequate arterial perfusion. Furthermore, when considering revascularization, direct revascularization of the ischemic angiosome should be the goal in order to achieve the greatest likelihood of healing and avoidance of major amputation [16]. Luckily, great advances in both open and especially endovascular evaluation and interventional techniques have paved the way for greater success in limb salvage.

Deformity

While every effort should be made to achieve limb salvage, it should be emphasized that limb salvage must also be functional. Indeed, there is little benefit to the patient if their limb does not allow for the demands placed upon it (i.e. weight-bearing and ambulation). While this may be intuitive in theory, there is still much to be learned about the mechanics of the foot and ankle and what truly constitutes a functional limb in any one patient. Indeed, there are many scenarios, too numerous to discuss in this chapter alone, which exist that may precipitate or complicate a partial foot amputation (Fig. 33.3). However, there are general principles to adhere to when it comes to amputation management of the foot and ankle with concomitant deformity. The identification of deformity or predisposition for its development is largely based on irregularity of alignment and/or stability. Deformity of the foot and ankle may present in a variety of manner from the subtle to the obvious. More specifically, deformity of the foot and ankle may be seen at varying levels (toes, forefoot, midfoot, rearfoot, ankle, and/or leg), planes (sagittal, coronal, and/or transverse), severities (mild, moderate, severe), flexibilities (flexible, partially flexible, rigid), and tissue types (soft tissue and/or bone). Again, although outside of the scope of this chapter, consideration for the presence or predisposition for foot and ankle deformity is paramount and the onus of its recognition and the formulation of an appropriate intervention(s) and/or referrals is ultimately placed upon the treating surgeon. The acquisition of proper alignment and/or stability for safe and efficient ambulation are the overarching goals of lower extremity deformity correction.

When addressing a pressure induced wound, local wound care alone and offloading may temporarily aid in healing the wound, only for the



Fig. 33.3 Clinical and radiographic images multiple views. Deformity of the foot and ankle is appreciated at varying levels of involvement. (**a** and **b**) Digital deformities in the form of hammertoes, crossover toes, and hallux malleus are appreciated. (**c**) Heterotopic ossification of bone status post-transmetatarsal level amputation is fraught with the potential for uneven force distribution from bony prominence. (**d**, **e** and **f**) Charcot's neuroarthropathy commonly leads to significant multiplanar deformity in the foot and ankle and ultimately poses increased risk of aberrant force distribution and wound formation. (**g**, **h**, **i**, and **j**) Multi-plane and multi-level deformity, specifically in the at-risk patient population, can pose exponentially added risk for the bearing of adverse forces within the foot and ankle and create scenarios of wound formation and stagnation, the possibility of infection and necessitate deformity correction or accommodation

wound to recur when ambulatory function is resumed. Thus, the musculoskeletal abnormality or deformity must be corrected via soft tissue balancing and/or exostectomy, osteotomy, or fusion. If a corrective osteotomy is planned, bone biopsy and culture should first be performed to confirm or refute the presence of infection involving the bone as deep chronic infection can not only contribute to nonhealing wounds but may also spread infection directly to other parts of the extremity, especially when internal or external fixation is used.

In cases of flexible biomechanical deformities, tendon transfer and/or lengthening may be used for correcting the deformity and may supplement healing wounds or pre-ulcerative lesions. A common example of this is the equinus or varus deformity that occurs after a midfoot amputation. A tendo-achilles lengthening at the time of the midfoot amputation of shortly thereafter may help to relieve plantar forefoot pressure that would otherwise lead to aberrant pressure distribution and ultimately new ulceration [17]. Additionally, when encountering the varus stump after midfoot amputation either tibialis anterior tendon or posterior tibial tendon transfer can be used to assist in correction of the flexible varus deformity and avoiding further plantar wound development (Fig. 33.4) [18, 19]. In such cases where the biomechanical deformity continues to



Fig. 33.4 Clinical images axial foot views: Transmetatarsal amputation before (**a**) and after (**b**) tibialis anterior tendon transfer. Significant clinical correction of the residual forefoot varus with resolution of the aberrant biomechanics is appreciated

be a major risk for re-ulceration, a major amputation may be considered for a permanent solution that allows for the patient to return to normal activities of daily life with a greatly reduced risk for recurrence.

Partial Foot Amputations

General

The surgeon must consider the following basic factors when performing a partial foot amputation: definitive level of amputation, anticipated means of soft tissue closure, and the resultant biomechanical function of the foot and limb. Additionally, perioperative management, rehabilitation management including appropriate orthoses and/or prostheses, and the patient's baseline and anticipated ambulatory status are helpful factors. The guiding principle in any lower extremity amputation, inclusive of partial foot amputation, is to maintain or improve the patient's ambulatory function and thus quality of life [20]. Clinicians should not sacrifice biomechanical alignment or stability, however promising or well-intentioned, in order to merely maximize foot length. It is of utmost importance that the surgeon properly conveys this message to the patient and their social support structure, as a failure to identify the most appropriate level of amputation can result in dire consequences.

Following the eradication of infection and the optimization of local and systemic healing factors, an assortment of options exist on the plastic and reconstructive ladder for definitive amputation closure including primary closure and delayed primary closure, secondary closure, skin grafting, intrinsic tissue flaps, extrinsic tissue flaps, and free tissue transfers [21]. It is incumbent upon the surgeon to choose the most appropriate method(s) of closure based on the availability of resources, logistical feasibility for both the patient and surgeon, wound characteristics including location, size, topography, and concomitant factors which may either advance or retard overall healing. In general, a majority of partial foot amputations will ascribe to a more simplistic manner of closure via primary closure or delayed primary closure. A minority of amputations will require definitive closure via tissue flap reconstruction and in these cases it is only when necessary to cover vital structures like bone, tendon, or capsule. It is dependent upon the surgeon to discern when and where to implement or supplement with each of these methods of reconstruction in order to provide the most expedient and durable result for the patient.

Maximizing lower extremity function is a significant consideration for every patient. Regardless of confounding factors associated with the successful closure or reconstruction of an amputation site, the ability to maximize a patient's ambulatory function is of the utmost importance. Poor consideration for a patient's functional demands and limitations can perpetuate a cascade of events that ultimately result in failure, recurrence, and the need for more proximal amputation. Although outside the scope of this chapter, supplementary procedures to afford a preservation or even increase in functional limb capacity may include soft tissue procedures like tendon lengthening or transfer, or bony procedures such as exostectomy, osteotomy, joint arthroplasty, or joint fusion. Notably, considerations for functional limb preservation can afford patients a more expedited recovery, greater likelihood for avoidance of recurrence, and ultimately a superior quality of life. For these reasons patient and limb functional abilities and demands should always be a consideration prior to definitive procedure performance.

Tissue Handling

Regardless of the precise level of amputation or method of closure, proper tissue handling is paramount and may quite literally "make or break" an attempted amputation closure, especially in the comorbid population. Bunnell [22] first coined the term "atraumatic technique" to describe how

soft tissues should be handled during surgery. An atraumatic technique should be implemented at all times in order to preserve vascularity to the existing tissues and maximize the potential for healing. This technique is especially paramount for the immunocompromised or diabetic patient population. Regardless of the exact location or presentation of amputation, one should minimize excessive traction and manipulation of the tissues. This is best accomplished with strictly intent motions and manipulations and blunt retraction only when necessary for appropriate visualization or performance of a surgical task. Proper instrumentation selection is key to preserving an atraumatic technique. A thorough understanding and knowledge of the available instrumentation and more importantly how well a particular surgical task can be accomplished in one's hands is crucial. For example, the authors often prefer to forgo the use of forceps for tissue handling unless absolutely necessary, especially during suturing as this may cause repeated trauma to the microvasculature of the remaining tissues. Rather, the use of strategically positioned and oriented sutures is best utilized for transposition, rotation, and overall manipulation of tissues during a definitive amputation closure. Ideally, when utilizing suture material one should use a nonabsorbable monofilament. The authors prefer a vertical mattress technique when reapproximating skin layers directly and absorbable monofilament when affixing grafts and supplementing with staples where warranted.

Toe Amputation

Toe amputations are extremely common procedures performed as disarticulations at the level of the interphalangeal joint, metatarsophalangeal joint, or as transection amputation through the phalanx. It is preferred to preserve the base of the toe for central digits to lessen the likelihood of digital crossover deformities with adjacent toes, which may lead to aberrant pressure distribution and subsequent ulceration (Fig. 33.5).

The toe amputation procedure begins with a fish-mouth incision at the level of the interphalangeal joint creating dorsal and plantar skin flaps. Free the soft tissues of the head of the more proximal phalanx bone and use a sagittal saw to resect the head of the phalanx bone. The wound is irrigated with saline. Hemostasis is obtained and the wound is inspected to ensure that the extensor and flexor tendons are not visualized in the wound. The dorsal and plantar skin flaps are closed full-thickness with monofilament suture. Alternatively, a clam-shell vertically oriented incision may be utilized with medial and lateral tissue flaps (Fig. 33.6). Still more, a full tissue flap from plantar, medial, lateral, or dorsal may be utilized if tissue availability and vascularity are restrictive (Fig. 33.7). Tissue availability and surgeon preference will ultimately determine the most appropriate mode of closure (Fig. 33.8).

Alternatively, a racquet type incision can be performed dorsal to a central digit, medial to the great toe, or lateral to the fifth toe. This incision curves circumferentially around the interphalangeal joint to disarticulate the distal portion of the toe. The soft tissues are freed from the head of the next phalanx bone and a sagittal saw is used to resect the head of the phalanx bone. The wound is irrigated with saline. Hemostasis is obtained and the wound is inspected to ensure that the extensor and flexor tendons are not visualized in the wound. The skin is closed full-thickness with monofilament suture.

The dissection and technique are the same for the toe amputation that is done at the interphalangeal joint or metatarsophalangeal joint. However, if the toe amputation is done at the level of the metatarsophalangeal joint, the cartilage should be removed from the metatarsal head with a curette or curved osteotome. The soft tissues adhere better to subchondral bone, minimize risk of infection from retaining avascular cartilage, and decrease risk of seroma forming from joint fluid.

It is preferred to allow the extensor and flexor tendons to retract proximally so they are not visu-



Fig. 33.5 Clinical images axial foot views (**a** and **c**) and radiographs dorsal-plantar foot view (**b** and **d**): Preoperative (**a** and **b**) and postoperative (**c** & **d**) status post partial third toe amputation secondary to the formation of osteomyelitis from an open wound

alized in the wound prior to closure. This allows the tendons to scar in an appropriate position to maintain extension and flexion of the remaining base of the toe. The authors do not recommend tenodesing the extensor and flexor tendons over the residual phalanx bone as this can result in unwanted contracture of the base of the toe resulting in deformity and ulceration.

Partial Ray Amputation

A partial ray amputation involves the removal of the entire toe and a portion of the distal metatarsal. An indication for this procedure would be osteomyelitis of the metatarsophalangeal joint involving both the head of the metatarsal and base of the proximal phalanx such as a diabetic

foot ulcer with osteomyelitis located at the medial first metatarsophalangeal joint due to bunion deformity. The exact technique and means of closure of partial ray amputations are quite variable but are often dictated by the location (first ray, fifth ray, or central rays) and the extent of soft tissue loss, presumably secondary to infection, ischemia, deformity, or combined pathologies.

Traditionally, a partial first ray amputation begins with a long racquet incision from the medial glabrous junction extending distally circumferentially around the base of the hallux (Fig. 33.9). This incision can include excision of the medial diabetic foot ulcer. Using atraumatic technique, the skin and soft tissues are freed from the first metatarsophalangeal joint and the hallux is disarticulated at the joint. Full-thickness dissection of the soft tissues off the bone is extended proximally to expose the head of the first metatarsal. A sagittal saw is used to cut across the first metatarsal neck angled 45 degrees from the coronal plane, creating a resected surface that is slightly shorter medially and parallel to the weight-bearing surface. The sesamoids are visualized and removed using curved Mayo scissors. The wound is irrigated with saline and hemostasis is achieved. The full-thickness skin flaps are reapproximated with vertical mattress stitches.



Fig. 33.6 Clinical images axial foot view: Clamshell oriented closure of a right second toe amputation at the level of the metatarsophalangeal joint is appreciated

The same technique can be applied for a partial fifth ray amputation with the racquet incision along the lateral glabrous junction circumferentially around the fifth toe proximal phalanx (Fig. 33.10). It is preferred to preserve the base of the fifth metatarsal bone with the peroneal brevis tendon attachment to prevent varus deformity of the foot. If the entire fifth ray is amputated, one should expect staged reconstruction and further surgery to correct varus deformity.

For a central ray amputation, the preferred incision is linear at the dorsal foot over the metatarsal extending distally circumferentially around the base of the proximal phalanx (Fig. 33.11). The toe is disarticulated at the metatarsophalan-

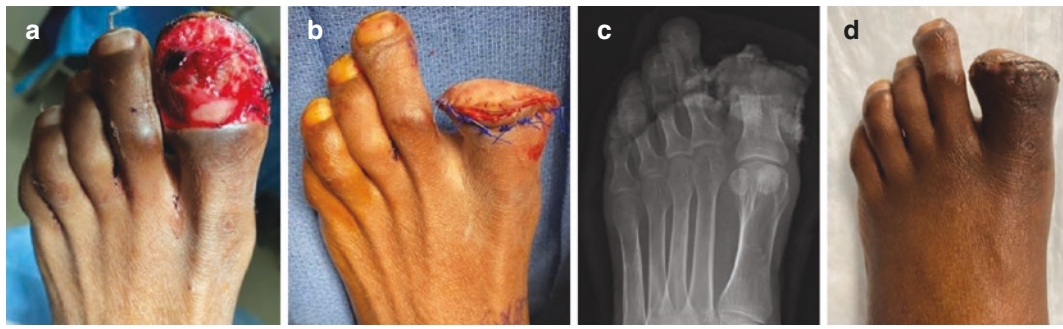


Fig. 33.7 Clinical images (**a**, **b**, **d**) and radiographs (**c**) dorsal foot view: Sequential performance of a plantar-based flap closure of a Left partial hallux amputation site is appreciated. (**a**) Initial presentation, (**b**) definitive closure, (**c**) immediate postoperative, (**d**) three weeks status post-definitive closure

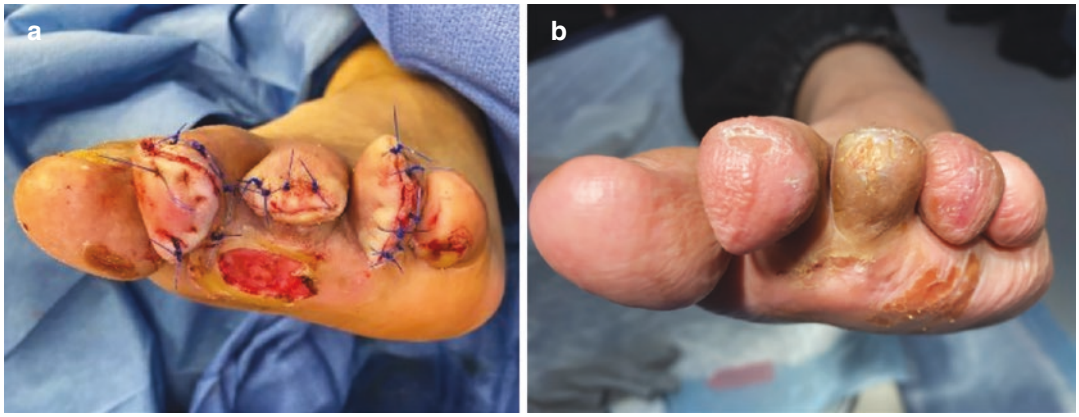


Fig. 33.8 Clinical images axial foot view: Sequential performance of three individual partial toe amputations of the left foot is appreciated, immediate postoperatively (**a**) and four-weeks postoperatively (**b**). The second toe utilized a medially based flap closure. The third toe utilized a fish-mouth horizontally oriented type closure. The fourth toe utilized a clam-shell vertically oriented type closure. Specific definitive closure technique is driven primarily by the amount and pliability of the remaining tissues utilized for closure

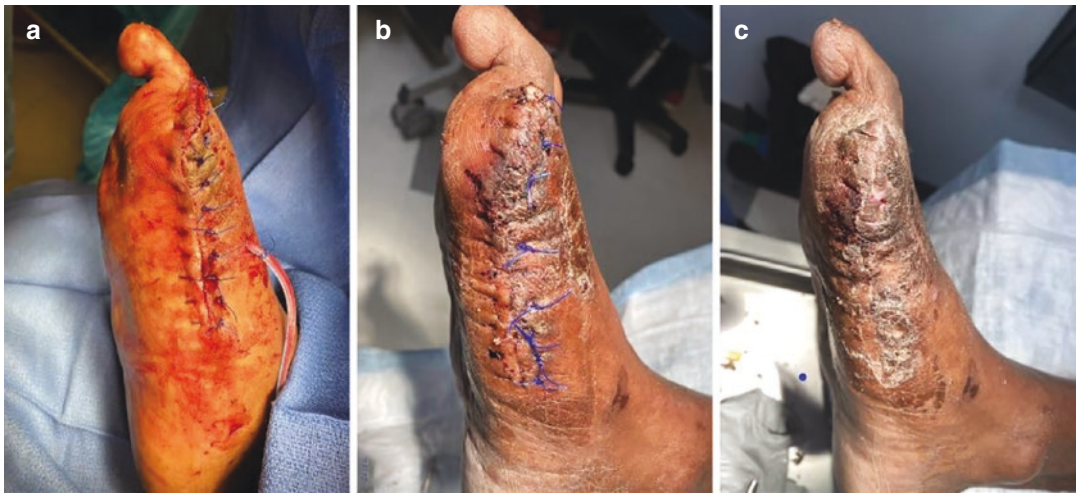


Fig. 33.9 Clinical images medial foot view: Sequential performance of a partial first ray amputation is appreciated (**a**–**c**)

geal joint. Retractors are placed on either side of the metatarsal neck to protect the soft tissues and a power saw is used to cut the metatarsal neck to remove the head of the metatarsal. The wound is irrigated and hemostasis is achieved. The skin is closed full-thickness. This technique is useful for ulcerations of the dorsal toe interphalangeal joint or infection of the metatarsophalangeal joint. However, a more common indication is an ulceration plantar to the metatarsal head due to neuropathy and bony deformity. The alternative incision for a central ray amputation begins plantar to the metatarsal excising the ulceration extending distally circumferentially around the toe proximal interphalangeal joint. The toe is disarticulated at the proximal interphalangeal joint. The soft tissues are dissected off the proximal phalanx bone which is disarticulated at the metatarsophalangeal joint preserving a small dorsal skin flap from the toe. Retractors are used to protect the soft tissues at the metatarsal neck and a saw is used to cut the metatarsal at the anatomic neck to remove the metatarsal. The wound is irrigated and hemostasis is achieved. The skin is



Fig. 33.10 Clinical images lateral foot view: Sequential performance of a fifth ray amputation is appreciated (**a**–**c**)



Fig. 33.11 Clinical image dorsal-plantar foot view: Open partial second ray amputation is appreciated. Central ray amputations often present many unique challenges for management, especially in the comorbid patient population

closed plantarly and the dorsal toe flap is used to obtain closure distally between the toes.

If more than two partial ray amputations are performed, regardless of location or distribution, progression to transmetatarsal amputation is preferred (Fig. 33.12). This provides for a more even distribution of ground reaction forces on the plantar foot and a lessened potential for aberrant accommodation in the form of deleterious toe, foot, and/or ankle contracture (Fig. 33.13).

Transmetatarsal Amputation

A transmetatarsal amputation involves removing the forefoot including the toes and the distal aspect of the metatarsals. Traditionally, a curved incision is made across the dorsal foot over the metatarsal heads just distal to the metatarsophalangeal joints and continued plantarly across the sulcus of the foot. Starting medially, all toes are disarticulated at the metatarsophalangeal joints. The incision can be extended medially and laterally along the glabrous junction and Bovie dissection is performed to raise a full-thickness dorsal tissue flap to expose the metatarsal heads. Sharp dissection is used to free the capsule and



Fig. 33.12 Clinical image dorsal-plantar foot view: Open concomitant partial first and fifth ray amputations are appreciated. Severely altered biomechanics of the foot and the precipitation of complication is so common that multiple partial ray amputations are preferably converted to the transmetatarsal amputation level in order to more adequately balance the altered mechanics of the foot



Fig. 33.13 Clinical image dorsal-plantar foot view: The altered biomechanics following partial first ray and partial second ray amputations have perpetuated severe multiplantar contractures of the remaining digits and precipitated abnormal force distribution with a resultant mechanical plantar wound (**a** and **b**). Multiple ray amputations place the patients at exponentially increasing risk for further complication

ligamentous structures from the metatarsal head and neck. A periosteal elevator is used to free the periosteum at the level of the metatarsal shaft. Hohmann retractors are used to protect the intermetatarsal soft tissues at each individual metatarsal where an osteotomy is made. A sagittal saw is used to cut all metatarsals across the metatarsal diaphysis, angled 15 degrees from the coronal plane following a normal metatarsal parabola when viewed in the transverse plane (Fig. 33.14). A small bone clamp or towel clamp may be used to hold the metatarsal head and neck to remove from the plantar flap. Curved Mayo scissors are used to remove the plantar plates of the metatarsals from the plantar skin flap. A hemostat is used to bluntly dissect and isolate the flexor tendons from the plantar skin flap which are tensioned and resected as proximal as possible to allow retraction back into the anatomy. The wound is copiously irrigated with sterile saline. The dorsal and plantar skin flaps are reapproximated and the wound is closed via vertical mattress sutures under minimal tension. A longer plantar skin flap typically covers the metatarsals allowing closure to be more dorsal and to provide better surface area for ambulation (Fig. 33.15).



Fig. 33.14 Radiograph dorsal-plantar foot view: Transmetatarsal level partial foot amputation. A normal metatarsal parabola without osseous prominence but with a preservation of length which is suitable for soft tissue closure is the primary goal

When soft tissue coverage is in short supply from the remaining available tissues, often secondary to either infection and/or ischemia, a filleted toe flap may be utilized in order to provide for additional coverage for soft tissue closure (Fig. 33.16). The phalanges of the toe of choice, most often the hallux as it possesses the most amount of shear soft tissue surface area for coverage, are skeletonized from the remaining soft tissues with meticulous sharp dissection. This provides for additional tissue which may be utilized to cover atypical soft tissue defects in the closure process. While this maneuver is quite useful for deficits at the transmetatarsal level, it may be utilized for closure purposes at any level. We find the hallux to be the most useful for such tissue deficits and the lesser toes to be of decreasingly usefulness due to lessening amounts of tissue surface area and pliability. Regardless, the fillet of toe flap should be considered a useful and viable mode of tissue closure in the surgeon's armamentarium.

Lisfranc's Amputation

The Lisfranc amputation is a relatively lesser performed level of partial foot amputation which involves disarticulation of the tissues distal to the level of the tarsometatarsal joints, or Lisfranc joints (Fig. 33.17). Often this level of amputation is predicated by soft tissue or osseous infection or relative ischemia just distal to this level or where a transmetatarsal level amputation does not have sufficient soft tissue envelope for primary closure.

Most pertinent to the alignment and stability in this level of amputation is the fact that in addition to the loss of the long extensor tendon insertions, as is seen in the transmetatarsal level amputation, the insertion of the peroneus brevis is lost. This creates a scenario where the ankle and foot are placed into a predisposed position of plantarflexion and inversion, respectively. In this instance it is perhaps more important to prophylactically address the potential for positional misalignment and instability with a combination of tendon procedures which address the sagittal plane predisposition for plantarflexion and the coronal plane predisposition for inversion (Fig. 33.18). This includes but is not limited to a posterior group lengthening in the form of a tendo-achilles lengthening, Achilles tenotomy/tenectomy or gastrocnemius soleus recession, long extensor tendon to long flexor tendon tenodesis, tibialis anterior tendon transfer (split or whole), and tibialis posterior tendon transfer (Fig. 33.19).

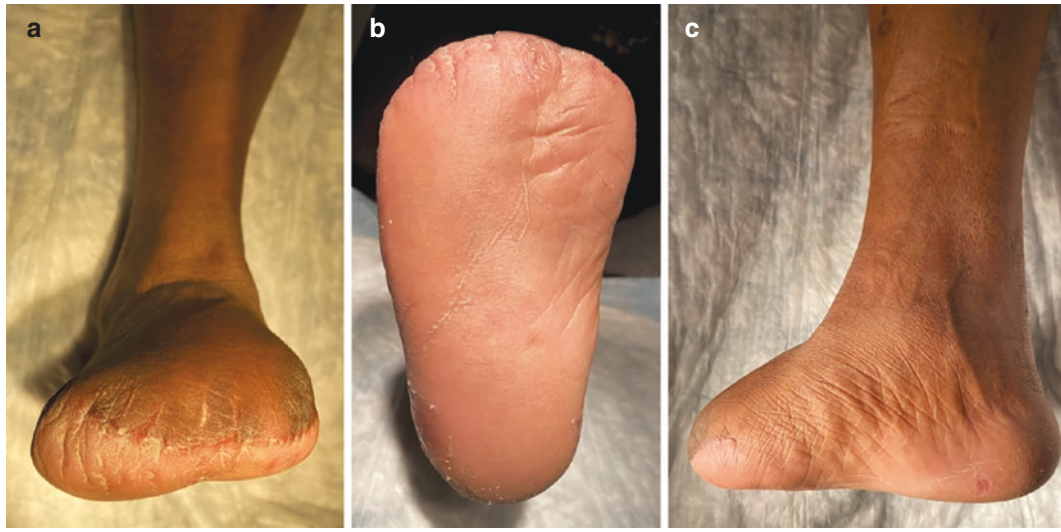


Fig. 33.15 Clinical images axial foot: (**a**) Plantar-dorsal foot (**b**) and medial-lateral foot (**c**)—Right foot well-healed and well-aligned transmetatarsal level amputation is appreciated. In this specific case, the patient received a prophylactic gastrocnemius recession posterior group lengthening at the time of final amputation site closure with an excellent clinical result



Fig. 33.16 Clinical images multiple views: Left foot well-healed and well-aligned transmetatarsal level amputation with utilization of a Fillet of Hallux toe flap for soft tissue envelope closure. In this specific case, the soft tissue of the hallux was rotated to the most lateral and proximal portion of the amputation site to provide definitive closure with an excellent clinical result

Chopart's Amputation

A Chopart's amputation is an even less commonly performed amputation which removes the forefoot and midfoot at the level of the talonavicular joint and calcaneocuboid joint, or Chopart's joint, preserving only the talus and calcaneus. This level of amputation tends to be more unstable as all the supporting tendons acting across the ankle and subtalar joint lose their insertions in the foot and no longer function. The only remaining tendinous attachment is the Achilles tendon insertion on the calcaneus which provides for powerful plantarflexion.

Special consideration for the patient's functional demands and age must be taken prior to considering a Chopart's amputation as the durability of the residual limb is considered to be questionable [23]. The authors consider this type of amputation for patients who are home ambulators, who merely require a full length limb for transfers or short periods of ambulating, or those who would otherwise do more poorly with a more proximal amputation. The Chopart's ampu-



Fig. 33.17 Clinical images dorsal-plantar and medial foot views (**a** and **b**) and radiograph dorsal-plantar foot view (**c**)—Right foot well-healed and well-aligned Lisfranc's level amputation is appreciated. The acquisition of a well-balanced foot and ankle is of the utmost importance at the Lisfranc level amputation secondary to loss of the insertion of the Peroneus Brevis tendon which predisposes the formation of an equinovarus contracture of the foot and ankle. Prophylactic performance of a posterior tibial tendon or anterior tibial tendon transfer with posterior group lengthening in the form of a tendo-Achilles lengthening or gastrocnemius-soleus recession is commonplace



Fig. 33.18 Radiograph lateral ankle view: Right foot Lisfranc's level amputation without appropriate soft tissue balancing resulted in significant equinovarus contractures with subsequent plantar foot wound and positive probe to cuboid bone

tation is not typically considered for younger patients with higher ambulatory demands as this level of amputation leaves a residual stump that is difficult to brace or shoe for moderate or high-demand ambulation [24]. An ankle equinus contracture deformity is a major complication of the Chopart's amputation due to increased pull of the Achilles tendon on the posterior calcaneus. This can result in distal plantar stump ulceration and shift of heel pad posteriorly requiring further surgical intervention or proximal amputation. An Achilles tenectomy is the preferred prophylactic treatment at the time of amputation in order to reduce the possibility of developing this equinus contracture deformity.

Again, incision placement can vary considerably depending on any prior surgery and tissue loss secondary to infection, ischemia, deformity, or combined pathologies. Incisions at the medial and lateral glabrous junction allow the surgeon to create dorsal and plantar skin flaps for bone exposure. A longer plantar skin flap is preferred as this

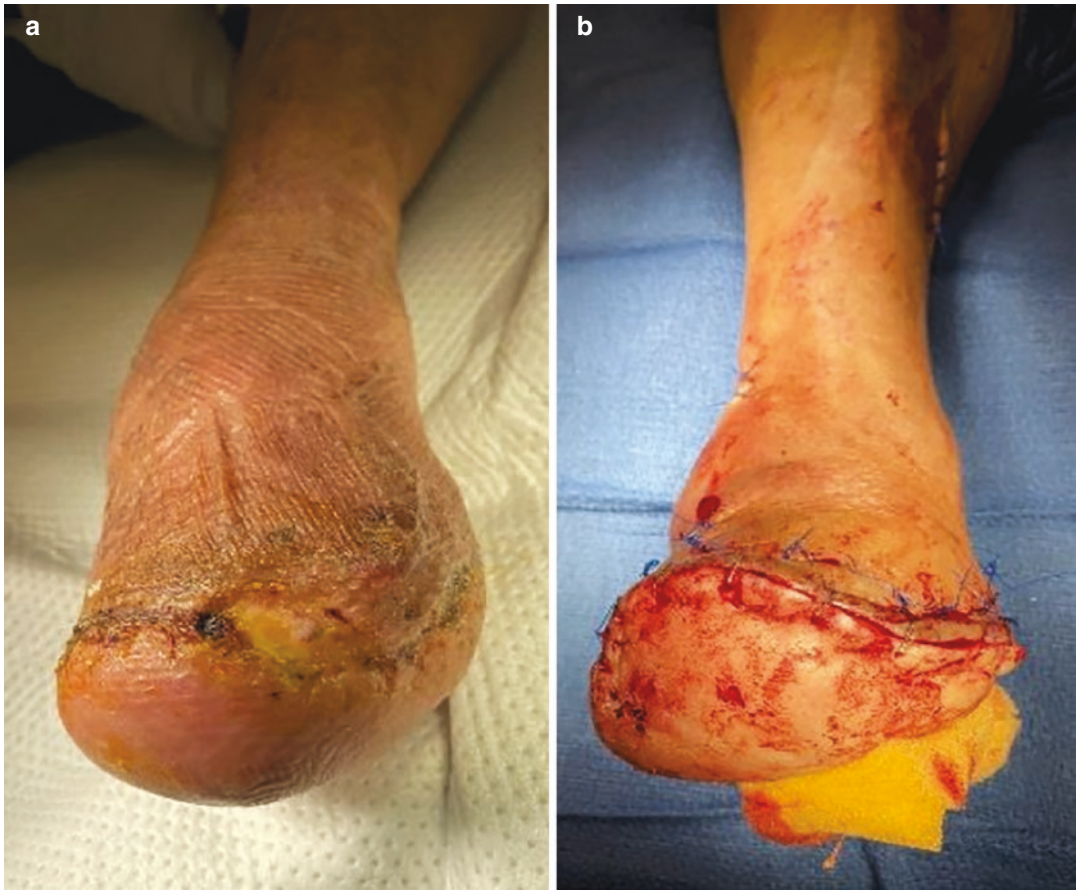


Fig. 33.19 Clinical images axial foot view: Lisfranc's level partial foot amputation before (**a**) and after (**b**) soft tissue balancing procedures in the form of posterior tibial tendon transfer and gastrocnemius recession

skin is sturdier for weight-bearing purposes; however, this may vary depending on the availability of viable soft tissue structures for closure (Fig. 33.20). The extensor tendons, flexor tendons, anterior tibial tendon, posterior tibial tendon, and peroneal tendons are all detached from their insertions. The forefoot and midfoot bones are removed preserving only the talus and calcaneus bones. The wound is irrigated and hemostasis is achieved. Skin flaps are closed meticulously to provide for direct dermal contact with minimal tension on the soft tissues (Fig. 33.21).

The Chopart's amputation has been described with tendon transfers such as anterior tibial tendon and posterior tibial tendon transfer into the talus to help reduce equinus contracture; however, the authors do not routinely perform these when performing Chopart's amputation. These tendon transfers are not significantly strong enough to counter the equinus deformity produced by an intact Achilles tendon or by the cumulative ground reaction forces which may perpetuate an equinus position. Additionally, the Chopart's level amputation is commonly performed in the acute setting of infection and every attempt should be made to avoid the implantation of foreign material such as anchors and nondissolvable sutures to reduce the risk of postoperative wound complication or recurrent infection, especially in the comorbid population.



Fig. 33.20 Clinical image anterior–posterior ankle view: Open left foot Chopart's level amputation is appreciated. The long plantar flap is preferred secondary to its generally stout arterial perfusion and for the generally thicker soft tissues of the plantar foot

Vertical Contour Calcanectomy Amputation

The partial calcanectomy amputation is considered a relatively common type of partial foot amputation where a significant portion of the calcaneus is resected necessitated by soft tissue and/or calcaneal bone infection or wound formation. There is significant distinction between plantar and posterior heel ulcer locations where posterior heel wounds are generally caused secondary to pressure and ischemia in non-ambulatory patients, whereas plantar heel wounds are generally the result of biomechanical abnormality during the gait of ambulatory patients, namely calcaneal gait. Regardless, the necessity for partial calcanectomy amputation is most often due to the presence of soft tissue and/or bone infection at the site of the calcaneus, most commonly via wound formation. Historically, the conventional partial calcanectomy amputation in the form of a flattened or non-contoured bone resection has several pitfalls related to its lack of reproducibility and a high risk of recurrence owing to residual calcaneal bony prominence,



Fig. 33.21 Clinical images axial foot and medial foot views (**a** and **b**) and radiograph dorsal-plantar foot view (**c**)—Right foot well-healed and well-aligned Chopart's level amputation is appreciated



Fig. 33.22 Plain film radiograph lateral ankle view: Pathologic fracture of the calcaneus bone with significant displacement is appreciated at the site of a previously performed traditional non-contoured calcanectomy. The traditional partial calcanectomy can place significant aberrant force distribution through the remaining calcaneus which significantly increases the risk of pathological fracture

lack of robust soft tissue coverage, and the formation of aberrant force distribution through the calcaneus which may ultimately result in pathologic fracture (Fig. 33.22).

The vertical contour calcanectomy (VCC) is a novel modification to the conventional partial calcanectomy amputation [25]. The VCC is an aggressive partial resection of the os calcis designed to ensure primary soft tissue closure and mitigate the risk of reoperation while respecting the basic tenets of surgical closure, wound healing, and force distribution upon the remaining calcaneus bone. The procedure promotes early wound closure without the need for complex soft tissue reconstruction and the osteotomy approach can be modified based on a patient's unique presentation in order to achieve similar results.

As in other amputation levels, a staged approach is recommended, as this strategy permits for tissue and bone culture and histopathology results to guide the exact timing of closure. The initial surgical intervention is directed at the removal of infected and nonviable soft tissue and bone to the level of healthy margins. Retention sutures may be used to approximate the wound edges to prevent loss of elasticity in the soft tissue between operative debridements. Once operative cultures confirm eradication of infection a completion VCC can be performed. Alternatively, a single-stage approach may be used in patients with overtly noninfected heel wounds following revascularization and in those high-risk surgical candidates.

Placing the patient in the prone position provides optimal visualization and accessibility to the surgical site. Alternatively, the lateral decubitus position can be used. A supine position can be challenging but is an option when aided with support triangles and leg holders. The soft tissue deficit generally dictates the extent of the incisional approach required to perform the VCC. A linear midline Gaenslen split heel incision is used to create full-thickness medial and lateral flaps, exposing the plantar and posterior calcaneus. Once the medial and lateral flaps are created, the Achilles tendon is then fully detached from its insertion and the plantar fascia is detached from its origin. A properly sized incision aids in visualization and dissection. Complete detachment of these structures enables removal of the calcaneus bone fragments. The full-thickness medial and lateral soft tissue flaps are protected to avoid injury to the neurovascular structures isolated within.

Using a sagittal bone saw the first osteotomy is made from the posterior aspect of the calcaneus and directed distally parallel to the long axis of the foot. The starting point of the osteotomy on the posterior calcaneus should be placed in the lower half of the bone. The blade should remain inferior to the sustentaculum tali, which is easily palpated. The osteotomy includes the medial and lateral tubercles of the plantar calcaneus. The second osteotomy is made parallel to the long axis of the leg and perpendicular to the first osteotomy. The osteotomy is initiated from the plantar aspect of the foot and aimed proximally. The blade should exit on the superior aspect of the calcaneus and should be within the posterior half of the superior cortex. If imaging is available, this point corresponds with the lateral process of the

talus. Alternatively, the osteotomy can be made from superior to plantar. The final osteotomy is made tangential to the first and second bone cuts at 45 degrees. On lateral projection imaging, the cut is generally made roughly parallel to the posterior facet of the subtalar joint. Generally, these osteotomies can be made without intraoperative imaging; however, intraoperative fluoroscopy may be of assistance (Fig. 33.23). The final step of the osseous component of the VCC is calcaneal contouring. Contouring is aimed at creating a rounded final surface with smooth cortical borders (Fig. 33.24). This goal can be accomplished with the use of manual or power rasps to ensure there are no sharp corners or projections and to produce a truly contoured posterior and plantar calcaneus.

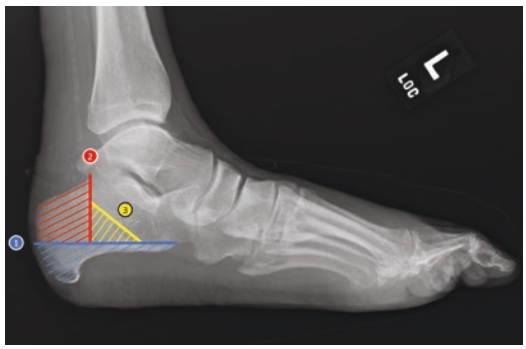


Fig. 33.23 Plain film radiograph lateral ankle view: Location, orientation, and order of the three osteotomies of the vertical contour calcanectomy



Fig. 33.24 Plain film radiograph lateral ankle view: Final vertical contour calcanectomy with closed soft tissue envelope is appreciated

In preparation for closure, the surgical site is copiously lavaged with normal saline. The calcaneus is a highly vascularized mainly cancellous bone and may require extra attention to achieve full hemostasis. To prevent hematoma formation, the use of a surgical negative pressure non-DME drain is encouraged, especially in those patients receiving anticoagulation. After the osteotomies, soft tissue closure may be achieved without significant soft tissue tension. Reattachment of the Achilles tendon is strictly not performed. Most cases require revision of the incisional flaps created after completion of the osteotomies as there may be redundant soft tissues. Interrupted vertical mattress technique using a nonabsorbable 0 or #2 monofilament suture is recommended. A posterior splint is applied in neutral to gravity equinus to decrease tension on the surgical incision, with robust padding and offloading of the heel. Alternatively, an external fixator may be applied to suspend the foot for offloading of pressure.

The postoperative course requires strict offloading and the patient must remain non-weight-bearing if they are normally ambulatory. Patients who are non-ambulatory should be provided with a means to maintain the surgical site suspended during the healing process. Once healed, they will require an offloading device to protect against recurrent ulceration in the form of a Charcot Restraint Orthotic Walker (CROW) boot or solid ankle foot orthosis (AFO). Continued offloading is required several weeks after suture removal to ensure incision healing. Generally, after six months of ambulation in CROW boot, progression into a custom solid AFO should be considered.

Conclusion

The fundamental tenets in the management of partial foot amputations are the eradication of infection, optimization of tissue healing factors, appropriate procedure selection, and adequate musculoskeletal alignment and stability with major consideration for residual functional abil-

ity and demands. In particular, the comorbid patient population requires adherence to a multifactorial algorithm which affords the greatest healing potential while mitigating costs and minimizing recidivism. A variety of management factors are essential to a successful partial foot amputation which includes, but is not limited to, patient comorbidities, nutrition, glucose control, smoking status, ambulatory status, amputation etiology, availability of resources, and ability to adhere to a rehabilitative course. Outside of the modifiable patient-centered factors as a means of ameliorating recurrence, the local establishment and maintenance of a stable and well-aligned foot and ankle is of the utmost importance. This is made possible with the proper procedure selection, including the appropriate level of amputation, mode of closure, with supplementation by vascular optimization, and musculoskeletal balancing or accommodation, where warranted.

Given the complexity of the comorbid patient population, the management of partial foot amputations is best suited for the multidisciplinary approach. This aspect of treatment cannot be overstated; however, it is often underappreciated and certainly underutilized in today's American healthcare market. This is perhaps due to a myriad of factors but most obvious may be secondary to an absence of resources and a lack of appropriate edification on part of the health system or a combination thereof. To be fair, the culmination of well-equipped, informed, and skilled podiatric surgery, plastic surgery, vascular surgery, and infectious disease teams is an increasingly elusive constellation in both the private and public settings. Many practices, hospitals, or healthcare systems simply lack the available infrastructure and/or physician expertise or enthusiasm to adequately support the demands of this type of patient population. However, the consortium offered by a multidisciplinary approach including specialized evaluation, intervention, and perhaps most importantly inter-specialty collaboration may truly be considered the ideal foundation for the management of this increasingly complicated patient population.

Acknowledgements No acknowledgements are made.

References

1. Banks M. The surgeon of old in war. JAMA. 1897;29(14):665–7.
2. Moxey PW, Gogalniceanu P, Hinchliffe RJ, Loftus IM, Jones KJ, Thompson MM, Holt PJ. Lower extremity amputations – a review of global variability in incidence. Diabet Med. 2011;28(10):1144–53.
3. Weledji EP, Fokam P. Treatment of the diabetic foot – to amputate or not? BMC Surg. 2014;14:83.
4. Altemeier WA, Fullen WD. Prevention and treatment of gas gangrene. JAMA. 1971;217(6):806–13.
5. Price P. The diabetic foot: quality of life. Clin Infect Dis. 2004;39(Suppl 2):S129–31.
6. Raspovic KM, Hobizal KB, Rosario BL, Wukich DK. Midfoot Charcot neuroarthropathy in patients with diabetes: the impact of foot ulceration on self-reported quality of life. Foot Ankle Spec. 2015;8(4):255–2559.
7. Beaulieu RJ, Grimm JC, Lyu H, Abularrage CJ, Perler BA. Predictors for readmission and reamputation following minor lower extremity amputation. J Vasc Surg. 2015;62(1):101–5.
8. Hobizal KB, Wukich DK. Diabetic foot infections: current concept review. Diabet. Foot Ankle. 2012;3(1):18409.
9. Yazdanpanah L, Nasiri M, Adarvishi S. Literature review on the management of diabetic foot ulcer. World J Diabetes. 2015;6(1):37–53.
10. Fernandez A, Schillinger D, Warton EM, Adler N, Moffet HH, Schenker Y, Salgado MV, Ahmed A, Karter AJ. Language barriers, physician-patient language concordance, and glycemic control among insured Latinos with diabetes: the diabetes study of northern California. J Gen Intern Med. 2011;26(2):170–6.
11. Glaser JD, Bensley RP, Hurks R, Dahlberg S, Hamdan AD, Wyers MC, Chaikof EL, Schermerhorn ML. Fate of the contralateral limb after lower extremity amputation. J Vasc Surg. 2013;58(6):1571–7.
12. Kim PJ, Attinger CE, Bigham T, Hagerty R, Platt S, Anghel E, Steinberg JS, Evans KK. Clinic-based debridement of chronic ulcers has minimal impact on bacteria. Wounds. 2018;30(5):114–9.
13. Pinzur MS, Slovenkai MP, Trepman E, Shields NN. Diabetes Committee of American Orthopaedic Foot and Ankle Society. Guidelines for diabetic foot care: recommendations endorsed by the diabetes Committee of the American Orthopaedic Foot and Ankle Society. Foot Ankle Int. 2005;26(1):113–9.
14. Anghel EL, DeFazio MV, Barker JC, Janis JE, Attinger CE. Current concepts in debridement: science and strategies. Plast Reconstr Surg. 2016;138(3 Suppl):82S–93S.

15. Wolcott RD, Kennedy JP, Dowd SE. Regular debridement is the main tool for maintaining a healthy wound bed in most chronic wounds. J Wound Care. 2009;18(2):54–6.
16. Neville RF, Attinger CE, Bulan EJ, Ducic I, Thomassen M, Sidawy AN. Revascularization of a specific angiosome for limb salvage: does the target artery matter? Ann Vasc Surg. 2009;23(3):367–73.
17. Armstrong DG, Stacpoole-Shea S, Nguyen H, Harkless LB. Lengthening of the Achilles tendon in diabetic patients who are at high risk for ulceration of the foot. J Bone Joint Surg Am. 1999;81(4):535–8.
18. Kim PJ, Steinberg JS, Kikuchi M, Attinger CE. Tibialis anterior tendon lengthening: adjunctive treatment of plantar lateral column diabetic foot ulcers. J Foot Ankle Surg. 2015;54(4):686–91.
19. Turan I. Tarsometatarsal amputation and tibialis anterior tendon transposition to cuneiform I. J Foot Surg. 1985;24(2):113–5.
20. Attinger CE, Brown BJ. Amputation and ambulation in diabetic patients: function is the goal. Diabetes Metab Rev. 2012;28(Suppl 1):93–6.
21. Attinger CE, Clemens MW, Ducic I, Levin MM, Zelen C. Chapter 23: the use of local muscle flaps in foot and ankle reconstruction. In: Dockery GD, editor. Lower Extremity Soft Tissue & Cutaneous Plastic Surgery. 2nd ed. Kidlington: Elsevier Science; 2011.
22. Bunnell S. An essential in reconstructive surgery: atraumatic technique. Calif State J Med. 1921;19:204.
23. Schade VL, Roukis TS, Yan JL. Factors associated with successful Chopart's amputation in patients with diabetes: a systematic review. Foot Ankle Spec. 2010;3(5):278–84.
24. Brodell JD, Ayers BC, Baumhauer JF, DiGiovanni BF, Flemister AS, Ketz JP, Oh I. Chopart amputation: questioning the clinical efficacy of long-standing surgical option for diabetic foot infection. J Am Acad Orthop Surg. 2020;28(16):284–91.
25. Elmarsafi T, Pierre AJ, Wang K, Evans KK, Attinger CE, Kim PK, Steinberg JS. The vertical contour Calcanectomy: an alternative surgical technique to the conventional partial Calcanectomy. J Foot and Ankle Surg. 2019;58:381–6.

34

Below Knee Amputation: Techniques to Improve Rehabilitation, Pain Management, and Function

Tanvee Singh, Kevin G. Kim, Grant M. Kleiber, and Christopher E. Attinger

Introduction

Although the rate of lower extremity amputations has been declining in the USA, there are still approximately 185,000 amputations performed annually with nearly two million living amputees [1, 2]. A transtibial or below knee amputation (BKA) is the most common level of major amputation and involves surgically removing the foot, ankle, and distal tibia and fibula, along with related soft tissue structures. The vast majority of patients undergoing a BKA have greater functional outcomes and a higher likelihood of ambulating with a prosthesis compared to their above-knee amputation counterparts [3]. This can be attributed largely to the mechanical advantage of preserving the knee joint and resulting greater functional baseline status postoperatively. Although there are functional and ambulatory benefits attributable to BKA, it is not without risks. For example, non-ambulatory patients may experience flexion contracture of the knee and subsequent pressure ulcers on the distal residual limb from prolonged immobility [3–5]. Furthermore, chronic pain syndromes of the resulting stump are not uncommon. BKAs are associated with various limitations on activities of daily living (ADLs), and adjusting to these changes poses additional physical and psychological morbidities for patients [1].

Indications for BKA vary widely and may include traumatic injuries, oncologic treatment requirements, vascular disease and critical limb ischemia, diabetic complications such as chronic nonhealing ulcers, congenital deformities, necrotizing infections, and other vasculopathies. BKAs are performed in both acute and non-urgent settings for a wide range of patients and are able to restore and improve patient function in addition to provide lifesaving and definitive treatment. Diabetic patients, for example, with nonhealing foot ulcers may improve ambulation and regain function with prosthesis after the removal of an affected limb [6]. Complicated diabetic foot infections may require major drainage amputation to limit progression of infection and maximize the

T. Singh
Columbia University Irving Medical Center, New York, NY, USA
e-mail: ts1216@georgetown.edu

K. G. Kim
Department of Plastic Surgery, MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: kgk31@rwjms.rutgers.edu

G. M. Kleiber
Department of Plastic and Reconstructive Surgery, MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: grant.m.kleiber@medstar.net

C. E. Attinger (✉)
Department of Plastic Surgery, Georgetown University School of Medicine and MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: christopher.attinger@medstar.net

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_34

optimal subsequent prosthesis fitting and ambulation. Further, patients with chronic pain after traumatic injuries may elect to undergo BKA for palliative improvement of pain and functional outcomes. BKAs may also be performed when limb salvage has failed to preserve a mangled extremity or in cases of full-thickness burns, serious neurovascular compromise, recalcitrant infection, and irreplaceable soft tissue defects [6–9]. Lastly, elective BKAs are appropriate in patients with lack of distal foot or ankle function with refractory pain, venous stasis ulceration, or multiple distal to mid-foot amputations with persistent infection or vascular insufficiency [6–9].

Several contraindications to BKA also exist. Patients with flexion contracture of the knee greater than 20 degrees, stroke, or neurologic deficits resulting in spasticity or rigidity on the side of amputation, and infections that have spread to the skin within 4 to 5 cm of the tibial tuberosity leaving too short a tibia for a prosthesis should not undergo a BKA. Vascular occlusion of the superifical femoral artery and popliteal artery also poses challenges to wound and stump healing secondary to severe ischemic conditions.

The purpose of this chapter is to discuss various multidisciplinary techniques to improve rehabilitation, pain control, and functional outcomes in patients undergoing BKA. First, we give an overview of the etiologies, anatomy and discuss surgical considerations to optimize pain after BKA. Next, we highlight morbidities associated with BKA, with a focus on pain, and the various treatment options that can be used to address it. Lastly, we discuss surgical interventions to treat neuromas and other multidisciplinary options such as nutritional support, physical therapy, and prosthesis.

Anatomy and Surgical Considerations

Musculocutaneous flaps for BKAs are planned according to the anatomy and blood supply of the lower leg compartments. There are four fascial compartments of the leg, with each containing muscle and neurovascular structures. The anterior tibial compartment lies anteromedial to the tibia and anterior to the fibula. The fascia encompasses the tibialis anterior, extensor hallucis longus, extensor digitorum longus, the deep peroneal nerve, and the anterior tibial artery and vein. The anterior tibial artery is the main blood supply to the anterior compartment of the leg with reinforcement by the perforating branch of the peroneal artery. The lateral compartment lies lateral and posterior to the anterior compartment and lateral to the fibula and contains the peroneus longus and brevis and the superficial branch of the peroneal nerve for much of its course. Its arterial supply derives from the anterior tibal artery proximally and pedicles from the peroneal artery distally. The posterior leg holds both the superficial and deep compartments. The superficial compartment contains the soleus, gastrocnemius, and plantaris muscles. The muscular deep compartment contains the tibialis posterior, the Flexor Hallucis Longus and Flexor Digitorum Longus. The peroneal and posterior tibial arteries as well as the posterior tibial nerve also lie within the deep compartment.

Advances in surgical technique have contributed to improved outcomes following BKA. Considerable clinical evidence continues to support the use of a long posterior musculocutaneous flap comprised of the gastrocnemius and soleus muscles for stump coverage [10]. The sural arteries, which originate proximal to the knee joint, are often the major blood supply for this type of flap. Many of our patients, especially those with diabetes, have preserved blood flow through the sural arteries despite having restricted blood flow through the popliteal artery and its major branches. Long posterior musculocutaneous flaps with no anterior flaps can prevent wound necrosis and rehabilitation failure [10]. Care should be taken to ensure the distal end of the fibula is shorter than the tibia (1–2 cm.), that it is smooth and that it has ample musculocutaneous padding to avoid potential pressure points within the socket of the prosthesis. Bony protrusions can impede weight-bearing on the residual limb and complicate prosthetic fittings (Fig. 34.1). Subsequent myodesis of the anterior tibial, peroneal and superficial distal muscles to the distal tibia restores their insertion so that they can still contract and avoid loosing their bulk. This helps pad the tibia and fibula in the distal stump over the long term. In addition, the myodesis of the gastrocnemius muscles to the distal tibia adds power to knee flexion.

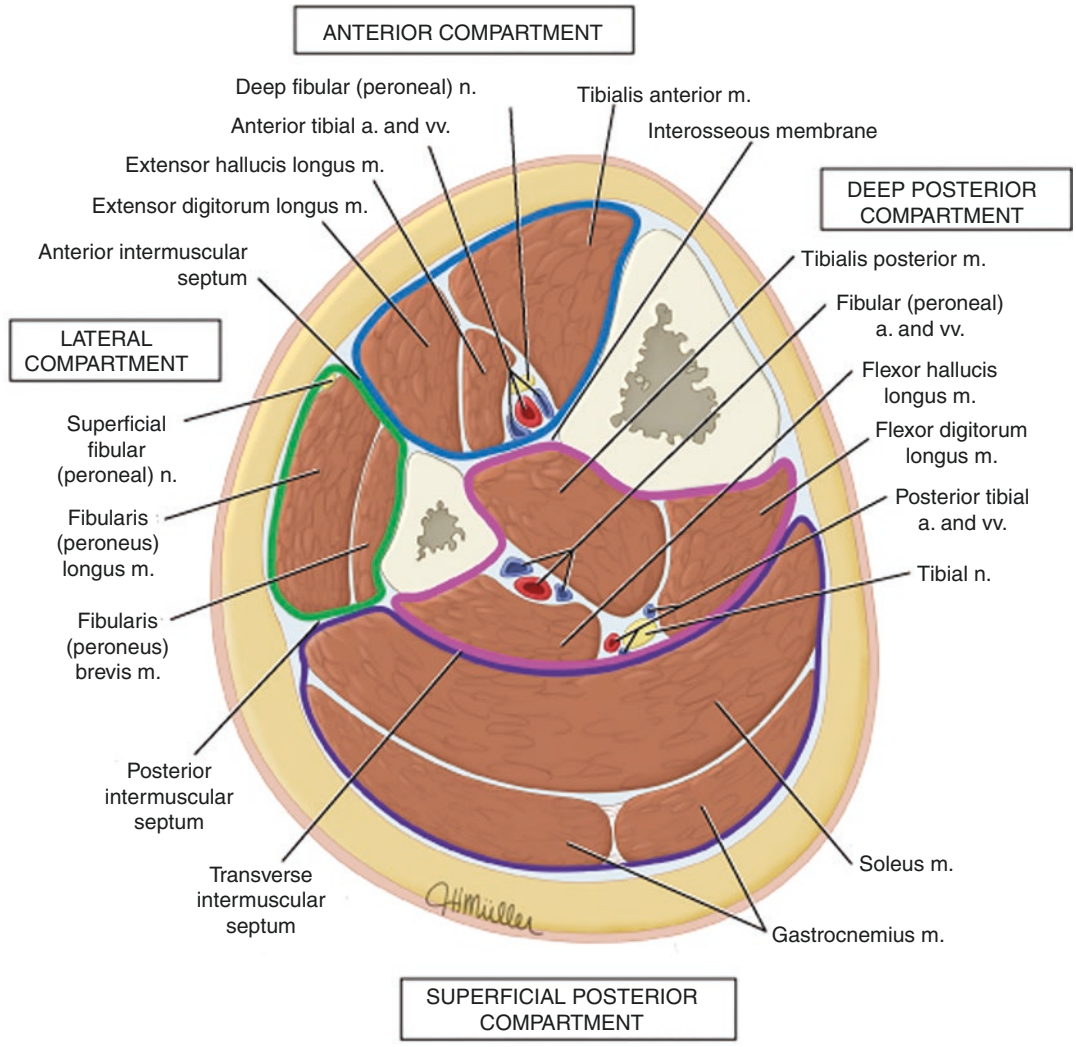


Fig. 34.1 Anatomy of muscle compartments of the leg

Understanding the anatomy of the amputation site is also critical to placing a successful nerve block for adequate postoperative pain control. BKAs require sciatic nerve blockade, whereas an above the knee amputation necessitates blockade of both femoral and sciatic nerves for successful pain control [11]. Tourniquet site placement is also paramount when planning a peripheral nerve block, to ensure access neurovascular structures of interest. Skin closure should be without tension to minimize the pressure applied per unit skin surface and facilitate wound healing [12].

A key underlying principle to improve rehabilitation and function after BKA is to provide a residual limb with functional length. This decreases the shear and torque pressures on the amputation stump. The anatomic level of bony transection is an important consideration to ensure proper soft tissue coverage of the residual limb. The incision line should be placed distal to the distal anterior tibia bone cut in order to prevent the scar from being at the highest friction and pressure point when wearing a prosthesis. The ideal length of the residual limb is 12–18 cm from the tibial tubercle [13]. Optimal prosthetic alignment promotes steady and comfortable mobility [14, 15]. We elaborate more on prosthetics in Chap. 28.

Morbidities Associated with BKA

Patients undergoing BKA are susceptible to a constellation of postoperative morbidities that are medical, psychological, social, and financial in nature. Beyond acute postoperative deficits in function, pain after BKA often has complex pathophysiological mechanisms and may manifest weeks, months, or years following amputation. This pain can be function limiting, a detriment to quality of life, as well as a negative impact to mental health and interpersonal relationships. It is estimated that 70–80% of amputees in the USA deal with chronic pain of varying etiologies, often necessitating revision surgeries and limiting prosthetic use [16, 17].

Pain at the amputation site can be classified into one of the four categories: residual limb pain (RLP), phantom limb pain (PLP), phantom limb sensations, and postoperative pain. Acute postoperative pain is pain at the surgical site due to surgical trauma that most patients experience after surgery. This pain is often described as sharp and stabbing in nature, due to the involvement of the nociceptive afferent nerve innervating the surgical site. Some patients also experience muscle spasms and tenderness at the amputation site due to prolonged immobility and use of surgical dressings [11, 18, 19].

RLP, or "stump pain," is localized, intense pain experienced in the residual limb after amputation. There are several possible etiologies to RLP including soft tissue inflammation, infectious processes such as osteomyelitis, heterotopic ossification, and neuromas. One of the most common causes of RLP is neuroma formation. Although neuromas may be asymptomatic, one in four of limb amputees will develop chronic localized pain because of symptomatic neuromas within their residual limb [8, 20–23]. Painful symptomatic neuromas are frequently the cause of RLP and are known to compromise prosthetic rehabilitation and diminish the quality of life after amputation.

Neuromas may form following transection of a peripheral nerve, as the nerve attempts to regenerate in response to intrinsic signals, as well as those from the distal targets they innervate [13, 24]. Following peripheral nerve transection injury, the nerve undergoes three biologic processes: Wallerian degeneration, axonal regeneration, and muscle reinnervation if end organs are present [25]. If the distal end of the proximal nerve stump is in proximity to the proximal end of the distal nerve stump, end-to-end neurorrhaphy may occur. In this process, proximal axons regenerate into distal endo-neural tubes and elongate until they reinnervate the end organ, achieving maximal functional recovery [26]. However, in the context of amputation, these end organ targets are surgically removed. Thus, peripheral nerves in the residual limb may sprout and regenerate in an uncoordinated fashion, forming a neuroma in the process, leading to symptomatic, focal pain. Neuroma pain may be attributable to the neuroma microenvironment, which has different mechanochemical sensitivity and excitability, as well as the neuroma itself, which has altered expression of transduction molecules, sodium channels, potassium channels, and axonal connections [27].

The pathophysiology of neuroma pain makes neuromas particularly difficult to treat using traditional medical interventions, requiring the use of surgical management for definitive treatment. Techniques for neuroma management are varied and can involve nerve grafting, nerve cap placement, use of regenerative peripheral nerve interface (RPNI), "end-to-side" neurorrhaphy, and targeted muscle reinnervation (TMR). These techniques are discussed further later in this chapter.

Perceived pain in the amputated limb was first described in 1462 by Dr. Ambrose Pare, a French surgeon, and the term "phantom limb" was coined in 1871 by Silas Weir Mitchell, a Civil War surgeon [18, 28]. PLP is the perceived pain in an area of the amputated limb that is no longer present. The etiology of PLP) is not well understood but is thought to be caused by functional reorganization of the somatosensory cortex and changes in inhibitory sensory feedback signals sent to the dorsal horn of the spinal cord, resulting in pain transmission [11, 18, 19]. In comparison, phantom sensations are nonpainful perceptions of the amputated limb that can be kinetic (perceived movements of the amputated

limb), kinesthetic (perceived shape or position of the amputated limb), or exteroceptive (perceived touch, pressure, itching, vibration in the phantom limb) [29, 30].

It is well understood that effective control of acute postoperative pain decreases the risk of residual and phantom limb pain development [31]. Thus, preoperative pain optimization is essential to control acute post-amputation pain and subsequently decrease the risk of lasting chronic and phantom pain. By doing so, amputation patients may maximize their chances of post-amputation pain control and successful ambulation with a prosthesis.

Preoperatively, patients undergoing non-traumatic BKA should have their medical conditions and nutritional status optimized for maximal wound healing, undergo narcotic evaluation for opioid tolerance, and be evaluated by physical therapy/occupational therapy to enhance postoperative recovery. Patients with underlying depression and high baseline pain scores are more likely to experience physical and psychosocial difficulties [32]; thus, it also appropriate for psychiatric conditions to be evaluated and managed through a psychological or psychiatric consult prior to BKA [33–35].

On the day of surgery, a multidisciplinary and collaborative approach is essential. Anesthesiologists and the Acute Pain Service team play a vital role in the formulation and execution of an optimized perioperative analgesia plan. Adopting a patient-tailored approach is important in perioperative pain management as individual pain perception accounts for variability and multifactorial etiologies of pain between patients [36, 37]. Perioperative catheter nerve blocks during the operation and subsequent hospital recovery allow for a 5 day relatively pain free period that helps minimize subsequent pain. A preoperative discussion with physical therapy and occupational therapy, when permitted, also allows for improved pain management and expectations.

If chronic pain develops following amputation, several modalities are available: pharmacological, psychological, and physical [23]. Pharmacological options include narcotics, peripheral nerve catheters, nonsteroidal anti-inflammatory drugs, antidepressants, muscle relaxants, anticonvulsants, nerve modulators, local nerve blocks, steroid injections, and lidocaine patches. Psychological methods include mirror box therapy, antidepressant therapy, and following up with a pain psychologist [38, 39]. Physical methods include transcutaneous electrical nerve stimulation to the limbs, spinal electrical stimulators, rehabilitation with exercise or massage, and surgery [23].

Targeted Muscle Reinnervation and Regenerative Peripheral Nerve Interface Surgery for Neuroma Prevention and Treatment

Traction neurectomy is a simple surgical option to treat symptomatic neuromas that entails neuroma excision, with high transection of the nerve while on traction [40, 41]. The nerve stump is proximally relocated into an area more protected by muscle and soft tissue, thereby making sure it remains undisturbed and asymptomatic [40, 41]. Regenerative peripheral nerve interface (RPNI) surgery and targeted muscle reinnervation (TMR) are innovative surgical techniques to prevent neuroma formation and chronic pain, ultimately improving prosthetic control. Originally designed to provide amputees better control of upper limb myoelectric and bioprostheses [42–47], TMR reestablishes function of the severed nerve through the creation of bio-amplifiers. This is accomplished using multiple nerve transfers to reroute transected peripheral nerves to motor nerves, increasing neuro-excitability and motor function [24]. TMR) is thought to decrease neuroma formation by exploiting the biology of regenerating peripheral nerves and minimizing the number of aimless axons available. It is important to recognize, however, that TMR involves sacrificing donor nerves, which may lead to central sensitization and additional neuroma formation, and denervating muscles that could potentially be useful in post-BKA rehabilitation [24].

Contrarily, RPNI surgeries do not carry the risk of neuroma formation. RPNI surgery is indicated for the treatment of symptomatic neuromas and is increasingly performed after major limb

amputation. It involves implanting the distal end of a transected peripheral nerve into a free skeletal muscle graft [24]. RPNI surgery offers a physiologic mechanism of decreasing neuroma pain by providing peripheral nerve axons targets for reinnervation [24]. Although RPNI surgery is an effective surgical technique that decreases neuroma pain by providing peripheral nerve axons targets for reinnervation, it is not a panacea [24]. Patients can experience incomplete pain relief, thus highlighting the crucial role of multidisciplinary approach to pain management after BKA.

In a preliminary cohort of BKA patients treated with traction neurectomy at our institution, 57% report RLP and 47% report PLP), with an average severity of 5.2/10; 24% were taking chronic opioids, and 42% on neuroleptic medications with an average daily dosage of gabapentin. We recently wrote a case report providing unique insight into a patient we treated with symmetric bilateral amputations, with TMR on one side and RPNI on the other. While the patient still experiences RLP which she attributes to chronic edema from her DVTs and pressure from her wheelchair, she does not have a symptomatic neuroma at either stump. Future studies must be conducted to compare the efficacy and safety of TMR and RPNI. Our recent experience of 100 consecutive BKAs with TMR has shown a 6% requirement for narcotics and an ambulatory rate of 91% at 3 months [48]

Pharmacological Agents and Regional Analgesia

Opiate Analgesics

Parenteral opioids are widely used for the management of acute perioperative pain in patients undergoing amputation surgeries [49, 50]. Tramadol is a weak opioid agonist and acts by inhibiting the reuptake of serotonin and norepinephrine. The use of both tramadol and morphine is well established for managing acute pain in the perioperative period [51, 52]. However, evidence supporting the use of opioids to reduce PLP is sparce. Additional research is needed to evaluate the role of perioperative opioids in preventing post-BKA pain.

N-Methyl D-Aspartate (NMDA) Receptor Blocker

Ketamine is a noncompetitive blocker of NMDA receptors and is effective in treating perioperative pain in its intravenous (IV) form [50]. Data from a randomized controlled trial by Hayes *et al.* found that patients receiving IV ketamine perioperatively developed lower rates of PLP); however, these results were not statistically significant at 6 months [53]. There is insufficient evidence, however, regarding the use of ketamine for chronic pain management.

Gabapentinoids

Gabapentin is an anticonvulsant and structural analogue of GABA. According to published literature, gabapentin and pregabalin are well established options for treating existing PLP [3, 54–56]. In a cross-over study, authors found gabapentin to be superior in relieving established PLP) but had no difference in its effect on mood, sleep, and functionality compared to placebo [57].

Calcitonin

Calcitonin is a hormone produced by the parafollicular C-cell of the thyroid gland. Its exact mechanism of action for pain management is unclear, but it is thought to have opioid like action on μ receptors and modulate voltage gated Ca^{2+} channels on nociceptive neurons [58, 59]. One study showed epidural calcitonin could be used as a preventive strategy for PLP; however, additional studies are needed in this regard [60].

Non-steroidal Anti-inflammatory Drugs (NSAIDs)

Non-steroidal anti-inflammatory drugs (NSAIDs) can be useful in postoperative pain relief and can be used to treat inflammatory pain, but they do not specifically treat neuropathic pain, which

derives from a largely different physiological mechanism [50, 61, 62].

Epidural Analgesia

The role of epidural anesthesia in immediate postoperative pain relief for patients undergoing amputation has been well-documented and is thought to be attributed to the interference of nociceptive inputs to the spinal cord [63–68]. Existing literature has not established epidural analgesia as a preventive strategy of PLP; however, a handful of randomized trials have reported promising results demonstrating the role of perioperative epidural anesthesia in combination with adjuvants such as opioid [63], ketamine [67], and calcitonin [60], in preventing PLP).

Perineural Catheters

Perineural catheters (PNCs) decrease the need for opioids and play an important role in providing postoperative pain relief after BKAs [49, 69, 70]. However, evidence is non-concrete on whether PNCs are effective in preventing PLP [69–74]. There is no definitive evidence demonstrating that PNCs can prevent PLP). Nonetheless, they are still used widely as they do not have the same hemodynamic effect (i.e., usage of pressors intraoperatively) as epidural blockade [75].

Psychological Treatment Modalities and Support Groups

Post-operative wound healing is considerably shorter-lived and less complex than the psychological healing that follows a BKA [76]. Psychological therapies can be very effective in helping patients modify their perception of pain. Modalities such as cognitive behavior therapy, mindfulness, brief interpersonal therapy, and biofeedback can play important and meaningful roles in pain management and improved outcomes [77]. In our institution, we have implemented monthly amputee support group meetings that empower patients with coping mechanisms and information about rehabilitation in a supportive environment. This is discussed in further detail in Chap. 38.

Nutrition

The environment into which amputees must assimilate has changed considerably since the passage of the Americans with Disabilities Act (ADA) in 1990. Not only has the ADA increased awareness of the biopsychosocial needs of amputee population, but it also expressly prohibits discrimination against people who have suffered major limb loss, among other disabilities [78]. It is not uncommon for patients undergoing BKA to experience a significant increase in metabolic demands following amputation, attributable to surgical stress in the postoperative period and increased use of lower extremity muscles unaccustomed to the new biomechanical distribution [77, 79, 80]. These metabolic changes emphasize the importance of postoperative nutritional support in optimizing recovery and wound healing. Otherwise, poor outcomes may ensue. For example, patients with poorly controlled diabetes, a population known to have poor nutritional status, face poor long-term survival following BKA due to high glucose levels [79, 81].

Therefore, it becomes paramount to provide tailored nutritional care and education, keeping in mind dietary preferences, allergies, and cultural restrictions. Lack of nutritional knowledge, nutritional counselling, and dialogue with nurses has previously shown to negatively affect patients' experiences [82–84]. Furthermore, nutritional counselling may better position patients to improve their own health and nutritional status through increased health literacy.

Physical Therapy, Rehabilitation, and Patient Education

Patient-centered education and counseling is applicable to many aspects of patient care following amputation. Patients undergoing BKA should

be provided with resources to manage stump pain, stump care, and prosthesis care and fitting.

Post-amputation rehabilitation is a multidisciplinary, collaborative effort between physicians, nurses, prosthetists, orthotists, physical therapists, occupational therapists, and nutritionists, among other members of the healthcare team. Success of rehabilitation depends on a myriad of factors such as patient age, baseline health, cognitive status, comorbid diseases, and sequence of onset of disability. The first step of rehabilitation consists of caring for the wound and managing pain and edema to increase joint and muscle flexibility. It is also critical to strengthen the trunk prior to prosthetic fittings, as patients take time to adjust to the new distribution of weight and are at increased risk of falls. Patient education and shared-decision making is a cornerstone of the rehabilitation process.

Physical therapy can have meaningful impacts on functionality and quality of life in patients after BKA. Patients who receive physical therapy post-amputation are more likely to have improved walking speed, prosthetic fit and mobility, musculoskeletal endurance, and increased survival [85–88]. Despite these benefits, only a fraction of patients undergoing amputation utilize physical therapy services due to multilevel barriers such as financial costs, accessibility, and availability [2, 89, 90]. It is important to develop and integrate a rehabilitation program that is able to address limitations specific to BKA patients, such as asymmetric use of lower limbs when performing ADLs such as walking, standing, rising from a chair, walking upstairs among others [2, 89–92]. Amputees often experience psychological and emotional complications and change in body image, in addition to the loss of physical functionality [76]. We discuss this topic in further detail in Chap. 38.

Prosthetics and Functional Scoring Scales

Close coordination with prosthetists is an essential component of the rehabilitation process. BKA prostheses can be subdivided into the following elements: socket, interface, suspension, shank, and foot and ankle. It is important to note that prosthetics are not a "one size fits all" modality. Each patient's baseline, unique needs, and functional status should be carefully considered. This topic is discussed in more detail in Chap. 28.

Functional scoring scales are a valuable tool to collect objective information regarding patient quality of life and function in society, which is inherently a subjective measure. One such scale, the amputee mobility predictor (AMP), is a validated performance-based outcome measure (PBOM) developed for patients with lower extremity amputations. It measures functional capabilities and mobility both with (AMPPro) and without prosthesis (AMPnoPro) or with a prosthesis [93]. Research demonstrates the AMP tool correlates with other measures of functionality such as self-reported measured of prosthetic mobility, Time-up and Go, and walking speed [93–98]. The utilization, importance, and applicability of functionals scoring scales are also further detailed in Chap. 28.

Financial Disclosure Statement The authors have no financial disclosures, commercial associations, or any other conditions posing a conflict of interest to report.

References

1. Ziegler-Graham K, MacKenzie EJ, Ephraim PL, Travison TG, Brookmeyer R. Estimating the prevalence of limb loss in the United States: 2005 to 2050. Arch Phys Med Rehabil. 2008;89(3):422–9. Accessed Dec 31, 2020. https://doi.org/10.1016/j.apmr.2007.11.005.
2. Dillingham TR, Pezzin LE, MacKenzie EJ. Limb amputation and limb deficiency: Epidemiology and recent trends in the United States. South Med J. 2002;95(8):875–83. Accessed Dec 31, 2020. https://doi.org/10.1097/00007611-200208000-00018.
3. Smith DG. Amputation. preoperative assessment and lower extremity surgical techniques. Foot Ankle Clin. 2001;6(2):271–96. Accessed Dec 31, 2020. https://doi.org/10.1016/s1083-7515(03)00096-2.
4. Ghazali MF. Awareness, potential factors, and post-amputation care of stump flexion contractures among transtibial amputees. Turk J Phys Med Rehabil. 2018;64(3):268–76. https://search.datacite.org/works/10.5606/tftrd.2018.1668. https://doi.org/10.5606/tftrd.2018.1668.

5. Crowe CS, Impastato KA, Donaghy AC, Earl C, Friedly JL, Keys KA. Prosthetic and orthotic options for lower extremity amputation and reconstruction. Plast Aesthet Res. 2019;6:4. https://parjournal.net/article/view/2987. Accessed Dec 31, 2020. https://doi.org/10.20517/2347-9264.2018.70.
6. Hong CC, Tan JH, Lim SH, Nather A. Multiple limb salvage attempts for diabetic foot infections: Is it worth it? Bone Joint J. 2017;99-B(11):1502–7. Accessed Dec 31, 2020. https://doi.org/10.1302/0301-620X.99B11.BJJ-2016-0793.R2.
7. Narula N, Dannenberg AJ, Olin JW, et al. Pathology of peripheral artery disease in patients with critical limb ischemia. J Am Coll Cardiol. 2018;72(18):2152–63. Accessed Dec 31, 2020. https://doi.org/10.1016/j.jacc.2018.08.002.
8. Harris AM, Althausen PL, Kellam J, Bosse MJ, Castillo R. Complications following limb-threatening lower extremity trauma. J Orthop Trauma. 2009;23(1):1–6. Accessed Dec 31, 2020. https://doi.org/10.1097/BOT.0b013e31818e43dd.
9. Busse JW, Jacobs CL, Swiontkowski MF, Bosse MJ, Bhandari M. Complex limb salvage or early amputation for severe lower-limb injury: A meta-analysis of observational studies. J Orthop Trauma. 2007;21(1):70–6. Accessed Dec 31, 2020. https://doi.org/10.1097/BOT.0b013e31802cbc43.
10. Amputation, prosthesis use, and phantom limb pain: An interdisciplinary perspective. New York: Springer-Verlag; 2010. https://www.springer.com/gp/book/9780387874616. Accessed Jan 26, 2021.
11. Neil M. Pain after amputation. BJA Education. 2016;16(3):107–12. https://doi.org/10.1093/bjaed/mkv028. Accessed Jan 6, 2021
12. Baumfeld D, Baumfeld T, Macedo B, Zambelli R, Lopes F, Nery C. Factors related to amputation level and wound healing in diabetic patients. Acta Ortop Bras. 2018;26(5):342–5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6220668/. Accessed Jan 6, 2021. https://doi.org/10.1590/1413-785220182605173445.
13. Hong JP. Reconstructive surgery: Lower extremity coverage. In: Plastic surgery: Volume 4: Lower extremity, trunk, and burns. 4th ed. Philadelphia, PA: Elsevier; 2018. p. 118–142.e3. https://www.clinicalkey.com/#!/content/book/3-s2.0-B9780323357067000051?scrollTo=%23hl0000422. Accessed Jan 6, 2021.
14. Pinzur MS, Cox W, Kaiser J, Morris T, Patwardhan A, Vrbos L. The effect of prosthetic alignment on relative limb loading in persons with trans-tibial amputation: A preliminary report. J Rehabil Res Dev. 1995;32(4):373–7. Accessed Jan 26, 2021
15. Chow DHK, Holmes AD, Lee CKL, Sin SW. The effect of prosthesis alignment on the symmetry of gait in subjects with unilateral transtibial amputation. Prosthetics Orthot Int. 2006;30(2):114–28. Accessed Jan 26, 2021. https://doi.org/10.1080/03093640600568617.
16. Rauck RL, Cohen SP, Gilmore CA, et al. Treatment of post-amputation pain with peripheral nerve stimulation. Neuromodulation. 2014;17(2):188–97. Accessed Jan 1, 2021. https://doi.org/10.1111/ner.12102.
17. Sadosky A, McDermott AM, Brandenburg NA, Strauss M. A review of the epidemiology of painful diabetic peripheral neuropathy, postherpetic neuralgia, and less commonly studied neuropathic pain conditions. Pain Pract. 2008;8(1):45–56. Accessed Jan 1, 2021. https://doi.org/10.1111/j.1533-2500.2007.00164.x.
18. Hsu E, Cohen SP. Postamputation pain: Epidemiology, mechanisms, and treatment. J Pain Res. 2013;6:121–36. Accessed Jan 6, 2021. https://doi.org/10.2147/JPR.S32299.
19. Kuffler DP. Coping with phantom limb pain. Mol Neurobiol. 2018;55(1):70–84. Accessed Jan 6, 2021. https://doi.org/10.1007/s12035-017-0718-9.
20. Jensen TS, Krebs B, Nielsen J, Rasmussen P. Immediate and long-term phantom limb pain in amputees: Incidence, clinical characteristics and relationship to pre-amputation limb pain. Pain. 1985;21(3):267–78. Accessed Jan 6, 2021. https://doi.org/10.1016/0304-3959(85)90090-9.
21. Jensen TS, Krebs B, Nielsen J, Rasmussen P. Phantom limb, phantom pain and stump pain in amputees during the first 6 months following limb amputation. Pain. 1983;17(3):243–56. Accessed Jan 6, 2021. https://doi.org/10.1016/0304-3959(83)90097-0.
22. Pierce RO, Kernek CB, Ambrose TA. The plight of the traumatic amputee. Orthopedics. 1993;16(7):793–7. Accessed Jan 6, 2021
23. Ducic I, Mesbahi AN, Attinger CE, Graw K. The role of peripheral nerve surgery in the treatment of chronic pain associated with amputation stumps. Plast Reconstr Surg. 2008;121(3):908–17. Accessed Jan 6, 2021. https://doi.org/10.1097/01.prs.0000299281.57480.77.
24. Bueno RA Jr, Neumeister MW. Pain management in plastic surgery an issue of clinics in plastic surgery, E-book. Amsterdam: Elsevier Health Sciences; 2020. Accessed Jan 6, 2021
25. Menorca RMG, Fussell TS, Elfar JC. Peripheral nerve trauma: Mechanisms of injury and recovery. Hand Clin. 2013;29(3):317–30. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4408553/. Accessed Jan 6, 2021. https://doi.org/10.1016/j.hcl.2013.04.002.
26. Grinsell D, Keating CP. Peripheral nerve reconstruction after injury: A review of clinical and experimental therapies. BioMed Research International Web site. https://www.hindawi.com/journals/bmri/2014/698256/. Updated 2014. Accessed Jan 6, 2021.
27. Mackinnon SE, Dellon AL, Hudson AR, Hunter DA. Alteration of neuroma formation by manipulation of its microenvironment. Plast Reconstr Surg. 1985;76(3):345–53. Accessed Jan 6, 2021. https://doi.org/10.1097/00006534-198509000-00001.
28. Weeks SR, Anderson-Barnes VC, Tsao JW. Phantom limb pain: Theories and therapies. Neurologist. 2010;16(5):277–86. Accessed Jan 6, 2021. https://doi.org/10.1097/NRL.0b013e3181edf128.

29. Mitchell SW. Injuries of nerves and their consequences. Am J Med Sci. 1872;64(127):229–32. insights.ovid.com. Accessed Jan 6, 2021
30. Trevelyan EG, Turner WA, Robinson N. Perceptions of phantom limb pain in lower limb amputees and its effect on quality of life: A qualitative study. Br J Pain. 2016;10(2):70–7. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4977953/. Accessed Jan 6, 2021. https://doi.org/10.1177/2049463715590884.
31. Karanikolas M, Aretha D, Tsolakis I, et al. Optimized perioperative analgesia reduces chronic phantom limb pain intensity, prevalence, and frequency: A prospective, randomized, clinical trial. Anesthesiology. 2011;114(5):1144–54. Accessed Jan 6, 2021. https://doi.org/10.1097/ALN.0b013e31820fc7d2.
32. Hanley MA, Jensen MP, Smith DG, Ehde DM, Edwards WT, Robinson LR. Preamputation pain and acute pain predict chronic pain after lower extremity amputation. J Pain. 2007;8(2):102–9. Accessed Jan 6, 2021. https://doi.org/10.1016/j.jpain.2006.06.004.
33. Nissen SJ, Newman WP. Factors influencing reintegration to normal living after amputation. Arch Phys Med Rehabil. 1992;73(6):548–51. Accessed Jan 6, 2021
34. Desmond DM, MacLachlan M. Affective distress and amputation-related pain among older men with long-term, traumatic limb amputations. J Pain Symptom Manag. 2006;31(4):362–8. http://www.sciencedirect.com/science/article/pii/S0885392406000479. Accessed Jan 6, 2021. https://doi.org/10.1016/j.jpainsymman.2005.08.014.
35. Fitzpatrick MC. The psychologic assessment and psychosocial recovery of the patient with an amputation. Clin Orthop Relat Res. 1999;361:98–107. Accessed Jan 6, 2021. https://doi.org/10.1097/00003086-199904000-00014.
36. Buckenmaier C, Mahoney PF, Anton T, Kwon N, Polomano RC. Impact of an acute pain service on pain outcomes with combat-injured soldiers at Camp Bastion, Afghanistan. Pain Med. 2012;13(7):919–26. Accessed Jan 6, 2021. https://doi.org/10.1111/j.1526-4637.2012.01382.x.
37. Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of postoperative pain: A clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. J Pain. 2016;17(2):131–57. Accessed Jan 6, 2021. https://doi.org/10.1016/j.jpain.2015.12.008.
38. Ramachandran VS, Rogers-Ramachandran D. Synaesthesia in phantom limbs induced with mirrors. Proc Biol Sci. 1996;263(1369):377–86. Accessed Jan 6, 2021. https://doi.org/10.1098/rspb.1996.0058.
39. Bowen JB, Wee CE, Kalik J, Valerio IL. Targeted muscle reinnervation to improve pain, prosthetic tolerance, and bioprosthetic outcomes in the amputee. Adv Wound Care (New Rochelle). 2017;6(8):261–7. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5564002/. Accessed Jan 6, 2021. https://doi.org/10.1089/wound.2016.0717.
40. Tintle SM, Donohue MA, Shawen S, Forsberg JA, Potter BK. Proximal sural traction neurectomy during transtibial amputations. J Orthop Trauma. 2012;26(2):123–6. https://journals.lww.com/jorthotrauma/Abstract/2012/02000/Proximal_Sural_Traction_Neurectomy_During.10.aspx. Accessed Jan 26, 2021. https://doi.org/10.1097/BOT.0b013e318214fd7b.
41. Pet MA, Ko JH, Friedly JL, Smith DG. Traction neurectomy for treatment of painful residual limb neuroma in lower extremity amputees. J Orthop Trauma. 2015;29(9):e321. https://journals.lww.com/jorthotrauma/Abstract/2015/09000/Traction_Neurectomy_for_Treatment_of_Painful.16.aspx. Accessed Jan 26, 2021. https://doi.org/10.1097/BOT.0000000000000337.
42. O'Shaughnessy KD, Dumanian GA, Lipschutz RD, Miller LA, Stubblefield K, Kuiken TA. Targeted reinnervation to improve prosthesis control in transhumeral amputees. A report of three cases. J Bone Joint Surg Am. 2008;90(2):393–400. Accessed Jan 6, 2021. https://doi.org/10.2106/JBJS.G.00268.
43. Kuiken TA, Dumanian GA, Lipschutz RD, Miller LA, Stubblefield KA. The use of targeted muscle reinnervation for improved myoelectric prosthesis control in a bilateral shoulder disarticulation amputee. Prosthetics Orthot Int. 2004;28(3):245–53. Accessed Jan 6, 2021. https://doi.org/10.3109/03093640409167756.
44. Kuiken TA, Miller LA, Lipschutz RD, et al. Targeted reinnervation for enhanced prosthetic arm function in a woman with a proximal amputation: A case study. Lancet. 2007;369(9559):371–80. Accessed Jan 6, 2021. https://doi.org/10.1016/S0140-6736(07)60193-7.
45. Kuiken TA, Li G, Lock BA, et al. Targeted muscle reinnervation for real-time myoelectric control of multifunction artificial arms. JAMA. 2009;301(6):619–28. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3036162/. Accessed Jan 6, 2021. https://doi.org/10.1001/jama.2009.116.
46. Dumanian GA, Ko JH, O'Shaughnessy KD, Kim PS, Wilson CJ, Kuiken TA. Targeted reinnervation for transhumeral amputees: Current surgical technique and update on results. Plast Reconstr Surg. 2009;124(3):863–9. Accessed Jan 6, 2021. https://doi.org/10.1097/PRS.0b013e3181b038c9.
47. Hijjawi JB, Kuiken TA, Lipschutz RD, Miller LA, Stubblefield KA, Dumanian GA. Improved myoelectric prosthesis control accomplished using multiple nerve transfers. Plast Reconstr Surg. 2006;118(7):1573–8. Accessed Jan 6, 2021. https://doi.org/10.1097/01.prs.0000242487.62487.fb.
48. Chang BL, Mondshine J, Attinger CE, Kleiber GM. Targeted muscle reinnervation improves pain and ambulation outcomes in highly comorbid amputees. Plast Reconstr Surg. 2021;148(2):376–86. https://doi.org/10.1097/PRS.0000000000008153. PMID: 34398088.

49. Ayling OGS, Montbriand J, Jiang J, et al. Continuous regional anaesthesia provides effective pain management and reduces opioid requirement following major lower limb amputation. Eur J Vasc Endovasc Surg. 2014;48(5):559–64. Accessed Jan 6, 2021. https://doi.org/10.1016/j.ejvs.2014.07.002.
50. McCormick Z, Chang-Chien G, Marshall B, Huang M, Harden RN. Phantom limb pain: A systematic neuroanatomical-based review of pharmacologic treatment. Pain Med. 2014;15(2):292–305. Accessed Jan 6, 2021. https://doi.org/10.1111/pme.12283.
51. Falzone E, Hoffmann C, Keita H. Postoperative analgesia in elderly patients. Drugs Aging. 2013;30(2):81–90. Accessed Jan 6, 2021. https://doi.org/10.1007/s40266-012-0047-7.
52. Byrne K, Nolan A, Barnard J, Tozer M, Harris D, Sleigh J. Managing postoperative analgesic failure: Tramadol versus morphine for refractory pain in the post-operative recovery unit. Pain Med. 2017;18(2):348–55. Accessed Jan 6, 2021. https://doi.org/10.1093/pm/pnw084.
53. Hayes C, Armstrong-Brown A, Burstal R. Perioperative intravenous ketamine infusion for the prevention of persistent post-amputation pain: A randomized, controlled trial. Anaesth Intensive Care. 2004;32(3):330–8. Accessed Jan 6, 2021. https://doi.org/10.1177/0310057X0403200305.
54. Abbass K. Efficacy of gabapentin for treatment of adults with phantom limb pain. Ann Pharmacother. 2012;46(12):1707–11. Accessed Jan 6, 2021. https://doi.org/10.1345/aph.1Q793.
55. Spiegel DR, Lappinen E, Gottlieb M. A presumed case of phantom limb pain treated successfully with duloxetine and pregabalin. Gen Hosp Psychiatry. 2010;32(2):228.e5-7. Accessed Jan 6, 2021. https://doi.org/10.1016/j.genhosppsych.2009.05.012.
56. Singh RK, Sinha VP, Pal US, Yadav SC, Singh MK. Pregabalin in post traumatic neuropathic pain: Case studies. Natl J Maxillofac Surg. 2012;3(1):91–5. Accessed Jan 6, 2021. https://doi.org/10.4103/0975-5950.102175.
57. Bone M, Critchley P, Buggy DJ. Gabapentin in postamputation phantom limb pain: A randomized, double-blind, placebo-controlled, cross-over study. Reg Anesth Pain Med. 2002;27(5):481–6. Accessed Jan 6, 2021. https://doi.org/10.1053/rapm.2002.35169.
58. Hagenacker T, Ledwig D, Büsselberg D. Additive inhibitory effects of calcitonin and capsaicin on voltage activated calcium channel currents in nociceptive neurones of rat. Brain Res Bull. 2011;85(1-2):75–80. Accessed Jan 6, 2021. https://doi.org/10.1016/j.brainresbull.2011.02.006.
59. Wall GC, Heyneman CA. Calcitonin in phantom limb pain. Ann Pharmacother. 1999;33(4):499–501. Accessed Jan 6, 2021. https://doi.org/10.1345/aph.18204.
60. Yousef AA, Aborahma AM. The preventive value of epidural calcitonin in patients with lower limb amputation. Pain Med. 2017;18(9):1745–51. Accessed Jan 6, 2021. https://doi.org/10.1093/pm/pnw249.
61. Alviar MJM, Hale T, Dungca M. Pharmacologic interventions for treating phantom limb pain. Cochrane Database Syst Rev. 2016;10:CD006380. Accessed Jan 6, 2021. https://doi.org/10.1002/14651858.CD006380.pub3.
62. Macario A, Royal MA. A literature review of randomized clinical trials of intravenous acetaminophen (paracetamol) for acute postoperative pain. Pain Pract. 2011;11(3):290–6. Accessed Jan 6, 2021. https://doi.org/10.1111/j.1533-2500.2010.00426.x.
63. Jahangiri M, Jayatunga AP, Bradley JW, Dark CH. Prevention of phantom pain after major lower limb amputation by epidural infusion of diamorphine, clonidine and bupivacaine. Ann R Coll Surg Engl. 1994;76(5):324–6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2502366/. Accessed Jan 6, 2021
64. Srivastava D. Chronic post-amputation pain: Peri-operative management—review. Br J Pain. 2017;11(4):192–202. Accessed Jan 6, 2021. https://doi.org/10.1177/2049463717736492.
65. Lambert AW, Dashfield AK, Cosgrove C, Wilkins DC, Walker AJ, Ashley S. Randomized prospective study comparing preoperative epidural and intraoperative perineural analgesia for the prevention of postoperative stump and phantom limb pain following major amputation. Reg Anesth Pain Med. 2001;26(4):316–21. Accessed Jan 6, 2021. https://doi.org/10.1053/rapm.2001.23934.
66. Ong BY, Arneja A, Ong EW. Effects of anesthesia on pain after lower-limb amputation. J Clin Anesth. 2006;18(8):600–4. Accessed Jan 6, 2021. https://doi.org/10.1016/j.jclinane.2006.03.021.
67. Wilson JA, Nimmo AF, Fleetwood-Walker SM, Colvin LA. A randomised double blind trial of the effect of pre-emptive epidural ketamine on persistent pain after lower limb amputation. Pain. 2008;135(1-2):108–18. Accessed Jan 6, 2021. https://doi.org/10.1016/j.pain.2007.05.011.
68. Sahin SH, Colak A, Arar C, et al. A retrospective trial comparing the effects of different anesthetic techniques on phantom pain after lower limb amputation. Curr Ther Res Clin Exp. 2011;72(3):127–37. Accessed Jan 6, 2021. https://doi.org/10.1016/j.curtheres.2011.06.001.
69. Grant AJ, Wood C. The effect of intra-neural local anaesthetic infusion on pain following major lower limb amputation. Scott Med J. 2008;53(1):4–6. Accessed Jan 6, 2021. https://doi.org/10.1258/RSMSMJ.53.1.4.
70. Malawer MM, Buch R, Khurana JS, Garvey T, Rice L. Postoperative infusional continuous regional analgesia. A technique for relief of postoperative pain following major extremity surgery. Clin Orthop Relat Res. 1991;266:227–37. Accessed Jan 6, 2021
71. Fisher A, Meller Y. Continuous postoperative regional analgesia by nerve sheath block for amputation surgery--a pilot study. Anesth Analg. 1991;72(3):300–3. Accessed Jan 6, 2021. https://doi.org/10.1213/00000539-199103000-00004.

72. Borghi B, D'Addabbo M, White PF, et al. The use of prolonged peripheral neural blockade after lower extremity amputation: The effect on symptoms associated with phantom limb syndrome. Anesth Analg. 2010;111(5):1308–15. Accessed Jan 6, 2021. https://doi.org/10.1213/ANE.0b013e3181f4e848.
73. Elizaga AM, Smith DG, Sharar SR, Edwards WT, Hansen ST. Continuous regional analgesia by intraneural block: Effect on postoperative opioid requirements and phantom limb pain following amputation. J Rehabil Res Dev. 1994;31(3):179–87. Accessed Jan 6, 2021
74. Pinzur MS, Garla PG, Pluth T, Vrbos L. Continuous postoperative infusion of a regional anesthetic after an amputation of the lower extremity. A randomized clinical trial. J Bone Joint Surg Am. 1996;78(10):1501–5. Accessed Jan 6, 2021. https://doi.org/10.2106/00004623-199610000-00007.
75. De Jong R, Shysh AJ. Development of a multimodal analgesia protocol for perioperative acute pain management for lower limb amputation. Pain Res Manag. 2018;2018:5237040. . Accessed Jan 6, 2021. https://doi.org/10.1155/2018/5237040.
76. Mckechnie PS, John A. Anxiety and depression following traumatic limb amputation: A systematic review. Injury. 2014;45(12):1859–66. Accessed Jan 6, 2021. https://doi.org/10.1016/j.injury.2014.09.015.
77. Castelnuovo G, Giusti EM, Manzoni GM, et al. Psychological treatments and psychotherapies in the neurorehabilitation of pain: Evidences and recommendations from the Italian consensus conference on pain in neurorehabilitation. Front Psychol. 2016;7:115. Accessed Jan 6, 2021. https://doi.org/10.3389/fpsyg.2016.00115.
78. West SL, McMahon BT, Monasterio E, Belongia L, Kramer K. Workplace discrimination and missing limbs: The national EEOC ADA research project. Work. 2005;25(1):27–35. Accessed Jan 26, 2021
79. Adams CT, Lakra A. Below knee amputation. In: StatPearls. Treasure Island. FL: StatPearls Publishing; 2020. http://www.ncbi.nlm.nih.gov/books/NBK534773/. Accessed Jan 6, 2021.
80. Gillis C, Wischmeyer PE. Pre-operative nutrition and the elective surgical patient: Why, how and what? Anaesthesia. 2019;74(Suppl 1):27–35. Accessed Jan 26, 2021. https://doi.org/10.1111/anae.14506.
81. Beyaz S, Güler ÜÖ, Bağır GŞ. Factors affecting lifespan following below-knee amputation in diabetic patients. Acta Orthop Traumatol Turc. 2017;51(5):393–7. Accessed Jan 6, 2021. https://doi.org/10.1016/j.aott.2017.07.001.
82. Johns N, Hartwell H, Morgan M. Improving the provision of meals in hospital. the patients' viewpoint. Appetite. 2010;54(1):181–5. Accessed Jan 6, 2021. https://doi.org/10.1016/j.appet.2009.10.005.
83. Cooper C, Burden ST, Molassiotis A. An explorative study of the views and experiences of food and weight loss in patients with operable pancreatic cancer perioperatively and following surgical intervention. Support Care Cancer. 2015;23(4):1025–33. Accessed Jan 6, 2021. https://doi.org/10.1007/s00520-014-2455-1.
84. Holst M, Rasmussen HH, Laursen BS. Can the patient perspective contribute to quality of nutritional care? Scand J Caring Sci. 2011;25(1):176–84. Accessed Jan 6, 2021. https://doi.org/10.1111/j.1471-6712.2010.00808.x.
85. Geertzen J, van der Linde H, Rosenbrand K, et al. Dutch evidence-based guidelines for amputation and prosthetics of the lower extremity: Rehabilitation process and prosthetics. part 2. Prosthetics Orthot Int. 2015;39(5):361–71. Accessed Jan 6, 2021. https://doi.org/10.1177/0309364614542725.
86. Kahle JT, Highsmith MJ, Schaepper H, Johannesson A, Orendurff MS, Kaufman K. Predicting walking ability following lower limb amputation: An updated systematic literature review. Technol Innov. 2016;18(2-3):125–37. Accessed Jan 6, 2021. https://doi.org/10.21300/18.2-3.2016.125.
87. Christiansen CL, Fields T, Lev G, Stephenson RO, Stevens-Lapsley JE. Functional outcomes after the prosthetic training phase of rehabilitation after dysvascular lower extremity amputation. PM R. 2015;7(11):1118–26. Accessed Jan 6, 2021. https://doi.org/10.1016/j.pmrj.2015.05.006.
88. Madsen UR, Bååth C, Berthelsen CB, Hommel A. A prospective study of short-term functional outcome after dysvascular major lower limb amputation. Int J Orthop Trauma Nurs. 2018;28:22–9. Accessed Jan 6, 2021. https://doi.org/10.1016/j.ijotn.2017.08.001.
89. Dillingham TR, Pezzin LE, Mackenzie EJ. Discharge destination after dysvascular lower-limb amputations. Arch Phys Med Rehabil. 2003;84(11):1662–8. Accessed Jan 6, 2021. https://doi.org/10.1053/s0003-9993(03)00291-0.
90. Dillingham TR, Pezzin LE. Rehabilitation setting and associated mortality and medical stability among persons with amputations. Arch Phys Med Rehabil. 2008;89(6):1038–45. Accessed Jan 6, 2021. https://doi.org/10.1016/j.apmr.2007.11.034.
91. Agrawal V, Gailey R, Gaunaurd I, Gailey R, O'Toole C. Weight distribution symmetry during the sit-to-stand movement of unilateral transtibial amputees. Ergonomics. 2011;54(7):656–64. Accessed Jan 6, 2021. https://doi.org/10.1080/00140139.2011.586060.
92. Agrawal V, Gailey RS, Gaunaurd IA, O'Toole C, Finnieston AA. Comparison between microprocessor-controlled ankle/foot and conventional prosthetic feet during stair negotiation in people with unilateral transtibial amputation. J Rehabil Res Dev. 2013;50(7):941–50. Accessed Jan 6, 2021. https://doi.org/10.1682/JRRD.2012.05.0093.
93. Gailey R, Gaunaurd I, Raya M, Kirk-Sanchez N, Prieto-Sanchez LM, Roach K. Effectiveness of an evidence-based amputee rehabilitation program: A pilot randomized controlled trial. Phys Ther. 2020;100(5):773–87. Accessed Jan 6, 2021. https://doi.org/10.1093/ptj/pzaa008.

94. Hafner BJ, Gaunaurd IA, Morgan SJ, Amtmann D, Salem R, Gailey RS. Construct validity of the prosthetic limb users survey of mobility (PLUS-M) in adults with lower limb amputation. Arch Phys Med Rehabil. 2017;98(2):277–85. Accessed Jan 6, 2021. https://doi.org/10.1016/j.apmr.2016.07.026.
95. Gailey RS, Scoville C, Gaunaurd IA, et al. Construct validity of comprehensive high-level activity mobility predictor (CHAMP) for male servicemembers with traumatic lower-limb loss. J Rehabil Res Dev. 2013;50(7):919–30. Accessed Jan 6, 2021. https://doi.org/10.1682/JRRD.2012.05.0100.
96. Resnik L, Borgia M. Reliability of outcome measures for people with lower-limb amputations: Distinguishing true change from statistical error. Phys Ther. 2011;91(4):555–65. Accessed Jan 6, 2021. https://doi.org/10.2522/ptj.20100287.
97. Muderis MA, Tetsworth K, Khemka A, et al. The osseointegration group of Australia accelerated protocol (OGAAP-1) for two-stage osseointegrated reconstruction of amputated limbs. Bone Joint J. 2016;98-B(7):952–60. Accessed Jan 6, 2021. https://doi.org/10.1302/0301-620X.98B7.37547.
98. Batten HR, McPhail SM, Mandrusiak AM, Varghese PN, Kuys SS. Gait speed as an indicator of prosthetic walking potential following lower limb amputation. Prosthetics Orthot Int. 2019;43(2):196–203. Accessed Jan 6, 2021. https://doi.org/10.1177/0309364618792723.

35 Complications and Revision Surgery in Complex Limb Salvage

Ali Rahnama, Noman Siddiqui, and Janet D. Conway

Introduction

Undoubtedly, surgeons will encounter complications and revision cases that need to be managed. Patients with surgical complications that require revision surgery may come from outside of your practice, referred to you for further management or may have been your own patients who return to you for further management of their complication. Regardless, while a complication may be secondary to iatrogenic factors, complications and the need for further revision surgery are not necessarily an indication of inadequate or incorrect surgical intervention. While the hope is to minimize the frequency of these cases through an evidence based surgical decision-making process and sound surgical technique, keys to ensuring these patients will have successful outcomes involve factors that extend beyond the operating room both before and after surgical intervention. While there are many complications that one may encounter in limb surgery, for the purposes of this chapter we will focus on infections, malunion, and nonunion. General considerations on the workup, physical exam, and overall evaluation of the patient will be discussed before moving on to give guidance on specific clinical scenarios in terms of surgical technique that will help guide the best management and outcomes possible. Furthermore, while we strive to practice in an evidence based manner, we do understand that many of the details that have helped drive successful outcomes have been through trial and error on the parts of the authors and we hope to share those "pearls" with you the reader.

Complication Workup

History

Various complications can point to different underlying issues stemming from the patient's existing metabolic disease, vascular insufficiency, or social practices. It is important when evaluating the patient and working them up to have a stepwise approach that evaluates all possible avenues for why the patient had their specific complication. Common complications include surgical wound dehiscence/infection, deep wound infection, nonunion, malunion, avascular necrosis, implant failure, nerve damage or neuroparalysis, limb length discrepancy, new or persistent pain after the procedure.

A. Rahnama (✉)
Department of Plastic and Reconstructive Surgery, Georgetown University School of Medicine, MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: ali.rahnamavaghef@medstar.net

N. Siddiqui · J. D. Conway
Rubin Institute for Advanced Orthopedics, Sinai Hospital, Baltimore, MD, USA
e-mail: jconway@lifebridgehealth.org

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_35

Situations requiring immediate attention such as surgical wound dehiscence and/or infection will often need aggressive and immediate attention in the form of systemic antibiotics and localized debridement (either in the clinic or operating room) before further workup can be done to understand the etiology of the issue at hand. While a simple superficial dehiscence of the surgical wound can be treated with relatively minor interventions such as a change in the type of dressings used, ignoring or undertreating wound complications early in the postoperative course can have severe ramifications for the high risk patient, particularly those with multiple medical comorbidities that may further contribute to the issue at hand and prove limb threatening.

A detailed history is an important first step in assessing the patient for potential barriers to healing. Particularly as it pertains to limb salvage and reconstruction, diabetes and glucose control/management needs to be paid close attention to. A HgA1C >8, for example, is grounds for pause and further referral to the endocrine specialist to help decrease the likelihood of further complications by better managing the patient's diabetes when possible [1]. Management of other underlying medical problems such as autoimmune disease and the medications needed to appropriately manage those disease processes need to be paid particular attention to. Indeed it may be necessary to discuss and coordinate with the rheumatologist a schedule to discontinue and alter the dosage and schedule of any steroids or disease modifying anti-rheumatic drugs (DMARDS) prior to any surgery [2].

In cases of nonunion, when the fixation construct selected in the initial surgical procedure is not thought to be a contributing factor, metabolic causes need to be evaluated. Vitamin D levels should be checked and supplemented when appropriate. If there is any doubt that the low vitamin D is secondary to any other contributing endocrine disorder, evaluation with an endocrine specialist is recommended.

Social factors such as smoking or excessive alcohol use should also be addressed and managed prior to any revision surgery to help decrease the likelihood of any further complications. Indeed smoking is well documented to have effects on bone and surgical wound healing both directly via the smoking itself and indirectly via the deleterious effects smoking has on the vasculature with long term use [3, 4]. Coordination with the primary care physician can help the patient be placed on nicotine supplementation to help with reducing or ceasing tobacco use completely. Additionally, excessive alcohol intake and alcoholism is thought to be associated with malnutrition as alcoholics are thought to consume too little carbohydrates, protein, and vitamins in addition to the direct inhibitory effects alcohol has on the absorption and digestion of these nutrients [5]. A better understanding in recent years of the effects of inflammatory markers on albumin and prealbumin levels has caused a shift from the reliance on these markers as the sole metric for nutritional status evaluation. Nevertheless, checking albumin and prealbumin levels, in addition to a detailed history and physical exam may further help quantify the level to which one is malnourished and therefore help in guiding appropriate avenues for nutrition supplementation prior to any further surgical intervention [6]. These social factors and habits can have direct effects on proper wound and osseous healing and can contribute to the incidence of complications if not addressed appropriately in the perioperative period.

Complications such as malunion/nonunion, nerve damage and neuroparalysis as well as an unintended limb length discrepancy can often point to improper technique (i.e. over aggressive bony resection, periosteal stripping, poor soft tissue handling leading to nerve, muscle and tendon damage). Unfortunately, due to the anatomic constraints present in limb surgery such as a limited soft tissue envelope between the skin and underlying osseous and tendon/nerve structures, the management of these complications often requires a high degree of skill in procedures that are not often performed in the community setting and referral to a revision surgeon in the tertiary care setting may be necessary for a chance at limb salvage. Complex constructs involving both internal and external fixation and advanced techniques such as bone transport, vascularized bone

grafting, nerve transfers, and others may be indicated in these difficult cases. Additionally, a center where a multidisciplinary approach to care involving vascular, plastic, podiatric, and orthopedic surgeons all offering their unique skill sets to the patients' care may help increase the likelihood of achieving an adequate outcome to not only save the limb but also allow for it to remain functional [7].

Physical Examination

After a detailed history, the physical exam is an important part of the workup that must not be brushed past with haste. The patient's vascular exam, for example, may demonstrate diminished pulses and can potentially predict or point to why a patient is having difficulty healing a wound (i.e. dehiscence). Vascular workup and potential intervention with a vascular surgeon may be indicated to help overcome the barriers of arterial and venous disease in the healing process. Furthermore, in areas where there is any concern for vascular compromise, even in the setting of adequate peripheral pulses, noninvasive vascular studies such as ankle brachial index/toe brachial index with pulse volume recordings as well as diagnostic angiography may be indicated to assess blood flow to specific angiosomes [8].

The orthopedic exam may help to uncover signs of complications from the primary procedure. Mobility and motion or swelling and persistent pain at joints where arthrodesis was previously attempted may point towards nonunion and warrant X-ray or other advanced imaging such as CT or MRI. Muscle tone and strength may help predict how the patient may do in any subsequent procedure, particularly if a tendon transfer is being considered. Flexibility vs rigidity of a deformity also helps in the surgical workup and helps to make decisions in regard to further procedure selection.

The dermatologic examination may demonstrate scar tissue and adhesions of the soft tissue envelope to the muscle and tendons below and may be reason to encourage consultation with plastic surgery in anticipation of issues related to closure and soft tissue mobilization in any subsequent procedure. Additionally, the quality of the soft tissue envelope is an important factor in whether the patient is a candidate for further revision surgery at all. Unfortunately, chronic processes such as venous stasis disease and chronic lymphatic insufficiency often make options for further surgery limited.

Finally, the neurologic examination may be consistent with absent sensation or neuropathy which may be in accord with chronic disease processes such as diabetes that have been shown to be associated with higher rates of complications and therefore an indication for a varying approach in construct or procedure selection in any further surgical procedure [1]. Additionally, new neuroparalysis may signify nerve damage from the index procedure and may need to be factored into any other procedure in the revision setting or require the nerve damage to be evaluated for potential repair before any further procedures are performed or considered.

Imaging

Imaging plays an important part in evaluating and managing the limb salvage patient from a musculoskeletal perspective. Radiographs should be a routine part of the postoperative visit to evaluate the patient after any procedure involving the skeletal anatomy. Radiographs help assess the integrity of any implants used, help to evaluate the patients healing, and can identify any complications such as periprosthetic fracture, hardware loosening, or signs of malunion or nonunion. Furthermore, radiographic evaluation and subsequent identification will determine the need for more advanced imaging (i.e. MRI, CT scan, or ultrasound).

MRI can aid in the evaluation of the soft tissues and assess any nerve, tendon, chondral, vascular damage, or injury from previous procedures as well as in the assessment of avascular necrosis and help to better formulate a surgical plan going forward based on the findings present. CT scanning can aid in the assessment of skeletal deformity and also for the evaluation of any malunion

or nonunion if there is any concern for these complications after the index procedure.

Ultrasound is also another imaging modality that can aid in the assessment of nerve, tendon, vascular injuries as well as in the evaluation of scar tissue and any fluid collection. While ultrasound can be done quickly and is usually more cost-effective than in comparison to imaging modalities such as MRI, its interpretation requires a high degree of skill, is user dependent, and relies on a well-trained radiologist for their interpretation as most surgeons are less likely to routinely evaluate their own ultrasound images in comparison to MRI or CT and this lack of comfort may explain why it is less often used in practice [9].

Other advanced imaging modalities that may help distinguish between complications such as infection, nonunion, Charcot neuroarthropathy, or other more subtle problems of the skeletal anatomy that may be causing problems for the patient include labeled white blood cell bone scanning or single-photon emission computed tomography (SPECT). Both of these imaging modalities may be valuable tools to help the surgeon make the appropriate diagnosis but are limited in their availability at all institutions and there is a general lack of widespread use in most clinical practices [10].

Laboratory Studies

Laboratory values have immense value in helping to determine what the underlying cause of a potential complication is, help to determine the best course of action in the near and long term, and also to help track progress.

In infection, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) when elevated can be signs of underlying infection and can be trended to monitor for progress and resolution of the inflammatory process associated with infection after antibiotics have been initiated. In a meta-analysis of more than 30 studies, it was found that the diagnostic accuracy for prosthetic joint infections was best for CRP and ESR only second to IL-6 levels. Pooled sensitivity and specificity for IL-6 were found to be 0.97 and 0.9, 0.88 and 0.74 for CRP, and 0.75 and 0.70 for ESR, respectively. Furthermore, the absence of an elevated ESR and CRP is a good predictor of an absence of prosthetic joint infection [11].

Procalcitonin level monitoring has also gained favor over the last decade because it is thought to have several advantages over ESR and CRP, mainly that it typically is unelevated in noninfectious cases and also tends to be detectable and peaks sooner than those other inflammatory markers [12].

In cases of nonunion, obtaining a vitamin D level is an appropriate first step for evaluation of the etiology of the nonunion. While the construct selected in the index procedure may have played a role, metabolic etiologies should be ruled out before surgical revision is attempted. Indeed it is thought that as many as 25–50% of patients can be vitamin D deficient. Large pulse dosing should be considered to help achieve the appropriate levels before any further surgery when appropriate [13]. At our institution we typically will "load" severely deficient (<10 ng/mL) patients with 50,000 IU weekly for 12 weeks with an end goal of 300,000 IU before initiating a maintenance dose of 2000 IU daily. When to initiate surgical intervention once treatment has been initiated for the severely vitamin D deficient patient is dependent on the surgeon and the amount of time the clinical scenario allows for optimization before further intervention is absolutely necessary to address the nonunion. Generally, if the clinical scenario is not considered urgent, this author will consider surgical intervention at 4–6 weeks after initiation of treatment and continue treatment throughout the perioperative period before transitioning to a maintenance dose.

Complications

Lower Extremity Nonunion

Tibial nonunions as well as ankle/hindfoot arthrodesis nonunions are very common. Traumatic injuries resulting in nonunion can often be secondary to the initial fracture with dis-

ruption of the blood supply to the bone and soft tissue, especially when the initial fracture is open. As it pertains to the ankle joint in the lower extremity, special considerations with ankle arthrodesis nonunions are whether the fibula was resected at the time of initial arthrodesis resulting in less bone stock, an anterior approach that resulted in disruption of the anterior tibial artery and the lack of good anterior soft tissue coverage.

As previously discussed, there are many host factors that can contribute to a nonunion including smoking, diabetes, patient noncompliance, vitamin D deficiency, malnutrition, steroid use, peripheral vascular disease, and peripheral neuropathy. Efforts made for the correction of these host factors preoperatively can optimize a successful outcome. Other host factors that complicate healing include renal and liver failure, anticoagulant use, and deep vein thrombosis with venous stasis of the leg. These patients with difficult underlying medical comorbidities must be counseled about prolonged nonweightbearing, chronic CROW boot protection, elevation and compression stockings for at least a year postoperatively [14, 15].

Important points from the history include whether the injury was open or closed and the degree of contamination. Previous culture results are helpful especially if the patient presents already on oral antibiotics. A thorough understanding of the previous procedures performed is critical as it may not always be obvious that a flap procedure has been performed. Furthermore, all previous autologous bone graft donor site locations need to be documented so that further harvesting from a prior site can be avoided. A notable exception to this is in the cases of a previously harvested intramedullary canal via the RIA (Reamer, Irrigator, Aspirator autologous bone harvesting system). It has documented that the intramedullary canal can be sequentially harvested as early as 3–6 months from the previous harvest without issue [16].

Sensation, joint range of motion, and palpable pulses as well as any preexisting scars must be documented. Any rotational malalignment is assessed by comparing the internal and external rotation of the femurs with the patient prone as well as comparing the thigh foot axis on each side. Since the patient will be receiving an operative procedure to address the nonunion, the malalignment should be corrected at the same setting. Any varus malalignment or malrotation, for example, can also contribute to nonunion by causing gait disturbances and uneven force distribution across the arthrodesis or fracture which may further lend to complications such as further nonunion if not addressed at the time or revision.

Plain radiographs and CT scan are the most useful imaging modalities to document a failed arthrodesis/nonunion. Underlying osteoporosis and osteopenia can be assessed with these tools as well [17]. MRIs and bone scans are not useful in these settings since there is typically hardware present and would therefore potentially obscure appropriate evaluation for nonunion. Osteoporosis and osteopenia can be addressed with the nonunion treatment by starting bisphosphonate therapy after the initial remodeling phase and choosing a surgical treatment plan that does not delay weight bearing unnecessarily [18].

A full set of preoperative labs is necessary. Nutrition markers are assessed with total protein, albumin, and prealbumin levels. CRP and ESR are used to determine if the nonunion is infected. Metabolic contributions to the cause of the nonunion are assessed with vitamin D levels and PTH. Any abnormal nutrition and metabolic parameters must be addressed as soon as possible preoperatively via the surgeon or with the assistance of an endocrine specialist [19]. In the case of an infected nonunion, additional immunology labs are sent to further assess the host immune system. Often there are abnormal values that contribute to the hosts inability to fight the infection. These values such as low IGG can be corrected preoperatively with IGG infusions to improve the patient's ability to clear the infection.

Bone biopsy as a separate procedure prior to definitive surgical intervention in nonunion surgery is typically avoidable. In the majority of nonunion cases, the question of infection is resolved preoperatively. We typically do bone

biopsy and cultures of every nonunion at the time of the definitive operation via fresh frozen section and stat gram staining. When planning an operative procedure for nonunion, infection is always a possibility and it is imperative to always enter the operating room with multiple plans based on the potential scenarios encountered. The amount of bone that is required to be resected down to healthy, bleeding bone often dictates the stabilization and fixation construct selection needed and the best method to determine live bone ends at the site of nonunion is still intraoperative evaluation via the naked eye.

Hypertrophic Nonunion

Hypertrophic nonunions are typically secondary to a problem with stability of the initial construct selected for fixation. The bone ends are viable but do not have enough stability to heal and often appear wider than the normal diameter of the bone involved. Treatment for this always includes increasing the stability of the bone with additional instrumentation. This type of nonunion is also amenable to distraction with an external fixator because the external fixator provides the increased stability and the hypertrophic nonunion can be distracted/compressed at a rate of 0.5 mm/day to get the bone to consolidate. No additional bone graft is typically needed for these cases.

Example of Hypertrophic Nonunion

Here is a case of a patient with a hypertrophic nonunion after a distal tibia/fibula fracture that was treated conservatively (Fig. 35.1a–d). The patient was initially distracted and the deformity corrected via hexapod external fixator. We elected to use this construct as it allows for gradual correction of the deformity and minimal insult to both the osseous anatomy and soft tissues. Once the deformity was corrected and the signs of radiographic consolidation were noted, the fixator was removed. Final clinical pictures of the patient showing the leg in anatomic position with the patient able to bear weight to the operative extremity.

Atrophic Nonunion

Atrophic nonunions are usually a result of inadequate blood supply. The bone ends are avascular and treatment will almost always involve resection of the distal ends of the nonunion down to bleeding and healthy appearing bone. As previously mentioned, the amount of bone resected will dictate one of the several treatment options that include acute shortening, tib/fib synostosis when working in the leg, or bone transport to deliver new, healthy bone to the site where the bone defect is. The distal tibia and ankle are not ideal places for acute shortening because of the difficulty with shoe wear as ankle circumference increases with shortening. It is important to note that acute shortening is not recommended for defects larger than 4 cm because of the potential for vascular compromise associated with kinking of the vessels. In these cases, gradual shortening using an external fixator with or without internal fixation is necessary and defects greater than 4 cm mandate bone transport [20]. Furthermore, our preference is to maintain length if there is more than a 2 cm defect via the use of bone graft, bone transport, or tib/fib synostosis.

Example of Atrophic Nonunion

Here is a case where we demonstrate how Tib-fib synostosis is ideal for a distal tibial nonunion where there is a poor soft tissue envelope anteriorly. From a lateral approach, the interval posterior to the fibula and the posterior tibia can be exposed where there is excellent soft tissue coverage and blood flow available from the posterior compartment musculature. The surface area of the tibia and fibula is large and can be prepared with a burr. Furthermore, the interosseous membrane and the posterior soft tissue envelope are used to maintain bone graft that is harvested from the patient or sourced as allograft and placed into the wound between the tibia and fibula. The postoperative radiographs show the patient at 6 months from revision surgery (Fig. 35.2a–c).

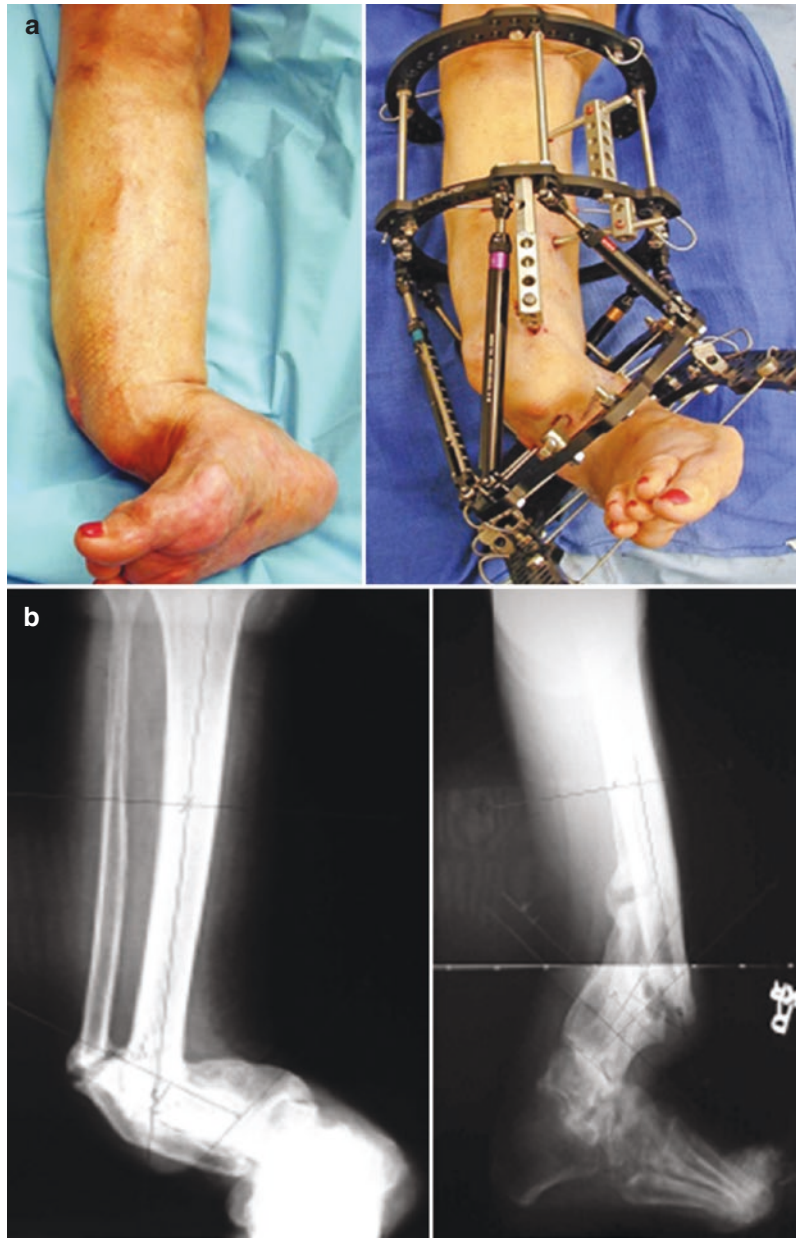


Fig. 35.1 (**a**) Preoperative and immediate postoperative clinical photos of the right lower extremity status post distal tibial and fibular hypertrophic nonunion with malposition surgical reconstruction via hexapod external fixator for gradual deformity correction. (**b**) Preoperative AP and lateral radiographs of the right leg. (**c**) AP and lateral radiographs demonstrating final corrected position of the tibia and fibula with resolution of the nonunion. (**d**) Final clinical photos demonstrating the right lower extremity in anatomical position with the patient weight bearing

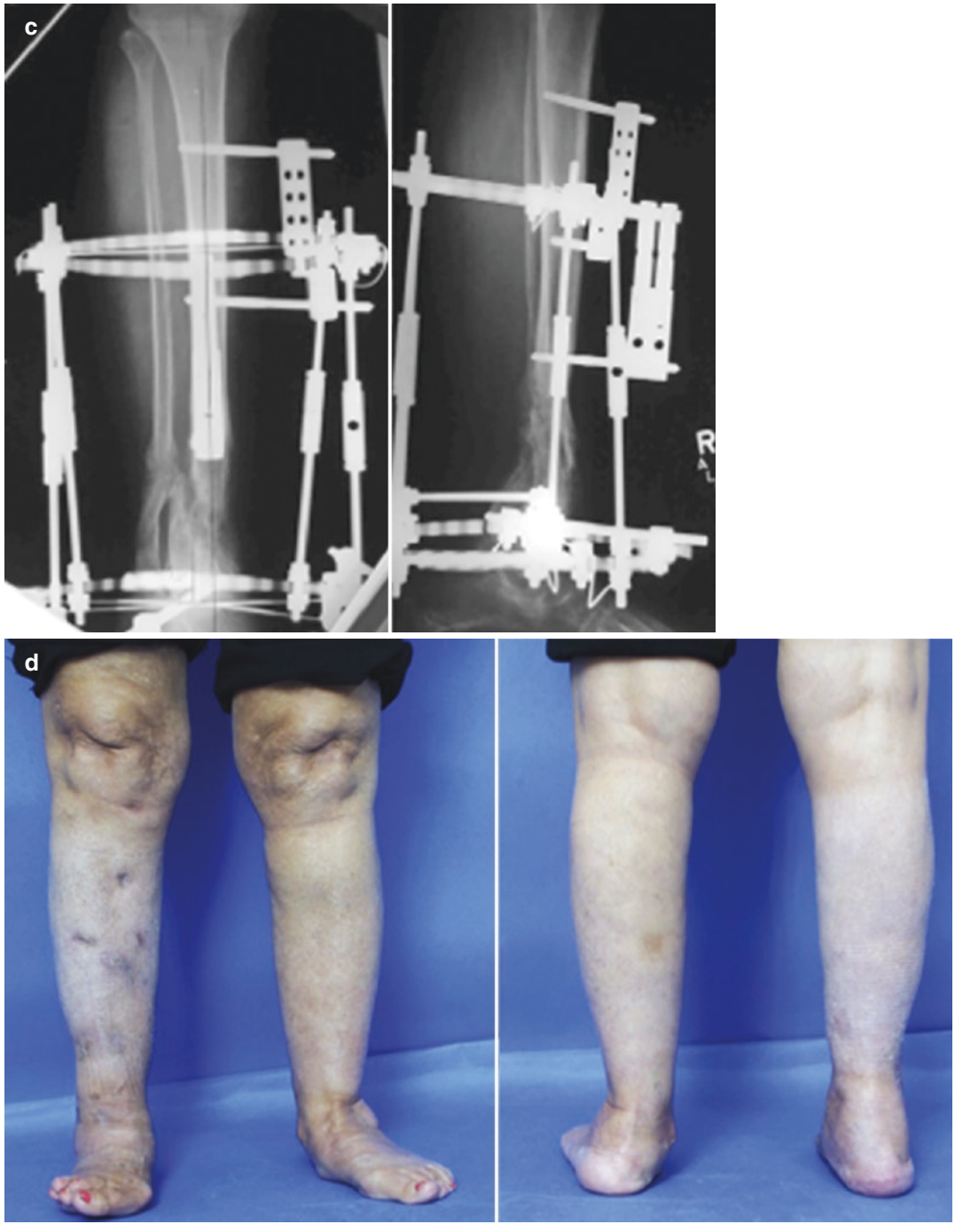


Fig. 35.1 (continued)

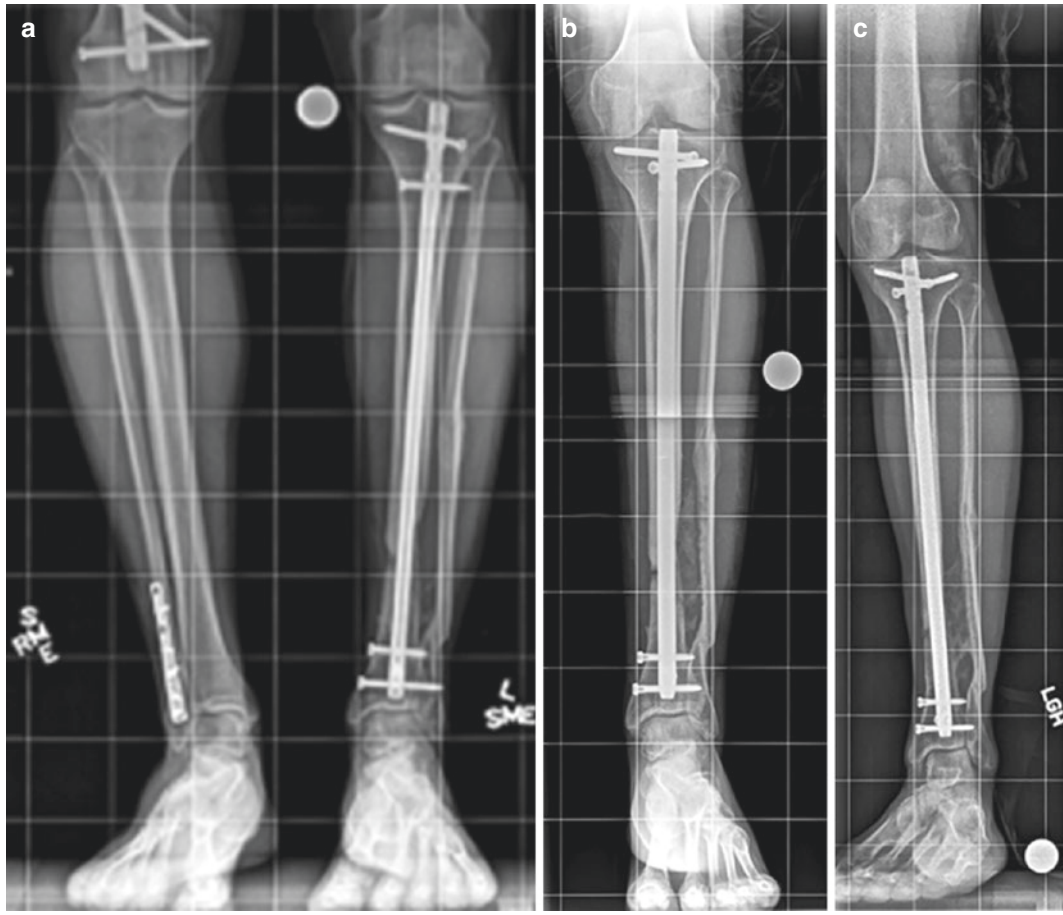


Fig. 35.2 (**a**) Atrophic nonunion of a tibial shaft fracture. (**b**) Patient 6 weeks status post tibial nonunion revision with preparation of the tibial and fibula and bone grafting of with signs of consolidation and synostosis formation. (**c**) Patient at 6 months demonstrating continued consolidation and synostosis formation in accord with healing and resolution of the nonunion

Infected Nonunion

This category of nonunion is the most complex as it usually involves a combination of a poor soft tissue envelope and infected bone. Much like cases of atrophic nonunion, the infected bone must be resected down to a healthy appearing, bleeding bone. The surgeon should anticipate and plan for the worst case scenario in terms of bone resection but again, the actual amount of bone resection is determined intraoperatively using visual inspection of the bone for bleeding when debrided with the high speed burr. Several options for stability after the bone resection include antibiotic coated rods or external fixation [21]. These cases are also among the most common cases to require additional blood supply to the nonunited area in the form of either local or free tissue/muscle flaps, as the soft tissue envelope and local blood flow are typically compromised. Plastic surgery consultation and a multidisciplinary approach should be utilized for a chance at the successful outcomes. The distal one-third of the tibia is amenable to a soleus muscle flap or a reverse sural flap. Often, the infected nonunion can be prepared, stabilized, and flapped in one session depending on the quality of the surrounding soft tissues (see Figs. 35.3 and 35.4). If the

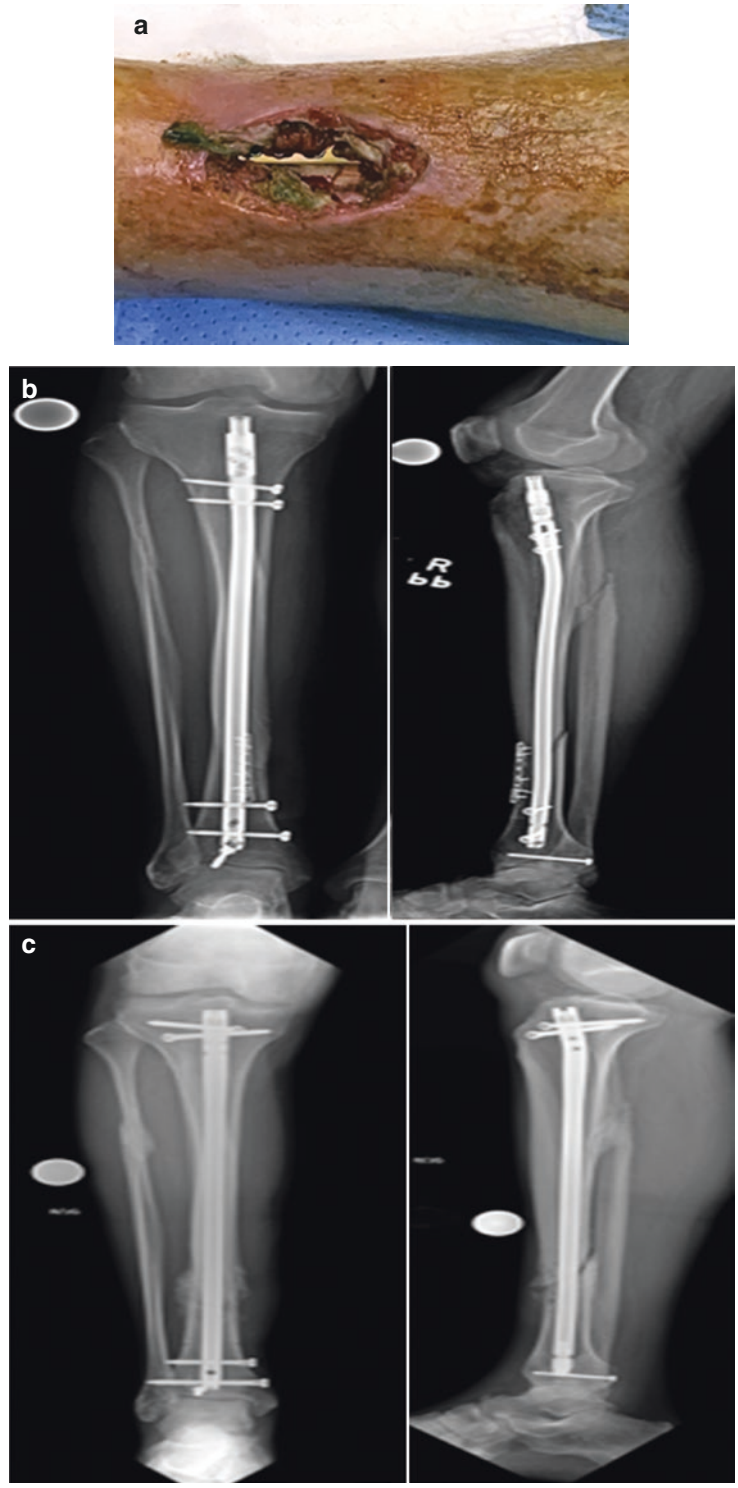


Fig. 35.3 (**a**) Clinical photo of an infected nonunion in a patient with a midshaft tibial fracture with an open wound and exposed hardware. (**b**) Preoperative AP and lateral radiograph of the tibia and fibula with nonunion noted at the midshaft of the tibia. (**c**) Post-revision AP and lateral radiographs of the tibial and fibula demonstrating signs of consolidation at the nonunion segment in accord with healing at 5 months from the date of revision surgery. (**d**) Immediate postoperative clinical photo status post local tissue transfer via gastrocnemius flap and split thickness skin grafting and at 5 months from the date of revision surgery demonstrating no open wound healed flap and skin graft



Fig. 35.3 (continued)

bone is too small to accommodate an antibiotic coated intramedullary rod, calcium sulfate paste containing antibiotics can be injected into the canal for local antibiotic delivery [22].

Example of Injected Nonunion

Here is a patient who presented after initial ORIF of a tibial shaft fracture via intramedullary nailing and plating of the anterior tibial fracture at an outside facility. The initial injury was reported as open. The patient subsequently went on to dehiscence and necrosis of the anterior tibial wound with exposed hardware and nonunion of the tibial fracture. The patient's biopsy and cultures were found to be positive and a decision was made for revision surgery. The patient's existing hardware was explanted, bone was debrided with high speed burr, and a new antibiotic cement coated nail was placed with simultaneous gastrocnemius local flap and split thickness skin grafting. The patient went on to heal without incident (Fig. 35.3a–d).

Example of Infected Ankle Arthrodesis Nonunion

Nonunited ankle arthrodesis and distal tibial nonunions can be challenging. The key to success is optimizing the patient prior to surgery and developing a surgical plan that is best suited for post-op patient compliance. The surgeon should have multiple plans in case the bone resection is larger than initially estimated. All options should be discussed with the patient so that everything can be done in one surgical setting in terms of rendering the bone clean, bleeding, healthy appearing, and the anatomy stabilized. Surgeons need to be comfortable with bone transport and bone lengthening technologies as tools to create and lengthen bone. Furthermore, rotational flap skills are helpful when there are compromised soft tissues or otherwise require the assistance of a trained plastic surgeon for a multidisciplinary approach. These challenging cases require surgeon patience and close patient follow-up to ensure success.



Fig. 35.4 (**a**) Radiographs of a patient with infected ankle arthrodesis nonunion in accord with post-traumatic arthritis of the ankle. X-rays are shown after hardware removal and radiographic nonunion is visible. (**b**) Clinical photographs of the open wound and local free tissue transfer to achieve closure as part of the revision procedure. (**c**) Radiographs after resection of the infected distal tibial segment with antibiotic cement bead placement, intramedullary hindfoot nailing, and proximal tibial osteotomy with bone transport of the tibia. (**d**) Radiographs at 9 months from frame removal and hindfoot arthrodesis via posterior plating demonstrating bony consolidation in accord with fusion. (**e**) Clinical photo demonstrating adequate clinical positioning and closed medial ankle wound after surgical revision



Fig. 35.4 (continued)

Here we present a case involving infected ankle arthrodesis nonunion with an open ankle wound that presented for a second opinion. What makes these cases particularly challenging is that since the foot is a long lever arm and the entire body weight force is concentrated on dorsiflexing the ankle with ambulation, the forces at the ankle extending from the leg and upper body down to the foot must be taken into consideration. Furthermore, post-traumatic arthritis involving talar AVN can prove difficult for fusion secondary to the tenuous blood supply to the talus. For these reasons, we prefer intramedullary fixation and the use of a long calcaneocuboid screw to neutralize the foot. This patient underwent a two stage approach where in stage one, the infected area of bone was resected to bleeding bone, antibiotic cement beads placed and local tissue rearrangement for coverage and closure of the wound. Additionally, we utilized placement of an antibiotic cement coated nail and bone transport was done via proximal tibial osteotomy. With exceptionally complex cases, a "belt and suspenders" approach is helpful where a hindfoot fusion intramedullary rod is supplemented with a posterior plate through a posterior trans-Achilles approach as shown below which was part of the second stage of the procedure where the external fixator was also removed. The approach for the posterior hindfoot plate is usually through a virgin soft tissue envelope and there is a large bony surface area along the posterior calcaneus and posterior tibia for bone grafting.

We prefer autologous bone grafting for ankle arthrodesis nonunion cases and typically there are several options for autograft. In cases where the operative procedure is performed prone, the posterior iliac crest or the RIA reamer retrograde from the femur can be a good option. In cases of hindfoot fusion via an intramedullary rod used for ankle and subtalar arthrodesis, the RIA reamer can be used to harvest bone graft from the proximal tibial canal and create a channel for the hindfoot fusion rod simultaneously as was done here (Fig. 35.4a–e).

Malunion

In cases involving malunion, host biology is not in question as can be the case with nonunion as the patient has demonstrated their ability to heal, albeit in a poor and nonfunctional position. Nevertheless, a great deal of consideration needs to be given to these deformities prior to any surgical intervention or revision procedure. This is particularly the case in a high risk patient population. A diabetic with peripheral vascular disease may not have a soft tissue envelope that is amenable to multiple revision procedures and a patient who previously healed uneventfully may not be guaranteed to heal without complication in the revision setting. Hence, care should be taken to avoid the need for excess surgery and meticulous planning should be done to allow for correction of any deformity in one stage when possible and with as little insult to the soft tissue envelope as possible when dealing with the skeletal anatomy.

Revision cases can be particularly challenging for the surgeon and a familiarity and comfort with a wide array of techniques and fixation constructs (i.e. internal vs external fixation) need to be had in order to achieve the best possible outcomes in each particular malunion case. The following case will demonstrate an example of a malunion that required revision surgery.

Example of Tibial Malunion in the Setting of Ankle Arthritis

As it pertains to the lower extremity and the ankle joint in particular, it is essential to assess the overall limb alignment when considering an ankle fusion. In certain cases, there is no subtalar joint or supple ankle to compensate for any amount of deformity proximally. Often when there are alignment problems secondary to a proximal deformity, the corrections are both done at the same surgical setting to prevent persistent deformity and subsequent pain.

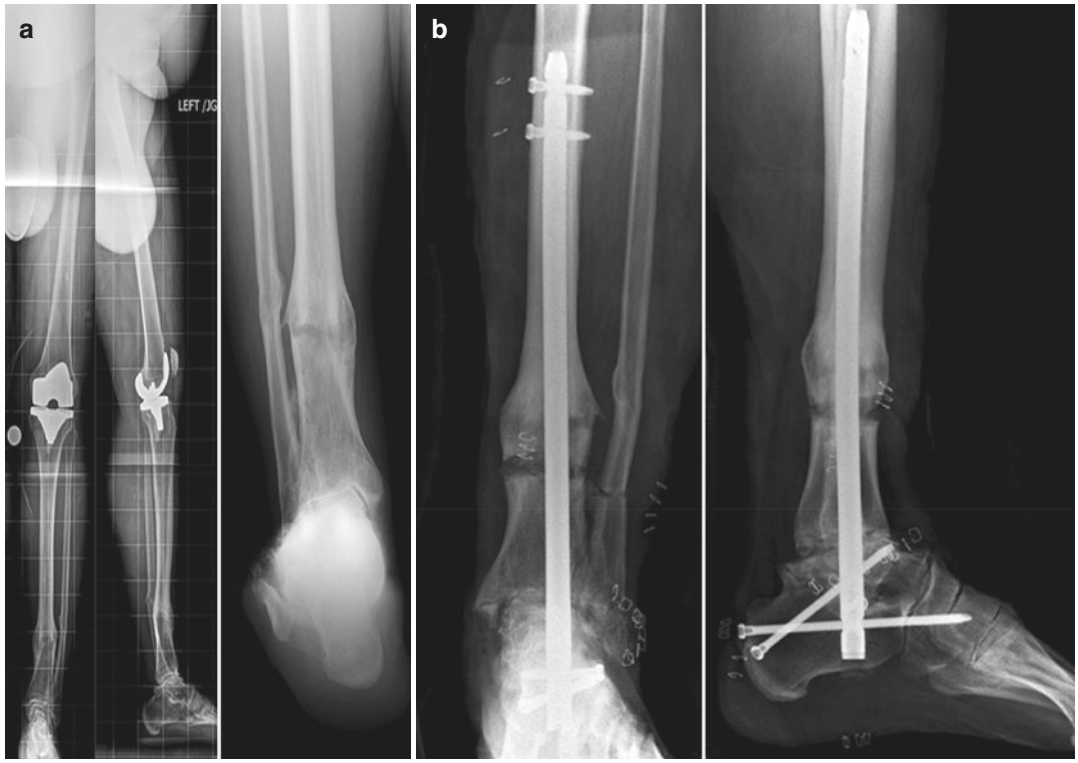


Fig. 35.5 (**a**) Long leg radiographs of the left lower extremity demonstrating varus and recurvatum deformity with malunion of the tibia in addition to equinus deformity of the ankle joint. (**b**) Postoperative AP and lateral radiographs status post clamshell osteotomy of the tibia with hindfoot ankle and subtalar joint arthrodesis via hindfoot intramedullary nailing

Here is a case where an ankle arthrodesis is necessary but there is a total knee arthroplasty above and a distal tibial oblique plane deformity with varus and recurvatum secondary to a precious shaft fracture of the tibia with malunion. This is also complicated by the ankle equinus. An isolated ankle arthrodesis with screws, without addressing the deformity, would leave the varus and recurvatum with subsequent stress being placed on the total knee arthroplasty or promoting uneven weight distribution across the fusion and foot. In this case, the ankle equinus and distal tibial recurvatum with varus were addressed at a single surgical setting with a hindfoot fusion rod transfixing the ankle arthrodesis and clamshell osteotomy of the tibia (Fig. 35.5a, b).

Advanced Surgical Techniques and Troubleshooting in the Revision Setting

There are a variety of challenging components to tackle when faced with a complication in limb salvage. Furthermore, different challenges can present during various phases. The goal of this section is to provide clinical examples that will provide guidance and strategies, along with a systematic thought process when encountering surgical challenges during the care of a limb salvage patient in the lower extremity. Indeed, for the highest chance at achieving a successful outcome, particularly in the revision setting and in a high risk patient population, it is important for

the surgeon to have familiarity and comfort with a number of fixation constructs (i.e. internal versus external fixation) and surgical techniques.

Paley subclassified challenges that are encountered during limb lengthening in an easier method by describing them as problems, obstacles, and complications. This classification differentiates challenges during care into the following method:

- *Problems* are difficulties that do not require operative treatment for resolution.
- *Obstacles* require operative intervention, but do not impact final outcome.
- *Complications* are those issues that do not resolve by the end of treatment.

We have utilized this simple classification to guide common to complex limb salvage complications. This decreases the stress associated with the different challenges and allows one to manage any complication appropriately in a systematic fashion. Furthermore, this can be applied to a number of possible scenarios that can occur when treating the patient undergoing limb salvage surgery. The following sections will demonstrate the application of this classification with case examples and how it can be applied to achieve successful outcomes.

Problems

External fixation is a common modality of stabilization when performing limb salvage procedures. One of the more common problems is pin site infections. In this scenario, treatment can often be rendered that requires no operative intervention, therefore, classified as a problem.

External fixation pin site infections are often a result of bacterial contamination presenting from the external environment along the path of the wire. A wire infection will present with localized redness, pain, and even purulent drainage. This may have started as local irritation or inflammation when wires are inadequately tensioned, lose tension, or secondary to excessive edema in the extremity as well as secondary to pistoning of the soft tissue against the wire such as in the proximal leg, among other factors [23]. Furthermore, pin site infections can be divided into three grades with grade 1 being inflammation, grade 2 is soft tissue infection, and grade 3 involving an infection down to bone [24]. To prevent pin site irritation and infection from occurring, the surgeon can utilize a number of local methods to prevent these issues such as placing foam sponges or rubber stoppers on the wire or wrapping betadine soaked gauze around each wire to prevent pistoning of the soft tissue due to swelling therefore, decreasing the likelihood of pin tract infection. If wires have lost tension, retensioning in the clinic with the tensiometer or manual tensioning via the "Russian" method can resolve the issue. If a pin tract infection does develop, however, it is important to start a short course of broad-spectrum antibiotics, typically an oral first-generation cephalosporin in our practice, for one week. If the pin infection does not respond to oral antibiotic therapy, intravenous antibiotics may be indicated and cultures from around the pin site or any drainage may help direct the best antibiotic regimen. Furthermore, removal of the wire in the clinic may be necessary in addition to the antibiotic therapy. For this reason, we will often advocate placing one or two additional wires to prevent loss of stability of the fixation segment in the event of an infected wire that necessitates removal.

Obstacles

As previously stated, obstacles are challenges that present during limb salvage that require a return to the operating room, however, they do not impact the final outcome. Hardware related infections can pose a significant challenge for management and often result in operative intervention for either removal/exchange. If a concomitant deep infection is present with osteomyelitis it can further complicate the management and salvage of such cases. The following case demonstrates this challenge and the stepwise approach taken to manage the infection.

Example of a Case Involving a Midfoot Obstacle

A 60-year-old male with chronic ulceration and Charcot neuroarthropathy of the midfoot presented for surgical consultation. The patient had a non-healing ulceration for greater than one year and was treated with offloading and total contact casting with no improvement. Patients initial preoperative diagnostic workup included standard weight bearing radiographs that demonstrated peri-navicular collapse and fragmentation of the midfoot joints. No acute bony signs of infection were noted and a preoperative nuclear medicine Indium-111 scan demonstrated negative uptake for bone infection. Notable in the medical history, the patient has hypertension, anemia of chronic disease, and stage one chronic kidney disease. The patient was taken for an initial wound debridement and bone biopsy given the long-standing history of ulceration. In these cases, it is imperative to be certain that there is no deep bone infection or contamination. The bone biopsy and cultures were both negative for osteomyelitis; therefore, a decision to proceed with formal arthrodesis with internal and external fixation was performed. There is much debate in regard to internal versus external versus a combined construct approach and each option can offer its own benefits and disadvantages. The patient underwent medial and lateral column arthrodesis with intramedullary foot fixation and application of external fixation [25, 26]. The patient had an uneventful postoperative course and after 12 weeks had his external fixator removed. Serial radiographs had demonstrated medial and lateral column arthrodesis, while clinically the patient had no open wounds and had returned to normal shoe gear. At two months from frame removal and five months from initial surgery, the patient presented to the emergency department with a red, hot, swollen foot with subjective complaints of a fever and malaise. Radiographic signs of bony fragmentation around the hardware and lucency along the fixation were noted in both the medial and lateral columns. Laboratory findings demonstrated an elevated erythrocyte sedimentation rate and c-reactive protein and a normal white blood count. Given the radiographic findings, constitutional symptoms, and clinical appearance of the foot a decision to go to the operating room was made. The medial and lateral column fixation was removed through percutaneous incisions and any drainage was swabbed for cultures. The long-cannulated screw tracts were further reamed with cannulated ACL reamers one to two millimeters larger than the size of the screws (6.5 mm–8 mm in diameter) until medullary bleeding was witnessed, followed by medullary irrigation. The hardware along with the reaming's was cultured and sent for gram stain evaluation and pathologic examination. The medullary defect was then filled with poly-methyl methacrylate cement impregnated with vancomycin and tobramycin. The cement was coated on 1.8 mm Ilizarov wires until the cement hardened and the diameter of the coated pins was between 7 and 10 mm. The pins were press-fitted into the reamed canals and 1–1.5 cm of the coated pin was left exposed to allow for easy retrieval at a later time. Coagulase Negative Staphylococcus species was determined to be the offending pathogen and six weeks of intravenous antibiotics was initiated with weekly laboratory studies to monitor CBC, ESR, and CRP. During this time, serial radiographs were obtained to monitor signs of infection resolution and it was noted that the talus had started to demonstrate signs of avascular necrosis. After six weeks of intravenous antibiotics and serial radiographs, the patient returned to normal ESR and CRP in accord with a resolution of the infection. However, talar avascular necrosis required stabilization and arthrodesis of the tibio-calcaneal component to maintain stability of the midfoot and hindfoot which was done via application of a new frame to stabilize both the hindfoot as well as also offer compression and stability to the foot and allow for healing. This went on to heal without any further complicating factors and the patient was able to ultimately transition back into diabetic shoes at about one year from the final revision surgery. In this case we elected to proceed with internal and external fixation as the dual construct allows for a more robust fixation construct that allows for the patient to also

weightbear immediately with the aid of a walker. The downfall of this being that it is possible the pintracts introduced bacteria to the internal fixation that was present deep within the osseous anatomy. This case demonstrated multiple obstacles while managing an initial complaint. The key features of this case demonstrate that hardware related deep infection and osteomyelitis spanning from the metatarsals to the talus does not have to result in limb loss. The key to managing the infection is predicated on having adequate perfusion, managing the bony and soft tissue infection, and providing stability through arthrodesis. Other technical aspects of this case have been borrowed from management of infected nonunions and segmental defects of long bones. In their study, Thonse et al. demonstrated successful outcomes with management of infected nonunions and segmental defects treated with antibiotic coated nails. In this cohort, ninety-five percent were able to achieve infection control and eighty-five percent were able to achieve bony union. This method has been shown to be effective when managing medial and lateral column fixation that spans from the metatarsals to the ankle and can successfully be utilized when managing these complex infections (Fig. 35.6a–g).

Example of a Case Involving an Ankle Obstacle

Here is a case of a 55-year-old male with ankle and subtalar joint neuropathic collapse. The patient was initially managed at another location and due to increased pain, instability in bracing, and an inability to continue working as a heating and ventilation technician he presented to our office for surgical evaluation. His only significant past medical history included hypertension and type 2 diabetes with a recent HgA1c of 7.8%. Preoperative medical clearance was obtained via the primary care physician and a decision to proceed with surgical intervention was made for arthrodesis of the hindfoot and ankle complex with concomitant distal tibial lengthening to address the limb length discrepancy that would otherwise result from talar loss. Additionally, the patient was notified that he would likely have a limb length discrepancy greater than 3 cm due to the loss of talar height and in the process of obtaining arthrodesis if the tibial lengthening was not performed and was counseled on gradual distraction osteogenesis to restore limb height to within 1 cm of the contralateral limb. The goal of height restoration is to improve and maintain near normal gait and minimize complications at proximal joints that could potentially accompany a limb length discrepancy. Furthermore, while no literature has been published on this topic to our knowledge, we hypothesize that the tibial lengthening encourages a more robust arthrodesis at our distal fusion site secondary to the proximal turnover of bone and regenerate formation that occurs as part of the lengthening process.

Intraoperative findings demonstrated significant fragmentation and dissolution of the talus and superior aspect of the calcaneus. The healthy remnants of the talar medullary contents were morselized and incorporated into the fusion mass of the distal tibia and calcaneus. We then proceeded with a distal tibial osteotomy which was made to facilitate distraction osteogenesis of the tibia and arthrodesis of the hindfoot. A hexapod external fixator was designed to include a tibial block with six hexapod struts that would gradually lengthen the osteotomy and a foot block was fixated to the distal tibial block with threaded rods that were acutely compressed between the tibial and calcaneal segment to allow for compression and promote arthrodesis. A prescription for gradual correction with distraction of 0.75 mm/day was given to the patient and the patient was able to complete the distraction of 20 mm per the prescription. This distraction amount is based on the average height of the talus. Unfortunately, the patient started having difficulty with maintaining the frame and due to recurrent pin site irritation and pain, a decision was made for removal of the external fixator at



Fig. 35.6 (**a**) AP radiograph of the right foot demonstrating Charcot breakdown at the hindfoot tarsal bones. (**b**) Lateral lower extremity radiograph immediately following midfoot beaming and application of circular external fixator. (**c**) Lateral radiograph of the foot demonstrating adequate positioning and intact hardware at 12 weeks from frame application and internal beaming fixation of the foot. Picture shown is just following frame removal at 12 weeks. (**d**) AP radiograph at 8 weeks from frame removal demonstrating signs of lucency and fragmentation around the hardware. (**e**) Lateral foot radiograph demonstrating the patient status post hardware removal and antibiotic cement beaming with operative debridement. (**f**) Patient at final follow-up after infection management and subsequent hindfoot arthrodesis with radiographic signs of consolidation and healing throughout the midfoot and hindfoot. (**g**) Final clinical result

10 weeks. Due to a lack of consolidation of regenerate at the distraction gap, an antibiotic coated medullary nail was placed to provide stability to the regenerate and the arthrodesis site [27]. One month after medullary nailing, the patient presented to the emergency department with fever, malaise, and a red, hot, swollen ankle and extremity. Duplex studies were negative for deep vein thrombosis. Radiographs demonstrated signs of bone infection, hardware lucency and a CT scan revealed an abscess within the anterior distal tibia. Elevated levels of ESR and CRP all but confirmed a likely active infection. The patient was taken to the operating room for removal of the infected hardware, aggressive medullary debridement, and multiple bone and soft tissue cultures. Cultures and sensitivities were sent from the hardware and bone. The medullary canal of the tibia and surrounding calcaneus was aggressively debrided with a reamer until bleeding bone was noted. A temporary antibiotic rod was inserted to provide local delivery while the patient was placed on IV antibiotics for six weeks of antibiotic management by the infectious disease service. Cultures were positive for coagulase negative staphylococcus. Once the patients ESR and CRP started to trend towards normal and subsequent radiographs demonstrated signs of bone remodeling, the patient was subsequently taken to the operating room for revisional arthrodesis via antibiotic coated intramedullary nail. The patient subsequently demonstrated radiographic signs of union and consolidation and has maintained an infection free limb at greater than one year from the last procedure performed and subsequently returned to regular shoe gear and work as a heating and ventilation technician (Fig. 35.7a–h).

The above cases demonstrate the required steps for managing complex infections that require revision and can further be summarized below:

1. Step 1 involves management of the infection both medically and surgically. This typically involves a staged approach that requires removal and aggressive debridement of infected hardware, bone, and soft tissue. Leaving any infected tissue allows for proliferation of biofilm and negates the benefits of systemic antibiotic delivery, therefore, decreasing the effectiveness of this staged approach to revision [28].
2. Bone and soft tissue cultures obtained during the debridement can determine the medical treatment with systemic antibiotics. A multidisciplinary approach with an infectious disease specialist will facilitate the identification of the most effective antibiotic regimen.
3. Once infection markers and radiographic parameters improve, a revision can be performed with antibiotic coated stable fixation to achieve union and stability for limb salvage.

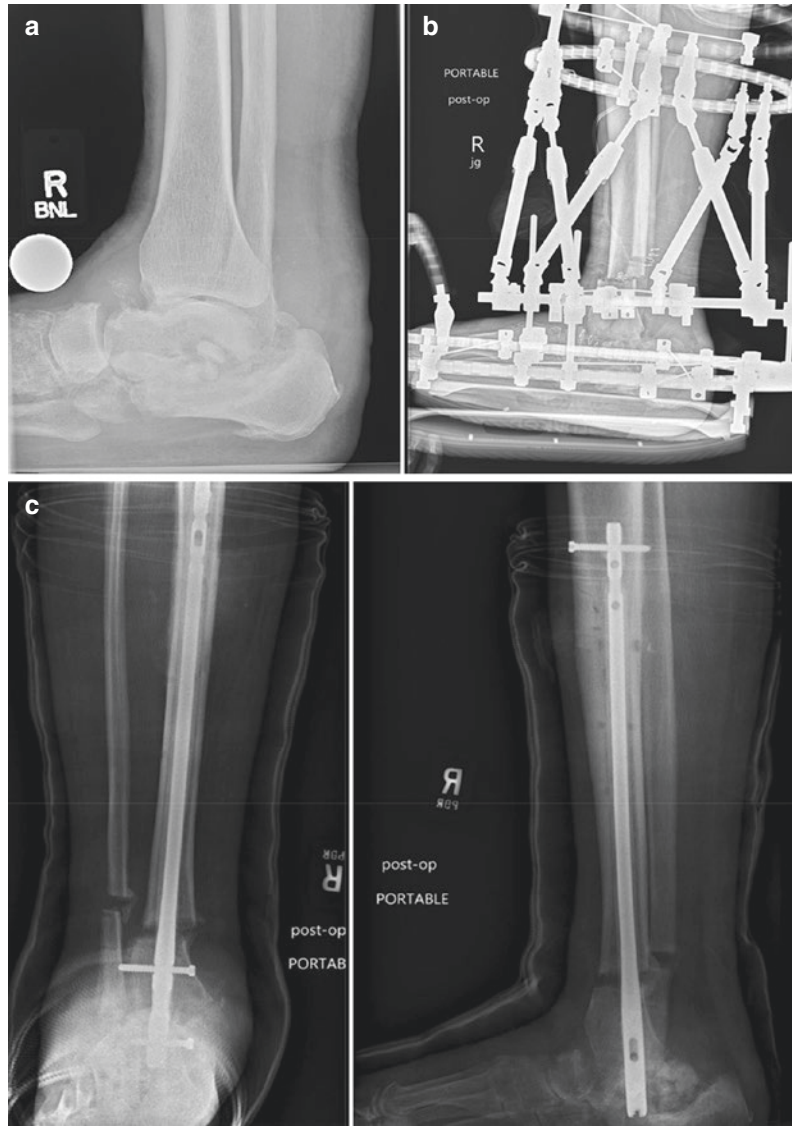


Fig. 35.7 (**a**) Lateral ankle radiographs demonstrating ankle and subtalar neuropathic collapse with fragmentation of the talus and calcaneus. (**b**) Radiographs demonstrating primary hindfoot arthrodesis with distal metaphyseal-diaphyseal tibial osteotomy and application of hexapod circular external fixator ready for tibial lengthening. (**c**) AP and lateral radiographs status post removal of external fixator following primary hindfoot arthrodesis and distal tibial lengthening demonstrating anatomic alignment and signs of regenerate formation at the lengthening segment. (**d**) Radiograph of the extremity demonstrating hardware lucency adjacent to the medullary nail. (**e**) CT scan of the lower extremity demonstrating nonunion and bone abscess formation to the distal tibia and hindfoot. (**f**) Radiograph shown status post removal of infected hardware, intramedullary reaming and placement of an antibiotic cement rod. (**g**) AP and lateral radiographs demonstrating signs of consolidation and healing of the hindfoot arthrodesis and lengthening segments with antibiotic coated nail placement. (**h**) Clinical photo at final follow-up demonstrating anatomic alignment of the foot and ankle with no open wounds present



Fig. 35.7 (continued)

Complications

As described earlier, true complications are operative injuries or problems that do not resolve by the end of treatment. A below knee amputation in limb salvage would be considered a complication. The goal of any attempt at limb salvage is to prevent complications in a high risk patient population. Important to note, however, that some cases can have complications that can be revised with a dedicated team of surgeons committed to functional limb salvage.

Example of a Complication Based on the Paley Classification

The following case is of a 60-year-old male with a chronic non-healing midfoot ulcer secondary to Charcot neuroarthropathy. Prior to surgical intervention, the patient went through preoperative medical and vascular surgery clearance. He had previously obtained a right sided below knee amputation secondary to complications associated with a diabetic foot infection and was eager to prevent another amputation to the contralateral extremity. At the vascular evaluation he demonstrated triphasic flow to his extremities and has no other medical comorbidities other than type II diabetes with a HgA1C of 7.5% in addition to hypertension. The patient had developed a chronic midfoot ulcer due to neuropathic collapse through the tarsal joints and a decision was made to correct his deformity acutely with an ankle and subtalar arthrodesis and a modified midfoot internal pedal amputation to allow for a single stage correction and closure of the midfoot ulceration. Koller described an internal pedal amputation in which a majority of the tarsal bones are removed to allow for soft tissue closure and make the foot ready for a stable brace [29]. In this case a wedge of midfoot tarsal bones was removed to allow for acute decompression and primary excision and closure of the plantar ulceration. The ankle was also fused in the neutral position to provide stability and to negate the effects of varus and valgus stress from the extrinsic musculature. The patient was placed in an external fixator after the acute correction. Within 2 weeks of the correction the patient started to demonstrate progressive ischemic changes to the digits which went on to fully demarcate to gangrene of the forefoot with a concomitant soft tissue infection of the excised plantar ulcer. Vascular consultation and angiography revealed the patient had distal occlusions at the level of the ankle of the posterior tibial and anterior tibial arteries with poor collateralization. A joint decision with the vascular team and the patient was made to proceed with removal of the gangrenous forefoot along with peripheral bypass beyond the occlusion and proximal to the infected wound. The goal was to increase flow to the proximal transmetatarsal amputation and, therefore, improve the likelihood of healing and prevent a below knee amputation. A successful peripheral bypass was performed after removal of the external fixator. The final procedure involved a transmetatarsal amputation after restoration of blood flow to the foot and hindfoot medullary rod placement for stabilization of the hindfoot. The patient was followed closely and he went on to heal without difficulty (Fig. 35.8a–g).

This case demonstrates a complication that still led to limb salvage by following sound surgical principles and a multidisciplinary approach to salvage. Furthermore, it demonstrates that even in some of the most complex clinical cases, salvage can be achieved via sound surgical principles and a multidisciplinary approach to patient management.

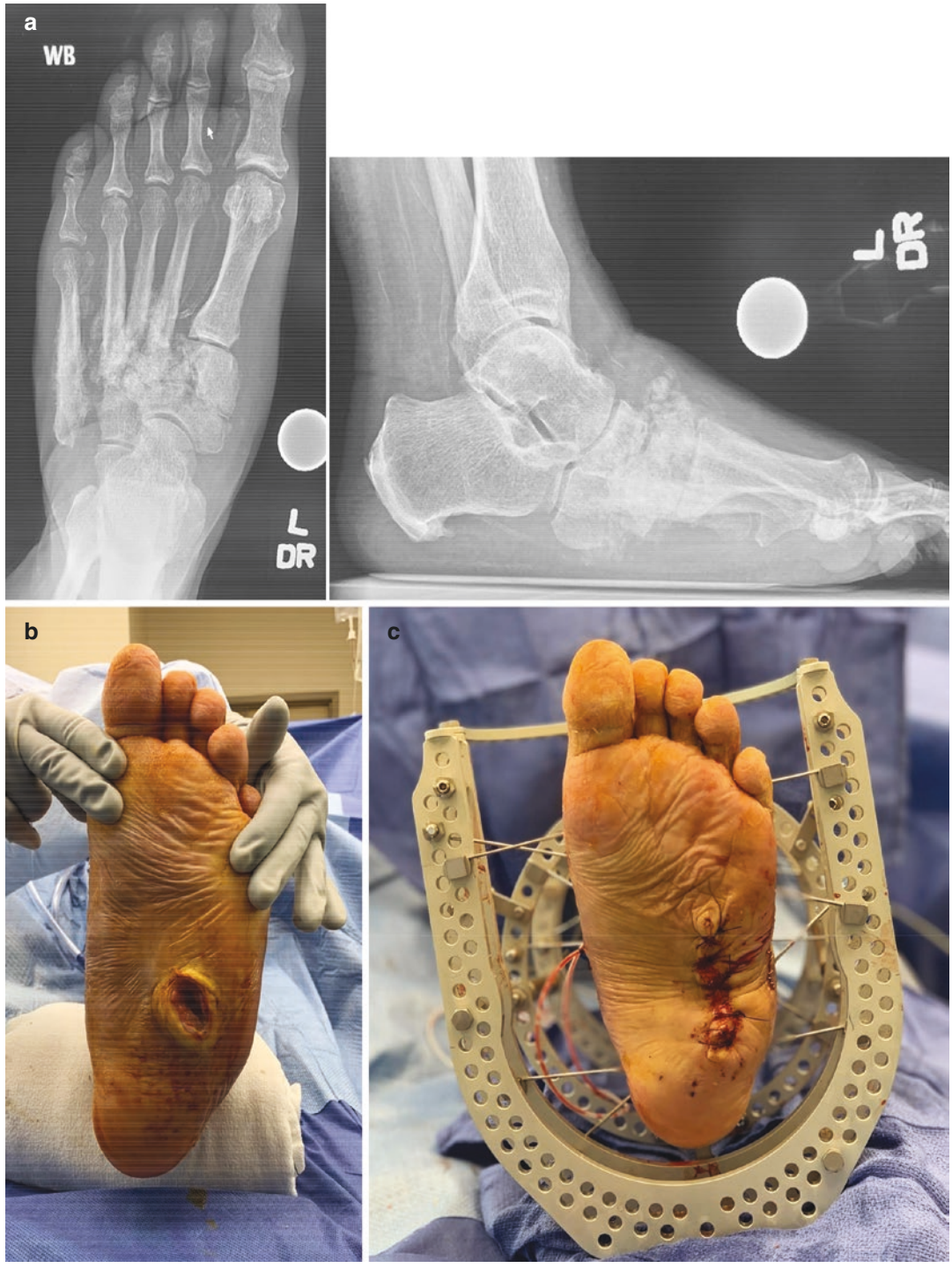


Fig. 35.8 (**a**) AP and lateral foot radiographs demonstrating midfoot collapse and rocker bottom deformity in accord with Charcot neuroarthropathy. (**b**) Preoperative clinical photo demonstrating plantar midfoot ulceration. (**c**) Clinical photograph immediately post midfoot reconstruction with application of external fixator and primary excision and closure of the plantar wound. (**d**) Gangrenous changes initially and after demarcation following the index procedure. (**e**) Clinical photo demonstrating the patient status post transmetatarsal amputation of the foot. (**f**) Lateral radiograph demonstrating hindfoot nailing of the left lower extremity. (**g**) Clinical photo at final follow-up demonstrating a healed midfoot amputation in anatomic alignment



Fig. 35.8 (continued)



Fig. 35.8 (continued)

Postoperative Management

When managing the patient who has recently undergone revision surgery, the details in regard to the postoperative course are not to be overlooked. Indeed, many patients leave the operating room with radiographic and clinically successful outcomes that can be significantly altered if not managed appropriately. This is especially true in a high risk patient population such as those with diabetes and other similarly immunocompromised patient populations where we know there is an increase in complications as compared to a nonimmunocompromised patient population [30]. Decisions such as when to advance weight bearing, etc. need to be tempered with the known fact that many of these patients will have delayed bone healing because of their underlying comorbidities [31]. For this reason many surgeons, including the authors of this chapter, advocate for delayed return to weight bearing after surgical intervention in a high risk patient population and in particular the patient undergoing revision surgery. It should be noted, however, that there is a lack of strong scientific evidence to support a definitive postoperative protocol and more work needs to be done to make definitive recommendations. Furthermore, it is important to have long term follow-up with these patients to assess their progress and look for signs of new problems or further late manifesting complications such as new bony collapse or new skin and soft tissue breakdown.

Conclusion

While complications and the need for revision surgery will undoubtedly arise for any surgeon, a number of factors will have a direct effect on the likelihood of success. Understanding and identifying the factors associated with the need for

revision surgery in the first place is an important first step at the time of index surgery and will optimize the care that the patient receives via appropriate workup, consultation with other specialists in a high risk patient population and surgical decision making that is tailored to the high risk patient (i.e. the diabetic, the immune impaired, etc.) and follows sound surgical principals in a stepwise fashion. Indeed, following these steps will decrease the need for revision surgery to begin with.

In the cases where this cannot be avoided, it is important to start the workup process from the beginning to make sure that no factor that may have led to an initial failure was missed by whoever performed the index procedure. Deficiencies in host such as nutritional status, comorbidity management, or anatomic deficiencies (i.e. vascular status) should be optimized and addressed before any further surgery if there is any hope for successful outcome in the revision setting.

Finally, understanding and knowing one's limitations is key to managing these patients successfully. While an initial hip/ knee arthroplasty or ankle fusion/replacement is well within the capabilities of the community surgeon, many of the revision techniques and procedures as highlighted in this chapter may require not just the skills of a surgeon in a tertiary setting but also the resources of those facilities. Indeed, in many of these cases the chance at having a successful outcome is not just dependent on the skills and abilities of the surgeon but also on the team that is around that individual and the tertiary setting is more well equipped for the aftercare of these patients.

While the topic of complication and revision surgery and the appropriate management of these cases can have a whole text dedicated to it, we hope that we have highlighted via the discussion and examples given in this chapter a small look into the complex nature of these clinical situations and some of the keys that are associated with obtaining successful outcomes and functional limb salvage. We hope that with a stepwise approach, consultation with other specialists and having a team of dedicated partners at all levels can help you, the surgeon, help your patients with these complex clinical cases.

References

1. Wukich DK, Crim BE, Frykberg RG, Rosario BL. Neuropathy and poorly controlled diabetes increase the rate of surgical site infection after foot and ankle surgery. J Bone Joint Surg Am. 2014;96(10):832–9. https://doi.org/10.2106/JBJS.L.01302.
2. Singh JA, Cameron C, Noorbaloochi S, et al. Risk of serious infection in biological treatment of patients with rheumatoid arthritis: a systematic review and meta-analysis. Lancet. 2015;386:258–65. https://doi.org/10.1016/S0140-6736(14)61704-9.
3. Hess DE, Carstensen SE, Moore S, Dacus AR. Smoking increases postoperative complications after distal radius fracture fixation: a review of 417 patients from a level 1 trauma center. Hand (N Y). 2020;15(5):686–91. https://doi.org/10.1177/1558944718810882. Epub 2018 Nov 22
4. Powell JT. Vascular damage from smoking: disease mechanisms at the arterial wall. Vasc Med. 1998;3(1):21–8. https://doi.org/10.1177/1358836X9800300105.
5. Lieber CS. Alcohol: its metabolism and interaction with nutrients. Annu Rev Nutr. 2000;20:395–430.
6. Keller U. Nutritional laboratory markers in malnutrition. J Clin Med. 2019;8(6):775. https://doi.org/10.3390/jcm8060775.
7. Sanders LJ, Robbins JM, Edmonds ME. History of the team approach to amputation prevention: pioneers and milestones. J Vasc Surg. 2010;52(3 Suppl):3S–16S. https://doi.org/10.1016/j.jvs.2010.06.002.
8. van den Berg JC. Angiosome perfusion of the foot: an old theory or a new issue? Semin Vasc Surg. 2018;31(2–4):56–65. https://doi.org/10.1053/j.semvascsurg.2018.12.002. Epub 2018 Dec 20
9. Kruse KK, Dilisio MF, Wang WL, Schmidt CC. Do we really need to order magnetic resonance imaging? Shoulder surgeon ultrasound practice patterns and beliefs. JSES Open Access. 2019;3(2):93–8. . Published 2019 Apr 26. https://doi.org/10.1016/j.jses.2019.01.004.
10. Scharf S. SPECT/CT imaging in general orthopedic practice. Semin Nucl Med. 2009;39(5):293–307. https://doi.org/10.1053/j.semnuclmed.2009.06.002.
11. Spangehl MJ, Masri BA, O'Connell JX, Duncan CP. Prospective analysis of preoperative and intraoperative investigations for the diagnosis of infection at the sites of two hundred and two revision total hip arthroplasties. J Bone Joint Surg Am. 1999;81:672–83.
12. Simon L, Gauvin F, Amre DK, et al. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection: a systematic review and meta-analysis. Clin Infect Dis. 2004;39:206–17.

13. Kennel KA, Drake MT, Hurley DL. Vitamin D deficiency in adults: when to test and how to treat. Mayo Clin Proc. 2010;85(8):752–8. https://doi.org/10.4065/mcp.2010.0138.
14. Jackson D. Addressing psychosocial factors preoperatively can improve outcomes. Orthop Today. 2005:82.
15. Zura R, Mehta S, Della Rocca GJ, Steen RG. Biological risk factors for nonunion of bone fracture. JBJS Rev. 2016;4(1):e5.
16. Conway JD. Autograft and nonunions: morbidity with the intramedullary bone graft versus iliac crest bone graft. Orthop Clin North Am. 2010;41(1):75–84.
17. Lund EA, Samtani R, Winston M, Anderson PA, Whiting PS, O'Toole RV, Hetzel S, Doro CJ. Association of Perioperative Computed Tomography Hounsfield Units and Failure of femoral neck fracture fixation. J Orthop Trauma. 2020;34(12):632–8.
18. McClung M, Harris ST, Miller PD, Kendler DL, Yuen CK, Lewiecki EM. Bisphosphonate therapy for osteoporosis: benefits, risks and drug holiday. Am J of Med. 2012;126(1):13–20.
19. Williams DGA, Molinger J, Wischmeyer PE. The malnourished surgery patient: a silent epidemic in perioperative outcomes? Curr Opin Anaesthesiol. 2019;32(3):405–11.
20. Conway JD. Osteomyelitis and Infected Nonunions. In: Rozbruch SR, Ilizarov S, editors. Limb Lengthening and Reconstructive Surgery. USA: Informa Healthcare; 2007.
21. Thonse R, Conway JD. Antibiotic cement coated nails for the treatment of infected nonunions and segmental bone defects. J Bone Joint Surg Am. 2008;90(Suppl 4):163–74.
22. Ferguson JY, Dudareva M, Riley ND, Stubbs D, Atkins BL, McNally M. The use of a biodegradable antibiotic-loaded calcium sulphate carrier containing tobramycin for the treatment of chronic osteomyelitis. Bone Joint J. 2014;96:829–36.
23. Finkler ES, Kasia C, Kroin E, Davidson-Bell V, Schiff AP, Pinzur MS. Pin tract infection following correction of Charcot foot with static circular fixation. Foot Ankle Int. 2015;36(11):1310–5.
24. Paley D. Problems, obstacles, and complications of limb lengthening by the Ilizarov technique. Clin Orthop Relat Res. 1990;250:81–104.
25. Siddiqui NA, LaPorta GA. Midfoot Charcot reconstruction. Clin Podiatr Med Surg. 2018;35(4):509–20.
26. Lamm BM, Siddiqui NA, Nair AK, LaPorta G. Intramedullary foot fixation for midfoot Charcot neuroarthropathy. J Foot Ankle Surg. 2012;51(4):531–6.
27. Thonse R, Conway J. Antibiotic cement-coated interlocking nail for the treatment of infected nonunions and segmental bone defects. J Orthop Trauma. 2007;21(4):258–68.
28. Patzakis MJ, Zalavras CG. Chronic posttraumatic osteomyelitis and infected nonunion of the tibia: current management concepts. J Am Acad Orthop Surg. 2005;13(6):417–27.
29. Koller A. Internal pedal amputations. Clin Podiatr Med Surg. 2008;25(4):641–53.
30. Lopez-Capdevila L, Rios-Ruh JM, Fortuño J, Costa AE, Santamaria-Fumas A, Dominguez-Sevilla A, Sales-Perez M. Diabetic ankle fracture complications: a meta-analysis. Foot Ankle Surg. 2021;27(7):832–7.
31. Gougoulias N, Oshba H, Dimitroulias A, Sakellariou A, Wee A. Ankle fractures in diabetic patients. EFORT Open Rev. 2020;5(8):457–63. https://doi.org/10.1302/2058-5241.5.200025.

36

Establishing and Running an Amputee Support Group to Empower Your Patients

Firras Garada and Holly Shan

Introduction

In the USA, there are approximately two million people living with limb loss currently, with an estimated 180,000 new amputees added annually [1]. Of those amputees, approximately 30% are currently suffering from anxiety, depression, or a combination of the two disorders [1]. In fact, some of the most common reactions toward amputations are feelings of isolation, denial, and loneliness. These feelings can continue long after an amputation, even if an amputee's loved ones are offering emotional support [2]. Anxiety and depression have been linked to numerous health problems, including headaches, heart disease, high blood pressure, stroke, sleep problems, weight gain/loss, memory impairment, and suicide [3]. As behavioral medicine continues to evolve, we now understand a combination of pharmaceutical and cognitive therapy works best to treat anxiety and depression. Understanding this, the authors of this chapter strongly believe amputee support groups are a key component in the acceptance of the trauma associated with losing a limb. Accepting this trauma will ultimately lead to more favorable metal health outcomes.

Importance of Support After Amputation

Injuries resulting in amputation is a major health burden on medical services and families of amputees. Some amputees view their limb loss as body distortion which leads to decreased self-esteem and believe that they are an incomplete human [4]. Limb loss also leads to lifestyle changes that often leave individuals unable to care for themselves which may prompt further psychiatric disorders in addition to physical adjustments.

Psychiatric comorbidities include depression in up to 30–70% of amputees, suicidality in 30%, and posttraumatic stress disorder (PTSD) in up to 20% in some studies [5].

Thus, it is imperative that we create a community where amputees can confide their feelings to others experiencing similar struggles. Support groups can provide resources, connect amputees, and be a stable source of information for amputees.

F. Garada
Department of Plastic and Reconstructive Surgery, Georgetown Medstar University Hospital, Washington, DC, USA
e-mail: firras.s.garada@medstar.net

H. Shan (✉)
Georgetown University School of Medicine, Washington, DC, USA
e-mail: hs730@georgetown.edu

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_36

The Amputee Coalition

In 1986, the Amputee Coalition was founded when "a small amount of amputee support group leaders recognized the need for an organization dedicated to the needs of people with limb loss, their families and healthcare providers" [6]. They are the leading Amputee Coalition in the USA that works to create guidelines and give structure to amputee support groups around the country. The Amputee Coalition has three key tenets that they believe should be incorporated into any amputee support group. These tenets are as follows [7]:

1. Limb loss is not uncommon and becoming less uncommon every day.
2. No amputee alone.
3. Living well with limb loss.

Understanding and teaching these tenets to amputees should be a keystone in therapy.

Since 1986 the Amputee Coalition has made significant strides in supporting amputees. In 2010, the Amputee Coalition convened the first Limb Loss Task Force Summit with the goal of improving amputee care and reducing limb loss in America [8]. In 2012, the Amputee Coalition was able to get a letter from the President of the United States recognizing April as National Limb Loss Awareness Month. The Amputee Coalition has also fought to have revisions to state and federal insurance laws to help cover prosthetic devices, having been successful in 20 states.

The Power of Peer Support

Healing from an amputation takes time. However, time alone is not enough [9]. There are amputees that recover from their amputations physically, but emotionally are not able to get back to who they were. This is where the power of peer support can come in.

It is well documented that support from peers in the wake of a life-altering event, like an amputation, is an invaluable part of the recovery process [9]. Since 1935, Alcoholics Anonymous has demonstrated the power and importance of peer support to help with the recovery process. Peer support can come in the form of a support group, or a visit from a trained individual. Immediately before or after amputation, peer support is essential. Hearing stories from fellow amputees has the potential to reach an individual on a level that no friend, family, or professional can while jump starting their transition into their new life.

Support groups are a form of peer support that allow individuals to find "others like me." Any time a group of individuals come together around a shared life experience, there is already a "common ground" connection noted between them. This understanding and connection allow for the opportunity to reestablish a sense of belonging to a community. Being able to mirror other amputees allows for another opportunity to come to terms with the limb loss and helps with the acceptance of losing a limb.

Establishing Your Own Amputee Support Group

In the twenty-first century, there are a multitude of ways to go about forming a group of like-minded individuals for support. Most commonly are through social media sites, such as Facebook, Discord, YouTube, Zoom and Teams. Also, groups can be created in person—the more common places are within libraries or churches, as both have been strong bulwarks of community. Advertising a group in a wound center where patients seeing the same physicians can gather can provide a great way for amputees to have common topics to discuss. The draw of online groups is that they can be far-reaching and need not be limited to only a singular geographic location. Zheng et al. presented strong evidence that online support groups are very popular. It was shown that almost 67% of US citizens alone used the popular social media site Facebook, and 1 in 7.7 people worldwide have an active Facebook account. It was also shown that having a group composed of like-minded individuals in which

National Suicide Prevention Hotline	1-800-273-8255
Substance Abuse and Mental Health Services National Hotline	1-800-662-4357
Nacional de Prevencion del Suicidio	1-888-628-9454
Crisis Text Line	Text"Home" to 741741

Fig. 36.1 Useful resources for group members

people can share their innermost thoughts, fears, and concerns about their medical health led to overall better physical and mental health outcomes [10].

After deciding whether you want to create a virtual or physical support group, one should survey their members to determine what interests they have. Some popular interests that are discussed in meetings include prosthetic issues, medical issues, daily living issues, sports and recreational issues, emotional issues, and legal issues [11]. It is also recommended to make sure to set aside time to discuss more positive and "fun" topics like humorous experiences of the attendees, pets, jobs, hobbies, and vacations.

As a support group leader there are important components to therapy that you should be able to provide for your group. These include [9]:

1. Providing a safe environment for your group.
2. Assisting group members with goals and objectives.
3. Providing educational information and referrals.
4. Avoiding giving advice on how to solve problems and instead facilitate the discussion and resolution of problems.

As a leader, you should recognize when your members' emotional states appear different than normal. Dealing with feelings of limb loss can affect everyone differently. A leader's job is not to diagnose psychiatric disorders, but to recognize signs of anxiety, depression, and suicidal ideation to ensure group members get proper referrals to assist them. Creating an atmosphere where members are encouraged to share feelings freely and confide in each other about their feelings is essential for the group's success (Fig. 36.1).

References

1. "15 limb loss statistics that may surprise you." Access Prosthetics, 1 Mar 2019. https://accessprosthetics.com/15-limb-loss-statistics-may-surprise/
2. A.B.L.E.: Benefits of Joining an Amputee Support Group. https://www.hortonsoandp.com/a-b-l-e-benefits-of-joining-an-amputee-support-group/
3. Mofatteh M. Risk factors associated with stress, anxiety, and depression among university undergraduate students. AIMS Public Health. 2020;8(1):36–65. . Published 2020 Dec 25. https://doi.org/10.3934/publichealth.2021004.
4. Mall CP, Trivedi JK, Mishra US, et al. Psychiatric sequelae of amputation. I: Immediate effects. Indian J Psychiatry. 1997;39:313–7.
5. Sahu A, Gupta R, Sagar S, Kumar M, Sagar R. A study of psychiatric comorbidity after traumatic limb amputation: a neglected entity. Ind Psychiatry J. 2017;26(2):228–32. https://doi.org/10.4103/ipj.ipj_80_16.
6. Nathan EP, Winkler SL. Amputees' attitudes toward participation in amputee support groups and the role of virtual Technology in Supporting Amputees: survey study. JMIR Rehabil Assist Technol. 2019;6(2):14887. . Published 2019 Aug 29. https://doi.org/10.2196/14887.
7. "Mission & Goals." Amputee Coalition, 10 Jan 2019, https://www.amputee-coalition.org/about-us/mission-goals/
8. "Mission & Goals." Amputee Coalition, 10 Jan. 2019, https://www.amputee-coalition.org/about-us/impact/
9. Support Group Manual—Amputee Coalition of America. https://www.amputee-coalition.org/wp-content/uploads/2015/01/lsp_support-group-manual_090115-065319.pdf

10. Zhang Y, He D, Sang Y. Facebook as a platform for health information and communication: a case study of a diabetes group. J Med Syst. 2013;37(3):9942. https://doi.org/10.1007/s10916-013-9942-7. Epub 2013 Apr 16

11. "U-CAN amputee support group: physical medicine and rehabilitation: Michigan medicine." Physical Medicine and Rehabilitation, 12 Jan 2022, https://medicine.umich.edu/dept/pmr/patient-care/therapeutic-other-services/orthotics-prosthetics/u-can-amputee-support-group

37 Analyzing the Population Dynamics of Limb Salvage

Kevin G. Kim, Paige K. Dekker, and Kenneth L. Fan

Introduction

An estimated 1–2% of the USA population will suffer from a chronic wound within their lifetime [1]. This may include pressure ulcers, diabetic ulcers, venous stasis ulcers, and arterial insufficiency ulcers [1]. Considering that successful wound healing is negatively correlated with age, this number is expected to increase as the American population continues to age [1, 2].

In 2017, nearly 25 million people in the USA were diagnosed with diabetes, representing 9.7% of the population [3]. In 2020, this number has increased to 34.2 million people, or just over 1 in 10 Americans [4]. Diabetic foot ulcers are estimated to affect 15–25% of diabetic patients, with 50% of these cases requiring hospitalization for serious infections [5, 6]. On risk analysis, an infected DFU increases risk of hospitalization by 55.7 times and amputation by 154.5 times, compared to non-infected DFUs [5].

K. G. Kim · P. K. Dekker
Department of Plastic Surgery, MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: kgk31@rwjms.rutgers.edu; pkd15@georgetown.edu

K. L. Fan (✉)
Department of Plastic and Reconstructive Surgery, MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: kenneth.l.fan@medstar.net

Based on emergency department discharge data from the Agency for Healthcare Research and Quality (AHRQ), over 54 million cases presenting to emergency departments between 2006 and 2010 involved a diagnosis of diabetes, representing 8.7% of all emergency department cases [7]. 1.2 million cases were due to complicated DFUs, with 81.2% of these cases requiring subsequent admission for inpatient care [7]. This represents a stark increase compared to the period between 1997 and 2007, in which 20.2 million cases involved diabetes, or just 1.7% of total emergency department cases [8]. This increase is likely related to the growing prevalence of diabetes in the USA: by 2050, the number of people in the USA with diabetes is expected to exceed 48.3 million [7, 9].

Conservative estimates reveal that annual Medicare spending on wounds exceeds $28 billion and that management of diabetic foot ulcers (DFU) accounts for over 20% of this spending [10]. DFUs not only have significant financial implications, but also carry serious morbidity and mortality. Patients with DFUs have decreased quality of life, increased psychosocial burden, and require an increased number of healthcare interactions [11]. Following amputation, mortality is estimated at over 33%, 53%, 64%, and 80% at 1, 3, 5, and 10 years, respectively [12].

While some surveys seem to suggest that rates of diabetes-related complications are trending downwards, these findings must be considered in

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_37

the context of broader population trends. One survey with data collected from 1990 to 2010 found that rates for diabetes-related complications, such as lower extremity amputation, end-stage renal disease, myocardial infection, stroke, and death, were on the decline. Importantly, the same period saw two- and three-fold increases in the incidence and prevalence of diabetes, respectively [13–15]. Lower complication rates applied to populations with higher prevalence of diabetes can lead to an overall decreased complication burden, and this has been the case with several diabetes-related complications. Annual rates of lower extremity amputations in diabetics, for example, decreased by 50% between 1990 and 2010; however, the same period witnessed an increase of more than 20,000 diabetic persons requiring amputation per year [13].

Data from the National Inpatient Sample (NIS) estimates that non-traumatic lower extremity amputation rates in diabetic patients declined by 43% between 2000 and 2009 but further data analysis demonstrated that the amputation rate changed course between 2009 and 2015. During this time, the non-traumatic lower extremity amputation rate increased by 50% to 4.62 per 1000 adults, with rates most pronounced in young and middle-aged adults [16]. This was largely driven by a significant increase in minor amputations, which increased by 62% in this time period, but it is of note that major amputations also increased in this period [16]. We should expect amputation rates to continue to rise in this population: in the USA, an estimated 1.6 million people underwent amputation in 2005 and this number is projected to more than double to 3.6 million by 2050 [17].

Disparities Faced by the Diabetic Foot Population

The development of diabetic foot complications is complex and multi-factorial, often with devastating consequences despite timely recognition and treatment. Unfortunately, the prevalence and distribution of DFUs and its complications are inequitable among its patient population. These disparities may lead to delay in care, loss to follow-up, and ultimately increased rates of amputation.

Geographical Location

A large study found that the majority of complicated diabetic foot cases presenting to emergency departments occurred in the Southern region (36.3%) of the USA, compared to the Northeast (22.9%), Midwest (22.1%), and West (18.6%). Using the Northeast as a point of reference, the relative risk (RR) of major amputation was significantly higher in the South (RR = 1.210) and the West (RR = 1.384) (Fig. 37.1) [7, 18].

Data suggests that patients treated in rural areas may be at increased risk of negative outcomes compared to their urban counterparts. Residing in a rural area is associated with a significantly increased risk of major amputation (RR = 1.513), minor amputation (RR = 1.149), and death during hospital admission (RR = 1.414) [7]. Diabetic black patients who are treated in rural areas may have amputation rates 9 times higher than those treated in urban areas [19]. This mirrors our institution's findings, where access to urban teaching hospitals was predictive of access to advance limb salvage modalities and decreased loss to follow-up [20, 21].

Access to Care

Differences in access to adequate care have a significant effect on health outcomes in the diabetic foot population. In a study encompassing over 155,000 admissions utilizing National Inpatient Survey (NIS) data, it was determined that access to urban teaching hospitals was the strongest protective factor against amputation, decreasing risk by 9% ($p < 0.01$) [21]. Furthermore, patients were significantly more likely to undergo limb salvage, whether with or without free flap reconstruction, when treated in an urban teaching hospital [21]. Physical proximity to any limb salvage center is important for longitudinal care; increased driving distance sig-

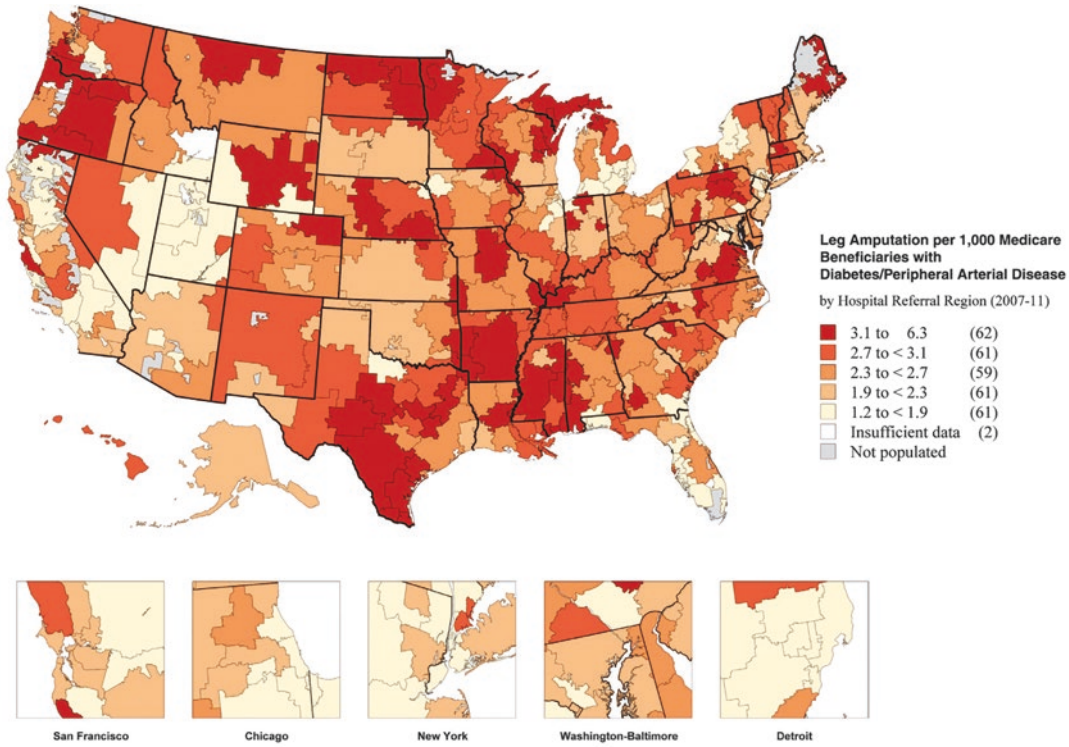


Fig. 37.1 Geographical portrayal of leg amputations per 1000 Medicare beneficiaries with diabetes and peripheral arterial disease (2007–2011). Rates adjusted for age, sex, and race. (Reproduced with permission from Goodney et al. [18])

nificantly increases odds of loss to follow-up in the limb salvage population (distance >20 miles; Odds Ratio = 2.95, $p = 0.045$), demonstrating the need for decentralized specialty care models [20]. Such models were proposed by Ibrahim et al. whereby patients requiring expertise within a given specialty can obtain expert care at smaller, regional facilities as opposed to having to travel to flagship, centralized institutions [22]. Through specialty care decentralization, healthcare networks can standardize evidence-based specialty care, increase healthcare access to patients, and streamline the patient care process. This can be accomplished through establishing treatment pathways, investing in regional facility infrastructure, and optimizing care coordination via health navigators and telehealth [22]. This is perhaps exemplified by the recent COVID-19 pandemic, in which access to care via telemedicine was dramatically increased in a relatively minute amount of time. In an institutional study, we determined that the increase in telemedicine, as a result of the COVID-19 pandemic, had a dramatic effect on the type of patients lost to follow-up at our wound center. Before the pandemic, Social Vulnerability Index (SVI), which incorporates factors such as transportation, housing, and socioeconomic status, was predictive of loss to follow-up [23, 24]. After telemedicine was incorporated, SVI was no longer predictive of loss to follow-up. Although its infrastructure and care pathways may be underdeveloped, telemedicine and remote technologies may offer solutions to disparities in access to care, especially for the diabetic foot population [23].

Race and Ethnicity

Diabetes disproportionately affects minority populations, with a prevalence that is significantly higher in Hispanic (22.1%), non-Hispanic black (20.4%), and Asian adults (19.1%) compared to non-Hispanic white adults (12.1%) ($p < 0.001$) [25]. These minority populations are also significantly more likely to have undiagnosed diabetes (Hispanic, 7.5%; Asian, 7.5%; non-Hispanic black, 5.2%; non-Hispanic white, 3.9%; $p < 0.001$) [25]. These disparities continue to be reflected in the number of diabetes-related emergency department visits. Both black race (OR = 1.8) and Hispanic ethnicity (OR = 1.6) carry significantly higher odds of having a diabetes-related visit [8].

These racial disparities persist with respect to risk of amputation. Both black (Hazards Ratio (HR) = 1.9) and Native American (HR = 1.8) patients have significantly increased risk of major amputation for DFUs or infection [26]. Black (OR = 2.9) and Native American (OR = 2.4) patients with peripheral arterial disease (PAD) also have significantly increased rates of major amputation compared to white patients [19]. Black patients who have undergone amputation are also less likely to have undergone revascularization, wound debridement, or hospital admission prior to amputation when compared to white patients who have undergone amputation [19].

Although race and ethnicity have been utilized as proxies for socioeconomic status, analysis of patients with PAD demonstrates that minority populations face significantly higher amputation rates, regardless of socioeconomic stratum [27]. Healthcare disparities facing minority populations is certainly multi-factorial, stemming from socioeconomic gaps, comorbidity burden, and physical access to healthcare facilities. Nonetheless, this increased risk of major amputation for DFUs in minority populations has been maintained on statistical analysis adjusting for sociodemographic and comorbidity confounders [26].

Socioeconomic Status

In patients with DFUs, the risk of major amputation significantly increases as income level decreases. Compared to the highest income quartile, the relative risk of major amputation for the third, second, and first quartiles is 1.152, 1.317, and 1.385, respectively [7]. Regardless of whether the patient has Medicare, Medicare, private insurance, or is uninsured, odds of amputation decreases from lowest quartile of median household income to the highest quartile [28]. Furthermore, beneficiaries of Medicaid and patients without insurance are significantly more likely to undergo major amputation [7, 26, 28]. Inpatient mortality appears to be less influenced by socioeconomic status [7, 28]. The reasons for these discrepancies in amputation rates across income levels remain unclear but may be due to selection bias secondary to insurance type, more severe disease, or delayed presentation [28].

When accounting for geographic factors using the area deprivation index (ADI), a study by Zhang et al. determined that geographic socioeconomic disadvantage is associated with both short-term and long-term outcomes following minor amputation in Maryland [29]. For example, patients considered the most deprived (ADI4) have 1.40 greater odds of reamputation compared to patients who are considered the least deprived (ADI1) [29].

Level of education also appears to play a role in lower extremity amputation rates and outcomes. A small, single-center study involving patients with major amputation(s) determined that over 50% of the studied cohort had a high school level education or less [30]. Furthermore, survival at five years is significantly higher for patients who have completed high school versus those who have not (OR 0.377) [31]. Lack of advanced education may result in decreased health literacy, which increases susceptibility to chronic disease, poor self-reported outcomes, and mortality [31].

Comorbidities

Patients with diabetes or previous foot ulcerations are susceptible to the development of new or recurrent ulcers [3]. Among patients who present to an emergency department with a DFU, certain underlying comorbidities are associated with significantly increased risk of major amputation. These include peripheral vascular disease (RR = 3.016), renal disease (RR = 1.281), and sepsis (RR = 3.875) [7]. It is estimated that roughly 50% of patients with DFUs have concomitant peripheral vascular disease [19]. Of the nearly 100,000 major lower extremity amputations performed in the USA annually, over half are attributable to diabetes and peripheral arterial disease [19].

The Multidisciplinary Limb Salvage Team

Achieving success in management of chronic wounds and amputation reduction is complex and multi-dimensional. The holistic approach required for successful chronic wound care has evolved into today's multidisciplinary limb salvage team. Although there is lack of consensus on team composition, wound care teams are often led by a core group of plastic surgeons, vascular surgeons, and podiatric/orthopedic surgeons [32]. Surrounding this group are other essential specialists, such as family medicine, endocrinology, hyperbaric medicine, and nurse practitioners [32]. In a study examining 27 multidisciplinary diabetic foot teams, 36 different disciplines were identified, with an average of five physician disciplines per team [33]. The most common surgical specialties were vascular surgery (74%), orthopedic surgery (67%), podiatry (52%), and plastic surgery (44%) [33]. The most common non-surgical specialties were endocrinology (82%), infectious disease (37%), general medicine (30%), and physical medicine and rehabilitation (22%) [33].

Single-center studies began reporting improved outcomes and cost savings achieved using a multidisciplinary approach to chronic wounds [32, 34]. Joret et al. reported a 25% total cost savings per wound care episode with the implementation of a multidisciplinary team to treat diabetic foot patients [35]. Subsequent studies have further supported the improved patient outcomes made possible by utilizing a multidisciplinary approach. A systematic review by Musuuza et al., for example, demonstrated that 94% of studies involving a multidisciplinary approach to care reported decreased amputation rates in patients with DFUs [33]. Although team composition greatly varied between studies, the authors cited efficient care algorithms and clear rereferral pathways as a unifying theme underlying success [33].

The multidisciplinary approach to the management of DFUs has revolutionized diabetic foot care and is now the gold standard. Expertise spanning across a variety of disciplines has resulted in reduced rates of amputation, improved wound healing, decreased lengths of stay, and less frequent recurrence of lesions [3]. As the literature continues to report the objective benefits of a multidisciplinary team, this approach has witnessed increased standardization and widespread use. For example, a practice guideline for the management of diabetic foot co-sponsored by the Society for Vascular Surgery, the American Podiatric Medical Association, and the Society for Vascular Medicine centers on an evidence-based multidisciplinary team approach [36]. These guidelines have evolved to include biomechanical offloading, various wound therapies, and surgical management requiring involvement of specialists across a multitude of specialties to adequately prevent and treat DFUs [36].

Studies utilizing large data-sets from the NIS have demonstrated that DFU patients are more likely to avoid amputation and undergo advanced limb salvage therapies when treated at an urban teaching hospital [21, 37]. A large underlying reason for this benefit is likely the access to

advanced surgical modalities available within academic centers, which house the necessary infrastructure and technology for a functioning multidisciplinary limb salvage team [21]. Within these centers, multidisciplinary teams are able to provide streamlined care, from preoperative management to postoperative wound care, that has enabled them to achieve remarkable limb salvage and ambulation rates [21]. When competition within hospital markets was accounted for, the protective factor for urban academic hospitals was removed, indicating regional competition may spur funding for advanced limb salvage capabilities [38]. Considering the complex technological and surgical skill associated with vascular intervention and free flap reconstruction, these surgical modalities may be limited to urban academic centers that not only have the infrastructure and finances to support this limb salvage option, but are incentivized to invest in it [38]. Further investigation into the role of infrastructure and institutional centrality of a multidisciplinary team would be of value.

The Future of Multidisciplinary Care

A Global Context

As previously discussed, the diabetic foot population in the USA faces a multitude of disparities, limiting access to care and manifesting as suboptimal medical outcomes. A large wage gap and inequitable distribution of low-quality insurance continue to remain a barrier to care for many patients. The Affordable Care Act largely expanded access to health insurance coverage but not without its challenges and criticisms [39, 40]. On balance, however, the Affordable Care Act has achieved positive gains in insuring minorities and reducing amputations [41, 42]. Future study needs to examine interventional approaches to disparity and amputation reduction.

It is perhaps worthwhile to examine the structure of healthcare systems in other countries to provide insight for the refinement of our own healthcare system. For example, the Netherlands has become a well-praised case of large-scale reform that has resulted in improved population health and superior mortality rates, compared to the remainder of the European Union [43]. Largely reformed in 2006, the Dutch healthcare system relies heavily on widely available primary care providers, well-developed tertiary care infrastructure, and privatized not-for-profit insurance coverage for inpatient care [43]. This, in theory, has created an expansive net to catch patients requiring specialized care, leading to reduced loss to follow-up and expedited care. In the management of DFUs, timely and available care is paramount. In fact, the Netherlands has witnessed a reduction in diabetes-related lower extremity amputations over the last several decades, decreasing from 5.5 per 1000 in 1991 to 0.8 per 1000 diabetic adults in 2011 [44, 45].

Although national legislative change regarding healthcare is a seemingly immense task, efforts to create a regional or statewide model are perhaps within reach. Many multidisciplinary limb salvage centers have emerged throughout the USA. However, despite providing expert care in the management of diabetic foot ulcers, many of these centers lack efficient and reliable referral pathways to ensure patients are treated in a timely manner and not lost to follow-up. Additional resources dedicated to creating regional limb salvage systems and screening centers may serve as a valuable focus for future health policy research.

Care Delivery Optimization

The treatment of DFUs requires a significant amount of medical and financial resources. In developed countries, the cost of amputation can range between $35,000 and $45,000, and in general, the cost of amputation in the USA is higher than that in European countries [46]. There are multiple factors affecting total cost per care episode. One of the largest underlying factors determining cost is the degree of management needed to adequately treat a DFU. One study found a significant increase in cost of admission correlating with progression of intervention: ~$4800 for primary healing, ~$13,500 for single minor

amputation, ~$31,800 for multiple minor amputations, and ~$73,800 for minor amputation necessitating major amputation ($p < 0.001$) [47]. Severity of patient presentation can also significantly affect cost of care. Increasing Society for Vascular Surgery Wound, Ischemia, and foot Infection (WIfI) score has been demonstrated to correlate with increased healing time, more surgical procedures, and increased cost of care [48]. Specifically, the total cost per wound care episode for Stage 1 wounds is ~$4000, which increases to ~$50,500 for Stage 4 wounds ($p < 0.001$) [48]. More complex procedures and increased lengths of stay are inherently related to increased costs [49].

The multidisciplinary limb salvage team is in a unique position to optimize care delivery and decrease the financial burden of diabetic foot management. In the outpatient setting, a well-organized multidisciplinary team with good communication and clear referral pathways can expedite the diagnosis of chronic wounds and provide proper treatment depending on severity. An outpatient multidisciplinary diagnosis and management model has already been shown to decrease hospitalization time, department transfer time, delay in undergoing surgery, and hospital length of stay [50]. As a result, total cost per care episode was significantly decreased [50]. Similarly, efficient clinical pathways and multidisciplinary treatment algorithms have decreased length of stay, amputation rates, and complication rates in the inpatient setting [49, 51]. The proportion of total costs attributed to inpatient care can double when escalating from primary wound care to amputation [49]; thus, a multidisciplinary outpatient approach aiming to reduce progression in severity of DFUs should be a priority.

Despite the multitude of studies demonstrating the clinical and financial superiority of the multidisciplinary limb salvage team, consensus on organization and structure is lacking. For example, team composition usually involves vascular surgery, plastic surgery, or podiatry/orthopedic surgery; however, it is otherwise highly variable between institutions [32, 33]. Limb salvage teams also rely on clear referral pathways and interdisciplinary optimization; in the USA, these resource-intensive teams are often organized and deployed without much evidence-based strategy or understanding [32, 34, 52–54]. The field is in need of standardized methods by which team organization and distribution are optimized for increased referrals and efficient patient care. Other healthcare systems have successfully implemented limb salvage teams with clear organization. In the UK, nearly 90% of primary care physicians have an identifiable limb salvage center they are able to refer patients to; 85% of the time, these centers are within 12 miles [55]. As a result, the rate of late referrals (>3 months) for DFU patients is less than 10% in the UK [56].

Collaborative Initiatives

National patient databases, such as the National Surgical Quality Improvement Program (NSQIP) from the American College of Surgeons (ACS) and the Nationwide Inpatient Sample (NIS) from the Healthcare Cost and Utilization Project (HCUP), have been instrumental in outcomes research, allowing large-scale analysis of outcomes following limb salvage and amputation. However, there are limitations in their applicability to limb salvage research. For example, both NSQIP and NIS do not capture wound characteristics or specific location of treatment, which are details often needed to properly assess clinical outcomes. Furthermore, the two databases are limited to short-term outcomes data and lack itemized cost-of-stays, which limits comprehensive analysis [57].

Collaborative quality initiatives are discipline-specific registries that aim to collect carefully curated quality measures to improve quality care [58]. These registries involve collaboration between multiple institutions, often sharing a geographic region, and collect data in a non-judgmental and non-punitive manner (Fig. 37.2) [58]. Already, collaborative initiatives have been established for other specialties, such as colorectal surgery, vascular surgery, and obstetrics and gynecology, resulting in improved outcomes and significant cost savings [58–61]. Such an endeavor within the realm of limb salvage may illuminate



Fig. 37.2 Collaborative initiatives are built upon institutions and providers sharing data, protocols, and strategies within an open forum to build and assess discipline-specific quality measures

areas in need of reform and improve both surgical and patient-centered outcomes for the chronic wound population. The US Wound Registry© is a Qualified Clinical Data Registry that collects deidentified patient records, specifically for wound care [62, 63]. Through their collective database, the organization acts in many ways similar to a collaborative initiative. For a fee, providers are able to access the database, contribute patient data, compare their benchmarks against those of other providers, and utilize quality measures specific to wound care already approved by the Centers for Medicare and Medicaid Services (CMS) [64]. In doing so, providers are able to avoid penalties imposed by the Merit-based Incentive Payment System (MIPS) in addition to improving quality care in their practice [64]. Collaborative initiatives may represent the next horizon of quality care in limb salvage.

Conclusion

The multidisciplinary limb salvage team has revolutionized medical care for the diabetic foot population. However, the discipline continues to face many hurdles that can only be overcome with careful systems-level examination, quality reform, and care delivery optimization. As the field continues to improve, chronic wound patients may bear witness to decreased amputation rates, improved postoperative function, and decreased financial burden.

Financial Disclosure Statement The authors have no financial disclosures, commercial associations, or any other conditions posing a conflict of interest to report.

References

1. Järbrink K, Ni G, Sönnergren H, Schmidtchen A, Pang C, Bajpai R, et al. Prevalence and incidence of chronic wounds and related complications: a protocol for a systematic review. Syst Rev. 2016;5(1):152.
2. Wicke C, Bachinger A, Coerper S, Beckert S, Witte MB, Königsrainer A. Aging influences wound healing in patients with chronic lower extremity wounds treated in a specialized wound care center. Wound Repair Regen. 2009;17(1):25–33. Available from: https://pubmed.ncbi.nlm.nih.gov/19152648/
3. Lavery LA, Oz OK, Bhavan K, Wukich DK. Diabetic foot syndrome in the twenty-first century. Clin Podiatr Med Surg. 2019;36(3):355–9. Available from: https://pubmed.ncbi.nlm.nih.gov/31079602/
4. CDC. National Diabetes Statistics Report 2020. Estimates of diabetes and its burden in the United States. Atlanta, GA; 2020.
5. Lavery LA, Armstrong DG, Wunderlich RP, Mohler MJ, Wendel CS, Lipsky BA. Risk factors for foot infections in individuals with diabetes. Diabetes Care. 2006;29(6):1288–93. Available from: https://pubmed.ncbi.nlm.nih.gov/16732010/
6. Lavery LA, Davis KE, Berriman SJ, Braun L, Nichols A, Kim PJ, et al. WHS guidelines update: diabetic foot ulcer treatment guidelines. Wound Repair Regen. 2016;24(1):112–26. Available from: http://www.acc.org/clinical/
7. Skrepnek GH, Mills JL, Armstrong DG. A Diabetic Emergency One Million Feet Long: Disparities and Burdens of Illness among Diabetic Foot Ulcer Cases within Emergency Departments in the United States, 2006–2010. Taheri S, editor. PLoS One. 2015;10(8):e0134914. https://doi.org/10.1371/journal.pone.0134914.
8. Menchine MD, Wiechmann W, Peters AL, Arora S. Trends in diabetes-related visits to US EDs from 1997 to 2007. Am J Emerg Med. 2012;30(5):754–8.
9. Deshpande AD, Harris-Hayes M, Schootman M. Epidemiology of diabetes and diabetes-related complications. Phys Ther. 2008;88:1254–64. Available from: https://pubmed.ncbi.nlm.nih.gov/18801858/
10. Nussbaum SR, Carter MJ, Fife CE, DaVanzo J, Haught R, Nusgart M, et al. An Economic Evaluation of the Impact, Cost, and Medicare Policy Implications of Chronic Nonhealing Wounds. Value Health. 2019;21(1):27–32.
11. Everett E, Mathioudakis N. Update on management of diabetic foot ulcers. Ann N Y Acad Sci. 2018;1411(1):153–65. Available from: https://nyaspubs-onlinelibrary-wiley-com.proxy.libraries.rutgers.edu/doi/full/10.1111/nyas.13569
12. Meshkin DH, Zolper EG, Chang K, Bryant M, Bekeny JC, Evans KK, et al. Long term mortality after nontraumatic major lower extremity amputation: a systematic review and meta-analysis. J Foot Ankle Surg. 2021;60(3):567–76. Available from: http://www.jfas.org/article/S1067251620303331/fulltext
13. Baba M, Davis WA, Norman PE, TME D. Temporal changes in the prevalence and associates of diabetes-related lower extremity amputations in patients with type 2 diabetes: The Fremantle Diabetes Study. Cardiovasc Diabetol. 2015;14(1):152. Available from: https://pubmed.ncbi.nlm.nih.gov/26684912/
14. Geiss LS, Pan L, Cadwell B, Gregg EW, Benjamin SM, Engelgau MM. Changes in incidence of diabetes in U.S. adults, 1997-2003. Am J Prev Med. 2006;30(5):371–7.
15. Boyle JP, Thompson TJ, Gregg EW, Barker LE, Williamson DF. Projection of the year 2050 burden of diabetes in the US adult population: dynamic modeling of incidence, mortality, and prediabetes prevalence. Popul Health Metr. 2010;8(1):29. Available from: http://pophealthmetrics.biomedcentral.com/articles/10.1186/1478-7954-8-29
16. Geiss LS, Li Y, Hora I, Albright A, Rolka D, Gregg EW. Resurgence of diabetes-related nontraumatic lower-extremity amputation in the young and middle-aged adult U.S. Population Diabetes Care. 2019;42(1):50–4. https://doi.org/10.2337/dc18-1380.
17. Varma P, Stineman MG, Dillingham TR. Epidemiology of limb loss. Phys Med Rehabil Clin N Am. 2014;25:1–8. Available from: https://pubmed.ncbi.nlm.nih.gov/24287235/
18. Goodney PP, Dzebisashvili N, Goodman DC, Bronner KK. Variation in the Care of Surgical Conditions: diabetes and peripheral arterial disease. Lebanon, NH: The Dartmouth Institute for Health Policy and Clinical Practice; 2014.
19. Barnes JA, Eid MA, Creager MA, Goodney PP. Epidemiology and risk of amputation in patients with diabetes mellitus and peripheral artery disease. Arterioscler Thromb Vasc Biol. 2020;40(8):1808–17. Available from: https://pubmed.ncbi.nlm.nih.gov/32580632/
20. Sharif-Askary B, Zolper EG, Deldar R, Tefera E, Tirrell AR, Abu El Hawa AA, et al. Risk Factors for Loss to Follow-Up in the Lower Extremity Limb Salvage Population. Plast Reconstr Surg. 148(4):883–93.
21. Fan KL, Delia D, Black CK, Zolper E, Singh T, Wirth P, et al. Who, what, where: demographics, severity of presentation, and location of treatment drive delivery of diabetic limb reconstructive services within the National Inpatient Sample. Plast Reconstr Surg. 2020;145(6):1516–27. Available from: https://pubmed.ncbi.nlm.nih.gov/32205544/
22. Ibrahim AM, Dimick JB. Redesigning the delivery of specialty care within newly formed hospital networks. NEJM Catalyst. 2017; https://catalyst.nejm.org/doi/abs/10.1056/CAT.17.0503 Acccessed May 8 2023.
23. Dekker PK, Bhardwaj P, Singh T, Bekeny JC, Kim KG, Steinberg JS, et al. Telemedicine in the Wake of the COVID-19 Global Pandemic. Plast Reconstr Surg—Glob Open. 2020;9(1):e3228.

24. CDC SVI Fact Sheet|Place and Health|ATSDR [Internet]. cited 2021 Jan 25]. Available from: https://www.atsdr.cdc.gov/placeandhealth/svi/fact_sheet/fact_sheet.html
25. Cheng YJ, Kanaya AM, Araneta MRG, Saydah SH, Kahn HS, Gregg EW, et al. Prevalence of diabetes by race and ethnicity in the United States, 2011–2016. J Am Med Assoc. 2019;322(24):2389–98. Available from: https://pubmed.ncbi.nlm.nih.gov/31860047/
26. Tan TW, Armstrong DG, Concha-Moore KC, Marrero DG, Zhou W, Calhoun E, et al. Association between race/ethnicity and the risk of amputation of lower extremities among medicare beneficiaries with diabetic foot ulcers and diabetic foot infections. BMJ Open Diabetes Res Care. 2020;8(1):e001328. Available from: https://pubmed.ncbi.nlm.nih.gov/32843499/
27. Arya S, Binney Z, Khakharia A, Brewster LP, Goodney P, Patzer R, et al. Race and socioeconomic status independently affect risk of major amputation in peripheral artery disease. J Am Heart Assoc. 2018;7(2):e007425. Available from: https://pubmed.ncbi.nlm.nih.gov/29330260/
28. Hughes K, Mota L, Nunez M, Sehgal N, Ortega G. The effect of income and insurance on the likelihood of major leg amputation. J Vasc Surg. 2019;70(2):580–7.
29. Zhang GQ, Canner JK, Haut E, Sherman RL, Abularrage CJ, Hicks CW. Impact of Geographic Socioeconomic Disadvantage on Minor Amputation Outcomes in Patients With Diabetes. J Surg Res. 2021;258:38–46. Available from: www.sciencedirect.com
30. Chernev I, Chernev A. Education Level Among Patients with Major Limb Amputation. Cureus. 2020;12(4):e7673. Available from: https://pubmed.ncbi.nlm.nih.gov/32426185/
31. Corey MR, St. Julien J, Miller C, Fisher B, Cederstrand SL, Nylander WA, et al. Patient education level affects functionality and long term mortality after major lower extremity amputation. Am J Surg. 2012;204(5):626–30. Available from: https://pubmed.ncbi.nlm.nih.gov/22906244/
32. Kim PJ, Attinger CE, Steinberg JS, Evans KK, Akbari C, Mitnick CDB, et al. Building a multidisciplinary hospital-based wound care center: nuts and bolts. Plast Reconstr Surg. 2016;138(3):241S–7S.
33. Musuuza J, Sutherland BL, Kurter S, Balasubramanian P, Bartels CM, Brennan MB. A systematic review of multidisciplinary teams to reduce major amputations for patients with diabetic foot ulcers. J Vascular Surg. 2020;71:1433–1446.e3.
34. Sinkin JC, Reilly M, Cralley A, Kim PJ, Steinberg JS, Cooper P, et al. Multidisciplinary approach to soft-tissue reconstruction of the diabetic Charcot foot. Plast Reconstr Surg. 2015;135(2):611–6.
35. Joret MO, Osman K, Dean A, Cao C, van der Werf B, Bhamidipaty V. Multidisciplinary clinics reduce treatment costs and improve patient outcomes in diabetic foot disease. J Vasc Surg. 2019;70(3):806–14.
36. Hingorani A, Lamuraglia GM, Henke P, Meissner MH, Loretz L, Zinszer KM, et al. The management of diabetic foot: a clinical practice guideline by the Society for Vascular Surgery in collaboration with the American podiatric medical association and the Society for Vascular Medicine. J Vasc Surg. 2016;63(2):3S–21S. Available from: https://pubmed.ncbi.nlm.nih.gov/26804367/
37. Fan KL, Bekeny JC, Kennedy CJ, Zolper EG, Steinberg JS, Attinger CE, et al. A Focus on Amputation Level: Factors Preventing Length Preservation in the National Inpatient Sample. J Am Podiatr Med Assoc. 2022;112(1):20–028.
38. Fan KL, Singh T, Bekeny JC, Zolper EG, Attinger CE, Evans KK, et al. Use of Flap Salvage for Lower Extremity Chronic Wounds Occurs Most Often in Competitive Hospital Markets. Plast Reconstr Surg Glob Open. 9(2):e3183.
39. Ho V. Refinement of the affordable care act. Annu Rev Med. 2018;69:19–28. Available from: https://pubmed.ncbi.nlm.nih.gov/28841383/
40. McIntyre A, Song Z. The US affordable care act: reflections and directions at the close of a decade. PLoS Med. 2019;16(2):e1002752. Available from: https://pubmed.ncbi.nlm.nih.gov/30807584/
41. Diaz D. Study finds minority patients in states with Medicaid expansion experience fewer leg amputations|ADA. Chicago, Illinois: American Diabetes Association; 2020. Available from: https://www.diabetes.org/newsroom/press-releases/2020/study-finds-minority-patients-in-states-with-medicaid-expansion-experience-fewer-leg-amputations
42. Buchmueller TC, Levy HG. The ACA's impact on racial and ethnic disparities in health insurance coverage and access to care. Health Aff. 2020;39(3):395–402. Available from: https://pubmed.ncbi.nlm.nih.gov/32119625/
43. Jeurissen P, van Ginneken E. The Dutch health system in 2019: many major reforms, but still work in progress. Health Policy. 2019;123:249–51. Available from: https://pubmed.ncbi.nlm.nih.gov/30832961/
44. Carinci F, Uccioli L, Massi Benedetti M, Klazinga NS. An in-depth assessment of diabetes-related lower extremity amputation rates 2000–2013 delivered by twenty-one countries for the data collection 2015 of the Organization for Economic Cooperation and Development (OECD). Acta Diabetol. 2020;57(3):347–57. Available from: https://pubmed.ncbi.nlm.nih.gov/31605210/
45. Van Houtum WH, Rauwerda JA, Ruwaard D, Schaper NC, Bakker K. Reduction in diabetes-related lower-extremity amputations in The Netherlands: 1991–2000. Diabetes Care. 2004;27(5):1042–6. Available from : https://care.diabetesjournals.org/content/27/5/1042
46. Petrakis I, Kyriopoulos IJ, Ginis A, Athanasakis K. Losing a foot versus losing a dollar; a systematic review of cost studies in diabetic foot complications. Expert Rev Pharmacoecon Outcomes Res.

2017;17:165–80. Available from: https://pubmed.ncbi.nlm.nih.gov/28283002/
47. Rinkel WD, Luiten J, van Dongen J, Kuppens B, Van Neck JW, Polinder S, et al. In-hospital costs of diabetic foot disease treated by a multidisciplinary foot team. Diabetes Res Clin Pract. 2017;1(132):68–78.
48. Hicks CW, Canner JK, Karagozlu H, Mathioudakis N, Sherman RL, Black JH, et al. The Society for Vascular Surgery Wound, ischemia, and foot infection (WIfI) classification system correlates with cost of care for diabetic foot ulcers treated in a multidisciplinary setting. J Vasc Surg. 2018;67(5):1455–62. Available from: https://pubmed.ncbi.nlm.nih.gov/29248237/
49. Apelqvist J, Ragnarson-Tennvall G, Larsson J, Persson U. Diabetic foot ulcers in a multidisciplinary setting an economic analysis of primary healing and healing with amputation. J Intern Med. 1994;235(5):463–71. Available from: https://pubmed.ncbi.nlm.nih.gov/8182403/
50. Peng M, Zhou Q, Fu X, Yu L, Xu J, Wu L, et al. Health economic indicators in patients with diabetic foot: outpatient multidisciplinary management. Int J Low Extrem Wounds. 2020. Available from: https://pubmed.ncbi.nlm.nih.gov/32524878/
51. Nather A, Bee CS, Lin WK, Valerie CXB, Liang S, Tambyah PA, et al. Value of team approach combined with clinical pathway for diabetic foot problems: a clinical evaluation. Diabet Foot Ankle. 2010;1:1–5. Available from: https://pubmed.ncbi.nlm.nih.gov/22396810/
52. Evans KK, Attinger CE, Al-Attar A, Salgado C, Chu CK, Mardini S, et al. The importance of limb preservation in the diabetic population. J Diabetes Complications. 2011;25(4):227–31. https://doi.org/10.1016/j.jdiacomp.2011.02.001.
53. Kim PJ, Evans KK, Steinberg JS, Pollard ME, Attinger CE. Critical elements to building an effective wound care center. J Vasc Surg. 2013;57(6):1703–9.
54. Driver VR, Fabbi M, Lavery LA, Gibbons G. The costs of diabetic foot: The economic case for the limb salvage team. J Vascular Surg. 2010;52:17S–22S.
55. Manu C, Lacopi E, Bouillet B, Vouillarmet J, Ahluwalia R, Lüdemann C, et al. Delayed referral of patients with diabetic foot ulcers across Europe: patterns between primary care and specialised units. J Wound Care. 2018;27(3):186–92. Available from: https://pubmed.ncbi.nlm.nih.gov/29509115/
56. Prompers L, Huijberts M, Apelqvist J, Jude E, Piaggesi A, Bakker K, et al. Delivery of care to diabetic patients with foot ulcers in daily practice: Results of the Eurodiale Study, a prospective cohort study. Diabet Med. 2008;25(6):700–7. Available from: https://pubmed.ncbi.nlm.nih.gov/18544108/
57. Albornoz CR, Cordeiro PG, Mehrara BJ, Pusic AL, McCarthy CM, Disa JJ, et al. Economic implications of recent trends in U.S. immediate autologous breast reconstruction. Plast Reconstr Surg. 2014;133(3):463–70.
58. Billig JI, Kotsis SV, Chung KC. The next frontier of outcomes research. Plast Reconstr Surg. 2020;145(5):1315–22.
59. Collaborative Quality Initiatives - Value Partnerships.com — Blue Cross Blue Shield of Michigan 2020 Jun 4. Available from: https://www.valuepartnerships.com/programs/collaborative-quality-initiatives/
60. Blue Cross Blue Shield of Michigan and Blue Care Network are nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association. 2018 Collaborative Quality Initiative Fact Sheet Michigan Surgical Quality Collaborative. Available from: www.valuepartnerships.com.
61. Behrendt CA, Venermo M, Cronenwett JL, Sedrakyan A, Beck AW, Eldrup-Jorgensen J, et al. VASCUNET, VQI, and the international consortium of vascular registries – unique collaborations for quality improvement in vascular surgery. Eur J Vasc Endovasc Surg. 2019;58(6):792–3.
62. Fife CE, Carter MJ. Wound care outcomes and associated cost among patients treated in US outpatient wound centers: data from the US wound registry. Wounds. 2012;24(1):10–7.
63. Fife CE, Carter MJ, Walker D, Thomson B, Eckert KA. Diabetic foot ulcer off-loading: the gap between evidence and practice. Data from the US wound registry. Adv Ski Wound Care. 2014;27(7):310–6.
64. What we do – US Wound & Podiatry Registries. [cited 2021 Jan 26]. Available from: https://uswoundregistry.com/what-we-do/

38 DLS Innovations: Landmark Publications and Innovations from Our Team

Samuel S. Huffman, Christopher E. Attinger, John S. Steinberg, Karen K. Evans, and Kenneth L. Fan

Evolution of Multidisciplinary Care

In the USA, up to 2.4–4.5 million people suffer from chronic lower extremity wounds, costing our health system $31.7 billion annually [1, 2]. The incidence of lower extremity wounds is rising as a result of the aging population and increased risk factors for atherosclerotic disease such as diabetes, smoking, and obesity. Lower extremity wounds are a major cause of disability as diabetes mellitus has moved to the second leading cause of disability-adjusted life years and years lived with disability [3]. With inadequate treatment, exacerbation occurs leading to a predictable pathway toward amputation. After a below the knee amputation, the 5-year mortality may be greater than 68%, primarily due to the deterioration of existing comorbidities and increase in cardiovascular events [4–8]. Associated emotional impact leads to depression, poor self-care, and physical decline [9, 10]. Substantial evidence exists suggesting the employment of a multidisciplinary approach is critical at both preventing and treating chronic lower extremity wounds [11–14].

Wound care centers are high functioning organizations that at their core provide broad methods to treat patients with complex wounds through four critical elements including organizational structure, facilities, finances, and a multidisciplinary approach, now the standard of care [15, 16]. Understanding and applying the combination of these four factors increases the odds of a beneficial outcome for the patient while adequately utilizing allocated health care funding [15, 16]. Due to the intensity of care required to treat complex wounds, effective management can be delivered through multiple specialists as a singular provider does not meet the medical, surgical, and nutritional needs of the patient [16]. The specific composition of multidisciplinary teams is loosely defined, although no consensus exists regarding the optimal team of specialists. The Georgetown DLS team believes patients are best served when the core group consists of plastic surgery, vascular surgery, and podiatric/orthopedic surgery, even though surgery may not be necessary for all patients (Fig. 38.1) [16–19]. For non-surgical care, consultation with internal medicine for optimization of glycemic control, infectious disease for treatment if an infection is present or suspected, and physical therapy,

S. S. Huffman (✉) · K. K. Evans · K. L. Fan
Department of Plastic and Reconstructive Surgery, MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: ssh91@georgetown.edu; Karen.K.Evans@medstar.net; Kenneth.L.Fan@medstar.net

C. E. Attinger · J. S. Steinberg
Department of Plastic Surgery, Georgetown University School of Medicine and MedStar Georgetown University Hospital, Washington, DC, USA
e-mail: Christopher.Attinger@medstar.net; John.Steinberg@MedStar.net

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2_38

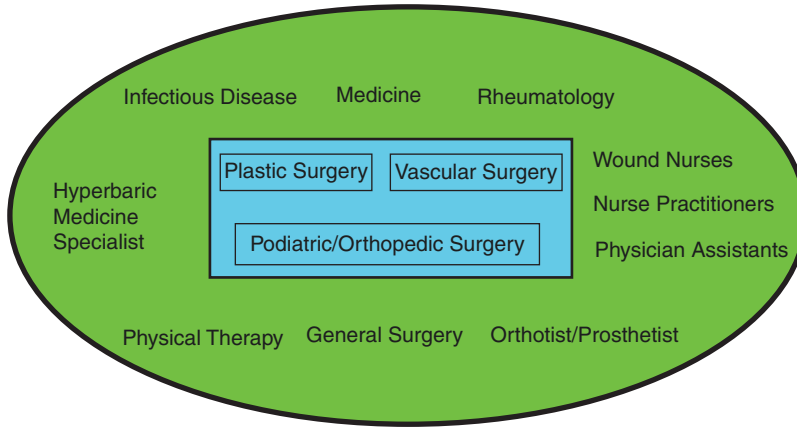


Fig. 38.1 Representation of the core and broad multidisciplinary care team members. The core team is defined by the central group of team members in the blue shaded box. Other essential team members are located within the shaded area. (Source Building a Multidisciplinary Hospital-Based Wound Care Center: Nuts and Bolts Plastic and Reconstructive Surgery138(3S):241S–247S, September 2016)

among other teams, is crucial [20]. Each of these team members supplies a key role in the evidence-based approach for treatment and prevention of foot ulcers proposed by Shaper et al. [20] Specifically, patients may require offloading of pressure placed on wounds by podiatric surgeons due to biomechanical stress of gait. Similarly, vascular surgeons aid in assessment and, when required, endovascular intervention to restore tissue perfusion. Plastic and podiatric surgeons additionally provide local wound care via routine inspection, application of wound dressings to maintain optimal healing conditions, and debridement of wounds. All team members can provide continuous patient education in diabetic foot care with the goal of achieving long-term prevention of foot ulcers [20, 21]. Multidisciplinary care under a singular comprehensive wound care center is critical to the adherence and provision of these evidence-based principles, although some center's capabilities may be limited by the lack of these key specialties.

Regardless of the combination of involved specialists, communication and shared ownership between all team members is paramount to increasing likelihood of successful outcomes. Moreover, the hospital-based wound center which employs the same electronic medical records (EMR) system for all team members provides access to a patient's entire history of wound and medical care in addition to a shared pager system, conducive for immediate communication [15, 16]. Ideally, outpatient clinics are structured under the same EMR and should parallel the inpatient management as patients' care extends beyond the hospital. This structure mutually benefits the patients and hospital system as the support and sustainability of wound centers can generate revenue for the hospital (Fig. 38.2) [22]. However, tertiary wound centers are only capable of providing these services to patients with complex chronic wounds if the community-based wound care centers refer patients for more advanced treatment modalities [15].

Even such, the clear advantages and success of a hospital-based wound care center are reliant on the core value of providing evidence-based and patient-centered care [12]. Kim et al. describe the ideal hospital-based model as a three tier system—inpatient service, clinic, and operating room—all of which interplay with one another in their provision of continuous care for a diabetic population who may require multiple hospital admissions [14–16, 23–25]. Implementation of a multidisciplinary care approach has been demonstrated as efficacious in reducing the rate of major amputations while simultaneously improving clinical outcomes and quality of life for patients [11–14, 17, 25–30]. Similarly, this approach has the potential to reduce healthcare costs through a

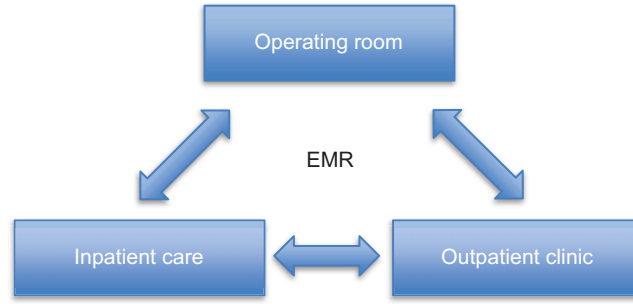


Fig. 38.2 Flow diagram depicting patient flow through a hospital-based wound care center model. The larger box represents the employment of the same EMR system for all parts of the wound care center. (EMR: electronic medical record)

more efficient delivery of care, all of which has been accomplished through varied applications of the multidisciplinary model [31, 32]. These alternative models of wound care centers exist through private practice offices or outpatient clinics; however, the hospital-based inpatient and outpatient model has been described as the most conducive for complex wounds that require intensive care [16]. The immediate access to resources and the wide array of ancillary services and personnel in continuity with outpatient clinics allow the hospital-based delivery model to provide a concerted effort toward amputation reduction and functional improvement [16].

The Effect of Multidisciplinary Care on Amputations

Among the Georgetown Diabetic Limb Salvage (DLS) team, the hospital-based multidisciplinary care approach has been the fundamental driving force to reduce mortality following amputation. Historically, the 5-year mortality rates following major lower extremity amputations were higher than breast, colon, or prostate cancer [8]. Furthermore, approximately three out of four patients who receive lower extremity amputations have diabetes [8]. One recent systematic review and meta-analysis by the Georgetown DLS team found that within both the type 1 and type 2 diabetic patient population, 1- and 5-year mortality was 27.3% and 63.2%. Moreover, it was found that 10-year mortality rates reached 80% [7].

As amputation rates vary from center to center, our experience in a team-based approach has helped reduce the primary amputation rate in patients with a threatened extremity [33, 34]. Utilizing free tissue transfer, Evans et al. illustrated the importance of limb preservation among the diabetic population, even with additional comorbidities of peripheral vascular disease and end-stage renal disease, which are known risk factors for increased complication rates during limb salvage (see section on Lower Extremity Reconstruction) [35]. In this population, limb salvage rates between 54 and 59%, with 64% of patients functionally ambulatory at 2-year follow-up can be achieved [35]. One reason for increased amputation rates in a non-multidisciplinary setting may be the ease of amputation for a clinic that does not have the multitude of resources as a hospital-based team [16].

When amputation is necessary, Attinger et al. demonstrated that by utilizing a team approach, limb salvage and below-knee amputation can both achieve a 64% ambulation rate. Additionally, it was determined the 2-year survival rate is higher in below the knee amputation patients treated with a multidisciplinary approach (80%) compared to standard care (52%) [36]. These findings highlight the need for a focus on function after amputation. Thoughtful preoperative planning in conjunction with pragmatic use of viable tissue optimizes potential for amputees to be highly functional [37]. Specifically, preoperative care should assess LE biomechanics, ambulatory functional status, and patient goals. In particular, preserving limb length and maximum number of joints is critical to augment function and preserve ambulatory status. Preoperative predictive factors aid in stratifying potential postop-

erative functional status. Preoperative popliteal patency in patients undergoing below-knee amputation was associated with higher postoperative ambulation rates when compared to patients without popliteal flow preoperatively and independently increased the likelihood of postoperative ambulation [38]. This illustrates that prioritization of functional status should be considered even in limbs with compromised vasculature. Furthermore, patients age > 60 years who underwent bilateral amputation and have a history of end-stage renal disease have lower likelihoods of ambulating [39].

Aside from the substantial psychological impact of amputation, maximizing limb length reduces the cardiopulmonary energy demand of amputation which has been associated with increased mortality and morbidity [4–6]. Therefore, limb-preserving amputations distal to the ankle joint with evaluations of LE biomechanics are performed when possible to avoid further amputation and maximize functionality [40]. However, due to advances in prosthetic technology some patients can attain better quality of life with a below-knee amputation than a salvaged LE [41–44]. Conversely, patients whose condition is not conducive to wearing a prosthetic device may do better with a limited functioning leg, as many patients never wear a prosthetic [45]. Predicting which patients will likely not wear a prosthetic device can help surgeons counsel patients to the most beneficial operative technique that maximizes functionality and quality of life. Specifically, it was found that preoperative factors independently associated with not wearing a prosthesis include non-ambulatory status prior to amputation, above knee amputation, homebound ambulation only, age > 60 years, presence of dementia, end-stage renal disease, and coronary artery disease [39]. Recognizing the determinants at play that may alter postoperative care is critical to the surgeon.

Research in lower extremity wounds has shifted from surgeon metrics, such as time to heal, to patient-based metrics [46–48]. Patient-reported outcomes (PRO) have become a cornerstone to assess postoperative functionality and quality of life, especially considering the healthcare shift to patient-centered care following the approval of the Patient-Centered Outcome Research Institute by congress within the Affordable Care Act [49]. These PROs following lower extremity reconstruction additionally include assessment of chronic pain and mental status which have been measured through tools such as the Short Form Survey-36 and the Sickness Impact Profile [10, 49, 50]. However, application of PROs has been inconsistent. One systematic review of studies assessing PROs following major LE amputation for peripheral arterial disease or diabetes mellitus found that eleven different amputation specific PROs were utilized, ten of which were developed only for prosthesis users [51]. Additionally, there were limited PRO tools for patients undergoing major LE amputation following limb-threatening trauma. Furthermore, the Georgetown DLS team discovered that over the last two decades there has been a significant research gap between clinical outcomes and PROs. Specifically, patient-reported outcomes for psychosocial measures, quality of life, and functional ability were reported in 24%, 21%, and 53% of articles, respectively [52]. This highlights the need for further development and increased utilization of PRO measures, which may help improve patient-centered healthcare delivery. Notably, ongoing development of LIMB-Q for both lower extremity and traumatic amputation patients exemplifies the progression in this field [53–55]. Similarly, [43–45] the development of WOUND-Q by international collaborators and members of the Georgetown DLS team represents an important step in assessment of the patient perspective in an evidenced-based medicine structure, and therefore, creating an avenue to improve patient-centered care for those with chronic wounds [56, 57].

Innovations in Lower Extremity Reconstruction

One way in which the Georgetown DLS team has been able to increase the rates of limb salvage and reduce major amputations is through innovations in free flap reconstruction. Early on, local

flaps were established as a primary method of reconstruction due to their versatility, reproducibility, and successful long-term functional outcomes for patients undergoing limb salvage [58]. With advancements in microsurgical reconstruction of the foot and ankle, free flaps emerged as a viable adjunct reconstruction modality [59]. Since success rates of microsurgical free flaps exceed 95% in tertiary centers, surgeons were able to achieve a higher salvage rate of limbs in those that were likely amputated prior to the option of microsurgical free flap reconstruction [59, 60].

In order to achieve a successful reconstruction and limb salvage, it is critical to identify risk factors for adverse long-term outcomes that may hinder functionality and quality of life. Additionally, recognizing that resource allocation required for limb salvage is extensive and understanding precluding elements of poor outcomes increases the odds of efficient healthcare delivery [61]. In the first microsurgical study committed to determining long-term risk factors of poor outcomes in patients undergoing microsurgical free flap reconstruction for limb salvage, Kotha et al. found that end-stage renal disease, hindfoot wounds, wound colonization, and elevated hemoglobin A1c were risk factors for amputation [61].

The detriment of diabetes for this patient population is significant as has been shown to increase the number of debridements, prolong healing times, and decrease long-term survival in patients undergoing local or free flaps [62]. However, diabetes does not affect limb salvage rates, and if successful limb salvage is achieved, it was demonstrated to prolong survival of diabetic patients [63]. The innovations in free flap tissue reconstruction at the Georgetown DLS team have expanded treatment modalities for lower extremity limb salvage. The anterolateral thigh (ALT) and vastus lateralis (VL) flap are known workhorse flaps of lower extremity reconstruction due to low donor site morbidity [64–68]. In the largest comparison study of the two flaps, it was found that ALT and VL flaps have similar complication rates, postoperative ambulatory rate, and flap success, with the most significant advantage of ALT flaps being the reduced need for skin grafting [69]. Other areas in which the Georgetown DLS team has improved free tissue transfer (FTT) success are through lower extremity vasculature. Prereconstructive targeted endovascular therapy as part of a multidisciplinary approach to functional limb salvage in patients with advanced arterial disease has been demonstrated to optimize recipient-site hemodynamics and promote flap survival in regions of compromised distal blood flow [70]. Furthermore, in a later study, it was found that both direct revascularization and indirect revascularization with collateral flow offer significantly improved wound healing rates and major amputation rates compared with indirect revascularization [71]. In the setting of unfavorable vascular anatomy, one novel approach is the hemirectus/ALT chimeric clap to cover complex defects and preserve donor site function [72].

At our tertiary referral center, we often receive complex patients that are deemed inoperable for FTT reconstruction, such as those with severe peripheral vascular disease or recalcitrant foot ulcers [73]. Through microsurgical advancements and the multidisciplinary model, it was demonstrated that flap success and lower extremity limb salvage of patients with diabetic recalcitrant wounds can reach 93% and 79%, respectively [74]. Additional use of longitudinal slit arteriotomy end-to-side anastomosis for patients undergoing FTT) reconstruction of life-threatening limb defects in the high-risk population has shown an overall limb salvage rate of 83.5%, and of those salvaged, 92.7% were ambulating without a prosthesis after one year [75].

Although no consensus exists regarding the ideal preoperative hypercoagulable workup in high-risk patients undergoing microsurgical reconstruction, in the Georgetown DLS patient population we perform preoperative screening protocol for inherited or acquired hypercoagulable traits which may predispose patients to thrombosis. Unidentified hypercoagulability can result in detrimental outcomes following FTT) reconstruction to the LE ultimately leading to difficult or nonsalvageable flaps [76–79]. Our tertiary limb salvage center implemented a novel,

risk-stratified algorithm for perioperative anticoagulation in July 2015 which parallels the assumed differences in hypercoagulable risk among our patient population. The decision to administer heparin—intravenous or subcutaneous—was determined by the presence or absence of thrombophilic risk factors for microvascular thrombosis (Fig. 38.3) [78]. Table 38.1 list the

Table 38.1 Preoperative thrombophilia screening panel

CBC, complete blood count
PT/INR, prothrombin time/international normalized ratio
PTT, partial thromboplastin time
MTHFR, methylenetetrahydrofolate reductase
PAI-1, plasminogen activator inhibitor 1
QST, quantitative sensory testing

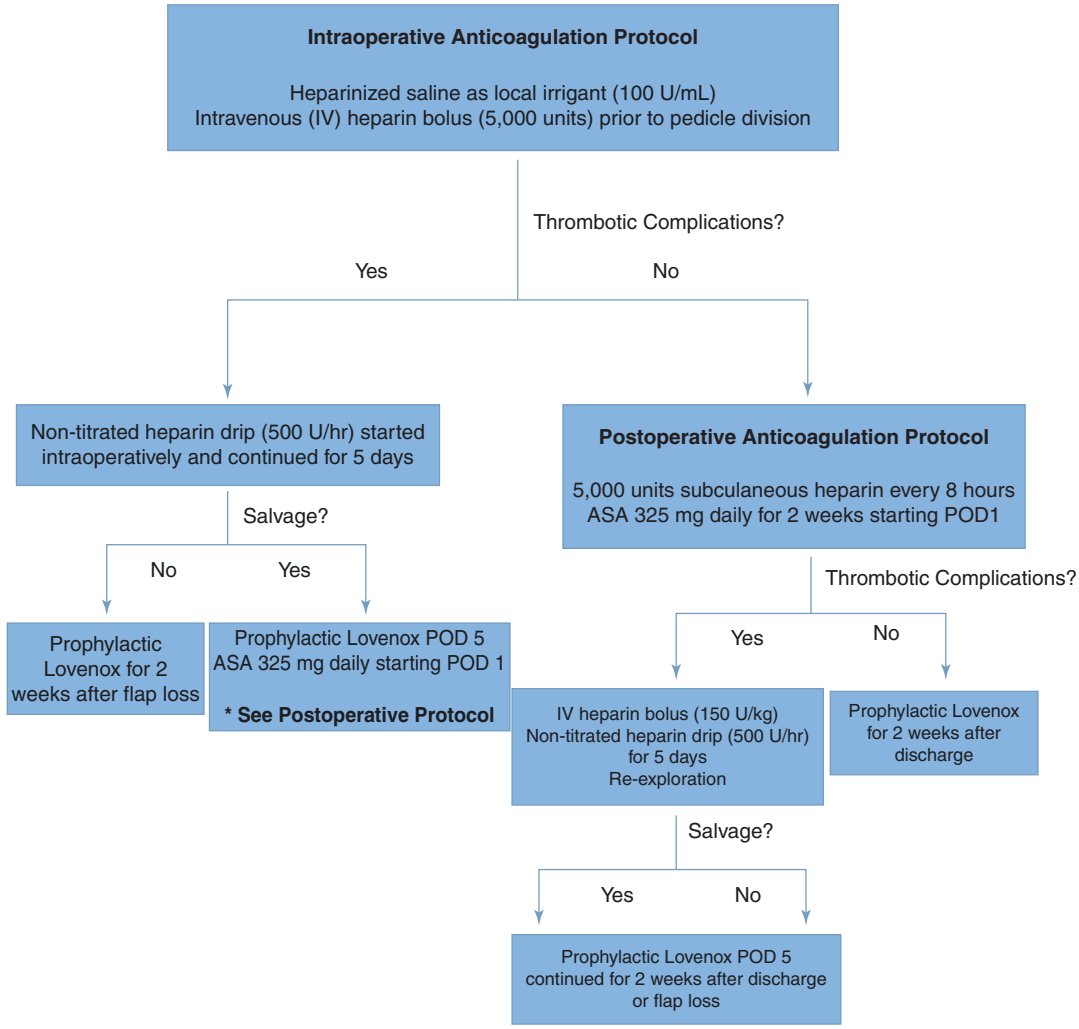


Fig. 38.3 Novel perioperative anticoagulation protocol based on the presence or absence of thrombotic complications. (Source. DeFazio MV, Hung RW, Han KD, Bunting HA, Evans KK. Lower Extremity Flap Salvage in Thrombophilic Patients: Managing Expectations in the Setting of Microvascular Thrombosis. J Reconstr Microsurg. 2016;32 (6):431–444. doi: https://doi.org/10.1055/s-0035-1571249)

factors included in the thrombophilia screening protocol. Prior to the anticoagulation protocol, DeFazio et al. found that 61% of patients undergoing FTT to LE for limb salvage had at least one of the 52 identified hypercoagulable traits, with the most common traits being the plasminogen activator inhibitor-1 4G/5G variant and the methylenetetrahydrofolate reductase A1298C and C677T polymorphisms [79]. Risk-stratified patients with identified thrombophilia who received a weight-based intravenous heparin were observed to have lower rates of total and partial flap loss, ultimately leading to a significant reduction in postoperative thrombotic events [78]. Conversely, surgeons must weigh this beneficial effect to the risk of bleeding complications following therapeutic heparin intervention which range between 20% and 60% [80–83]. However, recognition of the impact of morbidity following flap failure is critical to patient-centered care as patients face major LE amputation.

The diabetic patient population often presents with other challenges such as osseous destruction and/or superimposed infection. In the foot, absence of soft tissue coverage over the bony structures increases the risk of developing osteomyelitis, which ultimately compromises skeletal integrity resulting in altered biomechanical stresses [84]. In this case, Steinberg et al. illustrates the longevity and benefit of permanent polymethylmethacrylate cement spacers to prevent amputation by reducing the bacterial load on local tissue and filling soft tissue voids [85]. However, in patients with chronic calcaneal osteomyelitis, conservative management may no longer be considered. Conventional partial calcanectomy has been frequently utilized to address osteomyelitis of the calcaneus, but balancing calcaneus resection with maintenance of adequate soft tissue-to-bone ratio is challenging to achieve and often leads to closure under tension [86, 87]. The novel alternative surgical technique of vertical contour calcanectomy from the Georgetown DLS team ensures total resection of osteomyelitis, reduces risk of reulceration, and limits tension of the soft tissue during wound closure [86]. Moreover, patients who underwent primary closure at the time of vertical contour calcanectomy were nearly 80% more likely to achieve limb salvage [88].

Undoubtedly, patients still progress and ultimately receive amputations. However, innovations in targeted muscle reinnervation have led to improved patient outcomes and enhanced quality of life. Through tibial and common peroneal nerve coaptation during the index amputation and collagen nerve wrapping, patients report lower VAS pain scores, phantom symptoms, and neuroma formation, with higher ambulation rates after six months when compared with traction neurectomy alone [89]. The Georgetown DLS team has also demonstrated advancements in targeted muscle reinnervation, which reduces pain and improves ambulation in patients undergoing below-knee amputation [90]. These surgical techniques have the potential to improve morbidity and quality of life in the highly comorbid patient population.

Policy Implications

Despite advancements in limb salvage, access to wound care modalities to prevent amputation remains an issue for the US health system [10, 50, 51]. However, we have identified multiple patient- and hospital-level factors that decrease access to surgical limb salvage and multidisciplinary care. In the UK, primary care providers able to recall multidisciplinary wound centers, leading to amputation reduction upwards of 70%. Unfortunately, multidisciplinary wound care remains poorly organized and inefficient with amputations rates varying by region [91].

In patients admitted for chronic lower extremity wounds, the strongest protective factor against amputation was access to urban teaching hospitals, while receiving limb salvage without and with flaps was predictive of amputation [92]. When amputations are indicated, those living in urban areas and those having vascular intervention in the same hospital stay were predictive of limb-preserving amputations, such as a TMA, while patients living in rural areas who were treated in urban centers were more likely to proceed to a below-knee amputation [93]. Among

patients with chronic wounds, it has been shown that increased hospital competition is the strongest systems level predictor of receiving lower extremity flaps [94]. Presumably, competitive environments found in urban centers increase the likelihood hospitals will offer more services. In saturated markets, hospitals are less likely to offer services such as limb salvage and length preserving amputations.

Since length preserving amputations increase patient function and reduce mortality compared to higher-level amputations, addressing disparities can help to improve the quality of life in chronic lower extremity wound patients. Disparity reduction within the community will require a comprehensive strategy to address the severity of disease presentation in minority patients and the referral process to centers with limb salvage capabilities [93]. Furthermore, to fully address access to treatment modalities, the environment in which limb salvage centers operate should be dissected. Ultimately, developing healthcare policy that allocates focus to the utilization and distribution of lower extremity salvage will help to broaden access for minority patients and those systematically underserved.

References

1. Nussbaum SR, Carter MJ, Fife CE, DaVanzo J, Haught R, Nusgart M, et al. An economic evaluation of the impact, cost, and Medicare policy implications of chronic nonhealing wounds. Value Health. 2018;21(1):27–32.
2. Sen CK. Human Wounds and Its Burden: An Updated Compendium of Estimates. Adv Wound Care. 2019;8(2):39.
3. Leading causes of death, and disability—PAHO/WHO | Pan American Health Organization [Internet]. [cited 2022 Jun 3]. Available from: https://www.paho.org/en/enlace/leading-causes-death-and-disability
4. Moran SL, Illig KA, Green RM, Serletti JM. Free-tissue transfer in patients with peripheral vascular disease: a 10-year experience. Plast Reconstr Surg. 2002;109(3):999–1006. Available from: https://pubmed.ncbi.nlm.nih.gov/11884824/
5. Wukich DK, Raspovic KM, Suder NC. Patients with diabetic foot disease fear major lower-extremity amputation more than death. Foot and Ankle Specialist. 2018;1(1):17–21. Available from: https://journals.sagepub.com/doi/10.1177/1938640017694722
6. Attinger C, Ducic I. Foot and ankle reconstruction. In: Thorne CH, Beasley RW, Aston SJ, Bartlett SP, Gurtner GC, Spear SL, editors. Grabb & Smith's plastic surgery. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2007. p. 689–707.
7. Meshkin DH, Zolper EG, Chang K, Bryant M, Bekeny JC, Evans KK, et al. Long-term mortality after non-traumatic major lower extremity amputation: a systematic review and meta-analysis. J Foot Ankle Surg. 2021;60(3):567–76. Available from: https://pubmed.ncbi.nlm.nih.gov/33509714/
8. Armstrong DG, Swerdlow MA, Armstrong AA, Conte MS, Padula WV, Bus SA. Five year mortality and direct costs of care for people with diabetic foot complications are comparable to cancer. J Foot Ankle Res. 2020;13(1):16. Available from: https://pubmed.ncbi.nlm.nih.gov/32209136/
9. McCarthy ML, Mackenzie EJ, Edwin D, Bosse MJ, Castillo RC, Starr A. Psychological distress associated with severe lower-limb injury. J Bone Joint Surg Am. 2003;85(9):1689–97. Available from: https://pubmed.ncbi.nlm.nih.gov/12954826/
10. van der Merwe L, Birkholtz F, Tetsworth K, Hohmann E. Functional and psychological outcomes of delayed lower limb amputation following failed lower limb reconstruction. Injury. 2016;47(8):1756–60. Available from: https://pubmed.ncbi.nlm.nih.gov/27282688/
11. Sinkin JC, Reilly M, Cralley A, Kim PJ, Steinberg JS, Cooper P, et al. Multidisciplinary approach to soft-tissue reconstruction of the diabetic Charcot foot. Plast Reconstr Surg. 2015;135(2):611–6. Available from: https://pubmed.ncbi.nlm.nih.gov/25357158/
12. Almdal T, Nielsen AA, Nielsen KE, Jørgensen ME, Rasmussen A, Hangaard S, et al. Increased healing in diabetic toe ulcers in a multidisciplinary foot clinic-An observational cohort study. Diabetes Res Clin Pract. 2015;110(3):315–21. Available from: https://pubmed.ncbi.nlm.nih.gov/26515911/
13. Chiu CC, Huang CL, Weng SF, Sun LM, Chang YL, Tsai FC. A multidisciplinary diabetic foot ulcer treatment programme significantly improved the outcome in patients with infected diabetic foot ulcers. J Plast Reconstr Aesthet Surg. 2011;64(7):867–72. Available from: https://pubmed.ncbi.nlm.nih.gov/21216682/
14. Gottrup F. A specialized wound-healing center concept: importance of a multidisciplinary department structure and surgical treatment facilities in the treatment of chronic wounds. Am J Surg. 2004;187(5A):S38–43. Available from: https://pubmed.ncbi.nlm.nih.gov/15147991/
15. Kim PJ, Evans KK, Steinberg JS, Pollard ME, Attinger CE. Critical elements to building an effective wound care center. J Vasc Surg. 2013;57(6):1703–9. Available from: https://pubmed.ncbi.nlm.nih.gov/23402873/
16. Kim PJ, Attinger CE, Steinberg JS, Evans KK, Akbari C, Mitnick CDB, et al. Building a Multidisciplinary Hospital-Based Wound Care Center: Nuts and Bolts. Plast Reconstr Surg. 2016;138(3

Suppl):241S–7S. Available from: https://pubmed.ncbi.nlm.nih.gov/27556768/
17. Rogers LC, Andros G, Caporusso J, Harkless LB, Mills JL, Armstrong DG. Toe and flow: essential components and structure of the amputation prevention team. J Vasc Surg. 2010;52(3 Suppl):23S–7S. Available from: https://pubmed.ncbi.nlm.nih.gov/20804929/
18. Price P, Gottrup F, Abel M. Ewma study recommendations: for clinical investigations in leg ulcers and wound care. J Wound Care. 2014;23(Suppl 5(Sup5c)):S1–36. Available from: https://pubmed.ncbi.nlm.nih.gov/27292109/
19. Chung J, Modrall JG, Ahn C, Lavery LA, Valentine RJ. Multidisciplinary care improves amputation-free survival in patients with chronic critical limb ischemia. J Vasc Surg. 2015;61(1):162–169.e1. Available from: https://pubmed.ncbi.nlm.nih.gov/25073577/
20. Schaper NC, van Netten JJ, Apelqvist J, Bus SA, Hinchliffe RJ, Lipsky BA. Practical guidelines on the prevention and management of diabetic foot disease (IWGDF 2019 update). Diabetes Metab Res Rev. 2020;36(Suppl 1(S1)):e3266. Available from: https://pubmed.ncbi.nlm.nih.gov/32176447/
21. Dorresteijn JAN, Kriegsman DMW, Assendelft WJJ, Valk GD. Patient education for preventing diabetic foot ulceration. Cochrane Database Syst Rev. 2014;2014:12.
22. Attinger CE, Hoang H, Steinberg J, Couch K, Hubley K, Winger L, et al. How to make a hospital-based wound center financially viable: the Georgetown University Hospital model. Gynecol Oncol. 2008;111(2 Suppl):S92–7. Available from: https://pubmed.ncbi.nlm.nih.gov/18799210/
23. Rümenapf G, Geiger S, Schneider B, Amendt K, Wilhelm N, Morbach S, et al. Readmissions of patients with diabetes mellitus and foot ulcers after infra-popliteal bypass surgery - attacking the problem by an integrated case management model. VASA. 2013;42(1):56–67. Available from: https://pubmed.ncbi.nlm.nih.gov/23385227/
24. Beaulieu RJ, Grimm JC, Lyu H, Abularrage CJ, Perler BA. Rates and predictors of readmission after minor lower extremity amputations. J Vasc Surg. 2015;62(1):101–5. Available from: https://pubmed.ncbi.nlm.nih.gov/25827965/
25. Vartanian SM, Robinson KD, Ofili K, Eichler CM, Hiramoto JS, Reyzelman AM, et al. Outcomes of neuroischemic wounds treated by a multidisciplinary amputation prevention service. Ann Vasc Surg. 2015;29(3):534–42. Available from: https://pubmed.ncbi.nlm.nih.gov/25596408/
26. Yesil S, Akinci B, Bayraktar F, Havitcioglu H, Karabay O, Yapar N, et al. Reduction of major amputations after starting a multidisciplinary diabetic foot care team: single Centre experience from Turkey. Exp Clin Endocrinol Diabetes. 2009;117(7):345–9. Available from: https://pubmed.ncbi.nlm.nih.gov/19226478/
27. Sholar AD, Wong LK, Culpepper JW, Sargent LA. The specialized wound care center: a 7-year experience at a tertiary care hospital. Ann Plast Surg. 2007;58(3):279–84. Available from: https://pubmed.ncbi.nlm.nih.gov/17471132/
28. Sanders LJ, Robbins JM, Edmonds ME. History of the team approach to amputation prevention: pioneers and milestones. J Vasc Surg. 2010;52(3 Suppl):3S–16S. Available from: https://pubmed.ncbi.nlm.nih.gov/20804927/
29. Aksoy DY, Gürlek A, Çetinkaya Y, Öznur A, Yazici M, Özgür F, et al. Change in the amputation profile in diabetic foot in a tertiary reference center: efficacy of team working. Exp Clin Endocrinol Diabetes. 2004;112(9):526–30. Available from: https://pubmed.ncbi.nlm.nih.gov/15505761/
30. Hsu CR, Chang CC, Chen YT, Lin WN, Chen MY. Organization of wound healing services: the impact on lowering the diabetes foot amputation rate in a ten-year review and the importance of early debridement. Diabetes Res Clin Pract. 2015;109(1):77–84. Available from: https://pubmed.ncbi.nlm.nih.gov/26021976/
31. Vu T, Harris A, Duncan G, Sussman G. Cost-effectiveness of multidisciplinary wound care in nursing homes: a pseudo-randomized pragmatic cluster trial. Fam Pract. 2007;24(4):372–9. Available from: https://pubmed.ncbi.nlm.nih.gov/17602174/
32. Driver VR, Fabbi M, Lavery LA, Gibbons G. The costs of diabetic foot: the economic case for the limb salvage team. J Am Podiatr Med Assoc. 2010;100(5):335–41. Available from: https://pubmed.ncbi.nlm.nih.gov/20847346/
33. Apelqvist J, Larsson J, Agardh C-D. Long-term prognosis for diabetic patients with foot ulcers. J Intern Med. 1993;233(6):485–91. Available from: https://pubmed.ncbi.nlm.nih.gov/8501419/
34. van Gils CC, Wheeler LA, Mellstrom M, Brinton EA, Mason S, Wheeler CG. Amputation prevention by vascular surgery and podiatry collaboration in high-risk diabetic and nondiabetic patients. The operation desert foot experience. Diabetes Care. 1999;22(5):678–83. Available from: https://pubmed.ncbi.nlm.nih.gov/10332665/
35. Evans KK, Attinger CE, Al-Attar A, Salgado C, Chu CK, Mardini S, et al. The importance of limb preservation in the diabetic population. J Diabetes Complications. 2011;25(4):227–31. Available from: https://pubmed.ncbi.nlm.nih.gov/21447444/
36. Attinger CE, Brown BJ. Amputation and ambulation in diabetic patients: Function is the goal. Diabetes Metab Res Rev. 2012;28(Suppl. 1):93–6. Available from: https://pubmed.ncbi.nlm.nih.gov/22271731/
37. Brown BJ, Crone CG, Attinger CE. Amputation in the diabetic to maximize function. Semin Vasc Surg. 2012;25(2):115–21. Available from: https://pubmed.ncbi.nlm.nih.gov/22817862/
38. Alfawaz A, Kotha VS, Nigam M, Bekeny JC, Black CK, Tefera E, et al. Popliteal artery patency is an indicator of ambulation and healing after below-knee amputation in vasculopaths. Vascular. 2022;30(4):708–14. Available from: https://pubmed.ncbi.nlm.nih.gov/34134560/

39. Taylor SM, Kalbaugh CA, Blackhurst DW, Hamontree SE, Cull DL, Messich HS, et al. Preoperative clinical factors predict postoperative functional outcomes after major lower limb amputation: an analysis of 553 consecutive patients. J Vasc Surg. 2005;42(2):227–34. Available from: https://pubmed.ncbi.nlm.nih.gov/16102618/
40. Kotha VS, Ragothaman K, Walters E, Attinger CE, Steinberg JS. Lower extremity amputations in at-risk patients: a focus on tissue viability and function in the compromised limb. Clin Podiatr Med Surg. 2019;36(3):483–98. Available from: https://pubmed.ncbi.nlm.nih.gov/31079612/
41. Brown BJ, Attinger CE. The Below-Knee Amputation: To Amputate or Palliate? Adv Wound Care. 2013;2(1):30–5. Available from: https://pubmed.ncbi.nlm.nih.gov/24527321/
42. Qureshi MK, Ghaffar A, Tak S, Khaled A. Limb salvage versus amputation: a review of the current evidence. Cureus. 2020;12(8):e10092.
43. Busse JW, Jacobs CL, Swiontkowski MF, Bosse MJ, Bhandari M. Complex limb salvage or early amputation for severe lower-limb injury: a meta-analysis of observational studies. J Orthop Trauma. 2007;21(1):70–6. Available from: https://pubmed.ncbi.nlm.nih.gov/17211275/
44. Bosse MJ, MacKenzie EJ, Kellam JF, Burgess AR, Webb LX, Swiontkowski MF, et al. An analysis of outcomes of reconstruction or amputation after leg-threatening injuries. N Engl J Med. 2002;347(24):1924–31. Available from: https://pubmed.ncbi.nlm.nih.gov/12477942/
45. Raichle KA, Hanley MA, Molton I, Kadel NJ, Campbell K, Phelps E, et al. Prosthesis use in persons with lower- and upper-limb amputation. J Rehabil Res Dev. 2008;45(7):961.
46. Calvert M, Kyte D, Price G, Valderas JM, Hjollund NH. Maximising the impact of patient reported outcome assessment for patients and society. BMJ. 2019;364:k5267. Available from: https://pubmed.ncbi.nlm.nih.gov/30679170/
47. Nelson EC, Eftimovska E, Lind C, Hager A, Wasson JH, Lindblad S. Patient reported outcome measures in practice. BMJ. 2015;350:g7818. Available from: https://pubmed.ncbi.nlm.nih.gov/25670183/
48. Black N. Patient reported outcome measures could help transform healthcare. BMJ. 2013;346:7896. Available from: https://pubmed.ncbi.nlm.nih.gov/23358487/
49. Washington AE, Lipstein SH. The Patient-Centered Outcomes Research Institute--promoting better information, decisions, and health. N Engl J Med. 2011;365(15):e31. Available from: https://pubmed.ncbi.nlm.nih.gov/21992473/
50. Atiç R, Aydln A. Comparison of the demographic and clinical characteristics, functional status and quality of life of lower extremity amputees to identify the reason for undergoing amputation. J Back Musculoskelet Rehabil. 2018;31(5):973–9. Available from: https://pubmed.ncbi.nlm.nih.gov/30223383/
51. Miller R, Ambler GK, Ramirez J, Rees J, Hinchliffe R, Twine C, et al. Patient reported outcome measures for major lower limb amputation caused by peripheral artery disease or diabetes: a systematic review. Eur J Vasc Endovasc Surg. 2021;61(3):491–501. Available from: https://pubmed.ncbi.nlm.nih.gov/33388237/
52. Tirrell AR, Kim KG, Rashid W, Attinger CE, Fan KL, Evans KK. Patient-reported outcome measures following traumatic lower extremity amputation: a systematic review and meta-analysis. Plastic and Reconstructive Surgery Global Open. 2021;9(11):e3920.
53. Mundy LR, Klassen A, Grier J, Carty MJ, Pusic AL, Hollenbeck ST, et al. Development of a patient-reported outcome instrument for patients with severe lower extremity trauma (LIMB-Q): protocol for a multiphase mixed methods study. JMIR Res Protoc. 2019;8(10):e14397. Available from: https://pubmed.ncbi.nlm.nih.gov/31625944/
54. Mundy LR, Klassen A, Sergesketter AR, Grier AJ, Carty MJ, Hollenbeck ST, et al. Content validity of the LIMB-Q: a patient-reported outcome instrument for lower extremity trauma patients. J Reconstr Microsurg. 2020;36(9):625–33. Available from: https://pubmed.ncbi.nlm.nih.gov/32615610/
55. Mundy LR, Klassen A, Grier AJ, Gibbons C, Lane W, Carty MJ, et al. Identifying factors Most important to lower extremity trauma patients: key concepts from the development of a patient-reported outcome instrument for lower extremity trauma, the LIMB-Q. Plast Reconstr Surg. 2020;145(5):1292–301. Available from: https://pubmed.ncbi.nlm.nih.gov/32332555/
56. Klassen A, van Haren ELWG, Cross K, Fan KL, Gibbons C, Hoogbergen MM, et al. International mixed methods study protocol to develop a patient-reported outcome measure for all types of chronic wounds (the WOUND-Q). BMJ Open. 2020;10(3):e032332. Available from: https://pubmed.ncbi.nlm.nih.gov/32217558/
57. Klassen AF, van Haren ELWG, van Alphen TC, Cano S, Cross KM, van Dishoeck AM, et al. International study to develop the WOUND-Q patient-reported outcome measure for all types of chronic wounds. Int Wound J. 2021;18(4):487–509.
58. Paragas L, Attinger C, Blume P. Local flaps. Clin Podiatr Med Surg. 2000;17(2):267–318.
59. Attinger C, Colen L. The role of microsurgical free flaps in foot and ankle surgery. Clin Podiatr Med Surg. 2000;17(4):649–80.
60. Khouri RK, Cooley BC, Kunselman AR, Landis JR, Yeramian P, Ingram D, et al. A prospective study of microvascular free-flap surgery and outcome. Plast Reconstr Surg. 1998;102(3):711–21. Available from: https://pubmed.ncbi.nlm.nih.gov/9727436/
61. Kotha VS, Fan KL, Schwitzer JA, Youn R, Black CK, Attinger CE, et al. Amputation versus free flap: Long-term outcomes of microsurgical limb salvage and risk factors for amputation in the diabetic population. Plast Reconstr Surg. 2021;147(3):742–50. Available from: https://pubmed.ncbi.nlm.nih.gov/33587553/

62. Ducic I, Attinger CE. Foot and ankle reconstruction: pedicled muscle flaps versus free flaps and the role of diabetes. Plast Reconstr Surg. 2011;128(1):173–80. Available from: https://pubmed.ncbi.nlm.nih.gov/21399565/
63. Attinger CE, Ducic I, Cooper P, Zelen CM. The role of intrinsic muscle flaps of the foot for bone coverage in foot and ankle defects in diabetic and nondiabetic patients. Plast Reconstr Surg. 2002;110(4):1047–54.
64. Kuo YR, Jeng SF, Kuo MH, Huang MN, Liu YT, Chiang YC, et al. Free anterolateral thigh flap for extremity reconstruction: clinical experience and functional assessment of donor site. Plast Reconstr Surg. 2001;107(7):1766–71. Available from: https://pubmed.ncbi.nlm.nih.gov/11391197/
65. Celik N, Wei FC, Lin CH, Cheng MH, Chen HC, Jeng SF, et al. Technique and strategy in anterolateral thigh perforator flap surgery, based on an analysis of 15 complete and partial failures in 439 cases. Plast Reconstr Surg. 2002;109(7):2211–6. Available from: https://pubmed.ncbi.nlm.nih.gov/12045538/
66. Kimata Y, Uchiyama K, Ebihara S, Sakuraba M, Iida H, Nakatsuka T, et al. Anterolateral thigh flap donor-site complications and morbidity. Plast Reconstr Surg. 2000;106(3):584–9. Available from: https://pubmed.ncbi.nlm.nih.gov/10987464/
67. Spyriounis PK, Lutz BS. Versatility of the free vastus lateralis muscle flap. J Trauma. 2008;64(4):1100–5. Available from: https://pubmed.ncbi.nlm.nih.gov/18404081/
68. Gedebou TM, Wei FC, Lin CH. Clinical experience of 1284 free anterolateral thigh flaps. Handchir Mikrochir Plast Chir. 2002;34(4):239–44. Available from: https://pubmed.ncbi.nlm.nih.gov/12491182/
69. Black CK, Zolper EG, Ormiston LD, Schwitzer JA, Luvisa K, Attinger CE, et al. Free anterolateral thigh versus vastus lateralis muscle flaps for coverage of lower extremity defects in chronic wounds. Ann Plast Surg. 2020;85(S1 Suppl 1):S54–9. Available from: https://pubmed.ncbi.nlm.nih.gov/32539286/
70. Defazio M, Han KD, Akbari CM, Evans KK. Free tissue transfer after targeted endovascular reperfusion for complex lower extremity reconstruction: setting the stage for success in the presence of mutlivessel disease. Ann Vasc Surg. 2015;29(6):1316.e7–1316.e15. Available from: https://pubmed.ncbi.nlm.nih.gov/26028463/
71. Kim KG, Meshkin DH, Tirrell AR, Bekeny JC, Tefera EA, Fan KL, et al. A systematic review and meta-analysis of endovascular angiosomal revascularization in the setting of collateral vessels. J Vasc Surg. 2021;74(4):1406–1416.e3. Available from: https://pubmed.ncbi.nlm.nih.gov/33940077/
72. Economides JM, Fan KL, Black CK, Evans KK. The Hemirectus/Anterolateral Thigh Chimeric Flap: An Alternative in the Setting of Variable and Unfavorable Vascular Anatomy. Plast Reconstr Surg Glob Open. 2019;7(5):E2238. Available from: https://pubmed.ncbi.nlm.nih.gov/31333963/
73. Oh TS, Lee HS, Hong JP. Diabetic foot reconstruction using free flaps increases 5-year-survival rate. J Plast Reconstr Aesthet Surg. 2013;66(2):243–50. Available from: https://pubmed.ncbi.nlm.nih.gov/23098584/
74. Lu J, Defazio M, Lakhiani C, Abboud M, Penzler M, Elmarsafi T, et al. Limb salvage and functional outcomes following free tissue transfer for the treatment of recalcitrant diabetic foot ulcers. J Reconstr Microsurg. 2019;35(2):117–23. Available from: https://pubmed.ncbi.nlm.nih.gov/30099733/
75. Black C, Fan KL, Defazio MV, Luvisa K, Reynolds K, Kotha VS, et al. Limb salvage rates and functional outcomes using a longitudinal slit arteriotomy end-to-side anastomosis for limb-threatening defects in a high-risk patient population. Plast Reconstr Surg. 2020;145(5):1302–12. Available from: https://pubmed.ncbi.nlm.nih.gov/32332556/
76. Davis MR, Shell DH, Marques M, Long JN. Free flap failure secondary to dual thrombophilia. Microsurgery. 2009;29(1):62–5. Available from: https://pubmed.ncbi.nlm.nih.gov/18833574/
77. Wang TY, Serletti JM, Cuker A, McGrath J, Low DW, Kovach SJ, et al. Free tissue transfer in the hypercoagulable patient: a review of 58 flaps. Plast Reconstr Surg. 2012;129(2):443–53. Available from: https://pubmed.ncbi.nlm.nih.gov/21987047/
78. Defazio MV, Economides JM, Anghel EL, Tefera EA, Evans KK. Lower extremity free tissue transfer in the setting of thrombophilia: analysis of perioperative anticoagulation protocols and predictors of flap failure. J Reconstr Microsurg. 2019;35(4):270–86. Available from: https://pubmed.ncbi.nlm.nih.gov/30326523/
79. Defazio MV, RWY H, Han KD, Bunting HA, Evans KK. Lower extremity flap salvage in Thrombophilic patients: managing expectations in the setting of microvascular thrombosis. J Reconstr Microsurg. 2016;32(6):431–44. Available from: https://pubmed.ncbi.nlm.nih.gov/26789005/
80. Senchenkov A, Lemaine V, Tran N. Management of perioperative microvascular thrombotic complications - the use of multiagent anticoagulation algorithm in 395 consecutive free flaps. J Plast Reconstr Aesthet Surg. 2015;68(9):1293–303. Available from: https://pubmed.ncbi.nlm.nih.gov/26070491/
81. Kroll S, Miller M, Reece G, Baldwin B, Robb G, Bengtson B, et al. Anticoagulants and hematomas in free flap surgery. Plast Reconstr Surg. 1995;96(3):643–7. Available from: https://pubmed.ncbi.nlm.nih.gov/7543686/
82. Nelson JA, Chung CU, Bauder AR, Wu LC. Prevention of thrombosis in hypercoagulable patients undergoing microsurgery: a novel anticoagulation protocol. J Plast Reconstr Aesthet Surg. 2017;70(3):307–12. Available from: https://pubmed.ncbi.nlm.nih.gov/28089863/
83. Pugh CM, Dennis RH, Massac EA. Evaluation of intraoperative anticoagulants in microvascular free-flap surgery. J Natl Med Assoc. 1996;88(10):655.
84. Frykberg RG. Team approach toward lower extremity amputation prevention in diabetes. J Am Podiatr Med

Assoc. 1997;87(7):305–12. Available from: https://japmaonline.org/view/journals/apms/87/7/87507315-87-7-305.xml
85. Elmarsafi T, Oliver NG, Steinberg JS, Evans KK, Attinger CE, Kim PJ. Long-Term Outcomes of Permanent Cement Spacers in the Infected Foot. J Foot Ankle Surg. 2017;56(2):287–90. Available from: https://pubmed.ncbi.nlm.nih.gov/28089125/
86. Elmarsafi T, Pierre AJ, Wang K, Evans KK, Attinger CE, Kim PJ, et al. The Vertical Contour Calcanectomy: An Alternative Surgical Technique to the Conventional Partial Calcanectomy. J Foot Ankle Surg. 2019;58(2):381–6. Available from: https://pubmed.ncbi.nlm.nih.gov/30612862/
87. Cates NK, Wang K, Stowers JM, Attinger CE, Kim PJ, Steinberg JS. The Vertical Contour Calcanectomy, an Alternative Approach to Surgical Heel Ulcers: A Case Series. J Foot Ankle Surg. 2019;58(6):1067–71. Available from: https://pubmed.ncbi.nlm.nih.gov/31679660/
88. Cook HR, Cates NK, Kennedy CJ, Tefera E, Popovsky D, Delijani K, et al. Risks factors associated with major lower extremity amputation after vertical contour Calcanectomy. J Foot Ankle Surg. 2022;61(5):1046–51. Available from: https://pubmed.ncbi.nlm.nih.gov/35168902/
89. Economides JM, Defazio MV, Attinger CE, Barbour JR. Prevention of painful neuroma and phantom limb pain after transfemoral amputations through concomitant nerve coaptation and collagen nerve wrapping. Neurosurgery. 2016;79(3):508–12. Available from: https://pubmed.ncbi.nlm.nih.gov/27306717/
90. Chang BL, Mondshine J, Attinger CE, Kleiber GM. Targeted muscle reinnervation improves pain and ambulation outcomes in highly comorbid amputees. Plast Reconstr Surg. 2021;148(2):376–86. Available from: https://pubmed.ncbi.nlm.nih.gov/34398088/
91. Margolis DJ, Hoffstad O, Nafash J, Leonard CE, Freeman CP, Hennessy S, et al. Location, location, location: geographic clustering of lower-extremity amputation among Medicare beneficiaries with diabetes. Diabetes Care. 2011;34(11):2363–7. Available from: https://pubmed.ncbi.nlm.nih.gov/21933906/
92. Fan KL, Delia D, Black CK, Zolper E, Singh T, Wirth P, et al. Who, What, Where: Demographics, Severity of Presentation, and Location of Treatment Drive Delivery of Diabetic Limb Reconstructive Services within the National Inpatient Sample. Plast Reconstr Surg. 2020;145(6):1516–27. Available from: https://pubmed.ncbi.nlm.nih.gov/32205544/
93. Fan KL, Bekeny JC, Kennedy CJ, Zolper EG, Steinberg JS, Attinger CE, et al. A Focus on Amputation Level: Factors Preventing Length Preservation in the National Inpatient Sample. J Am Podiatr Med Assoc. 2022;112(1):20–028. Available from: https://pubmed.ncbi.nlm.nih.gov/35324459/
94. Fan KL, Singh T, Bekeny JC, Zolper EG, Dekker PK, Attinger CE, et al. Use of flap salvage for lower extremity chronic wounds occurs Most often in competitive hospital markets. Plast Reconstr Surg Glob Open. 2021;9(2):e3183. Available from: https://pubmed.ncbi.nlm.nih.gov/33680630/

Index

A
Abadeer, A.I., 187
Abductor hallucis (ABH) muscle flap, 431, 432
Acellular dermal matrix (ADM), 314
Achilles tendon, 74
  contracture, 513
  lengthening, 454
Acquired immunodeficiency syndrome (AIDS), 60
Active charcot foot, 245
Activities of daily living (ADLs), 545
Acute bacterial skin and soft tissue infections (ABSSI), 182
Acute coronary syndrome (ACS), 147
Acute ischaemia, 121
Acute kidney injury (AKI), 98
Acute pain service (APS), 36, 152
Acute rehab (AR) placement, 40
Acute reversible neuropathy, 113
Adductor digiti minimi (ADM) muscle flap, 430, 431
Adjunctive therapy, 394
Admin Pool, 22
Advanced plastic surgical reconstruction, in lower extremity
  algorithmic approach, 477
  flap selection
    ALT pedicle, 504
    dead space obliteration, 509
    MSAP, 504
    recipient vessel, 504, 507
    reulceration, 509
    SCIP, 505, 506
    suprascarpal plane, 509
  microsurgery, 467, 472, 513
  negative pressure wound therapy, 475
  orthoplastic surgery, 481
  patient population and selection, 468, 470
  pre-operative evaluation
    counseling, 472
    examination, 473
    history of, 473
    interdisciplinary consultations, 474
    studies, 473, 474
  preparation for, 474, 475
  recipient vessel selection, 500, 502
  supermicrosurgery, 467, 475, 479, 500, 502, 504, 507, 511
  technical considerations
    anastomosis, 512, 513
    antibiotic-impregnated cement/bone void fillers, 514
    anticoagulation, 514
    bony contouring, 513
    compression therapy, 516
    drains, 514
    external fixation, 516, 517
    flap inset, 514
    flap planning, 511
    HBOT, 517
    incision planning, 512
    positioning, 515
    postoperative monitoring, 515
    recipient vessel selection, 511
    tourniquet use, 512
    T-shaped/flow through anastomosis, 513
    wound preparation, 511
  wounds
    ankle, 490
    forefoot, 477, 478, 482, 484, 486
    hindfoot, 489, 490
    massive, 496
    midfoot, 489
"Advanced reconstruction", 477
Adverse effects, 270
Aerobic and anaerobic cultures, 454
Air plethysmography (APG), 293
Akbari, C.M., 1, 251–256, 258–260, 263–265, 267, 268, 270, 271, 273, 275–283
Alfonso, A.R., 305
Allergic contact dermatitis, 338
Allografts, 306
Alternburg, M.M., 87
Ambulation, 353, 355
American Diabetes Association (ADA), 91
American venous forum (AVF), 288
Amputation, 1, 8, 58, 59, 75, 178, 349, 521, 587, 603, 604, 606, 607, 609, 610
Amputee, 587, 588
  care coordinator, 353
  support group, 587–589

© Springer Nature Switzerland AG 2023
C. E. Attinger, J. S. Steinberg (eds.), *Functional Limb Salvage*,
https://doi.org/10.1007/978-3-031-27725-2

Amputee mobility predictor (AMP), 552
Anabolic resistance, 134
Anemia, 474
Angiogram, 40
Angiography, 259, 479
Angiosome, 259, 490
Angiosome-directed revascularization, 259
Angiosome-oriented revascularization, 278
Angiosome-specific reperfusion, 475
Angiosome-targeted revascularization, 278
Angiotensin converting enzyme inhibitors, 90
Angiotensin II receptor blockers, 90
Ankle-brachial index (ABI), 254, 255, 429
Ankle deformity, 369
Ankle foot orthosis (AFO), 229, 350, 458, 542
Ankle obstacle, 576, 578, 579
Ankle wounds, 490
Antegrade approach, 279
Anterior tibial tendon transfer (ATTT), 380, 381
Anterolateral thigh (ALT), 455, 504, 607
Antibiotic therapy, 50, 454, 473
Anticoagulation and antiplatelet management
  antiplatelet agents, 97
  background, 95
  bleeding risk, 96
  direct thrombin and direct Xa inhibitors, 96
  thrombotic risk, 95
  venous thromboembolism (VTE) prophylaxis, 97
  warfarin, 96
Anti-depressants, 71
Antidiabetic medications
  insulin, 92, 93
  non-insulin medications, 92
  perioperative insulin management, 93
Anti-epileptic agents, 70
Antimicrobial therapy, 195, 196
Antiphospholipid antibodies, 452
Antithrombotic therapy, 453
Aorto-bifemoral bypass, 267
Aortoiliac System, 279, 280
Area deprivation index (ADI), 594
Areeg, A., 1
Argenta, L.C., 436
Arizona Brace, 81
Armstrong, D.G., 142, 233, 394, 398
Arrhythmia, 147
Arterial calcification, 474
Arterial disease management in limb salvage patient
  CLTI, 263
  endovascular revascularization
    anatomic considerations, 277, 278
    choice of, 276
    general considerations, 276, 277
    inflow disease, treatment of, 280–283
    targets of, 277
    technical approaches in, 278, 279
    treatment of inflow disease, 279, 280
  inflow operation, 267, 268
  infrainguinal bypass, 270–273
  open surgery, 263–265
  patency rates, 275, 276
  preoperative consideration, 265, 267
  quality of life score, 276
  systemic and local complications, 274, 275
Arteriogram, 457, 459
Arteriography, 259
  FTT, 454
Arteriosclerosis, 134
Arteriotomy, 268
Arthropathy, 238
Artificial intelligence, 140
Aspergillus flavus, 337
Aspirin, 90
Assisted living facility (ALF), 38
Atherectomy, 260
Atherosclerosis, 251
Atherosclerotic cardiovascular disease (ASCVD), 147
Atraumatic technique, 165, 166
Atrophic nonunion, 564
Atrophy, 507
Attinger, C.E., 1, 157, 500, 545, 603
Attinger, T., 35
Atves, J.N., 157, 360, 521
Atypical mycobacterial infections, 336
Autogenous ipsilateral saphenous vein, 265
Autogenous saphenous vein, 270
Autogenous skin grafts, 415
Autogenous vein grafting, 264
Autoimmune blistering disease, 332, 333
Autolytic débridement, 161, 162
Autonomic neuropathy, 126

B

Bąk, E., 141
Bal, A., 109
Balloon angioplasty, 280
Baumhauer, J.F., 220
Beaulieu, R.J., 359, 522
Below knee amputations
  (BKAs), 455, 504, 545, 546
  anatomy, 546, 547
  calcitonin, 550
  epidural anesthesia, 551
  gabapentin, 550
  morbidities, 548, 549
  non-steroidal anti-inflammatory drugs, 550
  nutrition, 551
  opiate analgesics, 550
  perineural catheters, 551
  physical therapy, 552
  psychological therapies, 551
  targeted muscle reinnervation, 549, 550
Below the ankle (BTA) arteries, 282
Below the knee (BTK) arteries, 281, 282
Bertram, K.D., 73
BEST-CLI trial, 260
Beta-blockers, 89, 90, 274

Beta-lactamase inhibitor (BLI) clavulanic acid, 196
Bilateral neuropathic pain, 111, 112
Bilateral Oedema, 125
Billing analyst, 19
Bioavailability, 180, 181
Biobrane, 316
Biofilms, 180, 419
infections, 178
Biologic débridement, 162
Biologic skin substitute, 307, 323
Biomechanical deformities, 513
Biosynthetic dressing, 313, 316, 317, 321
Bone concentration, 181
Bone edema, 234
Bone imaging, 184
Boulton, A.J.M., v, 65
Brand, P.W., 68
Bunnell, Sterling, 166
Bypass versus angioplasty in severe ischaemia of the leg (BASIL) trial, 260

C
Caisson disease, 401
Calciphylaxis, 341, 345
Calcitonin, 550
Callus, 124
Candida albicans, 337, 457
Cardiac biomarkers, 89
Cardiovascular disease, 305
Carroll, P.J., 360
Case management (CM), 35
Case Management Society of America, 36
Case manager, 37, 39, 40
Case Manager Associate (CMA), 36
Casini, A., 263–265, 267, 268, 270, 271, 273, 275–283
Casts, 227, 228, 230
Catanzariti, A.R., 245
Cates, N.K., 239
Center for wound healing (CWH), 349
daily operations, 13, 14
Central nervous system (CNS), 410
Central scheduling, 27
Cerebrovascular disease (CVD), 147
Certified medical assistants (CWH), 17
CFA
BTA arteries, 282
BTK arteries, 281, 282
FP segment, 281
no-option patients with CLTI, 282, 283
Charcot bone, 242
Charcot foot disease, 123
active phase, 216
clinical presentation of, 216
diabetes factors
genetic predisposition, 219
obesity, 219
simultaneous pancreas-kidney transplant (SPKT) in type 1 diabetes, 219
skeletal fragility, 219
diagnosis of, 215
imaging, 222
etiology of, 217
history of, 216
inactive phase and recurrence, 217
mortality, 221
neuropathy
on joint capsule, 218
RANK/RANKL-NFkappaB and Wnt/β-catenin Pathways, 217, 218
on vasculature, 218
permissive factors, 219
pro-inflammatory cytokines, 221
expression, 220
Charcot, J.-M., 216
Charcot neuroarthropathy (CN), 74, 79, 81, 208, 227, 228, 237, 238, 361, 373, 473
charcot bone, 242, 243
charcot restraint orthotic walker, 231
conventional radiography, 234
deformity correction, 246
exostectomy, 245
foot with fractures, 228, 229
frame orthosis, 231
hindfoot internal fixation, 246
indications for surgery, 243, 244
midfoot internal fixation, 247
midfoot stabilization, 246
monitoring, 232, 233
MRI, 233
orthotic treatment, 229, 230
post-operative care, 248
postoperative follow-up treatment, 234, 235
prefabricated diabetic walker, 230, 231
preoperative evaluation, 241, 242
radiographic evaluation, 240, 241
shoes, 231, 232
surgical management, 239, 240
total contact cast, 230
two-stage reconstruction, 247, 248
Charcot reconstructive surgery, 81
Charcot restraint orthotic walker (CROW), 231, 350, 368
Chiu, E., 305
Chopart's amputation, 537
Chronic hyperglycemia, 187
Chronic inflammation, 134, 135
Chronic limb-threatening ischemia (CLTI)
CTOs, 278, 279
with foot ulceration/gangrene, 267
management of, 263
natural history, 263
no-option patients with, 282, 283
PAD, 263
treatment of, 263
Chronic obstructive pulmonary disease, 189

Chronic pain after amputation (CPAP), 150
Chronic peripheral vascular disease, 402
Chronic total occlusions (CTOs), 278, 279
Chronic venous disease (CVD), 285
  adhesive endovenous closure, 297
  anatomy, 286, 287
  causes and risk factors, 289
  clinical presentation, 290
  complications, 297
  compression therapy, 293, 294
  conservative management, 292
  diagnostic workup, 290, 291
  economic burden, 291
  elevation, 292
  epidemiology, 288, 289
  mechanochemical endovenous closure, 295, 296
  normal venous valves, 287
  pathophysiology, 287
  post-procedural care, 297
  quality of life, 291
  thermal endovenous closure, 295
Chronic venous insufficiency, 287
Chronic wounds, 604
Classical approach, 421
Claudication, 252
Claw toes, 122
Clerici, G., 263–265, 267, 268, 270, 271, 273, 275–283
Clindamycin, 197
Clinical management, 187
Clinical Nurse Manager, 16
Clinical pool, 22
Clinical social worker, 37, 38
Collateral-vessel-guided revascularization, 278
Collateral vessel network, 278
Combination therapy, 71
Commercial insurance, 37
Comorbid, 533
Complex discharge
  barriers, 42, 43
  case management, 42
  free-flap (*see* Free-flap)
  plan, 42
Complex limb patients
  hospital administration and limb service, 43–45
  mental health diagnoses and substance abuse issues, 38
  targeted discharge date (TDD), 39
  visits/conversations, 40
Complex regional pain syndrome (CRPS), 114
Compression therapy, 292
Computed tomography angiography (CTA), 258
Congestive heart failure (CHF), 148, 189, 425
Conservative fracture treatment, 228
Conservative surgery, 208
Contact dermatitis, 345
Context factors, 232
Contractures, 74
Contralateral saphenous vein, 265
Controlled ankle movement (CAM), 42, 77, 78
  walker, 78
Control of infection, 267
Conway, J.D., 559
Cook, J., 208
Cook-Swartz implantable Doppler probe, 462
Corns, 124
Coronary artery bypass graft (CABG), 148
Coronary artery disease (CAD), 147, 189
Cost per wound, 322
COVID-19 pandemic, 36, 38–39
C-reactive protein (CRP), 188, 195, 515
Critical limb ischemia (CLI), 418
Critical limb threatening ischemia (CLIT), 260
Cultured skin grafts, 306, 319, 320
Custom accommodative orthotics, 76, 77
Custom molded orthosis (CMO), 458
Cutaneous malignancy, 339
Cutler, B., 285

D
Daniels, H., 35
DC Medicaid, 38, 43
Débridement, 523, 524
  autolytic, 161, 162
  biologic, 162
  contraindications, 335
  defined, 157
  enzymatic, 161
  mechanical, 161
  surgical, 163
    atraumatic technique, 165, 166
    of bone, 168
    clinical determination, 171
    of deep tissue, 167, 168
    indications, 164
    instrumentation, 164
    methylene blue, 170, 171
    microbiological determination, 171
    of skin, 166
    of subcutaneous tissue, 166, 167
    staged approach, 168
    tissue viability, 171
Deep-learning image processing algorithm, 140
Deep tissue specimens, 209
Deep vein thrombosis (DVT), 285, 300
Definitive prosthesis, 355, 356
Deformities, 74, 122, 227–229, 239, 243, 526
  correction, 246
Degree of ischemia, 255
Dekker, P.K., 415–427, 449, 450, 452–462, 591
Del-Corral, G., 429–431, 433–446
Deldar, R., 57, 193
Delirium, 99
de Oliveira, A.L., 137
Deperio, T., 35
Dermal substitute, 313–317, 319, 321
Dermatologic wounds
  allergic contact dermatitis, 338, 339
  autoimmune and inflammatory diseases, 329, 330
  cutaneous malignancy, 339, 340
  fungal infections, 337
  Maverakis diagnostic criteria, 332

opportunistic infection, 334–336
vascular diseases, 341–343
Dermatomes, 421
Dermody, M., 298
De Vries, F.E.E., 396
Diabetes conference, v
Diabetes mellitus, 73, 237, 238
frailty
biomechanics of lower extremities, 135, 136
emerging technologies, 139
frailty phenotypes and frailty index, 138, 139
impact of, 141
mobility degeneration in, 136, 137
pre-frail diabetic patients, 142
screening frailty, 137
glucose management, 91
glucose range, 92
hyperglycemia, 91
hypoglycemia, 91
Diabetic foot, 251–253, 255
Arizona Brace, 81
bilateral neuropathic pain, 112, 113
biomechanics of, 74
callus, 124–127
Charcot restraint orthotic walker, 80, 81
classification, 110
complex regional pain syndrome, 115
components of examination, 74, 75
controlled ankle movement, 77, 78
custom accommodative orthotics, 75–77
custom shoes, 77
débridement
wound bed preparation, 160
wound healing, 158, 159
deformity, 122–124
diabetic shoes, 77
drug history, 116
examination, 116–128
family history, 116
felt padding, 75
femoral nerve, 114
footwear assessment, 128
gait, 128
infection, 119–121
ischaemic pain, 115
lumbar Spinal Stenosis, 114
past foot history, 116
past medical history, 116
patellar tendon brace (PTB), 81
presenting complaint, 110
psychosocial history, 116
saphenous nerve, 114
simple staging system, 109
skin, 117–118
breakdown, 119
soft tissue procedures
external fixation for offloading, 84
MIS invasive floating metatarsal osteotomy, 83, 84
modified Keller resection arthroplasty, 83
offloading options, by wound location, 85
percutaneous flexor tenotomy, 81, 82
tendoachilles lengthening, 82
tendon transfers, 83
sound offloading principles, 75
staging, 129
total contact cast, 78–80
ulceration, 74
Diabetic foot attack (DFA), 209
Diabetic foot infections (DFIs), 175, 203
antibiotics, 196, 197
antimicrobial therapy, 195–197
applied anatomy of, 205, 206
biomarkers of, 195
management, 189, 190, 195
microbiology of, 194
soft tissue infection, 193
biofilm, 199
diagnosis, 194
microbiological assessment of, 194, 195
surgical debridement of, 206
surgical treatment of, 206
Diabetic foot osteomyelitis (DFO), 179
with antibiotic therapy, 179
duration of therapy, 182, 183
epidemiology of, 176
intra-osseus/topical antimicrobials, 183
microbiology, 176, 177
outcome of treatment, 184
pathophysiology, 176
route of administration, 180
specific agents, 180, 182
surgical treatment, 178, 179
systemic antibiotic therapy, 179, 180
treating DFO, 184
Diabetic foot reconstruction, 467, 468
Diabetic foot ulceration (DFU), vi, 1, 2, 4, 73, 190, 203, 404, 417, 418, 591
amputation, 59
economic analyses, 58
guideline-based management, 59
healthcare costs, 58, 59
mortality, 60, 61
prevalence, 58
socioeconomic, 60
treatment algorithm, 73
Diabetic foot wounds, 57
Diabetic healing boot, 350
Diabetic healing shoe, 350
Diabetic limb salvage (DLS), 605, 606
communication barriers, 9
endocrinologist, 4 (*see also* Free tissue transfer (FTT))
infectious disease, 5
intraoperative risk mitigation, 149, 150
location, 7, 8
multidisciplinary needs, 7
multidisciplinary team, 3, 4
pediatric/orthopedic surgery, 4
phantom limb pain, 150
plastic and reconstructive surgery, 4
pre-operative optimization, 147, 148

Diabetic limb salvage (DLS) (*cont.*)
residual limb pain, 150, 151
team communication, 8, 9
vascular surgery, 4
wound management pathway, 6
Diabetic neuropathy, 66, 67, 69, 71, 252
classification, 67
diagnosis, 67
foot ulceration, 68, 69
pathogenesis, 66
pharmacological treatment, 69, 70
symptoms and signs, 68
Diabetic shoes, 77
Diabetics, perfusion assessment and treatment
history, 251–253
invasive diagnostic imaging, 259, 260
noninvasive diagnostic imaging, 254, 255, 258, 259
PAD, 251
physical examination, 251, 253, 254
symptomatic and asymptomatic, 251
therapeutic options, 260
Diabetic ulcers, 305
Dickkopf-1, 218
Dieckman, C., 306
Direct polymerase chain reaction (PCR), 195
Direct revascularization (DR), 277
Discoid lupus erythematosus (DLE), 333
Distal endovascular intervention, 268
Distal metatarsal metaphyseal osteotomy (DMMO), 366
Distal superficial femoral artery, 264
Division of Economic and Community Outreach (DECO), 38
Donor sites, 416
Doppler waveform, 258
Dorsalis pedis artery, 253
bypass, 265
Dramploas, E., 209
Drug coated balloons (DCBs), 260, 280
"Drug delivery", 280
Drug eluting stents (DESs), 260, 280
Duke activity score index, 89
Duplex arterial scanning, 258
Duplex ultrasound, 258, 265, 454, 473, 502
Durable medical equipment (DME), 37
Dysvascularity, 349–350, 354

E
Ecthyma gangrenosum, 338
Edema, 419, 424, 425
Edmonds, M., 107
Eichenholtz stages, 230
Electronic medical record (EMR), 9, 19
Ellis, A., 13
Emergency Department (ED), 39
Emergency Medicaid, 42
Endocrine Society, 91
guidelines, 92
Endocrinology, 457
Endothelial growth factor (EGF), 159
Endothermal heat-induced thrombosis (EHIT), 298
Endovascular revascularization, 457
aortoiliac system, 279, 280
CFA
BTA arteries, 282
BTK arteries, 281, 282
FP segment, 280, 281
no-option patients with CLTI, 282, 283
choice of, 276
chronic total occlusions crossing strategy, 278, 279
evaluation of collateral vessels, 278
general considerations, 276, 277
metabolic demands of tissue loss, 278
multivessel versus single-vessel, 278
targets of, 277
vascular territories of lower leg, 279
Endovascular therapies, 260
Endovenous glue- induced thrombus (EGIT), 299
Endovenous laser ablation (EVLA), 295
End stage renal disease (ESRD), 512
End-to-end (ETE) anastomosis, 489, 512, 513
End-to-side (ETS) technique, 512
Enhanced recovery after surgery (ERAS), 152
Enterobacteriaceae, 177
Enterococcus faecalis, 196
Enzymatic débridement, 161
Epidural anesthesia, 551
Equinus contracture, 482
Erythrocyte sedimentation rate (ESR), 188
Ethics of case management, 39
Ethylene vinyl acetate (EVA), 76
European guidelines, 90
Evans, K.K., 59, 415–427, 449, 450, 452–462, 603
Executive assistant (EA), 21
Exostectomy, 245
Extensor digitorum brevis (EDB) muscle flap, 433, 434
Extensor digitorum longus (EDL), 433
Extracellular matrix (ECM), 306

F
Fan, K.L., 449, 450, 452–462, 591, 603
Fasciocutaneous flaps, 455, 509
Felder, J.M., 467, 468, 470, 472–475, 477–482, 486, 489, 490, 500, 502, 504, 505, 507, 509, 511–516, 518
Felt padding, 75
Femoral nerve, 114
Femoro-Popliteal (FP) segment, 280, 281
Fernandez, A., 522
Fernando, M.E., 137
Ferraresi, R., 263–265, 267, 268, 270, 271, 273, 275–283
Fibroblast growth factor (FGF), 159
Fibrofatty padding depletion (FFPD), 123
Fillet flap of toe, 442, 443
First dorsal metatarsal artery (FDMA) flap, 435, 436, 484, 500, 501
Flexor digitorum brevis (FDB), 435
muscle flap, 434, 435

Flexor tenotomy, 364
Fluoroquinolones, 197
Folestad, A., 220, 221
Fontaine and Rutherford classifications, 254
Food and Drug Administration (FDA), 197
Foot ulceration, 65–68
Foot vein arterialization (FVA), 283
Forefoot osteomyelitis, 207
Forefoot wounds, 476–478, 482, 484, 486
Frame orthosis, 231
Free-flap, 39
  background on, 41
  case management, 41
  plan, 41
Free tissue transfer (FTT), 605, 607
  comparison to non-diabetic patients, 450
  free flap reconstruction, 449, 450
  indications, 450
  intraoperative optimization
    anesthesia, 455
    flap choice, 455, 461
    flap inset, 462
    microvascular anastomosis, 461
  for lower extremity, 449
  multidisciplinary approach, 451
  multiple debridements, 457, 459
  postoperative flap monitoring, 462
  preoperative stage
    endocrine pathways, 452
    medicine, 451–453
    podiatric and orthopedic surgery, 454
    surgical debridement, 454
    vascular, 453, 454
  risk-stratified anticoagulation protocol, 453
  targeted antimicrobial therapy, 457
  viability of, 449
Fried, L.P., 137, 138
Front Desk, 18
F-Scan systems, 77
Full-thickness skin grafts (FTSGs), 416
  aesthetic advantages, 416
  benefits of, 416
  disadvantages, 416
Functional morbidity, 455
Furlow, L.T., 435

G
Gabapentin, 550
Gabriel, A., 397
Gait analysis, 74
Game, F., 215
Garada, F., 587
Gastrocnemius recession, 378
Gastrocnemius-soleus recession (GSR), 380
Geirsdottir, O., 142
General internal medicine (GIM), 40
General Medicine (GM), 36
Genotypes, 452
Georgetown Home Care, 43
Georgetown NP Program, 43
Glaser, J.D., 523
Global Vascular Guidelines (GVGs), 277
Glucose control, 468
Glucose levels, 451
Glycemic control, 451
Gosh, A., 330
Grabb, W.C., 436
Graft infection, 270
Gram-negative bacilli (GNB), 196
Granulation tissue, 392
Great saphenous vein (GSV), 286
Greenhagen, R.M., 242
Grewal, G.S., 142

H
Haffner, Z.K., 58
Hallux valgus, 123
Hammer Toe, 122
Harding, J.L., vi
Haydek, J., 87
Hayes, C., 550
HbA1c, 426
Hemodialysis, 474
Hemoglobin A1c (HbA1c), 417, 474
Hemostasis, 420
Heparin-induced thrombocytopenia (HIT), 343
Herbst, S.A., 242
Herlin, C., 442
Herscovici, D., 373
Higgs, B.G., 349
High stakes defects, 502
Hindfoot wounds, 489, 490
Hoh, T.K., 521
Hollenbeck, S.T., 455
Hong, J.P., 467, 468, 470, 472–475, 477, 482, 486, 489, 490, 500, 502, 504, 505, 507, 509, 511–516, 518
Horn, D.M., 376
Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS), 54
Hubley, K.S., 1, 47
Huffman, S.S., 603
Hyperbaric oxygen therapy (HBOT), 14, 425, 475, 507, 517
  adverse effects, 409, 410
  clinical practice, 407–409
  diabetic foot ulcerations, 404, 405
  limb salvage, 403
  lipid peroxidation, 403
  microvascular cell walls, 403
  physiology, 402
  skin grafts and flaps, 405, 406
Hyperbarics Program, 18
Hypercoagulability, 452, 457, 459
Hyperglycemia, 91, 252, 305
Hyperlipidemia (HLD), 40
Hyperspectral imaging (HSI), 257
Hypertension (HTN), 39–40
Hypertrophic nonunion, 564

Hypertrophic obstructive cardiomyopathy (HOCM), 149
Hypoglycemia, 91, 305
Hypotension, 455

I
Ibrahim, A.M., 593
IGCA, 260
Iliac obstructive disease, 279
Ilizarov-type external fixation, 516
Immediate post-operative prosthesis (IPOP), 353
Immune system, 187
Incompetent perforator veins, 299
Indocyanine green angiography (ICGA), 260
Infected nonunion, 567–569, 572
Infection, 523
Infectious disease (ID), 5, 36
Infectious Diseases Society of America (IDSA), 188, 204
Inflow operation, 267
Infrainguinal arterial reconstruction, 264
Infrainguinal bypass, 270
Inherited/acquired traits, 452
Inosculation and capillary ingrowth phase, 417
Instability, 229, 231
Insulin, 92, 93
Insulin dependent diabetes mellitus (IDDM), 39
Insulin resistance, 134, 135
Integrated model of care (IMOC), 37
Interleukin-6 release, 187
Intermittency, 392, 394
Internal fixation, 564, 576
Internal tissue expansion, 443–445
International Working Group on Diabetic Foot (IWGDF), 178, 179, 194, 204
  classification, 188
Interqual Criteria, 36
Interventional procedures, 189
Intramedullary hindfoot nail (IMHN), 246
Intravascular ultrasound (IVUS), 300
Intrinsic muscles, 430
Isaac, A.L., 58
Ischaemia, 120, 253, 424, 524, 525
  foot, 107

J
Jeffcoate, W., 215
Johnson-Arbor, K., 401
Joret, M.O., 595
Joslin, E.P., 3

K
Kalani, M., 256
Kaloderm, 320
Kang, G.E., 133, 139, 141, 142
Karlakki, S.L., 396
Kavarthapu, V., 203, 237
Kesavan, R., 107
Kevin, G., 1
Kiguchi, M., 286
Kim, K.G., 283, 449, 450, 452–462, 545, 591
Kim, P.J., 391–399
Kiparizoska, S., 87
Kleiber, G.M., 545
Kleinpell, 47
Koller, A., 227
Kripalani, S., 50
Krishnan, S., 3
Kugler, M.C., 47

L
Lateral calcaneal artery (LCA) skin flap, 436, 437
Lawrence, P.F., 299
LeDran, Henry, 157
Left ventricular ejection fraction (LVEF), 88
Length-of-stay (LOS), 35
Lesser digits, 364
  arthroplasty, 364
Lessing, M.C., 393
Levine's technique, 194
Lewi, M.J, 2
Liao, A., 147
Life-threatening condition, 252
Limb salvage, 47, 50, 54, 57, 59–61, 349, 359, 361, 387, 609
  complications, 581, 582
    history, 559–561
    imaging, 561, 562
    laboratory studies, 562
    physical examination, 561
  diabetic foot population, 592
  geographical location
    access to care, 592, 593
    comorbidities, 595
    race and ethnicity, 594
    socioeconomic status, 594
  hypertrophic nonunion, 564, 565
  inpatients, 101
  lower extremity nonunion, 563, 564
  malunion, 572, 573
  multidisciplinary, 595, 596
  postoperative management, 584
Lipsky, B.A., 175
Lisfranc amputation, 536
Local antibiotic delivery, 208
Local flaps for foot and ankle reconstruction
  ABH muscle flap, 431–433
  ADM muscle flap, 430, 431
  angiosomes, 429
  EDB muscle flap, 433, 434
  FDB muscle flap, 434, 435
  FDMA flap, 435, 436
  fillet flap of toe, 442, 443
  internal tissue expansion, 443–445
  intrinsic muscles, 430
  LCA skin flap, 436, 437
  medial plantar artery flap, 438–440

pathologies management, 429
principles of, 429
random skin flaps, 443, 445, 446
reverse sural artery flap, 440–442
selection, 430
Logemann, N., 329
Low-density lipoprotein (LDL), 147
Lower extremity, 1, 6
biomechanics, 136
reconstruction, 605–607, 609
Lower extremity amputations (LEA), vi, 187, 313, 323
Lumbar spinal stenosis, 114

M
Macrodeformation, 393
MacRury, S., 8
Magnetic resonance angiography (MRA), 258, 259
Magnetic resonance imaging (MRI), 205, 221
Major adverse cardiovascular events (MACE), 148
Malunion, 572
Marjolin's ulcer, 340
Martin, D.Z., 429–431, 433–446
Massive wounds, 496, 497
Mathes-Nahai type B, 438
Mathes-Nahai type I flap, 440
Mathes-Nahai type II flap, 430, 431, 433, 434
Maturation phase, 417
Maximillian, 8
McCraw, J.B., 435
Mechanical débridement, 161
Mechanochemical endovenous closure (MOCA), 296, 297
Medial arterial calcification, 258
Medial plantar artery flap, 438–440
Medial sural artery perforator (MSAP), 455, 504
Medicaid, 38, 42
Medical Grand Rounds, 35
Medical therapy, 263
Megas, N.R., 47
Meta-analysis, 280, 282
Metabolic equivalents (METs), 148
Metatarsophalangeal joint (MTPJ), 362, 438
Methicillin-resistant *S. aureus* (MRSA), 177
nasal carriage, 195
Methylene blue, 170, 171
Methylthioninium chloride, 170
Metronidazole, 197
Microdeformation, 393
Microvasculature, 507
Micro water jet device, 165
Middle ear barotrauma (MEBT), 409
Midfoot exostectomy, 368, 369
Midfoot internal fixation, 247
Midfoot obstacle, 575, 577
Midfoot wounds, 489
Milisits, T.F., 73
Miller, J.D., 359
Minimal inhibitory concentration (MIC), 196
Mitochondrial dysfunction, 135
Mittlemeier, 240
Modi, N., v
Modified Keller resection arthroplasty, 83
Molines-Barroso, R.J., 245
Moore, Z., 137
Morrato, E.H., 136
Morykwas, M.J., 392
Motor neuropathy, 126, 468
Muchna, A., 135
Mucormycetes spp, 337
Mueller, M., 83
Multidisciplinary approach, 450
Multidisciplinary care team (MDT), 1–3, 8, 604, 609
limb salvage
care delivery optimization, 596, 597
collaborative initiatives, 597
Multidisciplinary diabetic foot care team (MDFT), 239
Multidisciplinary discharge rounds (MDRs), 37, 49
Muscle flaps, 476, 502, 507–509
Musuuza, J., 595
Myocardial infarction (MI), 61, 148
Myocardial injury after noncardiac surgery (MINS), 88

N
Nails, 125
Najafi, B., 133, 136, 137, 141, 142
National Fire Protection Association (NFPA), 408
Ndip, A., 216
Necrobiosis lipoidica diabeticorum (NLD), 426
Necrosis, 121
Negative pressure wound therapy (NPWT), 40, 50, 51, 419, 420, 423, 425, 511
advantages and disadvantages, 392
incisions, 391, 393, 394, 396
indications
chronic wounds, 395
closed incisions, 395, 396
infected/contaminated wounds, 396, 397
wound healing, 393, 394
innovation, 397, 398
for mechanisms of action, 392–394, 397
wound bed preparation, 395
Negative pressure wound therapy with instillation (NPWTi), 392–397
Neglen, P., 301
Neovascularization, 159
Neuropathic foot, 107
Neuropathic plantar ulcers, 207
Neuropathy, 126, 217, 241, 244, 248
Neuropathy disability score (NDS), 67
Neurothesiometry, 127
Neutrophilic vasculitis, 205
Neville, C., 135, 136
New molecular techniques, 195
Ngwe, 208
Nil per os (NPO), 148
N-methyl D-aspartate (NMDA), 550
Noncompliance, 473
Non-insulin medications, 92

Non-osteomyelitic soft tissue diabetic foot infections, 198
Nonsalvageability, 452
Non-steroidal anti-inflammatory drugs (NSAIDs), 550
Nonunion, 560
No-option patients with CLTI, 283
Nurse coordinator, 18
Nurse practitioners (NPs), 47, 49–51, 53
Nutrition, 551
screening, 452

O
Obesity, 255, 468, 507
Obstacles, 574
Obstructive sleep apnea (OSA), 149
O'Donovan, M., 141
Oedema, 125
Offloading, 73
Oh, T.S., 59, 449
Ollier, 415
Open endarterectomy, 280
Operating room (OR), 14
Opioid induced constipation (OIC), 100
Opsonophagocytosis, 187
Oral antibiotics, 180
Orbital atherectomy, 281
Osteomyelitis (OM), 190, 203, 429, 434, 468, 473, 475, 484, 491, 514, 518, 522, 523, 530
Osteoprotegerin (OPG), 217–218
Outcomes, 349, 352, 354
OVIVA study, 180
Oxidative stress, 135

P
Pantalar arthrodesis, 373, 374
Paola, L., 208
Parenteral antibiotics, 189
therapy, 196
Partial calcanectomy, 509
Partial foot amputation, 475, 521
Chopart's amputation, 537–539
deformity, 526, 527
indications, 521–523
infection, 523, 524
ischemia, 525
Lisfranc amputation, 536
partial foot amputations, 528
partial ray amputation, 531–533
toe amputation, 529
transmetatarsal amputation, 535, 536
vertical contour calcanectomy amputation, 540–542
wound, 523
Partial-foot amputee, 39
Partial ray amputation, 531
Pasieka, H.B., 329
Past medical history (PMH), 39
Patel, H., 49
Patel, N., 285
Patellar tendon brace (PTB), 81
Pathergy, 330
Patient-centered care plans, 39
Patient-controlled analgesia (PCA), 151
Patient discharge
education, 93, 94
goal hemoglobin A1c ranges, 94
home medication management, 94
outpatient follow-up, 94
prevention of atherosclerotic disease, 94
Patient Portal, 22
Patient registration associates (PRAs), 18
Patient-reported outcomes (PRO), 606
Patient services coordinators (PSCs), 19, 21
Patient Services Manager (PSM), 16
Patients' admission, 203
Peer support, 351, 352, 588
Percutaneous coronary intervention (PCI), 148
Percutaneous flexor tenotomy, 81, 82
Perforator flaps, 504
Performance-based outcome measure (PBOM), 552
Perineural catheters (PNCs), 551
Perioperative cardiac risk
condition, 87
functional capacity, 88
MINS protocol, 88
risk of procedure, 87
tools, 88
Perioperative cardiac testing
Ace-I/Arb, 90, 91
aspirin, 90
beta-blocker, 89, 90
cardiac biomarkers, 89
cardiac catheterization/CTA, 89
cardiac stress testing, 88, 89
EKG, 88
statin/lipid-lowering, 90
transthoracic echocardiography, 88
Peripheral arterial disease (PAD), 57, 65, 251, 260, 263, 276, 418, 594
screening, 254
Peripheral edema, 255
Peripherally inserted central catheter (PICC), 41
Peripheral nerve stimulation (PNS), 151
Peripheral neuropathy, 73
Peripheral vascular disease (PVD), 40, 470, 471, 476, 502
Periwound tissues, 475
Pes cavus, 122
Petrofsky, J., 136
Phantom limb pain (PLP), 150, 151, 548, 550, 551
Physical therapy, 552
Plain radiographs, 209
Plantar aponeurosis, 205
Plantar Callus, 74
Plasmatic imbibition phase, 417

Plastic Surgery (LIMB) service, 40
Platelet-derived angiogenesis factor (PDAF), 159
Platelet-derived growth factor (PDGF), 159
Plethysmography, 255
Polyarteritis nodosa (PAN), 342
Polymyositis, 115
Polyurethane, 398
Population dynamics, 591, 592
Portability, 398
Post-amputation rehabilitation, 552
Posterior interosseous artery (PIA) flap, 505
Posterior tibial (PT) artery, 254, 384
Postoperative complications
  acute kidney injury (AKI), 98
  antibiotics associated diarrhea, 101
  delirium, 99
  opioid induced constipation (OIC), 100
  postoperative ileus (POI), 100, 101
  postoperative nausea and vomiting (PONV), 99
Postoperative ileus (POI), 100, 101
Postoperative nausea and vomiting (PONV), 99
Posttraumatic stress disorder (PTSD), 587
Potter, J., 74
Powell, S.K., 39
Prader-Willi syndrome, 497
Prefabricated diabetic walker, 230
Preparatory prosthesis, 354, 355
Prevention, 350, 351
Primary revascularization, 417
Procalcitonin, 195
Prosthetic grafts, 273
Prosthetist consultation, 351
Provider Clinic Coverage schedules, 23
Provider Clinics, 13
Pseudomonas aeruginosa, 177, 196, 427
Pseudomonas spp., 194
Psychosocial assessment, 38
Pulse volume recording (PVR), 255
PVD, *see* Peripheral vascular disease (PVD)
Pylon, 355
Pyoderma gangrenosum, 329–331, 344, 402

Q
Quality adjusted life years (QALYs), 322
Quality of life (QOL), 69

R
Radiofrequency ablation (RFA), 295
Radiographs, 361
  evaluation, 74
Rahemi, H., 137, 142
Rahnama, A., 521, 559
Random skin flaps, 443, 445, 446
Randomized controlled multicenter trial, 180
Randomized controlled trials (RCTs), 70
Range of Motion, 74
RANKL/OPG/NFKappaB pathway, 220
Rasmussen, L.H., 295
Raspovic, K.M., 361, 522
Razmjou, K., 147
Reactive nitrogen species (RNS), 402
Reactive oxygen species (ROS), 402
Readmission, 49, 54
Reconstruction, 237, 238
Red–amber–green (RAG) model, 206
Reducing Amputation in People with Diabetes (RAPID), 8
Rehabilitation, 351, 352
  Rehab discharges, 38
Relative risk (RR), 592
Remission, 361
Remote monitoring, 398
Removable rigid dressings (RRD), 353
Residual limb pain (RLP), 150, 548
Residual volume fraction (RVF), 293
Restless legs syndrome, 115
Retiform purpura, 341
Retrograde approach, 279
Revascularization phase, 417
Reverse sural artery flap, 440–442
Revised Cardiac Risk Index (RCRI), 88
Rheumatoid arthritis, 115
Rifampi(ci)n, 182
Roberts II, A.H., 35
Robust soft tissue, 450
Rockwood, K., 138, 139

S
Safavi, P., 239
Safety, 472
Safety Director, 21
Sammarco, V.J., 246
Samsell, B., 322
Sanchez, J.A., 203
Saphenofemoral junction (SFJ), 286
Saphenopopliteal junction (SPJ), 286
Saphenous nerve, 114
Saphenous vein, 260
  graft, 270
Sayyed, A., 415–427
Sayyed, A.A., 57
Schon, L.C., 233
Schwenk, M., 137
Sclerostin, 218
Senneville, E., 193
Sensory neuropathy, 126
Shan, H., 587
Shanahan, 438
Shaper, 604
Shiroky, J., 50, 51
Siah, M.C., 251–256, 258–260, 263–265, 267, 268, 270, 271, 273–283
Siddiqui, N.A., 376, 559
Simon, S.R., 239
Singh, T., 545
Skin and soft tissues (SSTs), 193
Skin flap, 403, 406

Skin grafting, 404–406
classifications of, 415, 416
complications
factors impairing healing, 424, 425
revisional procedures, 425
diabetic foot ulcers, 417, 418
healing, 417
PAD, 418
postoperative healing
donor sites, 423
recipient site, 423, 424
presurgical evaluation
infection control, 418, 419
nutritional status, 419
vascular supply, 418
soft tissue reconstruction, 415
Skin temperature, 232, 233
Slit arteriotomy, 512
Smoking cessation, 452
Social vulnerability index (SVI), 593
Social Work (SW), 35, 39
Society of Vascular Surgery (SVS), 290
Socket, 355
Soft tissue reconstruction, 84
Spillerova, 278
Spinal cord simulation (SCS), 151
Split-thickness skin grafting (STSG), 415, 427, 458
advantages of, 416
benefits, 416
conservative approach, 416
disadvantages of, 416
donor site, 423
healing of, 424
indications, 416
operative steps, 420
application, 422, 427
harvesting stage, 420–422
wound bed debridement, 419, 420
Split tibialis anterior tendon transfer (STATT), 381, 382
Squamous cell carcinoma, 339
Staffing and day-to-day management
associate engagement, 30–32
attendings/residents coverage, 14
billing analyst, 19, 21
certified medical assistants (CWH), 17
clinical staff schedules, 28
CWH/HBOT staffing structure, 14–16
daily operations, 13, 14
executive assistant (EA), 21
hyperbaric oxygen therapy (HBOT), 14
hyperbaric technicians and safety director, 21
leadership, 16
managerial tracking of clinic operations, 30
managers' perspectives, 32–34
nurse coordinator, 18
nurse manager roles and responsibilities, 16
nurse practitioners, 18
nurse specialists, 17, 18
operating room (OR), 14
Outlook Master Calendar, 25
patient registration associates (PRAs), 18
patient services coordinators (PSCs), 19
patient services manager roles and responsibilities, 16, 17
Plans of the Day, 28
Provider and Orthotic/Prosthetic Coverage Template, 25
scheduling, 23
triage, 18
triage desk, 21–23
upcoming clinic numbers, 26, 27
Staggered Staff Schedules, 13
Standard of care (SOC), 305
Stannard, J.P., 396
Staphylococcus aureus, 177, 193
Statin/lipid-lowering, 90
Steinberg, J.S., 1, 359, 444, 603
Sterile bone biopsy, 190
Streptococcus agalactiae, 193
Subacute rehab facility (SAR), 40
Subfascial endoscopic perforator vein surgery (SEPS), 299
Superficial circumflex iliac artery perforator (SCIP) flap, 455, 478, 481, 500, 505, 506, 511
Superficial circumflex iliac artery perforator (SCIP) free flap, 458–460
Superficial circumflex iliac vein (SCIV), 484, 505
Superficial inferior epigastric artery (SIEA) flap, 493
Superficial inferior epigastric vein (SIEV), 505
Supermicrosurgical flaps, 504
Support group, 587, 588
Supramalleolar osteotomy, 376
Surgical consultation, 189
Surgical débridement, 163
indications, 164
Surgical intervention, 81, 359
Surgical management
clinical assessment and classifications, 203–205
of DFO, 206
of diabetic foot attack, 209
forefoot osteomyelitis, 207, 208
of infected heel ulcers, 208, 209

T
Tahan, H.H., 39
Takeji, Y., 141
Talectomy, 374
Tamir, E., 83
Target arterial path (TAP), 277
Targeted antimicrobial therapy, 459
Targeted discharge date (TDD), 39
Targeted intravenous antibiotic therapy, 209
Targeted muscle reinnervation (TMR), 549
Target lesion revascularization (TLR), 280
$TcPO_2$, 256

Tendon Achilles lengthening (TAL), 82, 377, 457
Tendon transfers, 83
TGF-beta, *see* Transforming growth factor (TGF-beta)
Thiersch, 415
Thonse, R., 576
Thoracodorsal artery perforator (TDAP) flap, 486
3-step algorithm, 477
Tibiotalocalcaneal arthrodesis, 370, 372
Tinea incognito, 336, 337
Tinea pedis, 337
Tissue handling, 529
Tissue necrosis, 205
Tissue product, 306
Tissue-engineered skin grafts, 415
Titrating therapy, 92
TNF-alpha, 187
Toe amputation, 529
Toe-brachial index (TBI), 255
Toe systolic pressure measurements (TSP), 255
Toosizadeh, N, 139
Topical oxygen therapy, 410
Total contact casting (TCC), 78–80, 230, 350, 516, 517
Traditional angiography, 473
Traditional workhorse type flaps, 500
Transcutaneous electrical nerve stimulation (TENS), 151
Transcutaneous oxygen measurements (TCOMs), 518
Transcutaneous partial oxygen pressure measurements ($TcPO_2$), 255, 257
Transcyte, 316
Transforming growth factor (TGF-beta), 159
Transmetatarsal amputation (TMA), 59, 475, 476, 478, 486, 513, 533
Transport media, 343, 344
Transthoracic echocardiography (TTE), 88
Transverse partial latissimus flap, 505
Traumatic amputee, 353
Tricyclic antidepressants (TCAs), 150
Trigger toe, 122
Trough, 512
T-shaped/flow through anastomosis, 513
2020 ADA Standards of Care and Endocrine Society guidelines, 92
2009 NICE-SUGAR trial, 92
Type II diabetes mellitus, 426, 497

U
Ucci, A., 263–265, 267, 268, 270, 271, 273, 275–283
Ulceration, 73, 522, 531
  debridement, 209
  gangrenous area, 252
Ultrasound, 258
United States, 73
US Veterans Health Administration, 182
Utilization Review (UR) Nurse, 36

V
Vacuum assisted closure (VAC) device, 40
Vainieri, E., 209
van Asten, S.A.V., 175
Van Eekeren, R.R., 296
Van Epps, P., 141
Vascular endothelial growth factor (VEG-F), 159, 402
Vascular insufficiency, 187
Vascular intervention, 475
Vascular network, 417
Vascular surgery, 4, 457, 459
Vasculitis, 342
Vasculopathies, 343
Vasopressors, 455
Vastus lateralis free flap, 455, 457
Vein harvest incision, 264
Venous clinical severity score (VCSS), 292, 296
Venous duplex studies, 459
Venous obstruction, 290
Venous studies, 457
Vertical contour calcanectomy (VCC), 541
  amputation, 540
Verzella, A.N., 305
Viability, 449, 453
Viable tissues, 172
ViOptix Tissue Oximeter, 462
Vitamin D, 560
V-Y advancement flap, 444

W
Wallace, T., 13
Warfarin, 96
Weaver, N.K., 87
Weight-bearing films, 74
Wheeler, M.G., 87
White blood cell count (WBC), 188
WIfi classification system, 254
William, H., 216
Wnt/β-catenin pathway, 218, 220
Workhorse flaps, 482, 504, 512
World Health Organization, 133
Wound Center Staffing, 15–16
Wounds, 523
  ankle, 490
  bed preparation, 160
  forefoot, 477, 478, 482, 484, 486
  healing, 158, 159, 321, 404, 405
  hindfoot, 489, 490
  massive, 496
  midfoot, 489
Wrobel, J.S., 136
Wukich, D.K., 237

X
Xenografts, 306, 313

Y
Yang, C., 394
Yang, F., 329
Yavuzer, G., 137
Yazdanpanah, L., 522

Z
Zahiri, M., 139, 140
Zarick, C.S., 73, 415–427
Zhang, C.Q., 588, 594
Zhou, H., 142, 143
Zulbaran-Rojas, A., 142