Supporting the Patient Journey

There are alternative methods of pain management in wound care.

BY WINDY COLE, DPM AND EMMA WOODMANSEY, PHD

Successful wound management outcomes primarily focus on objective measures such as rate of wound healing, number of ulcer-free days, occurrence of infection, amputation rates, recidivism, and mortality. This information can be obtained through data mining of electronic medical record (EMR) systems or wound care registries, but these commonly reported parameters rarely consider the patient experience. There is a push within the wound management community supporting the collection of patient-reported outcomes measures (PROMs) and patient-reported experience measures (PREMs).

The healing process for a chronic wound can take 6 to 8 months or longer; some patients live with their wounds for 15 years or more.

Through surveys and interviews, patients can provide useful information on all aspects of their care including overall satisfaction of treatments, symptoms and severity, quality of life, mental health, and social interactions. By analyzing this data, healthcare professionals and organizations can better understand if services and procedures are contributing to the health status of a given patient population.[1] Additionally, this information can be used to determine treatment algorithms, drive policy, impact health service offerings, and influence quality performance measures.[1]

Chronic or hard-to-heal wounds can be defined as wounds that have not reduced in size by 40% to 50% within 1 month after onset.[2,3] Chronic wounds affect over 10.5 million Medicare beneficiaries in the U.S. alone, representing a significant burden to the healthcare system.[4] Chronic non-healing wounds also take a significant toll on all aspects of patients' lives. Living with a chronic wound can be demanding and restrictive. Daily routines become dictated by clinic appointments, tests, and bandage changes—all taking many hours over the weeks of therapy.

Indirect consequences of living with a chronic wound such as pain, exudate, and odor often contribute to social isolation. Research has shown that chronic wound patients limit social interactions and experience impairments in all aspects of social interactions.[5] Social isolation can contribute to depression, anxiety and sleep disturbances, compounding the impact on quality of life. Additionally, many patients are unable to participate in the activities they love. Limited ability to engage in physical activities that help them cope can increase stress and even escalate pain.[6]

In fact, studies have reported that pain associated with chronic wounds is one of the symptoms that patients find particularly distressing.[7] Chronic wounds cause decreased functional ability and quality of life (QOL) for 1% to 3% of individuals 60 years and older.[8] QOL was a predictor of major amputation and death for patients who experienced all or some of the QOL deficits (mobility restrictions, self-care deficits, inability to perform usual activities, pain, and discomfort).[9]

The healing process for a chronic wound can take 6 to 8 months or longer; some patients live with their wounds for 15 years or more.

The prevalence of pain with chronic wounds is 48% to 81%, with 19% to 46% of patients reporting moderate to severe pain.[8] Wound pain can be classified as nociceptive or neuropathic, with differing characteristics for each.[7]

Nociceptive pain is the normal physiological response to a painful stimulus and serves as a biologic function

Continued on page 78

New Concepts and Studies

"Clinical Innovations" is PM's ongoing series of articles dedicated to introducing new concepts, technologies and studies to the podiatric community. Readers should be aware that Podiatry Management does not specifically endorse any of the technologies, concepts, or products being discussed.

to warn of injury.[8] Nociceptive pain usually presents as aching, throbbing, gnawing, and tender symptoms.[7,8]

Neuropathic pain is caused by dysfunction or damage in the nervous system, causing signals to travel in abnormal pathways[10] and can be described as burning, stinging, shooting, stabbing, cramp, and numbness.[7,8]

In addition to injury-associated pain, chronic wounds are characterized by endogenous inflammatory mechanisms that lower the threshold of peripheral nociceptor stimulation, which in turn intensifies pain levels.[10] Combined with the added problems that ischemic nerve injury may take time to resolve and ischemic wounds are higher risk to develop infection and subsequent infection-related pain, this causes a vicious cycle of ongoing pain as summarized in Figure 1.

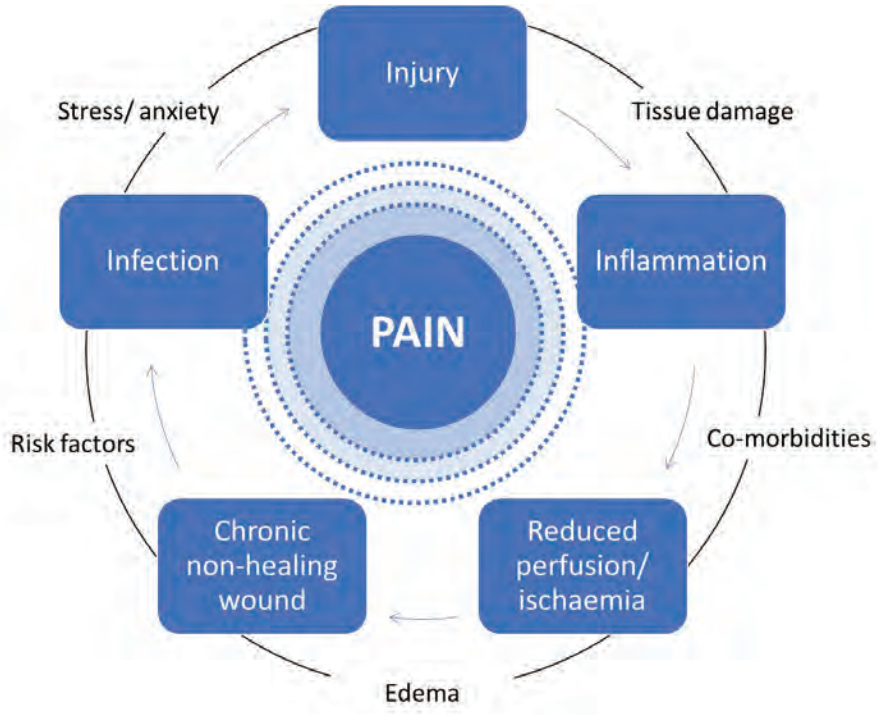

Figure 1: Cycle of pain in chronic wounds

Pitfalls in Pain Management

Effective pain management can improve patient QOL and reduce resource consumption related to global care management.[11] The World Health Organization (WHO) Analgesic Dosing Ladder, originally developed for cancer patients, is frequently applied for effective wound pain management.[7] This ladder employs a three-step system to recommend increasingly potent treatments based on increasing pain severity scoring, as detailed in Figure 2.

The Alarming Rise in Opioid Use

Opioid use is rising alarmingly with prescriptions in the United States increasing 272% from 76 million in 1991 to 207 million in 2013.[13] Furthermore, concurrent issues with opioid overuse, misuse, and addiction are much more prevalent.[14,15] In the United States, there were 142,557 opioid-involved overdose emergency room visits between July 2016 and September 2017, and over 60,000 opioid-related deaths in 2017.[13]

Drug overdose-related deaths escalated in the U.S. during the first year of the COVID-19 pandemic, noting a 30.6% increase in the first 12 months. This phenomenon was seen widespread across the country with as many as 47 states logging statistically significant increases in drug-related overdose deaths from 2019-2020.[13] To date, opioid addiction remains at epidemic levels in the U.S. and worldwide. The United States accounts for 80% of all opioid consumption in the world.

Opioids are still commonly prescribed for moderate to severe and persistent chronic pain in wound care,[7] even though opioids are known to have risks such as dependence and overdose. In 2022, the CDC published updated guidelines for prescribing opioids for pain control with the goal of equitable, safe, and effective individual pain management.[16] The consensus document recommends the judicious use of opioid use based on risk analysis after failure of a comprehensive non-opioid based treatment plan.[16]

Not only are opioids addictive with potentially serious complications, but this class of drugs can also have a negative impact on tissue

Continued on page 79

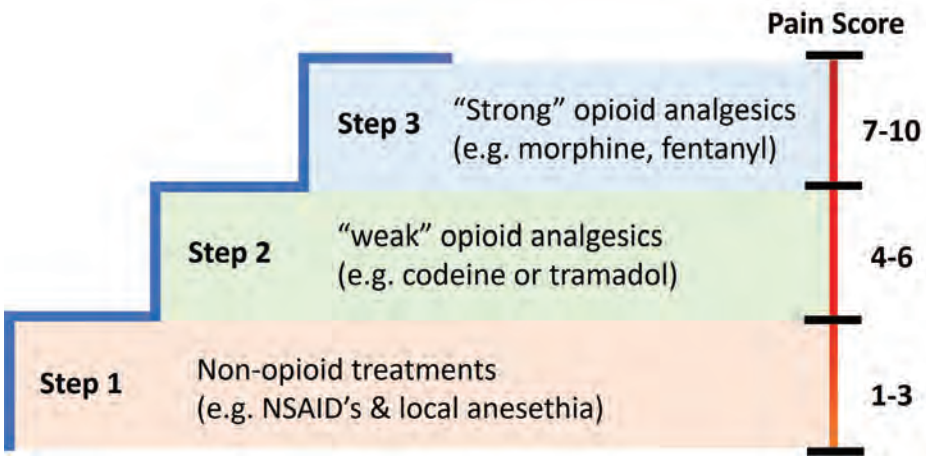

Figure 2: The WHO ladder of pain management. Modified from[12].

repair in wounds. Narcotic pain medications can reduce immune system activation, decrease endothelial proliferation, impact tissue oxygenation, alter fibroblast recruitment, and impact keratinocyte function.[17]

Interruptions in any one of these physiological functions can interfere with the wound repair process phases, thus causing improper or impaired wound healing and chronic non-healing wounds. These risks, combined with reports that certain pain such as ischemic pain can be refractory to NSAID and opioid treatment, highlight the unmet clinical need for alternative interventions to aid both pain management and healing in wounds.[18]

Topical Oxygen Therapy

Following injury, poor blood circulation, edema, injured microcirculation, and contraction of vessels in traumatized tissue limit oxygen distribution to a wound, thereby reducing the wound's capacity to heal.[19,20] Wound repair and tissue regeneration is heavily reliant on the presence of adequate oxygen levels within the injured tissues with essential roles in multiple wound healing processes including oxidative killing of bacteria, cellular signaling and proliferation, collagen deposition, and angiogenesis.[20,21]

Pain is often an indication that the underlying pathophysiology of the chronic wound has not been identified or treated effectively.

Despite a critical need for oxygen, levels are frequently insufficient in patients with chronic wounds due to a variety of systemic disease states causing poor circulation, inactivation of growth factors, and cellular senescence. Low levels of oxygen in the wounded tissues will prolong healing and cause physical symptoms such as wound pain.

The use of supplemental oxygen for wound healing can be traced back to the 1960s.[22] Nevertheless, the evidence supporting the utility of topical oxygen therapy in wound management has continued to mount in recent years. In February of 2022, the American Diabetes Association published a clinical compendium concluding that the "evidence supporting topical oxygen's efficacy in healing chronic DFUs can no longer be disputed".[23]

Figure 3: The continuous topical oxygen therapy device (cTOT), NATROX® O2

Similarly, the 2023 consensus document published by the International Working Group of the Diabetic Foot (IWGDF) made the recommendation to consider adjunctive topical oxygen therapy for the treatment of hard-to-heal DFUs.[24] These international guidelines reflect the results of published randomized clinical trials (RCTs), meta-analyses, and systemic reviews with statistically significant improvements in outcomes for chronic wound patients treated with topical oxygen therapy.[25–32]

Topical Oxygen Therapy and Pain Management

Pain is often an indication that the underlying pathophysiology of the chronic wound has not been identified or treated effectively. Untreated pain can contribute to lack of patient compliance or adherence to treatment regimens and prolong healing. Chronic wound pain is multifactorial. Tissue damage, nerve injury, blood vessel dysfunction, ischemia, bacterial contamination, and infection can all be contributing elements. Different pain characteristics have been associated with various wound etiologies (Table 1).

Management of wound pain requires a multifaceted approach. It is imperative to determine the underlying etiology and pathology causing the pain to break the cycle.[7] Wound healing often stalls in the inflammatory phase, causing the wound to become non-healing or chronic. Physiological features of chronic wounds such as high metabolic activity in the tissues, edema, poor microcirculation, diffusion constraints, and O2 consumption by bacteria affect tissue oxygenation.

Continued on page 80

TABLE 1

Pain Characteristics Associated with Different Chronic Wounds[33-35]

Wound Type	Pain Description
Venous Leg Ulcer	Aching, heaviness
Arterial Ulcer	Cramping or spasms with activity
Pressure Injury	Inflammatory or irritation from pressure and friction
Diabetic Ulcer	Burning, tingling, shooting, and or stabbing (continuous or intermittent)

NATROX® O_2

Continuous Topical Oxygen Therapy for Chronic Wounds

FDA CLEARED

A STEP FORWARD IN WOUND CARE

- **3x** — More likely to heal[1]
- **73%** — Greater reduction in wound size[2]
- **90%** — Patient satisfaction[3]
- **76%** — Felt rapid pain relief[4]
- **85%** — Remained healed at 1 year[5]

Chronic wounds just **became easier with NATROX® O_2**

To find out more
Call: 1-888-354-9772 or email: info@natroxwoundcare.com
https://bit.ly/46qbx1j

AD_US_09/23 (V6)

NATROX® is a registered trade mark of Inotec AMD Limited in EU, China, USA & UK.

1. Yu J, Lu S, McLaren AM, et al. 2016. Topical oxygen therapy results in complete wound healing in diabetic foot ulcers. *Wound Repair Regen*, [e-journal] 24:1066-72. doi:10.1111/wrr.12490.
2. Serena TE, Bullock NM, Cole W, et al. 2021. Topical oxygen therapy in the treatment of diabetic foot ulcers: a multicentre, open, randomised controlled clinical trial. *J Wound Care*, 30(Sup5):7-14.
3. Jones N, Curran G, Ivins N, et al. 2017. The role of topical oxygen therapy in the treatment of diabetic foot ulceration. [Poster] *Wounds UK*: Harrogate.
4. Jebril W, Nowak M, Palin L, et al. 2022. Topical oxygen treatment relieves pain from hard- to-heal leg ulcers and improves healing: a case series. *J Wound Care*, 31(1):4-11.
5. Al-Jalodi O, Kupcella M, Breisinger K, et al. 2022. A multicenter clinical trial evaluating the durability of diabetic foot ulcer healing in ulcers treated with topical oxygen and standard of care alone 1 year post healing. *Int Wound J*, [e-journal]:1-5. doi:10.1111/iwj.13789

Inotec AMD LTD Unit 7340 | Building 7300 Cambridge Research Park | Beach Drive | Waterbeach | Cambridge | England | CB25 9PD

Additionally, physical damage due to extensive tissue injuries disrupts the microvasculature and reduces tissue oxygenation.[36] Moreover, the requirement for oxygen is three times greater in wounded tissues than in intact tissue.[37] Tissue hypoxia can cause pain, decrease tissue repair and regeneration, and increase infection rates. Worsening or a change in the quality of pain may be a signal of wound deterioration or infection.[38]

Leukocyte production and function is compromised in low oxygen environments, allowing bacteria to persist and invade the wound environment and causing infection.[39] The presence of bacteria in a wound, particularly if multiplying rapidly due to an infection, cause additional drain on local oxygen availability. Thus, higher O2 levels are required to reverse local hypoxia in wounded tissues and facilitate the host response to wound infection, and aid antibiotic effectiveness and wound progression through the healing cascade.[20,36,40]

In a recently published manuscript by Jebril and colleagues,[41] the utilization of topical oxygen to treat chronic venous leg ulcers contributed to a 76% reduction in substantial pain in the study cohort. This 20-patient retrospective pilot study also reported that 69% of patients stopped opioid use while 53% had complete resolution of all pain symptoms.[41] While the exact mechanism of action is not yet understood, this initial trial illustrates the potential of topical oxygen therapy as a treatment option to support not only wound healing, but chronic wound pain management.

Wound Progression and Pain Management with Topical Oxygen Therapy: Case Example

The author has been using the NATROX® O2 (Figure 3), Inotec AMD, Cambridge UK) continuous topical oxygen therapy (cTOT) in her clinical practice for the past 4 years. The NATROX O2 device is FDA-cleared, compact, and battery-operated. The oxygen generator delivers 98% pure, humidified continuous oxygen 24/7 to the wound through a tube connected to an oxygen delivery system. The device is lightweight, portable, discreet, easy to use, and importantly allows patients to maintain mobility during treatment.

cTOT has been validated as a low-risk, adjunctive therapy for wound management in a variety of chronic wound types and across a wide range of care settings. Herein, we will provide a patient case report illustrating the utility of NATROX O2 cTOT to successfully treat a painful, non-healing venous leg ulcer.

Figure 4a: Wound at initial presentation

Figure 4b: Wound at 2 weeks

Figure 4c: Wound at 3 weeks

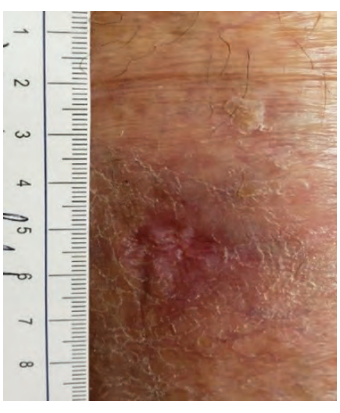

Figure 4d: Wound at 5 weeks

History

A 77-year-old female patient with a history of venous insufficiency, varicose veins, hypertension, and degenerative joint disease presented to the outpatient wound clinic with a non-healing wound of 2 months duration. The patient had originally hit her leg on a car door causing a small laceration that continued to deteriorate over the last 6 weeks. The patient had been seen by her primary care physician for this complaint without much success.

Initial Presentation

The wound base was covered with adherent slough and the wound area was measured at 3.06 cm2 (Figure 4a). She related that her pain was 10 out of 10 on the visual analog scale.

After a complete patient and wound assessment was performed, the diagnosis of a non-healing venous leg ulcer was made and a treatment regimen consisting of wound debridement, NATROX O2, alginate, and multi-layer compression bandaging was initiated.

The patient was seen weekly in the wound clinic for evaluation. By week 2, the base of the wound was beefy and granular, the wound dimensions had reduced to 1.77 cm2 and the patient's pain had dropped to 3 on a 10-point scale (Figure 4b).

The treatment plan, including continuation of NATROX O2 therapy, was adhered to. By week three the patient was completely pain-free and the wound continued to progress on a healing trajectory (Figure 4c). By week 5, the wound had reached complete closure with 100% epithelial tissue and no associated pain (Figure 4d).

Conclusion

Improving the patient journey and increasing QOL for patients suffering from chronic wounds is vital. PROMs, PREMs, and QOL data have given way to the concept of patient-centered care. Individualized care delivery and its application to wound management is becoming increasingly important to payers, facilities, and caregivers. At its core, individualized care focuses on addressing specific goals and addressing adverse factors affecting patients with wounds to promote their overall wellbeing.

Continued on page 82

Treatment plans and applied therapies must remain flexible and encompass the needs of the individual patient, diverting from a one-size fits all care regimen, with different underlying problems and care needs. Adequate pain management is an essential part of this journey and can help improve patient compliance with treatment plans.

Reversal of hypoxic conditions in any non-healing wound can support faster healing by supporting increased demand for oxygen tissue repair and the immune response and to minimize barriers to healing such as inflammation, infection, and biofilm—thus breaking the cycle of non-healing and wound pain. NATROX O2 cTOT is an option that supports wound healing and pain management and is well tolerated, easy to use, and readily adopted by patients, thus increasing patient quality of life.

Adequate pain management is an essential part of this journey and can help improve patient compliance with treatment plans.

As patient perspectives on wound care treatments will increasingly impact utilization, the use of novel and innovative therapies such as cTOT will continue to impact care algorithms. The need for additional studies to determine the exact mechanism of action and the application to a larger cohort of patients does exist, but early clinical reports are promising. **PM**

References

[1] Weldring, T. & Smith, S. M. S. Article Commentary: Patient-Reported Outcomes (PROs) and Patient-Reported Outcome Measures (PROMs). Health Serv Insights 6, HSI.S11093 (2013).

[2] Atkin, L., et al. Implementing TIMERS: the race against hard-to-heal wounds. J Wound Care 28, S1–S50 (2019).

[3] Kyaw, B. M., et al. Need for improved definition of "chronic wounds" in clinical studies. Acta Dermato-Venereologica vol. 98 157–158 Preprint at https://doi.org/10.2340/00015555-2786 (2018).

[4] Carter, M. J., et al. Chronic wound prevalence and the associated cost of treatment in Medicare beneficiaries: changes between 2014 and 2019. J Med Econ 26, 894–901 (2023).

[5] Klein, T. M., et al. Social participation of people with chronic wounds: A systematic review. Int Wound J 18, 287–311 (2021).

[6] Ribu, L. & Wahl, A. Living with diabetic foot ulcers: a life of fear, restrictions, and pain. Ostomy Wound Manage 50, 57–67 (2004).

[7] Price, P., et al. Managing painful chronic wounds: the Wound Pain Management Model. Int Wound J (2007) doi:10.1111/j.1742-481X.2007.00311.x.

[8] Newbern, S. Identifying Pain and Effects on Quality of Life from Chronic Wounds Secondary to Lower-Extremity Vascular Disease: An Integrative Review. Adv Skin Wound Care 31, 102–108 (2018).

[9] Siersma, V., et al. Health-Related Quality of Life Predicts Major Amputation and Death, but Not Healing, in People With Diabetes Presenting With Foot Ulcers: The Eurodiale Study. Diabetes Care 37, 694–700 (2014).

[10] Bechert, K. & Abraham, S. E. Pain Management and Wound Care. Journal of the American College of Certified Wound Specialists vol. 1 65–71 Preprint at https://doi.org/10.1016/j.jcws.2008.12.001 (2009).

[11] Franks, P. J., Barker, J., Laeuchli, S., Med, Priv.-D. & Mosti, G. Chief of Dermatologic Surgery, President of the European Wound Management Association (EWMA). www.markallengroup.com (2016).

[12] Anekar, A. A., Hendrix, J. M. & Cascella, M. WHO Analgesic Ladder. (2023).

[13] National Center for Drug Abuse Statistics (NCDAS). DrugAbuseStatistics.org.

[14] Mclellan, A. T. Substance misuse and substance use disorders: Why do they matter in healthcare? Trans Am Clin Climatol Assoc 128, (2017).

[15] Alghnam, S. & Castillo, R. Traumatic injuries and persistent opioid use in the USA: Findings from a nationally representative survey. Injury Prevention 23, 87–92 (2017).

[16] Dowell, D., Ragan, K. R., Jones, C. M., Baldwin, G. T. & Chou, R. CDC Clinical Practice Guideline for Prescribing Opioids for Pain—United States, 2022. MMWR. Recommendations and Reports 71, 1–95 (2022).

[17] Shanmugam, V. K., Couch, K. S., McNish, S. & Amdur, R. L. Relationship between opioid treatment and rate of healing in chronic wounds. Wound Repair and Regeneration 25, 120–130 (2017).

[18] Kogure, T., et al. Ischemic Ulcer Pain Is Both Nociceptive and Neuropathic Pain Based on a Discriminant Function Analysis Using the McGill Pain Questionnaire. J Pain Palliat Care Pharmacother 31, 98–104 (2017).

[19] Gottrup, F. Physiology and measurement of tissue perfusion. Ann Chir Gynaecol 83, 183–9 (1994).

[20] Frykberg, R., et al. Use of Topical Oxygen Therapy in hard to heal wounds. J Wound Care In press, (2023).

[21] Rodriguez, P. G., Felix, F. N., Woodley, D. T. & Shim, E. K. The Role of Oxygen in Wound Healing: A Review of the Literature. Dermatologic Surgery 34, 1159–1169 (2008).

[22] Mutluoglu, M., Cakkalkurt, A., Uzun, G. & Aktas, S. Topical Oxygen for Chronic Wounds: A PRO/CON Debate. Journal of the American College of Clinical Wound Specialists 5, 61–65 (2013).

[23] Boulton, A. J. M., et al. New evidence based therapies for complex diabetic foot wounds. America Diabetes Association (2022).

[24] Chen, P., et al. IWGDF Guidelines on interventions to enhance healing of foot ulcers in people with diabetes. www.iwgdfguidelines.org (2023).

[25] Serena, T. E., et al. Topical oxygen therapy in the treatment of diabetic foot ulcers: a multicentre, open, randomised controlled clinical trial. J Wound Care 30, 7–14 (2021).

[26] Al-Jalodi, O., Kupcella, M., Breisinger, K. & Serena, T. E. A multicenter clinical trial evaluating the durability of diabetic foot ulcer healing in ulcers treated with topical oxygen and standard of care versus standard of care alone 1 year post healing. Int Wound J 19, 1838–1842 (2022).

[27] Kaufman, H., et al. Topical oxygen therapy used to improve wound healing in a large retrospective study of wounds of mixed aetiology. Wounds International 12, 63–68 (2021).

[28] Carter, M. J., et al. Efficacy of Topical Wound Oxygen Therapy in Healing Chronic Diabetic Foot Ulcers: Systematic Review and Meta-Analysis. Adv Wound Care (New Rochelle) 12, 177–186 (2023).

[29] Sun, X. K., Li, R., Yang, X. L. & Yuan, L. Efficacy and safety of topical oxygen therapy for diabetic foot ulcers: An updated systematic review and meta-analysis. Int Wound J 19, 2200–2209 (2022).

[30] Sethi, A., Khambhayta, Y. & Vas, P. Topical oxygen therapy for healing diabetic foot ulcers: A systematic review and meta-analysis of randomised control trials. Health Sciences Review 3, 100028 (2022).

Continued on page 84

[31] Thanigaimani, S., Singh, T. & Golledge, J. Topical oxygen therapy for diabetes?related foot ulcers: A systematic review and meta?analysis. Diabetic Medicine 38, (2021).

[32] Connaghan, F., Avsar, P., Patton, D., O'Connor, T. & Moore, Z. Impact of topical oxygen therapy on diabetic foot ulcer healing rates: a systematic review. J Wound Care 30, 823–829 (2021).

[33] Barron, G. S., Jacob, S. E. & Kirsner, R. S. Dermatologic Complications of Chronic Venous Disease: Medical Management and Beyond. Ann Vasc Surg 21, 652–662 (2007).

[34] Briggs, M. & Closs, S. J. Patients' perceptions of the impact of treatments and products on their experience of leg ulcer pain. J Wound Care 15, 333–337 (2006).

[35] Buttke, J. Identifying the Charcot Foot. Adv Skin Wound Care 19, 189–191 (2006).

[36] Troitzsch, D., Vogt, S., Abdul-Khaliq, H. & Moosdorf, R. Muscle Tissue Oxygen Tension and Oxidative Metabolism during Ischemia and Reperfusion. Journal of Surgical Research 128, 9–14 (2005).

[37] Castilla, D. M., Liu, Z.-J. & Velazquez, O. C. Oxygen: Implications for Wound Healing. Adv Wound Care (New Rochelle) 1, 225–230 (2012).

[38] Swanson, T., et al. IWII Wound Infection in Clinical Practice consensus document: 2022 update. J Wound Care 31, S10–S21 (2022).

[39] Gottrup, F., et al. Use of oxygen therapies in wound healing. J Wound Care 26, S1–S42 (2017).

[40] Jensen, P. Ø., et al. Improving antibiotic treatment of bacterial biofilm by hyperbaric oxygen therapy: Not just hot air. Biofilm 1, 100008 (2019).

[41] Jebril, W., Physician, I., Nowak, M., Bachar-Wikstrom, E. & Wikstrom, J. D. Topical oxygen treatment relieves pain from hard-to-heal leg ulcers and improves healing: a case series. (2022).

Dr. Cole, an honor graduate from the Kent State University College of Podiatric Medicine, has practiced in Northeast Ohio for over 22 years. She is an adjunct professor and Director of Wound Care Research at KSU, is board certified by the ABFAS and the American Board of Wound Management. She has been a dedicated wound care advocate for two decades with interests focused on medical education, diabetic foot care, wound care, limb salvage, & clinical research. Additionally, she sits on the advisory board of multiple emerging biotech companies and has been integral in collaborating on innovative research protocols.

Dr. Woodmansey is Global Clinical Director of Natrox Wound Care. A medical microbiologist by background, initially working in the field of gastrointestinal microbiology at the University of Dundee where she completed her PhD and more recently in wound care. Emma has worked in the healthcare industry for 20 years with responsibilities for new product development and novel treatment solutions, global thought leadership, clinical and scientific strategy and evidence building and communication, focusing on infection, antimicrobials, debridement and advanced wound care pathways helping patients with wounds regain their lives.

Surgical Off-Loading for Diabetic Wounds

Here's an update on the prevention, treatment and long-term options for wound healing.

BY ROBIN TSAI, DPM AND LAURA SHIN, DPM, PHD

Diabetic wounds are costly and difficult. The economic strain associated with healing diabetic foot ulcers (DFUs) is substantial and multifaceted, impacting individuals and health systems. The typical direct mean cost per patient-year to heal a DFU was $3,368 (ulcer-only).[5] This number, however, does not highlight the change in quality of life, lost productivity, and loss of income during the course of treatment. In another study the expenditure of a DFU occurrence in the initial two years post-diagnosis was $30,724.[6]

Foot ulcerations (DFUs) are a significant complication of diabetes mellitus. DM impacts more than 37 million people in the United States. DFUs are linked to risks such as foot deformities, trauma, and diabetic peripheral neuropathy. Diabetic peripheral neuropathy is the main risk factor, constituting about 35-45%.[2,3] Studies demonstrate that DFUs occur in areas of highest plantar pressure.

A cornerstone principle of healing DFUs is to reduce or redistribute pressure from the ulcerated site, termed off-loading.[4] Although considered as first-line therapy, conservative off-loading entails high recurrence rates at the 1 year (40%) and 3 year (60%) mark; thus, even with resolution of the ulcer, the patient appropriately is termed as "in remission".[20,21]

Wounds that do not have sufficient healing after 4 weeks of standard care must be re-assessed to evaluate underlying pathologies and to determine if further advanced treatments are warranted.

The percentage area reduction (PAR) in wound size after 4 weeks of DFU treatment has been suggested as a clinical parameter to distinguish DFUs that will heal within 12 weeks.[1] Delaying the healing of diabetic foot ulcers (DFUs) significantly increases the risks of diabetic foot infections, leading to the potential for limb loss.

A cornerstone principle of healing DFUs is to reduce or redistribute pressure from the ulcerated site, termed off-loading.

Biomechanical abnormalities or bony deformities create alterations in gait patterns. Unstable gait with neuropathy poses challenges for off-loading, despite appropriate or advanced wound care. Managing diabetic foot ulcerations secondary to biomechanical deformities is as important as addressing the differing co-morbidities such as infection control, vascular disease, and neuropathy itself. These biomechanical etiologies can predispose individuals with diabetes to ulcer development. Surgical measures are considered when conservative approaches have proven ineffective.

Surgical interventions aim to alleviate pressure on the ulcerated area, promoting wound healing, and preventing further complications. Addressing biomechanical etiologies surgically for diabetic foot ulcerations should be considered when there are underlying osseous deformities that contribute to increased plantar pressure. Biomechanical factors play a significant role in diabetic foot pathology, and surgical intervention can help correct these issues to reduce the risk of ulceration and facilitate wound healing. Intervention may prevent further loss of mobility, prevent recurrence, and allow for return to activity.

Digital Flexor Tenotomies

DFUs are often linked to digital deformities such as hammer, mallet, or claw toes. Areas most commonly affected are distal plantar and dorsal parts of the toes.[7] Involvement of toes constitute a significant proportion of foot ulcers, ranging from 43% to 55.5% of cases. Despite their smaller size and generally quicker healing, they exhibit elevated rates of limb amputations in comparison to ulcers occurring in other foot locations.[8] Conservative treatments of digital ulcers include footwear, toe silicone orthosis, padding, and debridement. The effectiveness of conservative care, however, remains unclear due to limited evidence and poor patient compliance.[9]

Percutaneous flexor tenotomies

Continued on page 72

Surgical Off-Loading *(from page 71)*

have been effective in preventing and managing digital ulcerations. In an office setting, a 11 blade or 18-gauge needle can be used to minimize incision and tissue loss. Procedures can be done in the office with local anesthetic. Recent literature points to high healing rates of 92% to 100% with mean healing time of 2 to 4 weeks.[10]

an in-office treatment option that allows bone biopsy diagnosis while addressing osteomyelitis and biomechanical etiologies. To perform the procedure, local anesthesia is administered followed by an elliptical fish-mouth-type incision to the distal phalanx with complete removal of distal phalanx and nail bed. Studies have shown in-office Symes procedures are safe, reliable, and cost-effective with low complications.[11-12]

Tendon Lengthening

Achilles tendon lengthening is a fast and effective surgical procedure used to help treat forefoot DFUs, particularly when the ulcers are associated with increased plantar pressure from a tight posterior chord. Stiffness in the triceps surae limits the normal range of motion in the ankle joint, thus leading to high forefoot pressures. Several studies have explored Achilles tendon lengthening in cases

Figures 1A, 1B, and 1C: The patient highlighted in Figure 1A is a 42-year-old-female with a history of type 2 diabetes mellitus with a DFU sub the 2nd metatarsal who failed 5 months of conservative off-loading in an off-loading boot with local wound care. Figures 1B and 1C show clinical images status post 4 weeks after a dorsal approach floating distal metatarsal osteotomy procedure.

Distal Symes Amputation

Flexor tenotomy has shown significant benefit for distal digital ulcerations; however, indications are reserved for the superficial, non-infected, recurrent tip-of-toe ulcers associated with flexible deformities. Prior to tenotomy procedures, considerations of whether hammer digit strengthening would further elongate the digit should be addressed. Distal Symes amputations are an effective method to address rigid non-reducible hammer digit deformities, elongated digits, advanced toenail pathologies, or deep sores of digital tips complicated by osteomyelitis. Long courses of oral or IV antibiotics are commonly used in the presence of osteomyelitis; however, the underlying biomechanical etiology of the ulcer is not addressed.

The distal Symes amputation is

DMMO

Operative off-loading to the central metatarsal heads are indicated often to prevent recurrence or when conservative off-loading has failed. Surgical off-loading methods aim to directly correct the underlying osseous deformity. Minimally invasive distal metatarsal osteotomy (DMMO) has been successfully used in the treatment of plantar metatarsal head ulcerations. Benefits of DMMOs seen by our patients include immediate weight-bearing, minimal disruption to the patient's daily life, reduction of peak pressure to the respective metatarsal head as the cause of recurring DFUs. Floating metatarsal head osteotomies have been found to decrease peak pressure under the head of the osteomized metatarsal by 33% following surgery.[21] (see Figures 1A-1C)

where healing was not achieved using off-loading devices such as the total contact cast (TCC) or removable walker. They found 91% to 93% of plantar forefoot ulcers healed with Achilles tendon lengthening in a mean of 6 to 12 weeks.[13-15]

Another RCT comparing Achilles tendon lengthening vs. TCC groups noted 100% ulcers healing in the TAL group with 52% less risk of ulcer recurrence at two years than the TCC group.[16] Therefore, biomechanical evaluation of patients for the presence of soft tissue equinus should be performed as findings can indicate the need for a surgical off-loading approach.

Fat Grafting

Fat pad atrophy (FPA) or distal fat pad migration in the presence of

Continued on page 74

Surgical Off-Loading *(from page 72)*

neuropathy increases the risk of diabetic ulcer development. FPA in diabetic patients are thought to result from irregular arrangement of collagen fibrils as a result of glycation and reduction of adipocyte size. FPA leaves metatarsal heads vulnerable to increased peak plantar pressure.[18]

Fat grafting has been popular in plastic reconstructive surgery due to its low risk in complications, abundance of availability, and ease of harvest. It has been successfully utilized in contouring procedures for many years; however, use in prevention and treatment in diabetic foot ulcerations has yet to be popularized. Fat grafting, either via auto vs. allograft, reduces peak plantar pressure, friction, and shear forces by creating a cushioning effect and redistributing pressure.

Additionally, adipose tissue contains stem cells that promote tissue regeneration and wound healing. Mojallal, et al. paved the way for the use of autologous fat grafting in wound healing through their observation of enhancement in collagen fiber neosynthesis, vascularization, and the thickness of the dermis and subcutaneous tissue.[17] Studies have shown cases of allograft use in patients in thinning fat pads to have approximately 90% of average tissue thickness maintained after one year.[19]

Charcot Neuroarthropathy

Charcot neuroarthropathy among neuropathic patients often presents with deformity at the midfoot. The rocker bottom deformity is a debilitating condition where subluxation occurs in the midfoot joints, causing high peak plantar pressure at the apex of the deformity. Conservative off-loading often is the first line treatment, but if off-loading measures fail or there is an unbraceable deformity, ulcerations will occur.

Generally, the risk of limb loss and the complexity of surgical correction increase the more proximal the deformity. In the presence of ankle Charcot neuroarthropathy, the risk of amputation increases, the reconstruction is more challenging, and post-operative recovery is delayed.

Charcot neuroarthropathy reconstruction aims to create a braceable and stable plantigrade foot where the patient is able to ambulate following surgery. For the midfoot rocker bottom deformity, a plantigrade foot is achieved by plantar base wedge resection of the apex of deformity with plantar approach. The plantigrade foot can then be fixated via an internal vs. external circular fixator during a staged procedure where concern for infection is present.

It's important to recognize that the decision to pursue surgical off-loading is complex and should be made on a case-by-case basis.

It's important to recognize that the decision to pursue surgical off-loading is complex and should be made on a case-by-case basis. The patient's overall health, wound characteristics, vascular status, and the potential benefits and risks of surgery should all be taken into consideration. **PM**

References

[1] Sheehan P, Jones P, Caselli A, Giurini JM, Veves A. Percent change in wound area of diabetic foot ulcers over a 4-week period is a robust predictor of complete healing in a 12-week prospective trial. Diabetes Care. 2003 Jun;26(6):1879-82. doi: 10.2337/diacare.26.6.1879. PMID: 12766127.

[2] Fernando DJ, Masson EA, Veves A, Boulton AJ. Relationship of limited joint mobility to abnormal foot pressures and diabetic foot ulceration. Diabetes Care. Jan 1991;14(1):8-11. doi:10.2337/diacare.14.1.8

[3] Waaijman R, de Haart M, Arts ML, et al. Risk factors for plantar foot ulcer recurrence in neuropathic diabetic patients. Diabetes Care. Jun 2014;37(6):1697-705. doi:10.2337/dc13-2470

[4] Armstrong DG, Tan TW, Boulton AJM, Bus SA. Diabetic Foot Ulcers: A Review. JAMA. Jul 3 2023;330(1):62-75. doi:10.1001/jama.2023.10578

[5] Lo ZJ, Surendra NK, Saxena A, Car J. Clinical and economic burden of diabetic foot ulcers: A 5-year longitudinal multi-ethnic cohort study from the tropics. Int Wound J. 2021 Jun;18(3):375-386. doi: 10.1111/iwj.13540. Epub 2021 Jan 26. PMID: 33497545; PMCID: PMC8244009.

[6] Ramsey SD, Newton K, Blough D, McCulloch DK, Sandhu N, Reiber GE, Wagner EH. Incidence, outcomes, and cost of foot ulcers in patients with diabetes. Diabetes Care. 1999 Mar;22(3):382-7. doi: 10.2337/diacare.22.3.382. PMID: 10097914.

[7] Cowley MS, Boyko EJ, Shofer JB, Ahroni JH, Ledoux WR. Foot ulcer risk and location in relation to prospective clinical assessment of foot shape and mobility among persons with diabetes. Diabetes Res Clin Pract. 2008 Nov;82(2):226-32. doi: 10.1016/j.diabres.2008.07.025. Epub 2008 Oct 1. PMID: 18829126.

[8] Pickwell KM, Siersma VD, Kars M, Holstein PE, Schaper NC; Eurodiale consortium. Diabetic foot disease: impact of ulcer location on ulcer healing. Diabetes Metab Res Rev. 2013 Jul;29(5):377-83. doi: 10.1002/dmrr.2400. PMID: 23390115.

[9] Bus SA, Valk GD, van Deursen RW, Armstrong DG, Caravaggi C, Hlavácek P, Bakker K, Cavanagh PR. The effectiveness of footwear and off-loading interventions to prevent and heal foot ulcers and reduce plantar pressure in diabetes: a systematic review. Diabetes Metab Res Rev. 2008 May-Jun;24 Suppl 1:S162-80. doi: 10.1002/dmrr.850. PMID: 18442178.

[10] Calvo-Wright MM, López-Moral M, García-Álvarez Y, García-Madrid M, Álvaro-Afonso FJ, Lázaro-Martínez JL. Effectiveness of Percutaneous Flexor Tenotomies for the Prevention and Management of Toe-Related Diabetic Foot Ulcers: A Systematic Review. J Clin Med. 2023 Apr 12;12(8):2835. doi: 10.3390/jcm12082835. PMID: 37109172; PMCID: PMC10142834.

[11] Boffeli TJ, Goss MS. Distal Syme Hallux Amputation for Tip of Toe Wounds and Gangrene Complicated by Osteomyelitis of the Distal Phalanx: Surgical Technique and Outcome in Consecutive Cases. J Foot Ankle Surg. 2018 May-Jun;57(3):456-461. doi: 10.1053/j.jfas.2017.10.027. Epub 2017 Dec 19. PMID: 29273187.

[12] Boffeli TJ, Abben KW, Hyllengren SB. In-office distal Symes lesser toe amputation: a safe, reliable, and cost-effective treatment of diabetes-related tip of toe ulcers complicated by osteomyelitis. J Foot Ankle Surg. 2014 Nov-Dec;53(6):720-6. doi: 10.1053/j.jfas.2014.04.020. Epub 2014 Jul 22. PMID: 25060606.

Continued on page 75

Surgical Off-Loading *(from page 74)*

[13] Lazzarini PA, Jarl G, Gooday C, Viswanathan V, Caravaggi CF, Armstrong DG, Bus SA. Effectiveness of off-loading interventions to heal foot ulcers in persons with diabetes: a systematic review. Diabetes Metab Res Rev. 2020 Mar;36 Suppl 1(Suppl 1):e3275. doi: 10.1002/dmrr.3275. PMID: 32176438; PMCID: PMC8370012.

[14] Holstein P, Lohmann M, Bitsch M, Jørgensen B. Achilles tendon lengthening, the panacea for plantar forefoot ulceration? Diabetes Metab Res Rev. 2004 May-Jun;20 Suppl 1:S37-40. doi: 10.1002/dmrr.452. PMID: 15150812.

[15] Laborde JM. Neuropathic plantar forefoot ulcers treated with tendon lengthenings. Foot Ankle Int. 2008 Apr;29(4):378-84. doi: 10.3113/FAI.2008.0378. PMID: 18442451.

[16] Mueller MJ, 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 Aug;85(8):1436-45. PMID: 12925622.

[17] Chopinaud M, Labbé D, Creveuil C, Marc M, Bénateau H, Mourgeon B, Chopinaud E, Veyssière A, Dompmartin A. Autologous Adipose Tissue Graft to Treat Hypertensive Leg Ulcer: A Pilot Study. Dermatology. 2017;233(2-3):234-241. doi: 10.1159/000478009. Epub 2017 Jul 27. PMID: 28746927.

[18] Dalal S, Widgerow AD, Evans GR. The plantar fat pad and the diabetic foot—a review. Int Wound J. 2015 Dec;12(6):636-40. doi: 10.1111/iwj.12173. Epub 2013 Oct 17. PMID: 24131727; PMCID: PMC7950511.

[19] Rocchio TM. Augmentation of atrophic plantar soft tissue with an acellular dermal allograft: a series review. Clin Podiatr Med Surg. 2009 Oct;26(4):545-57. doi: 10.1016/j.cpm.2009.07.001. PMID: 19778688.

[20] Armstrong DG, Boulton AJM, Bus SA. Diabetic Foot Ulcers and Their Recurrence. N Engl J Med. 2017 Jun 15;376(24):2367-2375. doi: 10.1056/NEJMra1615439. PMID: 28614678.

[21] 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 May;42(5):536-543. doi: 10.1177/1071100720976099. Epub 2020 Dec 17. PMID: 33334148; PMCID: PMC8127671.

Dr. Robin Tsai attended the University of California, Los Angeles and earned his medical degree at Rosalind Franklin University, Dr. William M. Scholl College of Podiatric Medicine. He is currently a PGY2 resident at West Covina Medical Center.

Dr. Shin is an Assistant Professor of Clinical Surgery at Keck School of Medicine at USC in the Department of Vascular Surgery and Southwestern Academic Limb Salvage Alliance. She is a graduate of the University of Pittsburgh Medical Center Residency and Limb Salvage, Trauma and Reconstructive Fellowship. She completed her DPM PhD and studied stem cell mediated repair in the diabetic host.