Limb salvage provides an alternative to amputation in patients with limb-threatening conditions such as ischemia, infections, fractures and neoplasms. The total number of lower limb amputations performed each year in the USA is 113,000 [1]. According to the Amputee Coalition of America, lower extremity amputations (LEAs) occur at a much higher rate of 67% in people with diabetes compared to the general population.
with diabetes mellitus [2]. The majority of amputations each year occur secondary to complications of the neurologic and/or vascular system, especially from diabetes [3].

Limb salvage techniques have been described in the literature, with new advances in wound care as well as the introduction of a team approach to lower limb amputation prevention programs [4]. Given the fact that the prevalence of diabetes continues to rise, with an estimated worldwide prevalence of 425 million by 2030, a team of dedicated specialists is required to prevent and reduce the incidence of amputation in the lower extremity [5]. Understanding risk factors for limb loss and treatment options for limb salvage is essential in treating patients with complications of diabetes.

**Risk factors for limb loss**

Diabetic foot ulcers (DFUs) precede 70–84% of lower extremity amputations. It is estimated 25% of patients with diabetes will develop a DFU within their lifetime [5]. Several factors predispose patients to ulceration, most commonly peripheral neuropathy and ischemia, which can be complicated by infection.

Peripheral neuropathy results in impaired protective sensation and an altered pain response, predisposing the patient to trauma from extrinsic factors such as ill-fitting shoes and injury. Motor neuropathy causes muscle weakness and intrinsic muscle imbalance leading to deformities and elevated plantar pressures. Autonomic dysfunction leads to alterations in microvascular arteriovenous circulation (i.e., AV shunting), and this local diminution in the microcirculation perfusion causes dryness and atrophic skin changes [6].

Peripheral arterial disease (PAD) is characterized by narrowing or occlusion of the arteries, typically resulting in gradual reduction of blood supply to the limbs. Diabetes and smoking are the strongest risk factors in PAD [7]. In patients with diabetes, the risk of PAD is augmented by age, duration of diabetes and the presence of peripheral neuropathy. In the Roschester study, the cumulative incidence of PAD in people with diabetes was 15% 10 years after the diagnosis of diabetes mellitus and 45% 20 years later [8]. Noninvasive vascular studies such as the ankle brachial index (ABI), toe pressures and wave form analysis are reproducible and quantitative tests for vascular evaluation (an ABI value of <0.90 or >1.40 indicative of PAD) [9].

In a prospective study evaluating predictive factors of major amputations in patients with foot problems related to diabetes, significant univariate predictive factors for limb loss were age above 60 years, stroke, coronary artery disease, nephropathy, PAD, sensory neuropathy, elevated glycosylated hemoglobin level, ankle brachial index <0.8, gangrene and infection [10].

In a retrospective review of 119 hospitalized patients with a diabetic foot infection (DFI), a nonsignificant trend was observed that indicated higher rates of limb salvage in patients with moderate diabetic foot infections compared with patients with severe infections. Infection severity was determined utilizing the systemic inflammatory response syndrome (SIRS). Patients with severe DFI experienced a 2.55-fold higher risk of any amputation and a 7.12-fold higher risk of major amputation than patients with moderate DFI [11].

Charcot neuroarthropathy (CN) is a condition affecting the bones, joints and soft tissues of the foot and ankle. This destructive osteoarthropathy occurs as a result of peripheral neuropathy, with diabetes being the most common etiology. The varying stages of CN include patterns of bone destruction, subluxation, dislocation and deformity such as midfoot collapse or ‘rocker-bottom’ deformity [12]. Charcot neuroarthropathy by itself may not pose a serious amputation risk, but with the presence of an ulceration dramatically increases the risk of amputation. In a retrospective cohort of patients with CN and DFU, amputation risk relative to patients with CN without foot ulcer was seven-times higher for patients with an ulcer alone and 12-times higher for patients with CN and ulcer [13].

**Treatment options for limb salvage**

Prevention of major amputation begins with an interdisciplinary team approach, comprehensively addressing the challenges in the management of the diabetic foot. This involves early recognition and treatment of the underlying predisposing factors for ulceration, utilizing proper wound care, debridement and eradicating infection. Off-loading strategies, such as total contact casting (TCC) and removable walking boots, decrease external forces and accelerate healing times [14]. Wound care centers, employing physicians and nurses trained in specialized wound care techniques provide evidence demonstrating that comprehensive multidisciplinary programs increase quality of care and reduce
amputation rates by 36–86% [15]. Commonly employed advanced therapies in wound care include bioengineered tissue, negative-pressure wound therapy (NPWT) and hyperbaric oxygen therapy (HBO). Tissue-engineered skin replacements and cell-based therapies are being utilized to promote a shorter healing time by way of delivering exogenous growth factors to the wound bed in either an allograft or xenograft vehicle [16]. Prospective studies on bioengineered tissues are warranted to provide high levels of recommendation for treatment. NPWT was introduced in 1997 and has been associated with reducing the time between debridements and closure, as well as decreasing the number of dressing changes. Eginton et al. compared the healing efficacy of NPWT with conventional ‘wet to dry’ dressings to treat large diabetic foot ulcers, finding a significant decrease in wound volume and depth [17]. Hyperbaric oxygen therapy, treatment utilizing 100% oxygen in an enclosed chamber at a pressurized environment, has been described to reduce the risk of amputation for patients with DFU and increase the chances of healing at 1 year [18]. Although the healing benefits of HBO have high potential, according to the Centers of Medicare and Medicaid Services, only covered conditions regarding DFU include those meeting a classification of Wagner III to include osteomyelitis or abscess, and those that have failed an adequate course of standard wound therapy [19]. Proper blood flow to the distal extremities and eradication of infection are essential elements in achieving limb salvage. When amputations are deemed medically necessary, these components are essential as well, striving for a functional and biomechanically sound residual limb with a durable soft tissue envelope. Amputation prevention centers should include integrated team members that work to promote those goals. Along with the role of the reconstructive foot and ankle surgeon, vascular surgeons, plastic surgeons, therapists and certified wound nurses are indispensable in achieving limb salvage. The specific team members may vary from hospital to hospital, but the one common element should be a passion for amputation prevention. The development of distal revascularization techniques (open and endovascular) to restore blood flow to the foot has been a major advancement, highlighting the importance of the vascular interventionalist as an essential component in limb salvage. Essential to wound healing is the understanding of the angiosome concept as described by Taylor and Palmer [20]. An angiosome is an anatomic region of tissue that is fed by source arteries. If a given angiosome is not adequate for wound healing, the tissue depends on surrounding arteries directly through arterial–arterial connections or indirectly through choke vessels [21]. In these circumstances, revascularization techniques should be considered to optimize vascular status. Plastic surgeons can provide skin grafting, local flaps and microsurgical reconstruction to achieve expeditious wound closure. Ongoing interaction with the infectious disease specialists is imperative as infections in patients with diabetes is always limb threatening and occasionally life threatening. A prosthetist or pedorthist is also invaluable for modifying footwear and properly sizing offloading devices [4].

Limb salvage treatment commences with adequate debridement to achieve bleeding granular tissue and resection of all nonviable soft tissue and bone. Sheehan and colleagues examined the change in ulcer area of 203 patients over a 4-week period as a predictor of wound healing. In this prospective, randomized controlled trial, the absolute change in ulcer area at 4 weeks was significantly greater in healers verses non-healers [22]. This study provides clinicians with a simple tool that may serve as a pivotal clinical decision point in the care of DFU for early identification of patients who may not respond to standard care and may need additional treatment such as surgical operations or augmentation with biologics. Patients whose wounds did not decrease in size by 50% after 4 weeks were less likely to heal compared with patients whose wounds decreased by more than 50%. Multiple debridements may be needed for the infected limb and post-debridement cultures should be obtained for proper antibiotic therapy as indicated. Osteotomies, exostectomies and tendon-balancing procedures can be performed to address osseous prominences, which result in an increase in plantar pressure. Midfoot CN plantar exostoses contribute to recalcitrant neuropathic ulceration. Exostectomy has been deemed a viable and safe treatment option. Pinzur found that more than half of patients with mid-foot CN deformity can be managed without surgical intervention [23]. Achilles tendon lengthening (TAL) improves ankle dorsiflexion and results in a temporary reduction in forefoot pressure by weakening the plantarflexory power during gait, thus reducing the risk of ulcer recurrence in patients with diabetes [24].
In the case of unstable CN deformities or nonhealing wounds secondary to unbraceable deformity, more aggressive surgical options should be utilized, such as reconstructions incorporation fusions or osteotomies. These surgical options may employ techniques in both internal and external fixation. Despite success with major reconstruction, complications are common as the majority of these patients have multiple end-organ sequelae of uncontrolled, long-standing diabetes. Wukich and colleagues reported a sevenfold risk for any wire complication compared with patients without diabetes treated with external fixation [26].

**When to forgo limb salvage**

Despite limb salvage efforts, certain patients may ultimately require a major amputation. Amputation is one of the most feared complications of diabetes, but it provides an opportunity for improved quality of life for some patients [27]. Proceeding to major amputation is difficult decision for surgeons, patients and families to make, but it is essential to recognize that amputation does not mean failure. Physicians who treat these complex patients must know when to forgo limb salvage and proceed with amputation when it is in the best interest of the patient, such as circumstances when infection cannot be eradicated without amputation, especially in life-threatening conditions and chronic osteomyelitis, non-reconstructable soft tissue injuries, and distal vascular lesions not salvageable with revascularization techniques. In a select group of patients with CN and chronic osteomyelitis, trans-tibial amputation resulted in improvement in self-reported outcome measures. In this study, there was noted improvement in 12 out of 13 patients who underwent major amputation based upon the self-reported SF-36 Physical Component Summary score, Foot and Ankle Measure Activity of Daily Living and Sports score. Given these findings, amputation may be a viable and optimistic option that should be considered when limb salvage is no longer effective. The task of the physician should be to determine the highest likelihood of achieving the patient’s desired level of activity as quickly as possible [27].

**Current trends**

In January 2012, the CDC reported a large decline in lower-limb amputations among US adults with diagnosed diabetes [28]. The age-adjusted rate of nontraumatic lower limb amputations was 3.9 per 1000 people with diagnosed diabetes in 2008 compared with 11.2 per 1000 in 1996. Only partial toe amputations, which have less impact on quality of life, rose during that time period, demonstrating the effectiveness of amputation prevention centers. This was thought to be a result of improvements in blood glucose control, foot care, and diabetes management and early diagnosis. Improvements in diabetes control also identified a similar trend in the declining incidence of cardiovascular disease.

It has been estimated that the treatment of foot ulcers and amputations cost the US healthcare system US$49 billion in 2007 [29]. The direct costs of each major limb amputation are estimated to be US$70,434 including the cost of a prosthetic limb and hospitalization. The lifetime projected cost of a major amputation, considering rehabilitation and future prostheses, can reach upwards of US$500,000 per patient, with an estimated total expenditure for amputations in those with diabetes projected at US$11.7 billion. Diabetic foot ulcers can cost between US$7000 and 20,000 per episode, with an estimated US$19 billion being spent on care, including debridements and dressing supplies (2007 data). In a cost comparison study comparing limb salvage to amputation in CN patients, limb salvage patients’ average cost of care was US$56,712 compared with US$49,251 in patients with amputations [30].

**Conclusion**

Limb salvage provides an alternative to one of the most feared complication of diabetes, namely major amputation. With the implementation of specialized wound care centers coupled with an interdisciplinary team approach to limb preservation and amputation prevention, the rate of major amputation is declining as we direct our efforts for limb salvage. Further randomized clinical trials in advanced wound care products and techniques will continue to revolutionize the art of limb salvage. Despite these efforts, it is the task of the clinician to provide the patient with realistic goals on an individualized basis. While the goal is to avoid major amputation, consultation with physiatrists and physical therapists are advisable during the treatment course to discuss
possible amputation as an alternative if limb salvage techniques are not effective. Limb salvage is an extensive, time-consuming undertaking, and patients need to commit 12–18 months of compliance and patience in order to achieve high rates of successful limb salvage.

Future perspective
Limb salvage and amputation prevention continues to trend in the field of foot and ankle medicine and surgery. It is the goal of the patient provider to avoid major amputation. However, if limb salvage techniques are not effective, sometimes major amputation is the only viable option. Both patient and provider must understand the optimal treatment plan and share the same goal of healing and returning to base level of function.

In the authors’ opinion, limb salvage rates will continue to rise with the advancement in wound care technologies and a better understanding of wound-healing processes and randomized clinical trials. The authors believe that major amputations rates will continue to decline in the face of these new technologies and the promise of well educated and trained interdisciplinary treatment teams.

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