Multidisciplinary effort for the Healing of a Diabetic Foot Ulcer

Abstract
Diabetic foot ulcers figure as one of the most complex and hard to heal wounds. No isolated approach is the best approach. The best approach is made by a multidisciplinary team, by a very objective evaluation, that allows the identification of the most probable and significant barriers to the achievement of full healing. It is shown how important is a previous vascular assessment, the correct selection of the surgical technique, and the adequate follow up of the patient’s wound in terms of tissue viability, without forgetting the need of a podiatrist collaboration for the prevention of post-healing complications and ulcer recurrence.

Keywords: diabetic foot, Complex wounds, surgery.

Introduction

Foot problems are one of the most common complications of diabetes. There are between 2% and 6% of diabetic patients that will develop a foot ulcer/year. The risk of lower extremity amputation in people with diabetes is 15 to 46 times higher than in nondiabetic patients. One can easily claim it constitutes the most common underlying cause of lower extremity amputation in the western world. Recent data from the Centers for Disease Control (CDC) show in the United States of America an annual number of 111,000 hospitalizations for the diabetic foot in 2003, thereby surpassing the number attributed to peripheral arterial disease (PAD). Still we see that the annual rate of amputations in the United States has almost halved in the past decade, and most of this decrease has been in the above-ankle amputations. After the initial
amputation, the risk of re-amputation or amputation of the contralateral extremity, in the same year, is also high: 9% to 17%.⁸

The underlying pathology usually is not reversible, and most disease processes affecting the diabetic foot will continue to worsen over time. Three primary pathways or mechanisms of injury have been identified in the development of foot ulcers. These include wounds that result from ill-fitting shoes, ulcers on weight-bearing areas (mainly on the plantar area), and traumatic events. Neuropathy is one of the most common risk factors for lower-extremity complications in diabetic patient. Peripheral Sensory Neuropathy Diabetes affects sensory, motor, and autonomic nerve function. In patients with sensory neuropathy, pain is defective. Sensory neuropathy contributes to an inability to perceive injury to the foot due to what is commonly referred to as loss of protective sensation⁸, which implies a level of sensory loss where patients can injure themselves without recognizing the source of the injury. In the other hand motor neuropathy contributes to wasting of the intrinsic muscles of the foot, muscle imbalance, structural foot deformity, such as claw toes and subluxated metatarsophalangeal joints, as well as limited joint mobility. Autonomic neuropathy causes shunting of blood, and loss of sweat and oil gland function, which leads to dry, scaly skin that can easily develop cracks and fissures⁶. The combined effect of these neuropathies results in a foot with structural deformity and biomechanical faults, dry, poorly hydrated integument, which also has an inability to respond to pain and repetitive injury.

Another major complication source for the foot is peripheral arterial disease (PAD) in which perfusion is compromised. PAD in patients with diabetes is characterized by multiple occlusive 754 plaques of small- and medium-sized arteries of the infrapopliteal vessels.⁹,¹⁰ PAD puts the patient with diabetes at a significantly greater risk for foot ulcers, infections, and amputations.¹¹ Several theories attempt to explain the microvascular changes that occur in diabetes. One theory proposes that increased microvascular pressure and flow results in direct injury to the vascular endothelium, which in turn causes the release of extravascular matrix proteins. This leads to microvascular sclerosis and thickening of the capillary basement membrane. Capillary fragility also leads to microhemorrhage, which could be the reason that infection spreads through the tissue planes in patients with diabetes.¹⁰
Most authors state that any theory of microvascular involvement in the process of diabetic ulceration and healing must include both the direct effects of glycosylation and local inflammation and the indirect effect of alteration of microvascular hemodynamics associated with autonomic dysfunction. Regardless of the underlying mechanism, the result is a decrease in perfusion to the tissue thereby decreasing healing potential which places the diabetic limb at risk. Vascular evaluation should include a thorough history of symptoms of intermittent claudication, ischemic rest pain, and peripheral vascular surgery, as well as clinical signs of ischemia, such as skin temperature, dependent rubor, pallor, hair loss, and shiny skin with the most accurate assessment of lower-extremity pulses\textsuperscript{12}, using hand held doppler (vascular, 8 mHz) in determining bilateral resting ankle– brachial pressure indices (ABPI). However, in the advanced disease state of diabetes and particularly endstage renal disease, ABPI may have limited utility due to the lack of compressibility and may require vascular surgery consultation.

The use of surgery to heal wounds and prevent recurrence is very well supported, there are good evidence that elective or prophylactic foot surgery in patients who have diabetes might prevent bigger complications in the future. Armstrong et al.\textsuperscript{13} validated a four-tier surgery classification that consists of elective, prophylactic, curative, and emergent surgery. Elective surgery is planned reconstructive surgery in a patient with foot deformity to eliminate pain or to enhance function. Prophylactic surgery is intended to prevent ulcer recurrence. Curative surgery is intended to facilitate wound healing in a patient with an existing foot wound. Emergent surgery is intended to remove infection or devitalized tissue.\textsuperscript{13} There is no evidence that elective surgery alone, has a direct reduction of the risk of ulceration. Patients with diabetes should undergo elective foot surgery only if they have severe deformity, pain, or functional limitations that warrant surgery rather than an expectation that surgery will prevent a foot ulcer in the future. Prophylactic surgery includes toe and bunion deformity correction, Achilles tendon lengthening, and exostectomy. For example, percutaneous lengthening of the Achilles tendon has been shown to reduce plantar foot pressures in subjects with prior ulceration\textsuperscript{13}. The big question for physicians and patients is whether the risks of surgery are better than the risk of having a chronic foot ulcer. The risks of infection and amputation from a nonhealing foot ulcer are high. Approximately 10% to 20% of diabetic foot ulcers end in amputation,\textsuperscript{14,15} 56% are
treated for infection, and 20% develop osteomyelitis. Ulcer recurrence, as previously discussed, is about 30% per year when standard preventative therapies are provided. The incidence of ulceration is 50% to 80% when no additional prevention is provided. On the other hand, several authors have reported the results of planned surgical procedures to heal foot ulcers. These studies suggest a high rate of wound healing (91% to 100%) and a low rate of ulcer recurrence after 2 years (0% to 39%). If surgery is simply viewed as a prevention tool, in the correct subpopulation, surgery has the lowest reulceration rate. The goal of surgery is to reduce the longterm risk for reulceration by increasing joint motion where it is limited, reducing abnormal pressure points, and repairing structural foot deformities when they are an underlying cause of ulceration. Like the surgery described to increase ankle joint range of motion by lengthening the Achilles tendon, arthroplasty of the great toe has been reported to increase healing of ulcers that have failed other therapies with a much lower rate of ulcer recurrence. Armstrong reported the results of a cohort study of 41 diabetic patients with great toe ulcers. Patients either received resectional arthroplasty of the great toe or standard wound care. The surgery group had faster healing (24 vs. 67 days) and few recurrent ulcers after the surgery (5% vs. 35%). As the population continues to age, the incidence of diabetes will continue to increase, which will in turn lead to more diabetic wounds. A team approach—with total involvement of the healthcare system and the necessary partnership with the patient—will be the infrastructure for achieving better outcomes of care. Early assessment for the risk factors for foot ulceration in persons with diabetes is essential. A variety of methods must be used to identify at-risk persons.

When the elective/prophylactic surgery is no longer optional, and a surgical intervention is needed, curative and emergent surgery take place, in order to debride, help to remove infection and as earlier was mentioned, facilitate wound healing.

Transmetatarsal hallux amputation (TMHA) is, unfortunately, a frequently performed operation that aims to safeguard limb viability when no other option is available. The main candidates to TMHA are patients who develop ulcerations due to diabetic neuropathy, infection, necrosis, and/or gangrene.

TMA was first described by Bernard and Heute in 1855, but it was McKittrick et al in 1949 who performed it as an alternative to more proximal amputations in patients with the previous description. The goal of such procedures should be to
accelerate/make possible wound healing while maintaining function of the limb. To achieve this goal the surgeon must remove nonviable tissue while preserving the maximum amount of healthy foot.

The most important individual factor that should be taken into account is vascular sufficiency. This being said, we should not forget that a regular and dedicated post-op wound care performed by a specialized nurse staff is essential to a faster and successful recovery.

Infection is an important concern in diabetic ulcers and warrants prompt identification and treatment. Adjuvant therapies coupled with debridement and appropriate dressings can be critical in salvaging the diabetic limb. Soft tissue and bone infections are very common in persons with diabetic foot ulcerations. Most patients with diabetic foot ulcers (56%) will be treated for soft tissue infection during the course of their ulceration. Approximately 20% of these patients will develop infection of the underlying bone. Identification of foot infections in patients with diabetes requires vigilance because the normal signs of infection may be blunted or absent. Hyperglycemia impairs the humoral innate immune response by increasing the proinflammatory cytokine levels, dysregulating vasoactive cytokines, such as bradykinin and nitric oxide (NO), and decreasing complement activation. This, in turn, can lead to increased insulin resistance through several pathways, causing more hyperglycemia. The polymorphonuclear cells (PMNs) and monocytes of the cellular innate immune system show impaired chemotaxis, adherence, phagocytosis, and intracellular killing in patients with diabetes.

Lower-extremity wounds are often colonized with microorganisms regardless of the presence of a real infection. Routine cultures of the wounds and superficial swabs should not be done when the wound is clinically not infected. When cultures are obtained, deep tissue should be obtained rather than superficial swabs. In cases of mild or moderate infection, curettages from the ulcer base after debridement should be obtained prior to the initiation of antibiotics. In severe infections, empiric antibiotic therapy should be started as soon as possible. Deep tissue infection requires systemic antimicrobial agents. The classic signs of warmth, tenderness, swelling, and erythema can be supplemented for persons with chronic wounds by the mnemonic STONEES. If high exudate rate and odor are present, other criteria are needed to determine whether the infection is superficial.
or deep (again, according with Sibbald, Woo and Ayello’s NERDS and STONEES mnemonics).25,26

In the other hand, biofilm is a significant growing concern that is less understood, and its impact underappreciated, which makes it not effectively treated. Biofilm is a colony of bacteria, fungus, or yeast that can populate a wound within 10 to 24 hours.27,28 Once established, a complex and biodiverse community evolves protected by a glycocalyx shell.29,30 Thus, conservative debridement may not be able to reach these deeper layers. Unlike planktonic bacteria that are metabolically active and can be generally treated with antibiotic therapy, microbes within a biofilm are relatively senescent. Thus, the mechanism of action of antibiotics, which is to interfere with protein synthesis (disruption of cell wall, cell membrane synthesis) is largely ineffective against biofilm. Although biofilm under ideal circumstances provides a steady-state ecology and balances between the microbial species, the chronic wound may be dominated by one species that develops into wound chronicity and periods of limb-threatening acute infection. Further troubling is the fact that qualitative and standard quantitative culturing techniques selectively identify specific and limited number of bacteria, fungus, and yeast. Thus, the true pathogenic microbe may not be detected and subsequently not treated.31 Future research is needed to determine appropriate therapy combinations and individual treatment plans for patients with diabetic foot ulcers.

Case report

We bring a case of a 71-year-old male patient (Mr. P.A.), that used our services by the first time on March 11, 2019, with a neuro-ischemic diabetic foot ulcer, on the right foot, in the dorsal aspect of the distal third of the hallux, with a necrotic wound bed, without floating edges, except for the edge proximal to the lesion with a minimum locus of about 3 mm, but without discharge when pressed. Conservative sharp debridement of some necrotic tissue, maintaining a safe distance from the margins of healthy tissue, with the remaining tissue to be gradually debrided by autolytic method. Doppler performed with an 8 mHz probe, which reveals monophasic pulses of very weak amplitude in the anterior and posterior tibial territories (coinciding with the description in an arterial Eco-doppler report that documents the existence of severe pathology in the arterial axes of the lower limb), insufficient for calculating IPTB, despite
the fact that the skin of the lower limb appears to have a normal temperature in relation to the rest of the body. Easy pallor of the feet at elevation with flushing pending when lowered, time of re-perfusion of the nail bed greater than 3 seconds. He has a history of amputation below the knee in the contralateral limb also due to arterial insufficiency.

Fig. 1 - 11/03/2019

Initial treatment with Prontosan Gel X® (PHMB + Betain, a surfactant agent) and foam with silicone, following a 15 minutes application of Prontosan Solution. In terms of local care, debridement of slough or nonviable tissue should be actively promoted to create a clean wound. This may include careful sharp surgical debridement or the use of mechanical, enzymatic, or autolytic debridement methods with dressings (usually alginates and hydrogel-based products).

Topical antiseptics and wound cleansers are useful for their ability to remove devitalized tissue as well as reduce bioburden. Unlike antibiotic therapy, antiseptics are less likely to develop resistance to microbes, a concentrated localized effect, are generally better tolerated, and are widely available. In light of the troubling trend of growing antimicrobial resistance, topical antiseptics and wound cleansers may provide an important treatment modality. Antiseptic therapy can be applied in different ways. With every dressing change, the wound can be washed with an antiseptic solution. It
can also be applied onto the wound surface multiple times daily via an antiseptic saturated contact dressing.

Along the same category, another widely available yet generally underutilized topical therapy in wound care are surfactants. Surfactants are detergents that break up debris and prevent adherence of foreign materials. Surfactants have been utilized for orthopedic application for many years in the removal of acute contamination as well as biofilm reduction on hardware.33

Topical treatment for healable wounds with PAD, that are also critically colonized should include silver dressings (silver-alginate matrix paste), polyhexamethylenebiguanide (PHMB) gel, Hyaluronic acid gel or Manuka Honey. Agents such as sodium hypochlorite, quaternary ammonium agents, and various aniline dyes (mercurolchrome) have higher cellular toxicities and more limited antibacterial effects.32 As so, ulcers with adequate blood supply that are expected to heal (specially the one following TMHA in this case study) should be dressed with products that support moist wound healing principles. The surrounding intact tissue should be protected from fluid accumulation, which can macerate the healthy skin at the ulcer border, using a barrier film forming liquid acrylates. When treating diabetic foot ulcers, associated with PAD, it is wise to treat the cause: bypass, stents, or dilation with a consultation to a vascular specialist32. Therefore, we suggested to the family an evaluation for vascular surgery, and a consultation was scheduled for, March 23rd.

On March 13th, the lesion does not seem to be getting worse, and there are granulation foci in formation. By this time patient had ciprofloxacin.

![Fig. 2 - 13/03/2019](image-url)
The status of the wound bed shifted to dry necrotic tissue, probably when an accidental removal of the dressing led to the application of a dry dressing by informal caregivers, or either by a significant drop on the toe blood supply.

When a wound doesn’t have enough blood supply to heal, the surface of the wound or necrotic gangrenous tissue should be allowed to dry and demarcate, as we did in the early stages of treatment, prior to the TMHA. This can be facilitated by removing the soft slough around the proximal intersection of the necrotic and viable tissue but leaving the necrotic cap intact. Moisture and bacterial reduction may best be served with antiseptic and low moisture agents, such as provided by Cicarapid® Spray.
(kaolin associated with a complex of hyaluron, titanium dioxide, silver ions and benzalkonium), that usually reduce bacterial counts with acceptable tissue toxicity. Both of these agents have a broad spectrum of action, a sustained residual effect, and acceptable tissue toxicity for this indication.

On the March 25th, following the consultation with a vascular surgeon that had the opinion he should be submitted to endovascular procedures only after TMHA and only if this first intervention was proven inefficient. Therefore, the patient presented to the emergency room with a necrotic ulcer of the hallux with inflammatory edges that extended to the base of the toe. The patient mentioned intense pain that had worsened in the last 5 days. He brought a Doppler ultrasonography that revealed major atheromatous arteriopathy with a biphasic pulse of the deep and superficial femoral and popliteal arteries thus presenting multiple segment obstructive arterial disease with great hemodynamic repercussion. He had been going to General Surgery consultations for 10 months before this event with small improvements. The patient
had a history of prostatic and hepatocellular cancer and was allergic to Penicillin. He also had dyslipidaemia and insulin dependent type II diabetes with retinopathy, peripheral neuropathy and nephropathy (Chronic kidney disease stage IV) requiring haemodialysis. This being said, he was a high-risk patient. In this context the surgery was explained to the patient and he signed the informed consent. He was then submitted to TMHA.

A lateral cuneiform resection with resection of bone in a slide oblique technique was performed. The procedure had no complications to report. By the 1st post-operative day the patient was apiretic and with no algic complaint and was discharged on that same day under an 8-day course of Ciprofloxacin. In the post-operative consult (at day 15) the patient no longer needed analgesic medication.

On March 29th, the patient resumed treatment with the Clinical Nurse Specialist. The wound surface was a little de-hydrated, due to the no longer need of fibrous dressing. No drainage from the 1st metatarsal area, moderate odour, no major infection signs in superficial or deep compartment (based on NERDS and STONEES mnemonic). Surface sharp debridement was performed (curettage), followed by 15 minutes application of Prontosan® Solution. Calgitrol Paste® was applied (silver-alginate matrix paste), as a primary dressing. Due to the wound’s current high inflammatory status, an open cell foam was selected (Askina Foam®) as secondary dressing, in order to provide an adequate management for current more fibrinous exudate. Also, the moisture balance needed for proper healing achievement, is better provided by the combination of the primary dressing with a foam dressing. The foot was carefully protected of trauma with synthetic cotton bandage, followed by a support bandage.
On April 2\textsuperscript{nd}, the wound bed is more hydrated, no odour is detected, we can see some granulation tissue starting to take over. Exudate is still thick and fibrinous. The course of treatment is maintained. As the treatment goes on, some maintenance sharp debridment is made, no signs of infection are detected, moisture management seems...
to be adequate, still despite some wound contraction, it remains quite stagnant, with low quality granulation tissue, no formation of epithelial tissue, and with some necrotic hydrated tissue on the area of the first metatarsal, which seems to have healthy flat and non-rugged bone extremity, with deep wound probing. As so the primary dressing is shifted to Hyatoprol (Hyaluronic acid gel), from April 8<sup>th</sup> to May 3<sup>rd</sup>.
On May 3rd, some moderate odour is detected, we can see some granulation areas gone necrotic, even after sharp debridement, exudate was more fluid in the last weeks, but become thick and fibrinous again, facts that let us think about high levels of critical colonization. No other signs of infection were detected. Primary dressing was shifted to Prontosan Gel X®, in order to control the bacterial load thus helping the continuous wound cleaning process, specially taking in account the fact that the deeper area around the 1st metatarsal remains granulation free, with some necrotic/devitalized tissue, despite no bone detection on probing of the area. It seems also the area of the wound were the fibrinous exudate is originated. X-ray of the area was in equation, if we got no tissue improvement in the following weeks.
In the following weeks (May 3rd to 17th), we got some improvement, reducing non-viable tissue and associated colonization signs, better granulation tissue that now allows for some progress of epithelization tissue. Still we choose to maintain a small layer of Prontosan Gel X®, on the deeper part of the wound and to apply on the rest a non-adherent silver dressing (UrgoTull Ag®), keeping a foam dressing as secondary dressing (from May 24th to June 12th).
Fig. 14 - 24/05/2019

Fig. 15 - 31/05/2019
Fig. 16- 7/06/2019

Fig. 17- 12/06/2019

Fig. 18- 14/06/2019
Even without having applied gel on June 14th, in June 17th there is still maceration in the proximal area of the wound, that maintains 1 to 2 cm deep. The rest of the wound area is 90% epithelized. After deep probing with a curate, two loose bone fragments were removed, which probably were acting as a foreign body stalling the healing process of that area. The deep area was then cleaned with Prontosan® and filled with Calgitrol Paste®, from bottom to top, using a syringe with a 14G catheter (see 5th image of Fig.19), technique applied until full healing on June 26th).
Fig. 20- 21/06/2019

Fig. 21- 24/06/2019
Fig. 22 - 26/06/2019
Almost one month later, the patient was revisited, for a post-healing evaluation. Some scar keratosis was removed and Linovera® oil was applied due to its reinforced epidermal junction, hydrating and anti-inflammatory properties. Patient kept the application of Linovera® during one month, and start using regular hydrating crème in daily base. He was also advised to get a consultation with a podiatrist, in order to have a proper evaluation and correction of eventual new hyper-pressure areas on the foot, due to the absence of the Hallux.

Fig. 23- 24/07/2019
Conclusion

The post-op wound care is a vital part of a fast and effective rehabilitation after TMHA as represented in this successful case. The TMHA was performed in a slide oblique technique to facilitate wound healing maintaining a more physiological shape of the foot. Despite this, the patient should still wear adequate footwear to improve wound healing.

This procedure allowed the patient to salvage his lower limb thus maintaining his ability to walk. Advanced wound healing techniques, fully based on the best available evidence, provides great results even on this type of complex wounds were diabetes and PAD are main obstacles to full healing, and were sometimes time is short. Questioning the non-healing progression showed to be important in detecting another major barrier to healing (bone fragments) when all other parameters of the healing process were controlled. But the team work doesn’t end with the healed wound, prevention of future complications is very important, off-loading reduction of pressure and shear forces on the foot may be the single most important yet most often neglected aspect of neuropathic foot approach. Off-loading therapy is a key part of the treatment plan for diabetic foot. The goal is to reduce the pressure at the ulcer site and keep the patient ambulatory. Off-loading strategies must be tailored to the age, strength, activity, and home environment of the patient. Education is critical to improve compliance with off-loading. The patient must understand that the wound could result of a repetitive pressure and that every unprotected step could be hazardous.

References


