Prevention of Lower Extremity Amputations

Conservative modalities can lessen morbidity.

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Amputations have long been feared as one of the most tragic complications of diabetes mellitus. Non-healing diabetic foot ulcers (DFU) are most often key components in the pathway leading to non-traumatic amputation in this population. Although frequently necessary as a curative measure for chronic wounds, infections, and/or non-reconstructable ischemia, modern wound care protocols have been established to aim at minimizing the need for amputation. Once healed, prevention programs must focus on appropriate foot care, footwear, and early diagnosis of impending problems in order to avoid new or recurrent lesions. This article briefly outlines modern approaches to the management of DFUs and a new technology to aid in early detection.

Lower extremity amputations are one of the oldest surgical procedures that were performed, dating back to prehistoric times. Greater than one million people with diabetes suffer a limb loss, which equates to an amputation occurring every 20 seconds. Amputations may be indicated for limbs with peripheral vascular disease, trauma, tumors, infections, and congenital limb deficiencies. Peripheral vascular disease is the leading indication for lower extremity amputation in the United States. This is often seen in individuals with diabetes mellitus and peripheral neuropathy. Approximately 65,000 lower extremity amputations are a result of ischemic disease, leading to ulcerations and subsequent gangrene. It was also reported that 84% of lower extremity amputations are preceded by an ulceration. Though amputations in various cases are considered a limb salvaging technique and can be the best option for a compromised limb, it is vital to treat patients with all appropriate conservative methods prior to resorting to this surgical option.

Approximately 60% of both diabetic and non-diabetic, non-traumatic amputations that are performed might have been prevented with appropriate prevention programs including early pressure detection and annual check-ups in patients at high risk for ulcerations.

Basic Tenets of Wound Care

Identifying ulcerations, as well as continuing wound care of already identified ulcerations are vital components to preventing amputations. Routine foot checks are one way to help identify and follow ulcers. Patients who are at high risk for developing ulcerations should have rou-

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Peripheral arterial disease (PAD) should be taken into consideration, and patients with diagnosed or suspected PAD should have ankle-brachial index (ABI) measurements performed. Patients with diabetes are recommended to have ABI measurements performed once they reach the age of 50. Those patients with abnormal vascular examinations, a history of DFUs, prior intervention for peripheral vascular disease or atherosclerotic cardiovascular disease should have annual vascular exams performed. Revascularization is recommended in those individuals with DFUs and PAD.

Off-loading is a mainstay of therapy for wounds in high pressure areas, especially those on the plantar aspects of feet. In patients with plantar diabetic foot ulcerations (DFU), it is recommended to do so with a total contact cast (TCC) or an irremovable ankle walking boot. In patients who require frequent dressing changes, a removable option such as a walking CAM boot is preferred over a TCC. In patients whose wounds are not along the plantar foot, any modality that relieves the pressure at the site of the ulceration is recommended. Patients who are deemed to be at high-risk due to co-morbidities or a history of ulcerations are recommended to continue to wear diabetic footgear or an appropriate dressing, while avoiding maceration are recommended in those individuals with DFUs and PAD.

It is well accepted that the use of silver is a tried and true method in the prevention and treatment of infection. It supplies a broad spectrum of coverage while having very few side effects. Silver ions react by binding to negatively charged particles, including DNA, RNA, and chloride ions, preventing replication and altering cell membrane permeability. In this way, silver can act as an antimicrobial agent. Both creams and wound dressings containing silver have shown to be effective in the treatment of a wide range of infections, including bacteria, viruses, fungi, and molds. Nonetheless, the use of silver-containing products should be of a limited nature to avoid the development of resistant bacterial species.

Topical Gels, Creams, Dressings, and Other Biologics

In routine clinic visits, lower extremity wounds are typically treated with some sort of topical gel or cream and an appropriate dressing, whether it is the only treatment method, or in conjunction with other therapies. It is vital to identify the cause of the wound so that an appropriate treatment option can be employed. However, using appropriate topical wound care products and dressings can help to minimize or eliminate infections and can help prevent future infection.

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disrupting the extracellular polymeric substance (EPS) matrix, which is the main component of biofilm. Biofilm is the EPS matrix surrounding microbes, allowing them colony defenses against host immunity, host healing, and most wound care treatments. Biofilm is the "slime layer" that creates a physical barrier limiting chemicals from entering the bacteria. It has been seen that some wound care gels that work by disrupting this biofilm can reduce the number of bacteria present in the wound by 7 to 8 log. A prior study showed that applying a wound gel that disrupts the biofilm for four weeks helped reduce the volume of microbes 32% greater than when treated solely with standard of care. It was also reported that the use of wound gel improved the rate of healing in chronic wounds as 50% greater than with standard of care.15

There are also gels that contain recombinant human platelet-derived growth factor. Becaplermin, for example, is produced by recombinant DNA by inserting the gene for B-chains in platelet-derived growth factors (PDGF). These growth factors induce fibroblast proliferation and differentiation, potentiating healing, especially in those patients with decreased healing capacity. Gels that contain such growth factors that are utilized in ulcerations in conjunction with appropriate wound care, have been seen to heal approximately six weeks faster than those with only standard of care. Therefore, it is important for clinicians to be aware of various wound care products and their mechanism of action to appropriately decide on a wound care therapy based on the wound and the patient.15

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Topical Oxygen Therapy
It has been reported and widely accepted that topical oxygen for non-healing wounds can have beneficial effects. The partial pressure of oxygen (pO2) is a key factor in wound healing.14 A pO2 less than 40 mmHg is associated with poor wound healing. Many chronic non-healing wounds are stuck in the inflammatory phase, due to a lack

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of oxidative killing by neutrophils, which can occur due to a low pO2 level. Increasing the pO2 level at the site of a wound helps increase reactive oxygen species, which is a vital component in normal cell signal transduction and cell cycling. In addition, it is seen that adequate oxygen supply regulates cellular motility, angiogenesis, and extracellular matrix formation, all of which are vital for proper wound healing.16

Topical oxygen can be administered through various methods. One common method is delivering 100% oxygen for a total of 90 minutes once a day at the site of the wound. Another common method is applying continuous, atmospheric oxygen for three to seven days to the site of the wound through a cannula. Experimental studies have shown that patients using topical oxygen therapy for up to eight days had significantly more epithelialization on histologic examination compared to control wounds that did not have topical oxygen therapy. Various studies on topical oxygen treatment reported that subjects who were placed on topical oxygen in comparison to standard of care treatment healed in a shorter amount of time and had a significantly higher wound size reduction. It is, however, important to note that topical oxygen systems generally are able to diffuse through a maximum distance of 50-100 microns; therefore, the amount of biofilm layers and tissue over the wound should be taken into consideration before utilizing this conservative option.17

Skin Substitutes

Various advancements have occurred in both temporary and permanent skin substitutes. Allografts and xenografts can provide a temporary coverage option; however, they can come with the side-effect of rejection. Bioengineered skin substitutes are available to provide both temporary and permanent coverage, with negligible risk of infection or immunologic response. However, they can be very costly. It is important to appropriately utilize these options based upon the patient and the wound.

Human amniotic membranes have been successfully used to treat chronic cutaneous wounds. They are allografts that exhibit low immunogenicity, reduce inflammation, pain, scarring, and accelerate wound healing.18 Dehydrated human amnion/chorion membranes (dHACM) contain large numbers of pro-angiogenic growth factors that help with neovascularization and healing within chronic wounds. Clinical trials showed that diabetic foot ulcers treated with dHACM healed 77% at four weeks and 92% at six weeks when compared to standard of care methods.19 These results in healing rates and the advancements in allografts with decreased immune responses show promising outcomes.

New skin substitutes have been gaining popularity in clinics, especially due to their low immune response. In addition to porcine and bovine skin substitutes, an acellular fish dermal matrix as an alternative tissue source for chronic, non-healing ulcers is gaining popularity. This product is interesting because of the similar structure to human dermis. It also contains omega-3 fatty acids, thus providing a natural structure to the wound bed with additional bioactive lipids. Acellular fish skin also has antimicrobial peptides that help to repair wounds and work as a defense against bacteria, fungi, viruses, and parasites. Clinical studies have shown that after approximately five applications of fish-skin grafts, there was a significant reduction in the absolute wound area.20

Thermometric Pressure Detection Devices

Thermometric pressure detection mats are a novel product that have recently become available to help detect both new and recurring ulcers before they appear. Wireless floor mats with temperature sensors help to detect increased pressure points along the plantar aspect of the foot, and transmit information to the manufacturer’s monitoring center to help prompt clinicians and their staff to see the patient more routinely and alleviate pressure points in a timely manner. These types of devices detect inflammation that often precedes ulcerations by detecting a difference in temperature between the feet of 2.22°C. In a recent study, it was seen that 86% of patients averaged at least three uses per week. For 34 weeks, 132 patients who had a previously healed diabetic foot ulcer were followed, and it was seen that the mat detected 97% of diabetic foot ulcers five weeks before they were
clinically observed. Considering the high adherence rate by patients and the extremely high detection rate, these types of novel products that can prevent wounds and subsequent infections can make a significant difference in the success of amputation prevention programs.\(^5\)

**Conclusions**

Overall, it is vital to analyze the patient, the ability of the patient to abide by and follow the treatment plan, the wound, and the cause of the wound prior to utilizing conservative therapies. Though surgical intervention, such as amputations, in some cases may be the best course of treatment, various conservative therapies are available to the clinician to prevent this. Prevention of amputation by means of conservative therapy depends greatly on patient education and compliance, early diagnosis and treatment, and utilization of appropriate conservative therapies by the clinician. PM

**References**

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