The Wound Is Closed… Now What? So What?—Part 2

The closure of a wound does not define the endpoint of treatment.

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Part 1 of this article (Nov 2020 issue) dealt with why the closure of a wound does not define the endpoint of treatment but rather heralds the next phase in the management of a more complex condition. Part 2 (as follows) will discuss what should be done, after the wound is closed until complete healing takes place, to make the system work to address the critical supra-wound issues.

The Three Stages of Wound Healing

In order to answer the lead question: "The Wound is Closed…Now What?" we need to address the complex process of wound healing, which involves three identifiable stages:

1) The inflammatory stage defined by hemostasis, recruitment of inflammatory cells and secretion of cytokines and growth factors.

2) The proliferation stage defined by development of a matrix as well as the processes of angiogenesis and re-epithelialization.

3) The remodeling or maturation stage is when a mature scar is formed.

In the remodeling stage of diabetic wounds there is excessive breakdown of extracellular matrix proteins resulting in abnormal protein-protein bonds. This disrupts the normal maturation of collagen and leads to decreased scar thickness, which can reduce tensile strength of the eventual scar, eliciting decreased wound contraction. Thus, a greater portion of healed skin is composed of scar tissue, which is significantly weaker, more susceptible to damage and re-injury, and will break down quicker than skin that was not subject to these damaging influences of the diabetic condition. Specifically, hyperglycemia drives this process through non-enzymatic glycosylation and the development of advanced glycation end products (AGE'S); and hence the increased production of reactive oxygen species (ROS) as well as reduced antioxidant defenses. The imbalance created is a major factor in creating an extended inflammatory stage and over-production of damaging inflammatory elements. This shows up as chronicity and delayed healing of diabetic wounds.[2]

Figure 1: Fungus infections in the nails and skin in diabetes

The three phases of wound healing represent a more complex mechanism than previously understood.

Until recent years, these phases were thought to be distinct steps that occurred sequentially. But recent research has found that these three phases represent a more complex mechanism than previously understood. They are now known to overlap, and in some cases occur in parallel in time and space in the wound.[1] This means that extreme diligence must be done throughout the wound healing process, starting from the day the patient presents to the wound healing provider. The longer the wound takes to heal, the more inflammation occurs and the more chronic the wound will become, cre-

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ating a wound chemistry that will serve to adversely impact the eventual quality of the wound and the chances for reoccurrence, and will challenge the most skilled expert in wound healing. What takes place in all stages affects what situation the wound provider is faced with when the wound is closed. Keep in mind that *the wound is not healed just by virtue of the fact that it has closed.*

The wound is considered closed at the third stage of wound healing. This is the stage where granulation tissue is reorganized and collagen is being remodeled which aligns along the lines of tension. Water is reabsorbed so that collagen fibers lie closer together and undergo the process of cross-linking. This phase, which can last over one year, allows the wound to achieve maximum strength and promotes the attenuation of the thick fibrosis that may occur. Only after this process is completed can one say "the wound is healed."

Figure 2: Pressure areas under the heel and metatarsal heads because of increased loading time in these areas during gait.

Cutaneous Pathology

If one looks beyond the surface, it becomes apparent that knowledge of skin characteristics is not always used in daily clinical practice, where skin pathology can be underappreciated, neglected and frequently underdiagnosed.[3] Common complications are then allowed to occur, forcing patients with both type 1 and type 2 diabetes mellitus to endure a broad spectrum of disorders. Cutaneous pathology can show up any time in the course of diabetes but relevantly may appear in the foot before any other diabetic complications. It can't be overstated that close attention to the earliest skin changes can be one of the most important pre-emptive strategies employed in practice, and that such attention will likely lead to effective preventive measures.[4] A major challenge does exist, however, to this compelling concept: skin disorders in the person with diabetes are commonly written about in the literature, but there is insufficient research data available regarding early-stage skin conditions in these patients, especially information involving non-injured skin or skin that was previously ulcerated but now closed. Better understanding of the burdensome affliction of skin pathology in persons with diabetes may motivate those involved to accomplish a higher level of prevention and management.[5]

There are other comorbidities that co-exist as permissive factors before the wound develops and will remain such even after the wound is closed, reinforcing the concept that a closed wound is a risk factor, in itself, for the development of another wound.[1] Not mentioned frequently in this regard is the presence of *dystrophic, mycotic* toenails. It has been reported that both tinea pedis and onychomycosis are observed more frequently in the presence of poor glycemic control as well as peripheral neuropathy; and both were associated individually with and each portends the development of diabetic foot ulcerations (Figure 1). It is well-served then to add these conditions to the register of risk factors for lower extremity amputation.[2]

Other Cause and Effect Factors

Moreover, it is well documented that *psychologic factors* are associated with both cause and effect in the diabetic condition. As an example, a recent study focusing on the relationship between *depression* and major lower extremity amputations showed that this condition was associated with a 33% increased risk of amputation over those subjects that were not experiencing depression. In addition, evidence now suggests that depressive disorders are not only associated with mortality within 18 months of the appearance of a diabetic foot ulceration, but is also linked to a two-fold increase in mortality in persons with their first DFU at 5 years. The pathway through which depression relates to mortality in diabetic foot disease is unknown. What we do know, however, is that poor self-care and compliance has a strong association with depression. Studies suggest that professional treatment resulting in improved depression may decrease adverse outcomes in patients with diabetic foot ulcerations. This data raises the question of whether early treatment of depression decreases the risk of mortality. In any case, the presence of a DFW should alert health care providers to screen for depression as a routine matter.[6]

Persons with diabetic neuropathies, whether it be sensory, autonomic, motor or mixed, exhibit significant gait changes early on in the disease process.

Also, persons with diabetic neuropathies, whether it be sensory, autonomic, motor or mixed, exhibit significant *gait changes early on in the disease process.* These changes, which are often observed even before morphological changes take place in the foot, can be observed by the astute clinician.

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They include:

1) Increased peak plantar pressures.

2) Altered center of pressure stemming from restricted motion of the subtalar and first metatarsal phalangeal joints.

3) Increased loading time at the heel and metatarsals.

Dynamic plantar pressure analysis validates that these may lead to severe pre-ulcerative calluses (Figure 2), DFW's and also present definite risk factors for falls, which often lead to a tragic scenario of events.[7]

Additionally, recent research that shows that *psoriasis may predispose a person to develop type 2 diabetes mellitus*, just as it does for heart attack and stroke (Figure 3). A 13-year study with 52,000 participants concluded that people with psoriasis have a 49–56% greater risk of developing type 2 diabetes later in life.[14]

Along the same lines, a number of research papers have shown a *strong link between gout and type 2 diabetes.* In one study, the health records of people who participated in the well-respected Framingham Heart Study were studied. The researchers found that there was a direct relationship between the level of uric acid in the blood and the likelihood of developing type 2 diabetes. To be precise, the chance of diabetes went up 20% for every 1 milligram per deciliter (mg/dL) rise in uric acid. Other research showed that women with gout were 71% more likely to get diabetes; and men with gout had a 22% higher chance.

Scientists aren't sure of the reasons why psoriasis and gout are associated with type 2 diabetes. It is well to note, however, that both psoriasis and gout are inflammatory diseases and that inflammation is thought to play a role in the development of diabetes. Also, in type 2 diabetes, higher insulin levels promote hyperuricemia because of its effect on the kidneys.[8-11, 2]

One can readily see, then, that a person with diabetic foot syndrome can actually mirror a soup of comorbidities, some of which are normally considered in designing preventive strategies, and some are not. Having a wider view of the diabetic foot syndrome, *focusing more on the person who has a diabetic foot wound instead of just the wound* may provide big pay-offs in preventive dividends. Effective secondary prevention methodologies, then, require the practitioner to implement all of the clinical data that would be available, which could potentially mitigate the increased risk of a closed ulceration entering into a catastrophic cycle. Interestingly, meaningful information is often staring the provider right in the face; other times important knowledge is uncovered only below the surface; and observing the patient in this holistic context can lead to a more complete understanding of the particular clinical scenario.

Focusing more on the person who has a diabetic foot wound instead of just the wound may provide big pay-offs in preventive dividends.

Figure 3: Psoriatic lesions on the foot heralds a predisposition to diabetes

After Closure

It is generally safe to say the same underlying conditions that were present which allowed the wound to occur are still there when the wound becomes closed. One can readily see, then, that what is done for the patient with a wound that has closed, but not yet healed—and even after the wound is considered healed—can be formative. In that regard, there is work to be done after wound closure. What does this *"after wound care"* look like and how do we approach it?

To gain additional clarity, let us recap. Up to now, we have discussed many factors that may come into play when considering what therapeutics need to be employed after a wound has closed. Perhaps having the most influence on a wound that has yet to heal, regardless of what stage it's at, is *hyperglycemia*. Similarly, any *form of neuropathy* in a person with diabetes can negatively impact the affected limb through the many risk factors involved in the war of foot-related morbidities. Likewise, *peripheral vascular disease* can have an equivalent adverse impact on the patient with incomplete wound healing. Further, there are additional dynamics that have to be taken into account when developing an "after wound care" strategy. To illustrate, the condition of having dystrophic toenails, which are likely to become infected with fungus and yeast, or the development of tinea pedis, or both.

These causative pathologies, which are all interconnected, can then give rise to secondary complicating circumstances that set the stage for

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myriad *skin changes, bone and joint problems, Charcot deformity and altered biomechanics;* all of these could potentially result in *balance issues, gait instability and falls*. Psychological issues such as *depression*, as well as the social, financial and compliance issues that ensue, put a complex spin on the primary prevention, healing and *secondary prevention of diabetic foot wounds*. Also, it is germane to consider the role that diseases such as psoriasis and gout have in an individual's clinical assessment.

Strategies

Let us contemplate an *"after wound care" strategy* based on the above information. A good starting point, although exact statistics were not obtained, is to recognize that a large proportion, if not the majority, of diabetic foot wounds are treated at wound centers. Wound center protocols, by and large, do not call for referral of patients upon discharge to podiatric physicians and surgeons, who would have expertise in diabetic foot medicine and surgery. In fact, they are usually referred back to locations where there are *no diabetic foot specialists, nor are there any specific organized plans of podiatric care arranged.** To actualize optimal secondary preventive care, a referral to an establishment that provides the needed advanced wide-ranging services would be necessary.[15]

What services should be provided in this "after-wound care" setting? The first consideration, however, should be to address the context in which this care is given. There has been a recent "call to action" for more patient-centered care.[15] *A team-based approach* with patient-centered care as the focus has shown to be ideal for addressing the many personal issues that impact the well-being of patients with diabetic wounds. This concept allows for a patient advocate who could help navigate the patient through the maze of complex regulations and insurance issues; and would support compliance as well as address social, psychologic, financial and educational challenges. This approach provides the opportunity for the aggregation of assessment data such that a unified and organized plan of care among providers is generated. In addition, this plan implements referral mechanisms that are efficient and time sensitive. Perhaps the most important ingredient in this recipe for successful "after wound care" is the supporting of a person's ability to rely on their own judgement, knowledge and resources, thereby taking responsibility and being an active participant in their own health care. This level of self-reliance and the ability to engage community and/or family support is vital to this healthful mission.

The piece of the pie that tackles the actual medical, physical and orthopedic needs of the patient has to involve access to a podiatric physician and surgeon. This would provide the needed expertise in diabetic foot care, surgery, biomechanics, shoe therapy, wound, skin and nail issues, neuropathic and vascular conditions as well as the myriad complications that could arise. Studies have shown the positive impact that podiatric care has in the secondary prevention of ulcerations in diabetic subjects.[12]

It is essential to include the availability of *physical therapy modalities*, such as massage, which would address the local inflammation, scar tissue and scar formation created during the healing process. Importantly, management and care for the joint stiffness and muscle tightness, often a part of the clinical picture, must be included. Offering an exercise program or recommendations would reinforce commitment to the physical health goals. Incorporating nutritional support to the post-wound care patient not only speaks to the glycemic and systemic inflammatory constraints, but also the caloric and nutritional balance between carbohydrates, proteins and fats. This aspect is a fundamentally important element in the person's overall conditioning and wellness.

In summary, there is so much involved in "after wound care", that in this discussion, we just touched the surface of what needs to be said and done. It was the goal of this paper to introduce and highlight the major topics that this author, through many years of experience, is confident will add some insight into some of the challenges we face, in our little corner of the health care universe, with lower extremity amputation prevention.

Conclusion

To quote Henry Ford: *"If you always do what you've always done, you'll always get what you've always got."* We can't afford these results any more, and the trends out in the real world do not appear to be heading in the right direction.[13] We, as a profession, need to change the paradigm in which this high risk patient is treated, because what we're doing now just isn't working. There are still too many people losing their legs…. unnecessarily.

To ask the question again: *Does closure of a wound define the endpoint of treatment or should it herald the next phase in management of a more complex condition? We should enter the next phase with alacrity. Let the games begin!* **PM**

Physical therapy modalities, such as massage, can be helpful in addressing the local inflammation, scar tissue and scar formation created during the healing process.

*This comes from personal experience as I have started and have been involved with institutional wound centers in a director and physician capacity for over 30 years.

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