



REVIEW ARTICLE

Commentary on the Conversion to an Advanced Standard of Care for the Treatment of Diabetic Foot Ulcers and Other Chronic Wounds

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Abstract There have been notable contributions in the literature regarding the consensus for a new standard for the treatment of diabetic foot ulcers. The more recent advances in wound care therapies, modalities, and evidence-based research have demonstrated that an advanced standard of care for wound healing should exist. Failure of treatment protocols, which center on a 50% area of wound reduction within 4 weeks as a response to standard conventional care, should indicate the use of adjuvant therapies. Negative pressure wound therapy (NPWT), hyperbaric oxygen therapy (HBOT), growth factors, human-derived bioengineered tissue, and extracellular matrix products are readily available. This commentary will explore a brief selection of the current wound care literature as it relates to the acceptance of a new advanced standard of care. Furthermore, the intention is to stimulate further discussion and thought on the relevance of this approach in the treatment of diabetic foot ulcers and chronic wounds and how it may correlate with the ultimate outcome of healing in general.
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Standard conventional care involves a thorough vascular, neurologic, and nutrition assessment, as well as prudent diabetes or other comorbidity control. Initially, surgical or sharp debridement, appropriate off-loading, wound bed preparation, infection control, and maintenance of a moist wound environment are paramount to success in the treatment of wounds. The advent of new research and the current body of knowledge have ensured that moist wound healing is now accepted practice.¹ Therefore, no longer is a wet-to-dry gauze dressing acceptable wound care.² Additionally, the availability of options for the treatment of

diabetic foot ulcers and chronic wounds has made major strides in the past 20 years. The introduction of new wound care products and advanced adjuvant therapies has afforded the wound specialist an even greater armamentarium to manipulate the wound bed at the cellular level and achieve active healing. In patients with chronic wounds, such as diabetic foot ulcers, the treatment decision process often must go beyond merely maintaining a moist wound environment. Chronic wounds are full of senescent fibroblasts as a result of the failure of neutrophil activation.³ The physiology of the diabetic foot wound or chronic wound is dynamic and often unpredictable. Much too often, wound clinicians are stuck month after month in stagnant, unremitting treatment strategies that are not readily justified. Treatment, therefore, should be based on the timely response of the wound to the clinician's plan of care. A deficiency of timely response to

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standard conventional care should indicate the use of adjuvant therapies. Negative pressure wound therapy (NPWT), hyperbaric oxygen therapy (HBOT), growth factors, human-derived bioengineered tissue, and extracellular matrix products are readily available. These will promote further the active stimulation and passage of the wound from a senescent state into a healing state. Thus, the clinician more readily accomplishes the desired change from the chronic to the acute phase of healing.

The task at hand for the modern wound clinician is to base care strategy decisions on evidence. The modern wound clinician, however, needs to have parameters to define a timely response to his or her treatment strategy. During the past several years, a consensus has begun to emerge regarding the time that a wound takes to show signs of healing and of its overall healing potential. In 1999 the American Diabetes Association Consensus Development Conference on Diabetic Foot Wound Care concurred that a wound remaining open and unhealed after 4 weeks is a cause for concern and is associated with worse outcomes, including amputations.⁴ Sheehan et al.⁵ assessed the ability of the 4-week healing rate to predict complete healing over a 12-week period in a large, prospective, multicenter study. Findings revealed that those patients who did not reach 50% healing, or reduction in ulcer size, by the first 4 weeks were unlikely to heal over a reasonable time. Additional findings of this study revealed that 58% of those patients who had 50% or more healing at 4 weeks had full healing by 12 weeks. Only 9% who did not reach this 50% criterion healed at 12 weeks. Those who had ulcerations that healed had a mean percentage reduction in ulcer area of 82%, which, compared with the nonhealing group's rate of 25%, shows a significant difference.

The Wound Healing Society convened in 2006 and concluded that emerging adjuvant therapies—topical, device, and/or systemic—may offer benefits and increase healing in selected patients with difficult-to-heal wounds that lack response to traditional treatment.⁶ Boulton et al.⁷ discussed tissue-engineered skin, noting consideration of this advanced therapy in those patients in whom standard good wound care does not result in reduction of wound size after 4 weeks. Furthermore, in 2007, Armstrong et al.⁸ made a strong argument that the use of active therapy such as bioengineered skin substitute to stimulate healing in nonresponding wounds after 4 weeks is optimal care. Most recently (2010), Snyder et al.⁹ found similar reproduced results in their post hoc analyses of control participant data extracted from two previous randomized controlled studies. Snyder et al.'s trials treated diabetic foot ulcers using human fibroblast-derived dermal substitutes. Outcomes again showed that greater than 50% healing at 4 weeks had a significant correlation with complete healing, defined as 100% epithelialization at 12 weeks with no evidence of drainage. The Wound Healing Society's Provisional Guidelines for Chronic Wound Care, dated June 21, 1999,¹⁰ further confirm the consideration of adjuvant therapies, specifically

HBOT, as standard of care. The Arterial Subcommittee, chaired by Harriet Hopf and Judith West, generally stated that in communities where it is accessible, HBOT should be considered standard of care for wounds that are hypoxic because of ischemia. The subcommittee further stated that tissue hypoxia is reversible by hyperbaric oxygenation. The June 2001 issue of the *British Journal of Medicine's Clinical Evidence* related that for patients with diabetic ulcers, systemic HBOT is likely to be beneficial and, when compared with routine care, reduces the risk of foot amputations in those with severely infected foot ulcers.

There are numerous published studies of NPWT, including randomized clinical trials. To date, it has been shown to result in faster wound healing than conventional methods do. A large, multicenter, randomized, intention-to-treat trial involving 162 patients investigated whether NPWT improves the proportion and rate of wound healing after partial foot amputation in patients with diabetes. NPWT was delivered through the V.A.C. Therapy system, and control patients received standard moist wound care. A greater number of patients, 56%, in the NPWT group achieved complete closure during the 16-week assessment, compared with 39% of the control group. The study also found that among patients who presented with 0% to 15% granulation at baseline, the median time to reach 76% to 100% granulation was 42 days in the NPWT group but 84 days in the control group.¹¹ Other retrospective studies have shown that early intervention with NPWT in stage III and stage IV pressure ulcers and surgical wounds demonstrated a significant reduction in length of home care services, hospitalization, and emergent care.¹²⁻¹⁴

With the introduction of regenerative medicine, bioengineered tissue derived from the extracellular matrix has shown great potential for active reconstruction of wounded tissue. The extracellular matrix products all have the common feature of not only providing structural support but also supplying growth factors and cytokines efficiently to the cell surfaces' receptors while protecting them from degradation.¹⁵ Preliminary trials have shown evidence of complete timely healing with less scarring when these therapies are used.¹⁶

Finally, a study by Armstrong et al. in 2007¹⁷ illustrates the need for an advanced standard of care in the treatment of diabetic foot ulcers and potentially other chronic wounds. This study examined the 5-year mortality rates of various disease entities. Included were neuropathic ulcers, which had a 45% mortality rate, and ischemic diabetic foot ulcers, which had a 55% mortality rate after 5 years. Moreover, investigation of diabetes-related amputations and common carcinomas revealed that almost half the patients receiving a diabetes-related amputation died within 5 years; prostate and breast cancer, however, had an 8% and 18% 5-year mortality rate, respectively. While one is examining these statistics, it is important to realize that the mortality rates for these carcinomas in the past were much higher. Treatment for these carcinomas has encompassed a standard of care with

an approach that is consistent and evidence-based, thus reducing mortality rates.

The appropriate timely response a clinician should use to judge the effectiveness of treatment is a 50% reduction in wound size within 4 weeks. The wound clinician's use of an advanced standard approach based on these parameters has adequate evidence. Correlation and use of these parameters for chronic wound states of vascular, pressure, or other non-diabetes-related wounds possibly exist as well. There is a need for further trials and studies of the adjuvant therapies that result in reproducing advantageous healing timelines. Universal concurrence on the early use of advanced therapies, as part of a new standard of care, may reduce the mortality rates for diabetic, neuropathic, ischemic, and other ulcers. Implementing these active wound healing concepts on a timely basis may also reduce not only expense but patient suffering as well.

Conclusion

The preceding discussion serves as a springboard to concepts for the modern wound clinician's decision-making process. First, a patient's healing potential must be determined. Second, the clinician must determine the time to act and implement the strategies necessary to obtain full wound healing. The wound practitioner is encouraged to recognize the prognostic value of the 50% area reduction in 4 weeks and use it as a precedent for integration of advanced therapies. Clinical judgment based on the length of treatment time and the response or lack of response by the wound will ensure that the decision to initiate advanced adjuvant therapies is supported by evidence. The adjuvant therapies, displaying more rapid healing rates despite their initial expense compared with conventional wound treatments, may actually offer an advantage in terms of less frequent dressing changes, professional intervention, and hospitalization. This advantage may also allow for faster discharge from the hospital and continued treatment at home, and thus increased mobility and improvement in quality of life for the patient. A progression toward the development of a practice that integrates more advanced standards and has healing rather than management as its priority will advance the standard of care for all wound specialists.

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