New Study Finds Diabetic Wound Patients Healed Faster When Treated with Kerecis Fish Skin

By Patrick McEneaney, DPM, CEO of Northern Illinois Foot & Ankle Specialists and Immediate Past President of Illinois Podiatric Medical Association

A prospective, randomized, controlled clinical trial found that diabetic foot ulcers (DFUs) treated with **Kerecis® Omega3 fish skin** healed at statistically significant faster rates compared to DFUs treated with Fibracol, a collagen-alginate dressing.[1]

Kerecis Omega3 fish skin has been used successfully to treat thousands of patients around the world. The superior clinical performance and economic benefits of Kerecis Omega3 fish skin have been demonstrated in numerous clinical studies and two other randomized controlled trials.[2]

The multicenter study, described in more detail below, sought to compare the fish-skin graft with the standard of care (SOC) for treatment-resistant DFUs. The researchers stated that their findings and other supporting studies indicate that the Kerecis "fish-skin graft is an attractive therapy for DFUs" and that the "findings support the use of fish-skin grafts for nonresponsive DFUs."

In this study, the primary efficacy endpoint was complete wound closure over a 12-week period. Secondary outcome measures included the time to heal (for those DFUs that healed) and the percentage reduction in wound area at 12 weeks.

The 49 patients were randomized and included in the intent-to-treat analysis. Of the DFUs treated with Kerecis Omega3 Wound, 67% healed after 12 weeks of treatment versus 32% in the control group. The p value was .0152 (significant at $P < .047$). At six weeks, the wound area reduction was 72.8% in the fish-skin group and 41.2% in the control group.

The researchers concluded that the "application of fish-skin grafts to previously nonresponsive DFUs resulted in statistically significantly more fully healed wounds at 12 weeks than SOC alone."

Results of the clinical study were published in the peer-reviewed journal *Wounds*.[1]

Properties of Fish Skin That May Affect Healing

Kerecis Omega3 is intact fish skin that, when grafted onto damaged human tissue, recruits the body's own cells and ultimately is converted into living tissue.

The graft is the intact skin of wild-caught Atlantic cod, which has been decellularized and sterilized. Because no disease-transfer risk exists between cold-water fish and humans, the Kerecis fish skin is only gently processed and retains its similarity to human tissue. The gentle processing preserves the skin's original three-dimensional structure, and maintains its natural structure and elements, such as Omega3 fatty acids.

The researchers noted that "(t)he fish skin closely resembles human skin in composition and structure. However, the fish skin graft is thicker, with a porosity and three-dimensional microstructure that provide a foundation for efficient ingrowth of dermal and epidermal cells as well as for supporting vascularization. Moreover, the unique biomechanical properties of fish skin promote cell proliferation and differentiation, which are hallmarks for tissue regeneration. While devoid of fish scales, fish skin graft retains three basic layers of skin: epidermis, dermis, and hypodermis."[2]

The superior clinical performance and economic benefits of Kerecis Omega3 fish skin have been demonstrated in numerous clinical studies.

Clinical Trial Process

The study defined DFUs as superficial ulcers that didn't involve tendons or bone. The patients were first treated for two weeks with SOC, including offloading, appropriate debridement and moist wound care. Of the 58 patients initially enrolled in the study, nine healed more than 20% during the screening period or dropped out. The remaining 49 patients were randomized to either receive SOC alone or SOC plus the fish-skin graft, applied weekly for up to 12 weeks.

Those receiving the SOC treatment only had their wounds dressed four times weekly, as per the instructions for the Fibracol Plus Collagen Wound Dressing with Alginate. Those receiving the fish-skin treatment had the Kerecis graft re-applied and the dressing changed once a week.

The researchers compared the wound area after weeks six and 12 with the measurements from the first week. The trial was single-blinded concerning wound-healing assessments. An independent wound-care adjudicator confirmed wound healing. Also, an independent panel of wound-care experts reviewed all study-related decisions and confirmed the healing status.

Complete ulcer healing was based on the site investigator's assessment, as evidenced by complete (100%) re-epithelialization without drainage and the need for a dressing. A follow-up validation visit was conducted one week after the closure was first observed to confirm durability of closure.

Drs. John C. Lantis II and Eric J. Lullove led the national trial, which was conducted at nine research centers across the United States from June 20, 2019, to November 30, 2020. The study met all the criteria for evaluation set by the 2019 AHRQ Technological Assessment of Clinical Trials for Skin

Kerecis Fish Skin *(continued)*

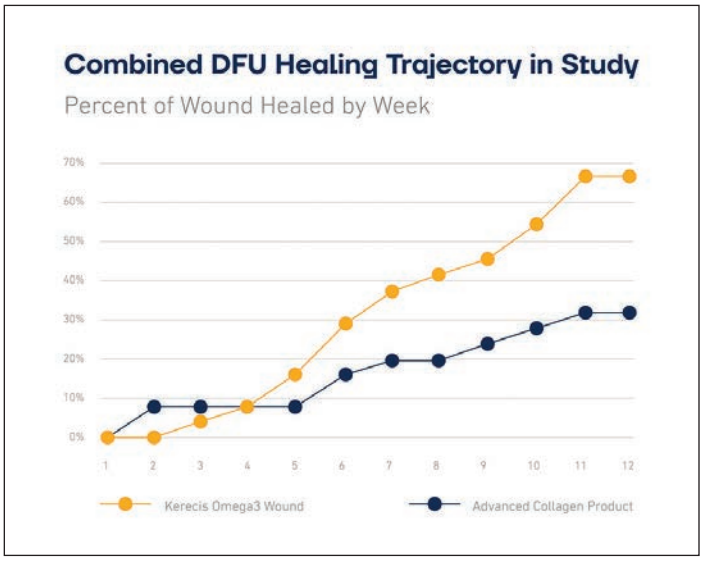
Substitutes for Treating Chronic Wounds. This study is registered with ClinicalTrials.gov (ID: NCT04133493).

The Economic Case

As part of their analysis, the researchers discussed the economic burden of diabetic foot ulcers, which are estimated to cost Medicare alone from $6 billion to $19 billion annually. Also, chronic diabetic foot wounds often lead to amputations, which affect the patient's quality of life and increase medical expenses. "Therefore, the availability of advanced therapies is crucial to improve healing rates, reduce the risk of amputation, improve patient outcomes, and decrease treatment costs," the researchers concluded.

In this study[1], "there was a significant two-fold enhancement in healing rate for DFUs compared with SOC treatment alone. The (Kerecis) xenograft is cost effective to produce and has been shown to have the potential to reduce the cost of DFU treatments compared with SOC."

The study's authors also reviewed a cost analysis by Winters et al.[3] which showed the fish-skin graft results in lower overall costs due to reduced hospitalization, fewer amputations and a lower chance of ulcer recurrence. That analysis was also published in the peer-reviewed journal *Wounds*.



In a blinded, randomized, controlled clinical trial, more previously non-responsive DFUs treated with the Kerecis fish skin grafts were healed at 12 weeks than wounds treated with SOC alone.

Other Clinical Studies

In addition to the Winters study, the researchers reviewed previous evidence[4-7] that showed that the fish skin improved healing when compared to SOC, to amnion/chorion membrane products and to mammalian-sourced extracellular matrixes (ECMs).

For example, two double-blind, prospective, randomized clinical trials found that the fish-skin graft resulted in significantly faster healing outcomes compared with the use of porcine intestinal submucosa and dehydrated chorion amniotic membrane.[4,5]

In a study by Dorweiler et al.,[6] weekly application of the fish skin graft to 25 amputated and bone-exposed wounds resulted in closure of 17 wounds (68%) between nine and 41 weeks. Participants also reduced their intake of analgesics after the fish-skin-graft treatment started.

In 2019, Michael et al.[7] published a retrospective study of 51 patients with 58 full-thickness DFUs that were treated with the fish-skin graft. The study compared the initial wound surface area at first application of fish skin with the final surface area after a 16-week treatment period. A mean reduction in surface area of 87.57% was noted, and more than 60% of the wounds (35 of 58) were fully healed.

Overall Conclusions

Eric J. Lullove, DPM; Brock Liden, DPM; Christopher Winters, DPM; Patrick McEneaney, DPM; Allen Raphael, DPM; and John C. Lantis II, MD, co-authored the paper, "A Multicenter, Blinded, Randomized Controlled Clinical Trial Evaluating the Effect of Omega-2-Rich Fish Skin in the Treatment of Chronic, Nonresponsive Diabetic Foot Ulcers," which appeared in the July 2021 issue of *Wounds*.[1]

According to these researchers, their findings and findings from studies such as these described above "indicate the fish-skin graft should be included in the list of CTPs for patients with DFUs for whom four weeks of standard off-loading has not resulted in appropriate wound area reduction."

For more information, visit kerecis.com or click here.

References

[1] Lullove EJ, et al. A Multicenter, Blinded Randomized Controlled Clinical Trial Evaluating the Effect of Omega-3-Rich Fish Skin in the Treatment of Chronic, Nonresponsive Diabetic Foot Ulcers. Wounds. 2021;33(7):169-177. doi:10.25270/wnds/2021.169177

[2] See https://kerecis.com/publications for a listing of clinical studies.

[3] Winters C, et al. Cost Effectiveness of Fish Skin Grafts Versus Standard of Care on Wound Healing of Chronic Diabetic Foot Ulcers: A Retrospective Comparative Cohort Study. Wounds. 2020;32(10):283-290.

[4] Baldursson BT, et al. Healing Rate and Autoimmune Safety of Full-Thickness Wounds Treated with Fish Skin Acellular Dermal Matrix Versus Porcine Small-Intestine Submucosa: A Non-inferiority Study. Int J Low Extrem Wounds. 2015;14(1):37-43. doi:10.1177/1534734615573661

[5] Kirsner RS, et al. Fish Skin Grafts Compared to Human Amnion/Chorion Membrane Allografts: a Double-Blind, Prospective, Randomized Clinical Trial of Acute Wound Healing. Wound Repair Regen. 2020;28(1):75-80. doi:10.1111/wrr.12761

[6] Dorweiler B, et al. The Marine Omega3 Wound Matrix for Treatment of Complicated Wounds: A Multicenter Experience Report. Gefasschirurgie. 2018;23(suppl 2):46-55. doi:10.1007/s00772-018-0428-2

[7] Michael S, et al. Acellular Fish Skin Graft Use for Diabetic Lower Extremity Wound Healing: A Retrospective Study of 58 Ulcerations and a Literature Review. Wounds. 2019;31(10):262-268.