Utilization of Rich Omega-3 Fatty Acid Fish Skin in Healing Soft Tissue Deficits in the Presence of Infection

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Statement of Purpose

Osteomyelitis, abscesses, and Charcot neuroarthropathy have the predilection to leave substantial soft tissue deficits for many patients. The diabetic population are highly predisposed to these pathologies and often undergo surgical procedures to eradicate disease and restore function. In the latter portion of staged procedures, often these patients are faced with the complicated task of achieving full wound healing. Thus, the aim of this study is to exhibit the success of rich omega-3 fatty acid fish skin xenografts in healing detrimental wounds in various compromised conditions.

Level of Study

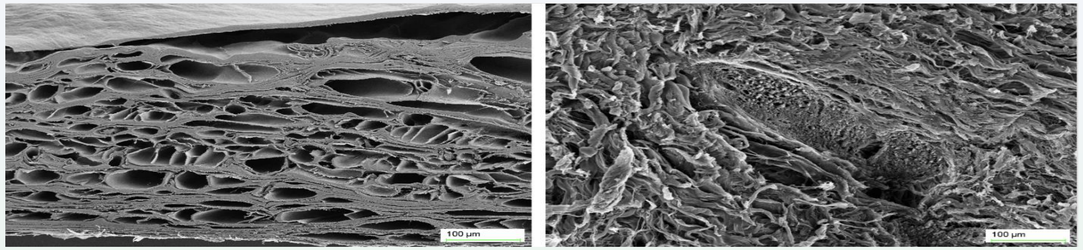
Level IV, Case Series

Introduction

Healing infected lower extremity wounds is marked by elimination of infection and by epithelialization of the wound. There are a multitude of factors that affect healing potential; metabolic, biomechanical, tissue vascularity, and infection bioburden to along with many others. When primary closure of surgical wounds is not a viable options, skin substitutes have been a reasonable modality to assist with secondary healing. There is a wide range of graft materials, with autologous skin grafts, allograft materials, and even xenografts available to the reconstructive surgeon. WIth regards to diabetic infections, biologics, negative pressure wound therapy (NPWT), and skin grafting have shown promising outcomes where amputation used to be the standard of care.[1, 2, 3]

Comparative studies have demonstrated that split thickness skin grafts applied to wounds on individuals with diabetes and ESRD, have equivocal healing potential to wounds in those without systemic illness.[4] Wound healing in diabetics and renal patients are a challenge that foot and ankle surgeons manage on a frequent basis. The longer these wounds stay open and in a chronic inflammatory state, the more prone they are to infection. A recent meta-analysis have connected skin graft applications with faster healing, and in certain populations, grafted wounds are 1.67 times more likely to heal after 3 months versus wounds with conventional dressings.[5] In the past two decades, acellular dermal matrices (ADMs) have made their mark on the wound healing arena. Specifically, Omega-3 fatty acid ADM has shown promising applications in wound care. The porous lattice demonstrated on a microscopic level, which is similar to the structure in native skin, is hypothesized to set it apart from other, thicker, detergent treated wound grafts, yielding better integration and stimulation of healing factors.

In cases of burn trauma, prospective studies of burn wounds treated with ADMs with Omega-3 have a significant difference in healing rate versus conventional dressings, with virtually no complications.[6] Faster healing of wounds with Omega-3 ADMs extend to the diabetic and compromised communities, with recent findings connecting them with less analgesic use.[7] The utilization of Omega-3 fatty acid ADMs in lower extremity soft tissue infections has not until recently been investigated, but there have been promising early clinical outcomes. With the only treatment to address certain lower extremity infections being an amputation, ADMs with Omega-3 fatty acid have the potential to be a viable treatment adjunct to stave off limb loss.



Electron microscopic images of graft processed fish skin (left) and human skin (right) showing structurally similar properties.

Methods

Twenty-two subjects all with either type I or type II diabetes mellitus undergoing surgical eradication of infection by means of amputation, incision and drainage, and/or ostectomy/resection were included in the study. Demographics consisted of females a males, with an average age of 52.7 years (range 29-74). Multiple patients suffered from additional comorbidities including but not limited to organ transplantation on chronic immunosuppression, congestive heart failure, hypertension, obesity, chronic tobacco abuser, and charcot neuroarthropathy. All patients possessed concern for remnant infection and large soft tissue deficits, thus primary closure was unable to be completed. Serial debridements, resections, and washouts were performed when necessary in addition to negative pressure assisted therapy via wound vacuums in 46% of the subjects. Of note, all 22 subjects sustained bone exposure of wounds, and grafts were applied once an adequate wound bed was encountered. In some of the cases where an adequate wound bed was unable to be obtained, the graft was applied directly over bone. All wound beds were prepared for graft application via debridement in the intra-operative setting or in the outpatient clinic. Serial graft applications were performed for large and/or complex wounds with full healing being deemed complete once full epithelialization of all deep, exposed soft tissue took place. Repeat applications took place every 3 weeks for all patients but one which was every four weeks due to missed appointments. When necessary, infectious disease consultations were placed for multi-drug resistant infections as well as for positive proximal margins for a microbiology and pathology standpoint. Three of the ten cases did not obtain a clean proximal margin, however patients wanted to pursue limb salvage. Patients remained non-weight bearing to the affected limb in a post-op shoe or CAM boot for the duration of graft applications to prevent failure of graft uptake.

Results

All twenty-two patients progressed to full healing of their respective wounds with fish skin grafts being used as the only skin substitute to facilitate tissue coverage. Twelve patients underwent operations due to abscesses including one patient with a confirmed septic fifth metatarsophalangeal joint as well as an additional patient with Charcot Neuroarthropathy. Ten of the Twelve patients also had confirmed osteomyelitis via pathology specimens treated with long-term antibiotics. The other two subjects suffered from gas gangrene infections (figures above) necessitating serial debridements and long term antibiotics as well. The average wound size was measured at 10.26 cm^2 (range 1.6 cm^2 - 26.3cm^2) with the average hemoglobin A1c % recorded at 9.2% (range 7.0% - 16.2%) which was taken place no further than 3 months prior to the first graft application. Zero of the ten patients developed wound recurrence once full epithelization was obtained. An average of 2.0 graft applications (range 1.0 - 4.0) were applied per patient with a direct correlation being observed with increase applications to larger wound measurements. Average time to complete healing was measured at 15.3 weeks (range 9 weeks - 19 weeks) and this incorporated the duration of time of presentation to time of healing.

Discussion

This case series clearly demonstrates the remarkable success of fish skin xenografts in facilitating wound healing in overtly compromised conditions. Previous studies with similar patient comorbidities and surgical procedures have graft uptake leading to healing recorded as low as 65%.[8] Although possessing a relatively small sample size, the alarming 100% success rate exhibits promise for advanced limb salvage in cases of proliferative infection causing exuberant soft tissue deficits. This study incorporated “healing time” to begin at the time of initial presentation due to many of the subjects undergoing multiple surgical procedures due to the extent of infection as well as having to undergo NPAT. This attribute can explain why other similar studies with split-thickness skin grafts exhibit healing times closer to 4-7 weeks on average due to the duration of healing beginning directly after the graft is first applied.[9,10]

The ability to heal such detrimental soft tissue deficits in the presence of infection in immunocompromised individuals is an obstacle that plagues many physicians daily. The staggering 9.2% average of hemoglobin A1c’s encountered in this study further illustrates the potential of fish skin xenografts in healing wounds in the diabetic cohort. A retrospective study deemed concluded each 1.0% point increase in HbA1c, decreased by 0.028 cm^2 /day with statistical significance.[11] Promising data illuminating the homeostatic, antimicrobial, and biologically similar properties of fish skin xenografts presents optimal healing potential similar to that of human skin.[12] In many cases with patients with advanced comorbidities and extensive wounds, STSG are avoided due to the principle of not wanting to obtain already “non-optimal” tissue and advancing it elsewhere. Thus, finding a comparable product that possesses those previously mentioned critical factors in the state of non-optimal native skin is of the utmost importance in healing wounds.

Further research is absolutely essential via randomized control trials and/or cohort studies to evaluate the efficacy of fish skin xenografts with obtainable statistical significance. This case series lays the foundation for such further studies to take place and provides aspirations for those suffering extensive tissue loss that limb salvage is possible despite non-optimal and complicated healing conditions.

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