Acellular Fish Skin Graft Use in Open Abdomen Management

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ABSTRACT

Introduction: Open abdomen (OA) management post damage control laparotomy (DCL) is common in complex abdominal trauma and intra-abdominal catastrophe (IAC). Use of polyglactin 910 mesh (VICRYL™, Johnson & Johnson, New Brunswick, New Jersey) to cover the intra-abdominal contents and wound vacuum-assisted closure (VAC) is current practice in the management of temporary abdominal closure (TAC). This may have complications and requires two to three weeks for granulations to be ready for skin grafting. Acellular fish skin graft (AFSG; Kerecis™, Reykjavik, Iceland), use in wound care management has proven beneficial in the management of both chronic and acute wounds, such as burns, by increasing wound granulation. However, to our knowledge, its utility in OA management has not been reported.

Objective: The objective of this report is to introduce a novel use of AFSG (Kerecis™) in open abdomen to decrease the time of TACs by accelerating formation of granulation tissue and placement of skin grafts in patients with post damage control laparotomy (DCL) for trauma and IAC when committed to open abdomen management is presented.

Materials and Methods: Illustration of application of AFSG (Kerecis™) in two patients who underwent DCL for IAC and OA management is presented.

Results: Two patients with intra-abdominal catastrophe post-DCL and fistulae were enrolled; one with postoperative enteric fistula and the other with post-anastomotic ileo-colonic fistula breakdown and major intra-abdominal sepsis resulting in multiple organ system failure (MOSF). In both cases, a hostile abdomen was present. The application of AFSG accelerated the placement of skin grafts in both patients and decreased the use of wound VAC and hospital length of stay.

Conclusion: This report illustrates the use of AFSG (Kerecis™) to accelerate placement of skin grafts in patients post-DCL and OA management. AFSG (Kerecis™) could be considered as part of the OA management strategy.

INTRODUCTION

Damage control surgery (DCS) or damage control laparotomy (DCL) and open abdomen (OA) management post major abdominal trauma was popularized by Rotondo et al.[1] Subsequently, this technique has been adopted for intra-abdominal catastrophe (IAC) and emergency general surgery. While it is a life-saving technique in appropriate cases, it may be associated with significant complications,[2] and it has been overused.[3] Although DCL is practiced less often in recent years, when applied, there is a need for temporary abdominal closure (TAC) and wound vacuum-assisted closure (VAC). TAC also has complications,[4] but it depends on the length of its use, technical factors, and the patient's conditions and characteristics. While several techniques have been invented and applied to reduce the period of use of TAC,[5-7] none have become a standard technique due to the associated complications. Irrespective of length of time of TAC, application of wound VAC is mandatory. While wound VAC has revolutionized wound care management overall, including that of the OA, it has its own complications as well.[8]

Temporary abdominal closure (TAC) length of use is dependent on the patients' factors (intra-abdominal pathology), hospital resources, and the experience of the surgical team. Irrespective of those, TAC requires a wound VAC to cover the abdominal contents (poor man's wound VAC, or any other VAC, such as AbThera Advance™, 3M, Saint Paul, Minnesota). Once the infection is controlled, the abdominal contents are covered with polygalactil 910 mesh (VICRYL™, Johnson & Johnson, New Brunswick, New Jersey), followed by the placement of wound VAC with white and black foam sponges, which needs to be changed every two to three days, while waiting for granulations tissue to be created over the polygalactil 910 mesh (VICRYL™), which may take two to three weeks. Other challenges of wound VAC management for OA are the associated pain during the applications, cost of the material used, and time that it takes for granulation tissue to mature.

We always place double layers of mesh over the omentum (if there is an omentum left), to reduce the chances of fistula, which adds more delays to complete degradation of polygalactil 910 mesh (VICRYL™) and provides longer times to granulations that will accept skin graft. The longer the time of TAC, the higher the chances for creation of entero-atmospheric fistulae (EAF), bleeding from the raw sites of the wound edges, skin excoriations, and malfunctions of wound VAC, requiring changes of the entire set up, in addition to other problems such as intestinal evisceration, particularly in intubated and those with tracheostomies patients. With or without EAF, almost always there is loss of abdominal domain with retraction of abdominal muscles laterally and major abdominal defects. When to apply skin grafts is a clinical decision based on how granulation tissue looks.

Recently[9] it was reported that for optimal results, split-thickness skin grafts should be delayed at least 14 days after polyglactin 910 mesh (VICRYL™) placement. These authors concluded that attempts to place a skin graft after the first two weeks following polyglactin 910 mesh (VICRYL™) placement was the only modifiable risk factor associated with the graft failure. Decision to place a skin graft, however, commits the patient to a two-staged abdominal wall reconstruction which has been a standard of care for years,[10,11] with definitive closure of the abdomen six to 12 months later through complex abdominal wall reconstruction (CAWR) with some kinds of mesh prosthesis.[12-14] In the last decade, in patients with WHG grade 3 and 4,[15] or in those with a history of intra-abdominal infections[16] requiring CAWR, we have been using biologic mesh, placed in a sublay position. Others have used synthetic or biosynthetic mesh.[17,18] If a skin graft is placed too early, there are higher chances of graft failure,[9] and if placed too late, there is an increased risk for EAF. To reduce the TAC period, there is a need for either early abdominal closure while avoiding the two-stage abdominal closure altogether or accelerating the granulation tissue formation and placement of skin grafts. Early abdominal reconstruction has been demonstrated safe and possible, and it should occur at the same hospitalization for the majority of patients post-DCL and OA[12-16] for trauma and intra-abdominal catastrophe. Despite this, many clinicians continue to use a two-stage closure. Acellular fish skin graft (AFSG; Kerecis™, Reykjavik, Iceland) used in the management of complex burn and other wounds has proven to accelerate wound healing. Current indications for AFSG (Kerecis™) are partial and full-thickness wounds, soft tissue reinforcement, trauma wounds, burns (e.g., abrasions, lacerations, second-degree burns, and skin tears), other surgical wounds (e.g., donor sites/grafts, post-Mohs surgery, post laser surgery, podiatric, and wound dehiscence), pressure ulcers, venous ulcers, chronic vascular ulcers, diabetic ulcers, and draining wounds.[19] The objective of this paper is to illustrate a novel use of AFSG (Kerecis™), in patients undergoing DCS for abdominal catastrophe and OA management and propose its use as a novel application in cases when the patient was committed to long-term OA and skin grafting, before definitive closure.

MATERIALS AND METHODS

Patient #1

A 62-year-old morbidly obese male with complete mechanical small bowel obstruction and recurrent giant ventral hernia presented to an outside community hospital. He previously had several operations, including gastric bypass for obesity complicated by sepsis, OA management, and more than two months in the ICU. Subsequently, he developed a hernia that was repaired with synthetic mesh, which was infected and managed with long-term antibiotics. The small bowel obstruction was secondary to adhesive disease synthetic mesh and granulation tissue of large chronic wounds (30 x 25cm), recurrent hernia, and hostile abdomen.[20] He was taken to the operating room where excision of chronic wounds and granulations tissue, extensive lysis of adhesions, explantation of large synthetic mesh, and about 30cm segmental small bowel resection with side-to-side anastomosis were performed. He had a large abdominal defect of 800cm^2 . Complex abdominal wall reconstruction (CAWR) using the standard technique with posterior component release and sublay (retrorectus) placement of biologic mesh (STRATTICE™, Allergan Aesthetics, Chicago, Illinois) technique was performed.[15] Due to the loss of the abdominal wall, including the posterior rectus sheet, a portion of the posterior rectus sheet was unable to be approximated. This gap was bridged with a polyglactin 910 mesh (VICRYL™). The recti muscles

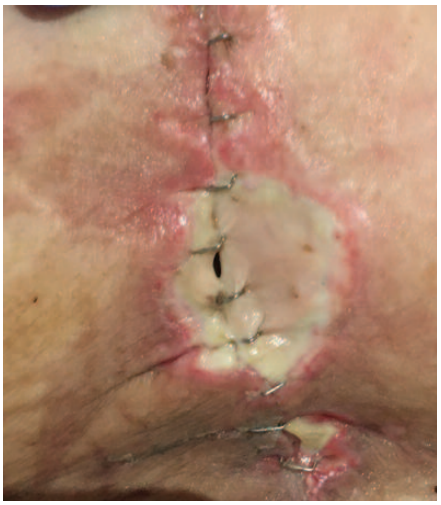

Figure 1. Infected wound that was found to be a result of enteric fistula.

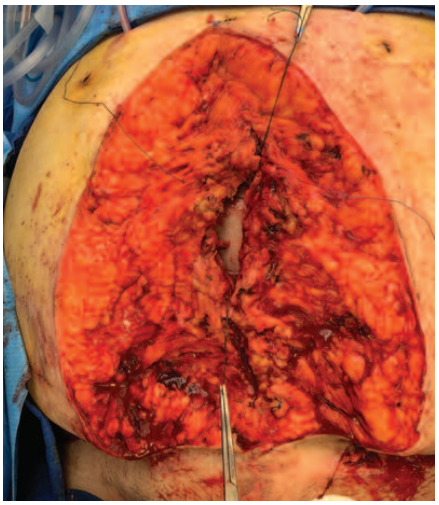

Figure 2. Debrided bed of the wound with opening of the fascia (visible is the biologic mesh).

were approximated with continuous polydioxanone (PDS) suture. Due to repeated and long-term abdominal sepsis, he developed large ossifications of the wound on each side of the midline,[21] which were resected too. In addition, partial xyphoidectomy was performed to facilitate closure of the upper portion of the wound. Three large drains (19 Fr) were placed, and the skin wound VAC was applied.

There was no intraoperative complication. Postoperatively, he did very well and was discharged from the hospital on postoperative day 10. However, he was seen in the follow-up visit a week later with a midline wound as illustrated in Figure 1, having mild fever and not feeling well. He was taken to the operating room for abdominal wall exploration and was found to have a large amount of foul-smelling fluid collection and fat necrosis of a large portion of the abdominal wall pannus (Fig. 2). He had developed a small bowel fistula approximately 30cm distal to the side-to-side anastomosis. Following major debridement of the abdominal wall pannus with skin and cutaneous tissue, massive irrigation was performed, open abdomen management was initiated, and wound VAC was placed. On postoperative day 5, he was taken back to the operating room. The preoperative plan was to create a floating stoma. However, upon exploration, we were able to release approximately 15cm of intestines from the mouth of the fistula distally and proximally and performed a primary handsewn single-layer closure of fistula mouth with 2.0 silk interrupted sutures and pushed back (dunk in) the intestines in the abdomen (Fig. 3). At this stage, we decided to cover the entire open abdomen operative field with AFSG (Kerecis™) (Fig. 4), including the operative site where we dunked the intestinal anastomosis, followed by covering it with petroleum jelly gauze (Fig. 5) and wound VAC. He did very well postoperatively, and five days later, the wound VAC was changed in the OR. There were no signs of fistula leak or sepsis. Although the wound bed was ready for skin graft on postoperative day 5 (Fig. 6), due to concerns that fistula may reoccur later, we reapplied AFSG for another four days before we placed a skin graft. He was discharged home without any complication, was able to eat, and regained his GI tract function.

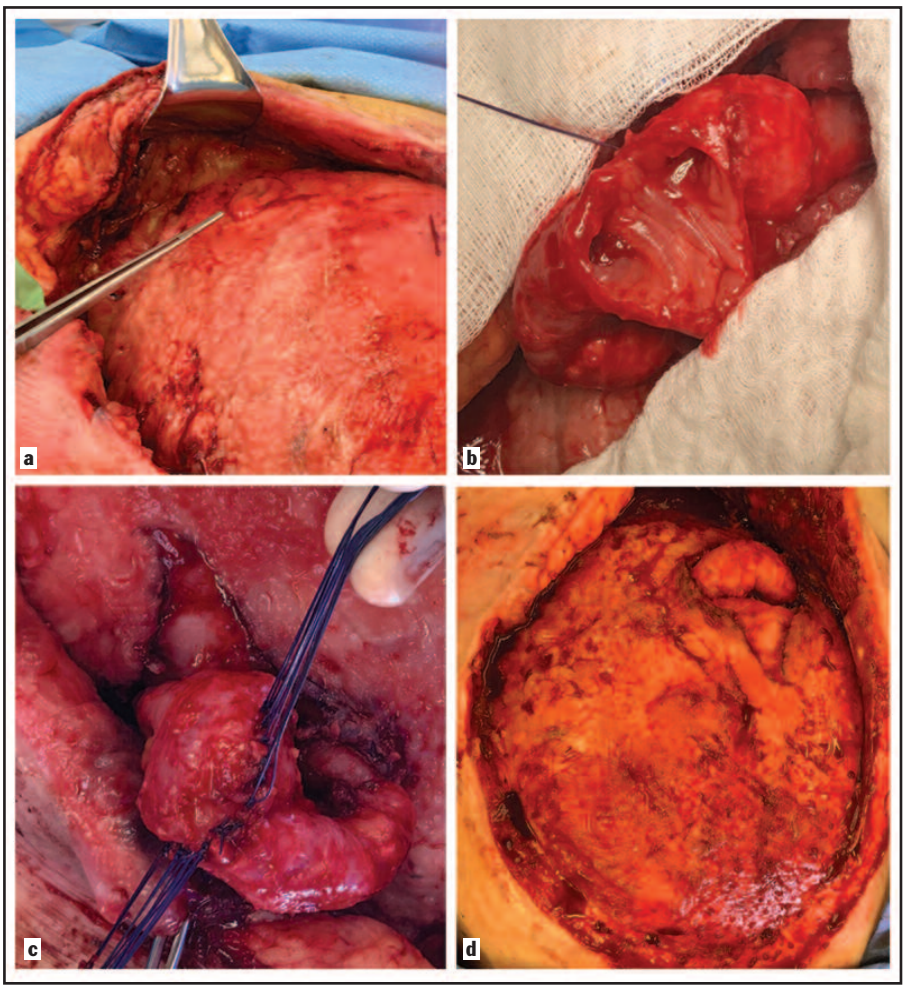

Figure 3a. Visible fistula in the right lower quadrant. b) Released small bowel with distal and proximal bowel visible and ready to be anastomosed. c) After reconstruction of the GI tract with single-layer suture. d) Anastomosis dunked into the peritoneum.

Patient #2

Previously, we published a case of a 42-year-old male but in the context of the use of the direct peritoneal resuscitation (DPR) technique[22] for intra-abdominal catastrophe. He had a past medical history of Crohn's disease and underwent an exploratory laparotomy for small bowel resection and ileocecal mass resection, DCL, and TAC at a

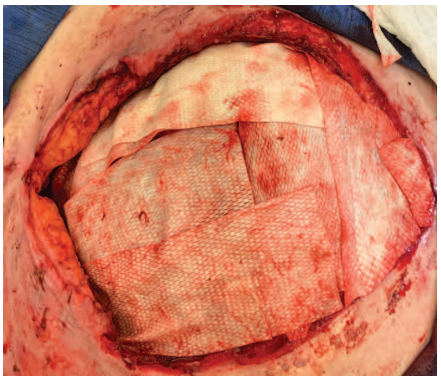

Figure 4. Wound covered with AFSG (Kerecis™).

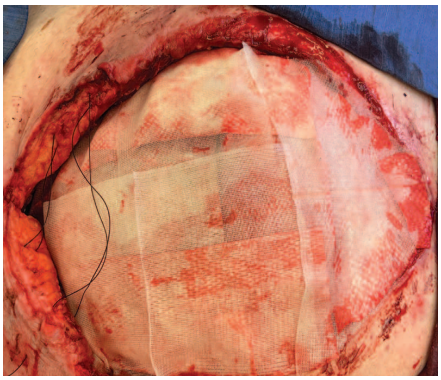

Figure 5. Wound covered with petroleum jelly gauze over the FSG.

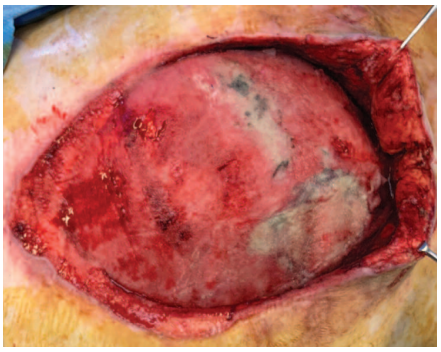

Figure 6. Excellent granulation post AFSG placement ready for skin grafting.

community hospital. On postoperative day 3, he was taken back to the OR for ileocecal anastomosis. He continued to be managed with an open abdomen, with few more returns to OR for an abdominal washout. Eventually he was diagnosed with complete disruption of the anastomosis. He developed a hostile abdomen, and an attempt to create a diverting ostomy was not successful. The anastomotic site was drained with a Malecot, and Jackson-Pratt (JP) drains, and the patient was transferred to our institution, intubated, on major vasopressors, and multiple organ system failures. While being resuscitated, a non-intravenous contrast CT of his abdomen was performed (Fig. 7a). Subsequently, the patient was taken to the operating room for an abdominal exploration. He was found to have a frozen and hostile abdomen with the bowels severely inflamed, dilated, and adhered together (Fig. 7b). We initiated a DPR wound VAC to reduce inflammatory process and assist with eventual closure.[23] Three days later, he underwent an exploration with the abdomen significantly less swollen and a floating loop ileostomy in the right lower portion of open abdomen was created. He continued on DPR for another four days, and reexamination of the bowel (Fig. 8) revealed almost complete resolution of bowel edema (Fig. 9). At this stage, a Kerecis™ omega-3 wound graft was placed and covered the entire open abdomen to aid with the formation of granulation tissue (Fig. 10). The wound VAC was placed as well. He went back to the operating room five days later for one more placement of the Kerecis™ omega-3 wound graft and a subsequent skin graft. Clearly, the use of AFSG (Kerecis™) accelerated the granulation tissue of the open abdomen and allowed for the rapid formation of granulation tissue to enable placement of a skin graft to close the abdomen. He was discharged to a rehab unit and eventually to home. Approximately eight months later, he was brought back to the hospital and underwent excision of the skin graft, a taken down loop ileostomy, with resection of distal (5cm) ileum and cecum, and an ileo-transverse colonic anastomosis using a combined stapler and handsewn method. Finally, a CAWR,[15] using posterior approach with a sublay placement of STRATTICE™ mesh, was completed without any difficulties. The patient recovered very nicely and was discharged to home.

RESULTS

Two patients with intra-abdominal catastrophe post-DCL and fistulae were enrolled; one with postoperative enteric fistula and the other with post-anastomotic ileo-colonic fistula breakdown and major intra-abdominal sepsis resulting in MOSF. In both cases, a hostile abdomen was present. The application of AFSG accelerated the placement of the skin graft in both patients, decreased the use of wound VAC, and subsequently the hospital length of stay. To our knowledge, this has not been reported before. A detailed postoperative course of each patient is imbedded into the materials and methods.

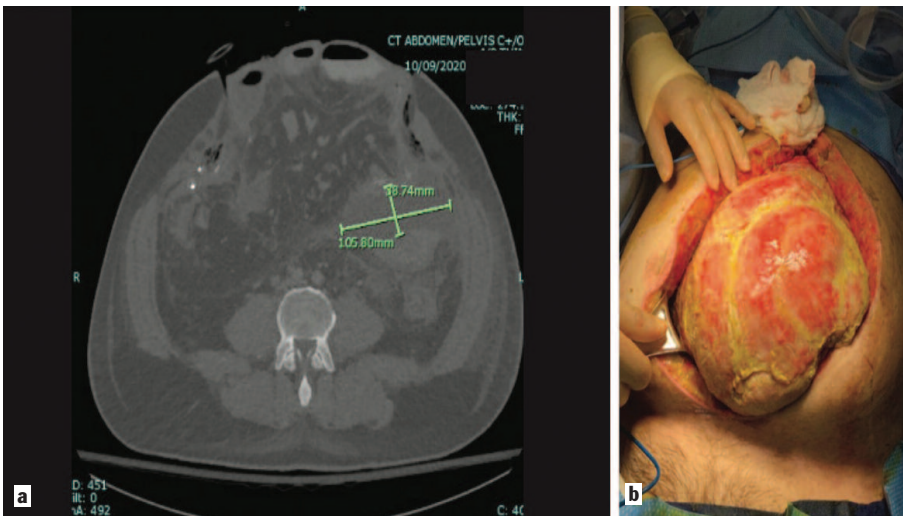

Figure 7a. CT scan of a patient with intra-abdominal catastrophe. b) Entire abdomen as one large inflammatory mass.

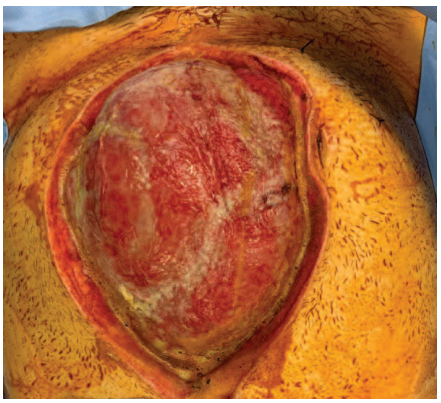

Figure 8. Same abdomen as in Figure 7b but with significant improvement.

DISCUSSION

Open abdomen management after damage control laparotomy is common in complex abdominal trauma and intra-abdominal catastrophe. Although DCL is practiced less commonly in recent years, when performed, there is a need for TAC until the definitive abdominal closure can be achieved or the patient is committed to OA management. While OA has proven to be very beneficial, at the same time, it has its own complications, such as intestinal fistula. A considerable amount of time is required for granulation tissue to be created. Surgeons have always been in search of ways to accelerate granulation tissue and skin grafting of OA when committing a patient to a long-term open abdomen.

In this paper, we illustrated a novel use of the AFSG (Kerecis™) application in two patients who underwent damage control surgery and open abdomen management due to intra-abdominal catastrophe. We propose that AFSG (Kerecis™) become part of the armamentarium of TAC, when patients are submitted to long-term open abdomen management, and eventually skin grafting as it greatly accelerates the formation of granulation tissue.

Tissue engineering processes and decellularization methods have tremendously advanced the technology of wound care in the last decade,[24] but there is still no defined, or widely accepted, standard of care to skin substitutes.[25]

Several mechanisms of improved wound healing of AFSG (Kerecis™) have been identified including cell ingrowth/healing and bacterial barrier which has been demonstrated by S. Magnusson et al.[26] and Stone et al.[27] The benefits of AFSG (Kerecis™) have been attributed to immune properties of omega-3 fatty acids.[28-30] Wound healing has been clearly illustrated by many authors, including Esmaeili et al.[31] (Fig. 11), and it is considered as a constant natural process).

The AFSG (Kerecis™) supports all these processes of wound healing. In our hands, the Kerecis™ has hemostatic properties suggesting a platelet mediated response. Further, the homogeneous architecture, including 3-dimensionality and porosity, polyunsaturated fatty acids, proteins, and mechanical properties augment the phases of wound healing.[26,29,32] In a study by Magnusson et al.,[26] fish skin grafts showed superior ability to support 3-dimensional ingrowth of cells compared to dehydrated human amnion/chorion membrane. Furthermore, fish skin acted as a bacterial barrier for 24 to 48 hours. Another proposed mechanism is the rapid cellular ingrowth. Fish skin recruits and supports migration and proliferation of fibroblasts, keratinocytes, and endothelial cells compared to bovine collagen.[32] Evidence suggests that scaffolds with homogeneous biochemical and biophysical properties facilitate angiogenesis.[32]

Although the use of AFSG (Kerecis™) has not been reported on the open abdomen, the process of acceleration to healing and granulation has been demonstrated in many clinical conditions, particularly in burns.[33] In this systematic review, the authors present the evidence on the use of acellular fish skin which indicates an acceleration of wound healing, reduction in pain, and necessary dressing changes as well as the treatment-related costs compared to conventional treatment options. Other authors in their systematic review of 10 studies concluded that AFSG showed superior healing in comparison to collagen alginate dressings, silver sulfadiazine cream 1%, and allografts.[34]

In a preclinical trial study by Stone et al., mentioned above,[27] using an animal model, two cellular and tissue-based products (CTPs) were evaluated on deep partial thickness (DPT) burn wounds in anesthetized Yorkshire pigs. Wounds were excised one day post-burn and the bleeding wound beds were subsequently treated with

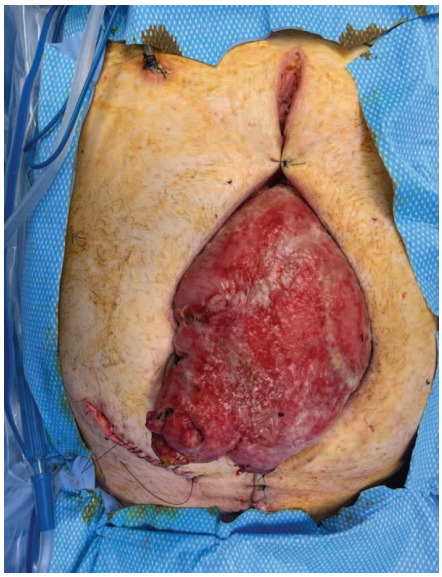

Figure 9. Still some swelling, but improved.

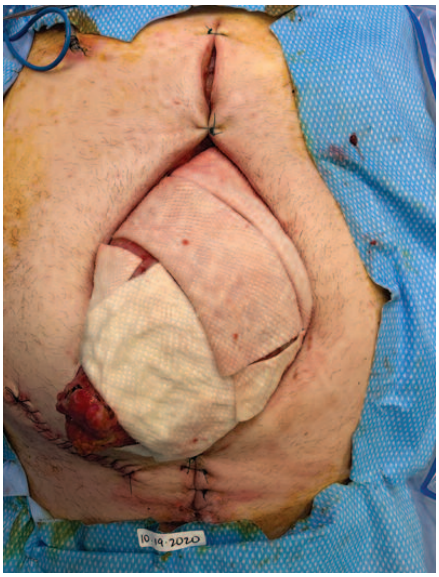

Figure 10. Wound covered with AFSG.

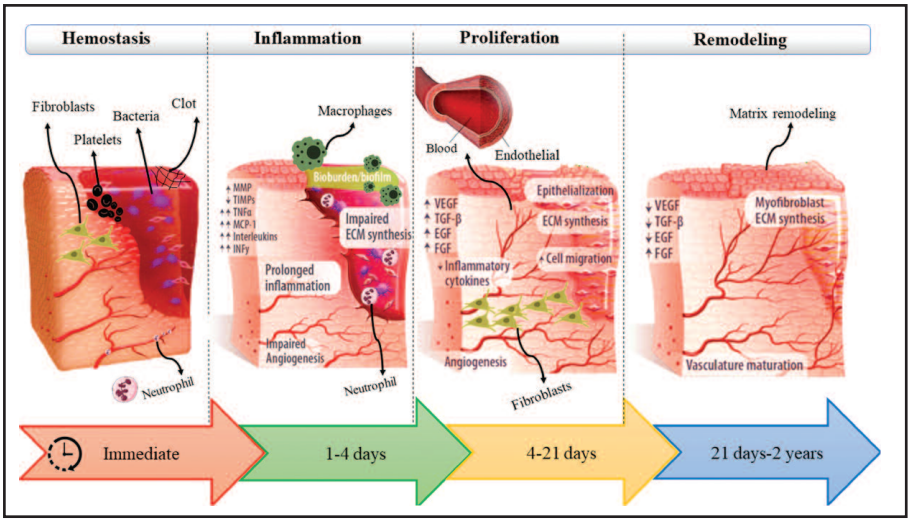

Figure 11. The phases and timeline of wound healing (reproduced from Esmaeili et al., with permission).[31]

omega-3 rich acellular fish skin graft (FSG) or fetal bovine dermis (FBD). FSG was reapplied after seven days and wounds healed via secondary intentions. The researchers used digital images, non-invasive measurements, and punch biopsies during rechecks performed on days 7, 14, 21, 28, 45, and 60. In addition, they used multiple qualitative measurements, including re-epithelialization, contraction rates, hydration, laser speckle, and trans-epidermal water loss (TEWL). They demonstrated superior wound healing properties of AFSG (Kerecis™) over FBD and demonstrated that the use of FSG enhanced wound closure as evidenced by quicker integration and reepithelization without increased contraction.

The use of AFSG (Kerecis™) in a few clinical settings has been demonstrated and the biology of the AFSG (Kerecis™), in advancing the healing process, has been discussed. Its clinical impact in lower extremity chronic wounds,[35] complex diabetic foot wounds,[36-40] second-degree burns, excised full-thickness burns[27,32,33,41-43], or in donor sites[44] have been demonstrated. Other beneficial properties of AFSG (Kerecis™), including reduced pain and less need to change the wound VAC, make AFSG (Kerecis™) very appealing for the management of large abdominal wounds, particularly in OA patients post-DCS and OA management. The current practice of changing the wound VAC in the open abdomen, often in the operation room, is every two to three days. Using AFSG (Kerecis™) extends the frequency of wound VAC changes to every five days. This cuts down significantly on both expenses and pain as well as other resources.

CONCLUSION

Based on the biology of fish skin grafts, and a milder form of decellularization and presence of current data, it appears that AFSG (Kerecis™) can be considered as a great alternative to its use in open abdomens in patients who have undergone DCL for major trauma or intra-abdominal catastrophe. However, while there are some evidences including RTC of its utility in difficult diabetic foot ulcers, burns, venous ulcers, and difficult wounds, decreased pain and the cost-effectiveness in these clinical conditions, further studies are warranted to delineate exactly the amount of time shortened by using AFSG (Kerecis™), the frequency of wound VAC changes, and the cost effectiveness associated with the fish skin. Other elements that need to be studied are postoperative complications and the number of applications of AFSG (Kerecis™). Ideally, multi-center international RCTs could address all these questions. **STI**

AUTHORS' DISCLOSURES

Dr. Latifi serves on the speaker's bureau for Kerecis, the producer of the fish skin graft. Dr. Smiley has no conflicts of interest to disclose.

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