

Background: The newly-approved Kerecis is a piscine acellular dermal xenograft. This piscine acellular dermal matrix (ADM) has specific bioactive lipid mediators, omega-3 polyunsaturated fatty acids, and has a positive effect on the process of wound healing. This study aimed to explore the utility of this novel material by comparing healing rates, and suggest the proper timing for applying Kerecis.

Methods: Patients who visited the hospital with acute or chronic deep dermal wounds from June 2019 to May 2020 were enrolled in the study. A total of 48 patients were assessed. All wounds in the experimental group (n=16) were treated only once with Kerecis and a non-adherent absorptive foam material (Therasorb) to cover the ADM. In the control group, daily conventional dressings were provided. All wounds sizes were measured with mass-market computer software in a method suggested by the authors for the first time.

Results: The mean healing rate proved to be faster in the Kerecis group ($P<0.05$) versus the control group, and no complications were observed. It was statistically proved that treating burn wounds with the ADM showed better healing rates than the conventional method ($P<0.05$).

Conclusion: This study establishes that managing wounds with the ADM is likely to heal wounds faster than traditional dressings. In addition, for burn wounds, a prolonged application (10 days vs. 5 days after the onset) showed a better wound healing rate ($98.8\% \pm 2.5\%$ vs. $67.0\% \pm 14.3\%$, respectively, $P=0.029$).

In general, wounds are classified into two types depending on the progress of healing: acute and chronic. Improper wound management causes delayed wound healing, which leads to chronicity. A wound is for the most part considered chronic if it has not healed in 4 weeks. Delayed wound healing is also often associated with complications such as infections, scar formation, and incomplete wound healing. Whether the wound is caused by direct trauma or a burn, proper wound management is one of the essential concerns for early wound healing. In general, wound management contributes to the healing process by protecting the wound fluids, preventing infection, controlling mechanical influences, and influencing the collagen maturation course. Physiologically, growth factors, chemokines, cytokines, and their receptors are critical in normal wound healing.

Many therapies promoting early wound healing by accentuating spontaneous healing at molecular levels have been recently introduced. Acellular dermal matrix (ADM) is one of such treatments, and it has shown potential for accelerating wound healing. ADM helps wound healing by stimulating angiogenesis, and providing a scaffold for granulation tissue formation. Many kinds of ADM products have been reported to promote tissue regeneration and wound healing, and are in wide clinical use, such as AlloDerm from human skin (LifeCell Corp.), Integra from bovine tendon type I collagen (Integra Lifesciences) and EZ Derm from porcine aldehyde cross-linked dermal collagen (Molnlycke HealthCare).

A total of 48 patients with acute and chronic deep dermal-layered wounds were enrolled. Of the 16 patients in the ADM group, 10 were women and six were men with ages ranging from 0 to 89 years (mean, 43.3 ± 25.2 years). There were eight acute burns, and five wounds in the acute stage created by direct trauma such as knife, machine, and glass. Of the other three chronic wounds, one patient had a diabetic foot ulcer on his right fifth toe, one had developed a wound on his right great toe due to venous insufficiency, and one had a pressure sore on her left heel. The average treatment duration in the ADM group was 10.1 ± 5.5 days. The ADM was applied 2 to 3 days (average, 2.40 ± 0.55 days) after the onset of the injury in traumatic acute wounds. For burn wounds, the application was later, from 5 to 12 days (average, 8.00 ± 3.02 days) after the onset.

The Kerecis was not fully absorbed until an average of 5.56 ± 1.60 days after its application. The average healing rate was $77.7\% \pm 18.2\%$, which was measured on when Kerecis was fully absorbed, which was 2 weeks after starting treatment. The mean healing rate for the traumatic acute wound was $71.4\% \pm 18.4\%$ when Kerecis was fully absorbed after its application, and $52.7\% \pm 24.1\%$ in the control, which represented no statistical difference ($P=0.310$). For the burn wounds, the mean healing rate was $86.5\% \pm 15.2\%$ in the ADM group and $61.1\% \pm 20.7\%$ in the control group ($P=0.021$). The average healing rate of all wounds with the ADM application in this study was $77.7\% \pm 18.2\%$ and $53.3\% \pm 22.0\%$ for the control group, demonstrating statistical significance with a P-value of <0.05 .

Meanwhile, for the burn wounds, the mean healing rate for the wounds on which Kerecis was applied over 10 days ($n=4$) after the onset of injury was $98.8\% \pm 1.0\%$, which is much faster compared to the burn wounds (average, $74.2\% \pm 11.7\%$; $n=4$) treated with the ADM 5 days after the onset ($P<0.05$).

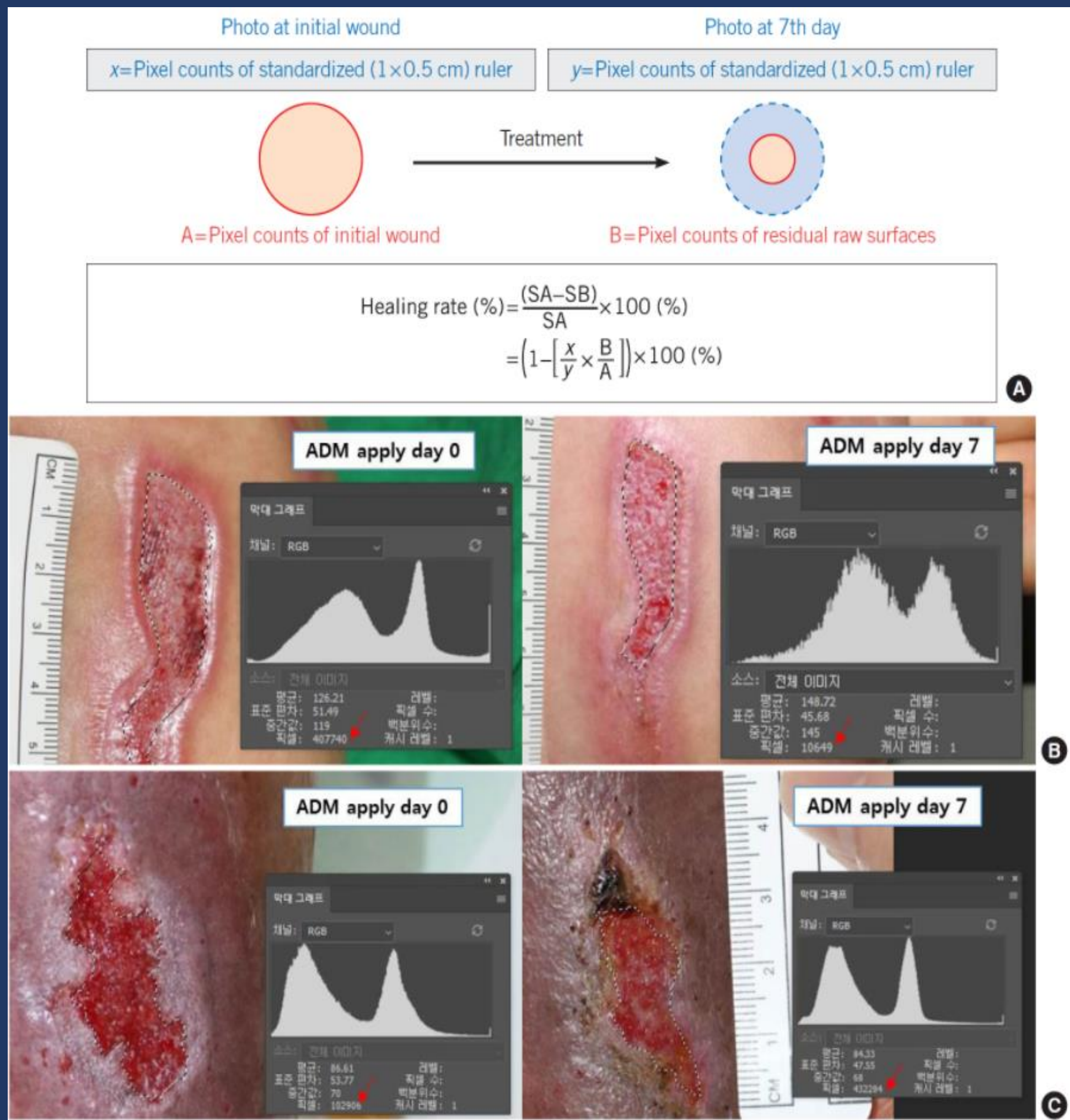
ADM is widely used in managing wounds. Its use accelerates wound healing and helps diminish wound complications. A novel acellular fish-skin graft product, Kerecis Omega3, is commercially available. Our study found that managing wounds with the piscine ADM is more effective than with conventional dressings. In addition, we suggest that application of the ADM in managing burn wounds should be delayed until discharges are sufficiently reduced. A 10-day postburn delayed application showed a better wound healing rate than applying the ADM 5 days after the onset.

Wound dressing using Kerecis

First, we removed most of the necrotic tissue, measured the size of fresh tissue surface, and cut the material 1 mm to 2 mm larger than the wound to cover the wound margin. The cut material was then bathed in saline solution for 60 seconds at room temperature. The Kerecis sheet was then directly applied on the wound, its rough side face down. Lastly, a non-adherent absorptive foam material (Therasorb 5 mm) was used to cover the ADM. Wounds were treated only once with Kerecis; those that were managed with other dermal substitutes were excluded. Foam change was performed daily after the ADM was used. In the control group, the wound was covered with the same foam material after applying antibiotic ointment once a day.

Clinical outcomes

Digital images, including a ruler (cm scale) within the frame of each image, were photographed with a Canon D750 Camera at a resolution of 6,000×4,000 pixels by a single trained photographer. In order to measure the wound sizes, based on clinical photos, their size and depth were assessed by three different board-certified plastic surgeons (SYW, HGJ, and JHP). The three reviewers all evaluated the wound as completely healed when it recovered with full epithelialization, and as healing state when it started to form healthy granulation tissue. To measure the size of the wounds, the digital photos were opened on Adobe Photoshop version 21.2.4 (Adobe, California, LA, USA) and the areas of the initial wounds and epithelialized wounds were calculated by their number of pixels. We compared the initial wound size when Kerecis was applied, with the wound size at 7th post-application day. The healing rate was calculated by the change in epithelialization over the course of a week in each group. We represented and recorded the progress of the wound based on clinical photography. In addition, the number of days until full recovery was recorded. The wounds were also examined for complications such as infection and dermal component loss for further follow-up in 2 months.



Patient 1
Acute trauma wound on the thumb. (A) At the time of initial application of the acellular dermal matrix (ADM). (B) Three days after application. (C) 8 days after application, the ADM was fully absorbed.



Patient 2
Acute burn wound on the lower leg. (A) At the time of initial application of the acellular dermal matrix (ADM). (B) Three days after application. (C) 5 days after application, the ADM was fully absorbed.