Clinical Outcomes Following the Use of Ovine Forestomach Matrix (Endoform Dermal Template) to Treat Chronic Wounds

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ABSTRACT

The suitability of the ovine forestomach matrix (OFM) for the treatment of recalcitrant wounds was evaluated in 19 patients. At 12 weeks, 50% of wounds had closed, and the average reduction in surface area was 73.4%. Promising outcomes of this initial series support the clinical consideration of OFM.

KEYWORDS: ovine forestomach matrix, chronic wound, venous ulcer, diabetic ulcer

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INTRODUCTION

Chronic wounds are characterized by a complex etiology that, in addition to an underlying medical condition, can also include aberrant cell–extracellular matrix (ECM) interactions, imbalances of matrix metalloproteinases, bioburden, and bacterial biofilm, and an unresolved inflammatory response—all of which contribute to the disruption or damage of the ECM.[1] Extracellular matrix components are important during tissue regeneration as they provide an essential pool of signals and substrates for cellular migration, proliferation, and differentiation.[2] Decellularized ECM (dECM)–based biomaterials have been developed to overcome tissue ECM deficits by providing a native collagen structure and functional secondary macromolecules to orchestrate tissue regeneration with concomitant capillary ingrowth.[3]

A dECM-based biomaterial termed "ovine forestomach matrix" (OFM) (Endoform Dermal Template; Mesynthes Ltd, Lower Hutt, New Zealand) has been cleared by the US Food and Drug Administration for dermal applications, including chronic wounds. Ovine forestomach matrix retains the authentic structure of native tissue ECM[4] and a complex mix of ECM-associated secondary molecules, whereas cellular and antigenic components (eg, cell debris and nucleic acids) are removed.[5] Although processed OFM is predominantly composed of collagens I and III, also present are elastin, fibronectin, laminin, and glycosaminoglycans.[5] Ovine forestomach matrix has been shown in vivo to support cell attachment and differentiation and is completely remodeled during the regenerative process.[6] Based on positive preclinical findings, a study was conducted to evaluate OFM in treating lower-extremity wounds.

METHODS

Participants with at least 1 chronic, lower-extremity wound were enrolled with consent in a prospective, noncomparative, open-label evaluation. Inclusion and exclusion criteria are described in Table 1. Product indications, contraindications, and precautions were followed (Table 2). All wounds were surgically debrided and irrigated with hypochlorous acid solution (Vashe Wound Therapy; PuriCore, Malvern, Pennsylvania) prior to a 7-day qualifying period. During the qualifying period, chronic wounds resulting from a prior surgery and venous ulcers were treated with a silver calcium alginate dressing and compression, whereas diabetic foot ulcers were treated with once-daily collagenase ointment and off-loading. Following the qualifying period, wounds remaining free of visible symptoms of infection were continued in the study, and silver calcium alginate dressings and collagenase ointment treatments were stopped.

Table 1.

STUDY INCLUSION AND EXCLUSION CRITERIA

Inclusion	Exclusion
Patient ≥18 y old	Exposed bone, tendon, or fascia
Noninfected chronic venous, arterial, incisional, and diabetic wounds	Wound over bony prominence
Wound duration ≥1 mo	Visible signs of infection (swelling, pain, purulent drainage, or tracking into the deep tissue planes) following a 7-d qualifying period
	Third-degree burns
	Known sensitivity to ovine or collagen materials
	Unable to remain in trial for 12 wk or until wound epithelialized (whichever shorter)
	Declined, unable, or unwilling to make informed consent

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Table 2.

OFM INDICATIONS, CONTRAINDICATIONS, AND PRECAUTIONS FOR USE

Indications	Contraindications	Precautions
Partial- and full-thickness wounds	Known sensitivity to ovine (or collagen material)	Uncontrolled clinical infection
Pressure ulcers	Third-degree burns	Acute inflammation
Venous ulcers		Excessive exudate
Diabetic ulcers		Excessive bleeding
Chronic vascular ulcers		
Surgical wounds		
Traumatic wounds		
Draining wounds		
Tunneled/undermined wounds		

Using aseptic technique, OFM was trimmed to slightly overlap the wound margins, placed on the wound bed, and rehydrated with sterile saline until moist. Light pressure was applied to the matrix to ensure conformity to the underlying wound bed, and the OFM was secured with a nonadherent secondary dressing. Compression stockings, exudate control, and off-loading were used as required.

At follow-up appointments (weekly or less frequently), wounds were debrided and irrigated to remove loose debris, residual OFM that appeared in the wound bed as an off-white gel was left in place, and OFM was reapplied. Changes in granulation tissue and wound dimensions were recorded, and the wound was photographed. Application of OFM was discontinued when the wound was partially or fully re-epithelialized, or at the end of 12 weeks. Demographic and wound healing data were analyzed using SAS version 9.2 (SAS Institute Inc, Cary, North Carolina).

RESULTS

This series consisted of 19 participants with 24 wounds. Demographic and outcomes data are summarized in Tables 3 and 4. The mean wound area decrease at study end was 73.4%, and the average weekly wound area decrease was 0.259 cm^2, as determined through linear regression. There was no correlation between initial wound size and time to healing (Spearman correlation, $P = .09$). Of the 24 wounds, 8 (33%) were closed by 8 weeks of treatment, and this number increased to 12 (50%) at 12 weeks (Tables 4 and 5). The mean time to closure was 7.3 weeks for the 12 wounds (50%) that had completely closed at 12 weeks. Given that the remaining 12 wounds were still open after 12 weeks of treatment, the mean time to complete closure for all wounds could not be calculated. Mean duration of OFM treatment was 5.9 weeks, and mean time between clinic follow-up visits/OFM reapplication was 8.5 days. No serious adverse events were reported. The physician found the OFM easy to apply. Cases are highlighted in Figures 1 and 2.

Table 4.

FREQUENCY OF COMPLETE WOUND CLOSURE BY WOUND TYPE

Wound Type	Total Completely Closed (%)
Pressure ulcer	0/1 (0)
Chronic surgical wound	2/4 (50)
Venous stasis ulcer	2/5 (40)
DFU	8/14 (57)

Abbreviation: DFU, diabetic foot ulcer.

DISCUSSION

Wound dimensions decreased in 21 of 24 wounds, including patients with multiple comorbidities. Of the 2 wounds that increased n wound area, 1 (wound 23) was treated for only 7 days then lost to follow-up, and 1 wound (wound 6) became infected. The infection was thought to be unrelated to OFM and was treated with a silver-containing dressing (over the OFM) and systemic antibiotics. The silver dressing did not appear to negatively impact the underlying OFM. The infection resolved within 2 weeks, and OFM treatment was continued. Because of differences in study designs and samples, the authors' results are not directly comparable with existing wound studies. For example, some wounds (n = 7) enrolled in the study were less than 1 cm^2 in area and therefore may have closed with

Table 3.

SUMMARY OF PARTICIPANT DEMOGRAPHICS

Mean Age, y	Sex (n)	Wound Type/ Etiology (n)	Wound Location (n)	Mean Surface Area of Wounds at Initial Visit, cm^2	Mean No. of Visits	Mean Treatment Time, wk	Mean Time Between Follow-up Visits, d
61 (SD, 12.9; range, 19–84)	M (9)	DFU (14)	Leg (7)	3.0 (SD, 3.9; range, 0.1–14.8)	5 (range, 1–23)	5.9 (range, 1–12)	8.5 (range, 5–21)
	F (10)	Pressure ulcer (1) Chronic surgical wound (4) Venous stasis ulcer (5)	Toe/foot (17)				

Abbreviation: DFU, diabetic foot ulcer.

Table 5.

WOUND CLOSURE RESULTS WITH OFM

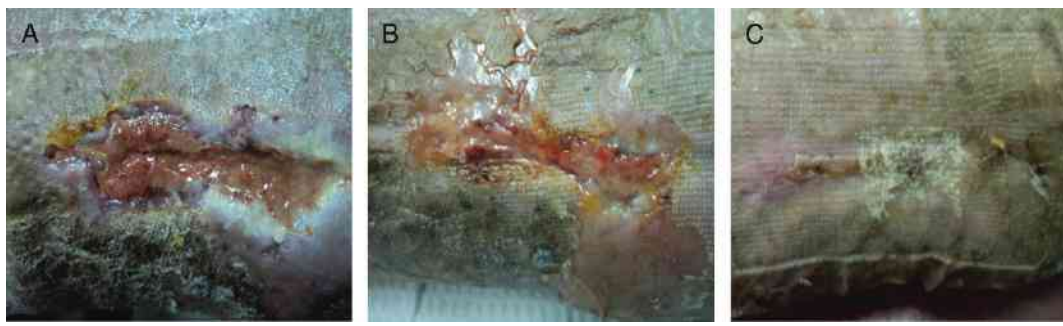
Wound No.	Age, y	Sex	Wound Type	Wound Duration, wk	Initial Wound Area (T = 0 wk), cm^2	Total OFM Treatments	Wound Area at End of Patient Study Period, cm^2	% Closure at End of Patient Study Period	Total Time to Closure, wk
1	60	F	VSU	12+	14.8	9	0.0	100	11.3
2	58	M	Surgical (foot)	4–6	5.0	6	0.0	100	7.0
3	41	M	DFU	4–6	2.6	6	0.0	100	6.9
4	56	F	DFU	12+	2.6	8	0.0	100	11.1
5	64	F	VSU	12+	1.4	6	0.0	100	8.9
6			VSU	12+	1.4	17	5.2	−271	
7			VSU	4–6	1.7	3	0.3	82	
8	69	M	DFU	4–6	1.2	9	0.0	100	9.9
9	67	M	DFU	12+	1.8	4	0.0	100	4.9
10	56	F	DFU	Unknown	1.3	6	0.3	77	
11	57	F	DFU	Unknown	2.9	3	0.9	69	
12			DFU	Unknown	10.9	3	7.4	32	
13	75	M	DFU	4–6	1.9	5	0.4	79	
14			DFU	4–6	3.5	6	0.3	91	
15	53	M	Surgical (ankle)	12+	8.7	8	0.0	100	8.0
16	70	M	DFU	4–6	0.9	6	0.0	100	6.9
17	84	F	DFU	4–6	0.9	2	0.0	100	1.9
18	64	F	DFU	6–12	0.2	3	0.0	100	3.0
19	50	F	Surgical (Achilles)	4–6	6.1	8	2.0	67	
20	60	F	DFU	4–6	0.1	2	0.0	100	2.0
21	72	F	PrU	Unknown	1.3	4	0.2	82	
22	56	M	DFU	Unknown	0.4	4	0.1	85	
23	72	F	VSU	Unknown	0.5	2	0.7	−44	
24	19	M	Surgical (foot)	4–6	0.2	1	0.2	0	

Abbreviations: DFU, diabetic foot ulcer; F, female; M, male; PrU, pressure ulcer; VSU, venous stasis ulcer.

standard care. Wounds in this series reached a 50% wound closure rate at 12 weeks, a finding consistent with the pivotal evaluation of small intestinal submucosa-treated diabetic wound closure rates (18/37; 49%) at 12 weeks.[7] Veves et al[8] reported a lower healing rate (37%) at 12 weeks of diabetic ulcers with collagen/oxidized regenerated cellulose matrix and an average wound area decrease

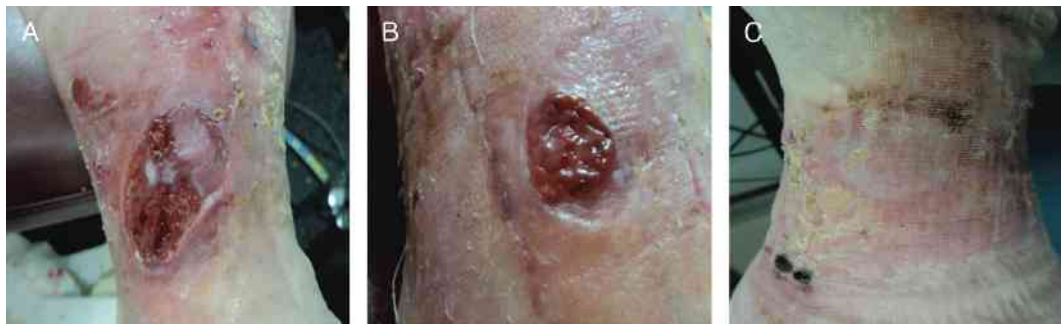
Figure 1.

CASE STUDY 1: VENOUS STASIS ULCER ON ANKLE



A, *T* = 0 weeks. Venous stasis ulcer of 2 years' duration on ankle. Patient had history of hypertension. Prior treatments included compression, debridement, collagenase enzymatic therapy, living cell–based product (x1), human fibroblast-derived dermal substitute (x8), porcine tissue bioscaffold, and xenograft. B, After 4 weeks of OFM treatment, wound was granulated, and epithelial tissue was present. C, *T* = 8 weeks. Complete healing occurred by week 9 with no recurrence.

Figure 2.
CASE STUDY 2: VENOUS ULCER ON THE ANKLE OF A DIABETIC PATIENT



A, *T* = 0 weeks. Patient had history of diabetes mellitus, congestive heart failure, and edema. Prior treatments included compression, debridement, oxidized regenerated cellulose, silver collagen, and steroid therapy. B, *T* = 7 weeks. Wound was granulated and epithelializing. C, *T* = 11 weeks. One week after complete healing.

Table 6.

CLINICAL IMPRESSIONS REGARDING USE OF OFM

Well-tolerated by patients and does not need to be removed at dressing change
Robust handling characteristics, quick rehydration, conforms well to underlying wound bed and adheres within 2–3 d
No suturing required, allowing application by a wide range of wound care practitioners
Available off-the-shelf, no special storage requirements, and 3-year shelf life
Available in large sizes (up to 400 cm^2)

of 64.5% at 12 weeks. The authors' current findings are promising and suggest OFM may assist closure of chronic wounds. Table 6 illustrates the clinical impressions regarding the use of OFM. A large, comparative clinical study is warranted. ●

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