Use of an Ovine Collagen Dressing with Intact Extracellular Matrix to Improve Wound Closure Times and Reduce Expenditures in a US Military Veteran Hospital Outpatient Wound Center

Daniel T. Ferreras, DPM, FAPWCA, AAWC
Chief/Lead Podiatrist
Surgical Services
Carl Vinson VA Medical Center
Dublin, Georgia

Sean Craig, RN, CWCN
Wound Care Nurse
Nursing
Alexandria VA Health Care System
Pineville, Louisiana

Rebecca Malcomb, RN
RN Care Manager for Primary Care
Nursing
Alexandria VA Health Care System
Pineville, Louisiana

ABSTRACT

A novel, comprehensive decision-making and treatment algorithm was established within a US government-run military veteran hospital in an attempt to standardize the process of outpatient wound care and streamline costs. All patients were systematically evaluated and treated using the comprehensive algorithm over a span of nine months. After three months of adherence to the algorithm, the algorithm was modified to include ovine-based collagen extracellular matrix (CECM) dressings as a first-line conventional treatment strategy for all appropriate wounds. The purpose of this retrospective analysis was to evaluate the hospital's change in cellular and/or tissue-based graft usage and cost, as well as wound healing outcomes following modification of the wound care standardization algorithm. Data from the first quarter (Q1; three months) of protocol implementation were compared to the subsequent two quarters (six months), during which time the first-line dressing modification of the protocol was implemented. Results showed that between quarters 1 and 3, the percentage of wounds healed increased by 95.5% (24/64 to 80/109), and the average time to heal each wound decreased by 22.6% (78.8 days to 61.0 days). Cellular and/or tissue-based

graft unit usage decreased by 59.7% (144 units to 58 units), and expenditures on cellular and/or tissue-based grafts decreased by 66.0% ($212,893 to $72,412). Results of this analysis displayed a trend toward decreased expenditures, faster healing times, and a greater number of healed wounds following modification of an evidence-based algorithm to incorporate CECM dressings as a first-line treatment strategy in managing chronic wounds.

INTRODUCTION

Chronic ulcers affect more than 6.5 million people in the US and are a major growing health problem due to an aging population, increasing health care costs, and a steep rise in diabetes and obesity worldwide.[1] The prevalence of venous insufficiency ulcers in the US is approximately 600,000 annually,[2] and venous leg ulcers (VLU) account for at least 70% of all chronic ulcers found on the lower leg.[2,3] In 2014, approximately 22 million people in the US were living with diagnosed diabetes,[4] and, of these diabetics, an estimated 10–15% will develop a foot ulcer during their lifetime.[5] These foot ulcers represent a substantial cost burden, estimated at a one-year cost of over $9 billion among US Medicare beneficiaries with diabetes.[6] In 2013, the average cost of treating a diabetic foot ulcer (DFU) patient was approximately $49,209 for the two-year period after diagnosis.[5] Compared to matched non-VLU patients, a large database analysis showed VLU patients incurred annual incremental medical costs of $6,391 in Medicare costs and $7,030 in private insurance costs, suggesting an annual US payer burden of $14.9 billion for VLUs.[7]

A focus on reductions in acute care spending has transferred care to the outpatient setting, and a growing number of hospitals are offering outpatient wound services as part of this cost shifting. Currently, there are more than 1,000 outpatient wound care centers in the United States[8] with alarming estimated annual expenditures on wound care services of over $50 billion.[9] These expenditures have captured the attention of US Centers for Medicare and Medicaid Services (CMS) administrators who have been moving to gain control of the overwhelming costs of outpatient wound services. CMS introduced several sweeping cost saving measures in 2014, and there is a major shift underway toward value-based payments, versus the present fee-for-service payments.[10,11]

Along similar lines of quality improvement and cost savings, within the US Veterans Affairs (VA) hospital system, there has been a major push toward standardization since the August 2001 launch of a Healthcare Failure Mode and Effect Analysis (HFMEA) process.[12] HFMEA is a five-step process that uses an interdisciplinary team to proactively evaluate a health care process. It involves process flow diagramming, a hazard scoring matrix, and a decision tree to identify and assess potential vulnerabilities. This standardization process was originally designed to assess and address prospective risk of a health care process to enhance safety, but the process is now also used to streamline cost.

Basic tenets of HFMEA were used to standardize the process of wound care within a US VA hospital in an attempt to improve outcomes and reduce cost. Prior to standardizing the wound care process in this VA hospital, inpatient and outpatient wound care was performed on all floors and in all departments by numerous physicians and clinicians with varying levels of wound care training. A substantial proportion of hospital expenditures were spent on wound care, outcomes were not tracked, and patients were regularly lost to follow-up. Diabetic foot and venous leg ulcers were reported causes of extended lengths of stay and increased emergency department admissions. Following committee analysis of the problem, a wound healing center was established within the hospital and a two-part wound care standardization algorithm was developed and implemented.

Goals of the wound healing center and the algorithm were to standardize wound care efforts and product usage throughout the facility, to increase the rate of wound resolution, and to decrease overall expenditures on wound care. After three months of adherence to the algorithm, the algorithm was modified to include an ovine-based collagen extracellular matrix dressing (CECM; Endoform® dermal template, Hollister Incorporated, Libertyville, Illinois) as a first-line treatment strategy for all appropriate wounds based on its understood effects in reducing elevated metalloproteinases (MMPs)[13] and its relatively low cost. The purpose of this retrospective analysis was to evaluate the hospital's change in cellular and/or tissue-based graft usage and cost, as well as wound healing outcomes following modification of a wound care standardization algorithm to include CECM dressings as a first-line treatment strategy.

MATERIALS AND METHODS

A 1,150 ft^2 outpatient wound healing center was established within the VA hospital, and all ancillary departments were educated about the wound healing center services and how to refer patients to the center. A dual algorithm that combined decision-making and wound treatment protocols was developed and implemented by the wound healing center program director (Daniel T. Ferreras) (Fig. 1). Wound healing staff members were educated about the systematic use of the algorithm for each patient.

Decision protocol

Part one of the algorithm (Decision Protocol) is a decision tree honoring the fundamentals of wound care and was used to determine that both the patient and wound bed were ready for treatment. The Decision Protocol was based

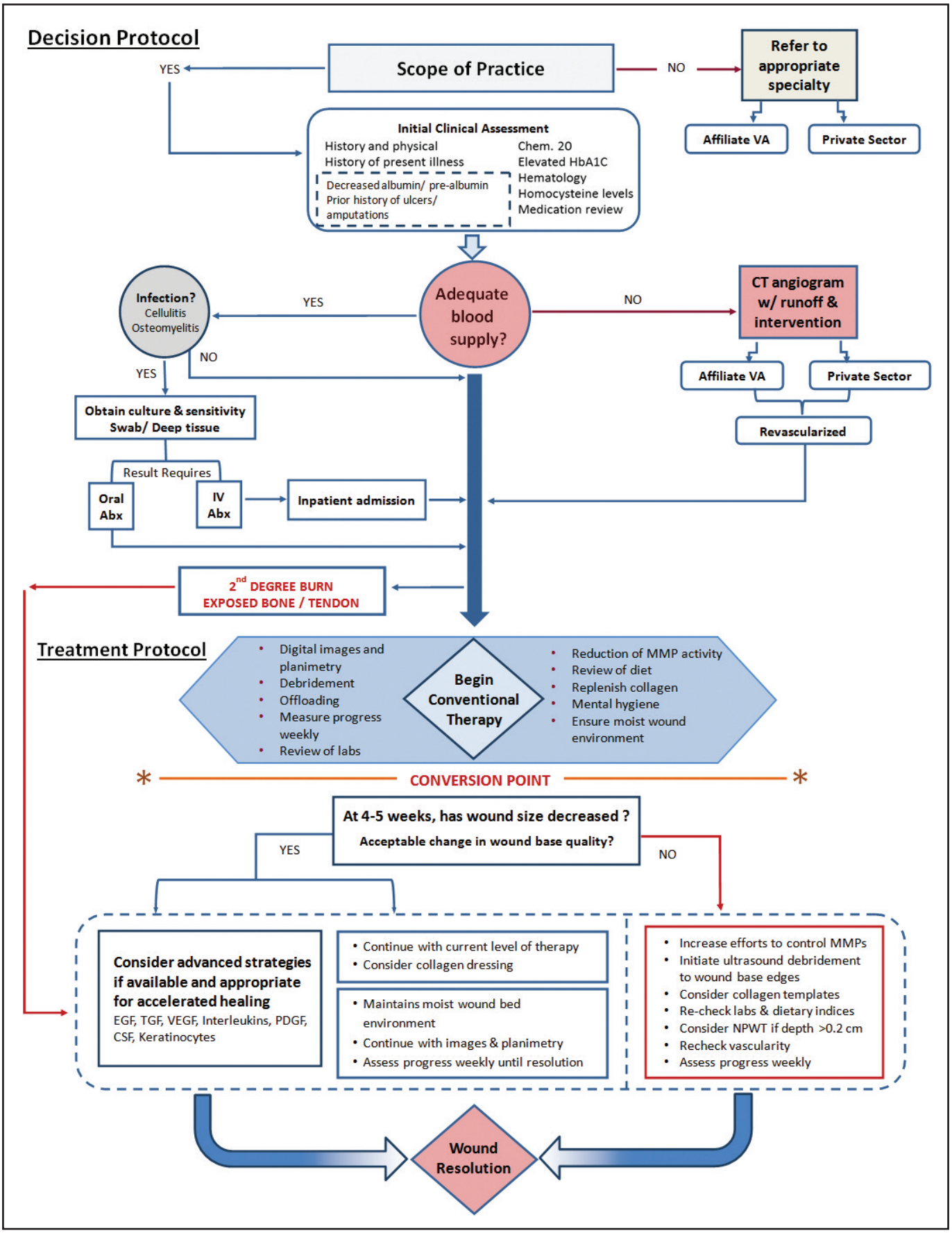

Figure 1. Dual protocol algorithm.

Table I
Patient demographics and outcomes

	Q1 Sept-Nov. 2014	Q2 Dec. 2014-Feb. 2015	Q3 Mar-May 2015
Patients (n)	79	78	73
Male, n (%)	76 (96.2)	76 (97.4)	71 (97.2)
Female, n (%)	3 (3.8)	2 (2.6)	2 (2.7)
Average age (years)	66.5	64.5	65.4
Wounds treated (n)	64	84	109
DFU, n (%)	35 (54.7)	65 (77.4)	82 (75.2)
VLU, n (%)	25 (39.1)	17 (20.2)	21 (19.3)
Heel PrU, n (%)	4 (6.2)	2 (2.4)	6 (5.5)
Clinic visits (n)	274	343	336
Healed wounds (n;%)	24 (37.5)	55 (65.5)	80 (73.3)
DFU, n (%)	18 (51.4)	44 (67.7)	61 (74.3)
VLU, n (%)	3 (12.0)	9 (52.9)	16 (76.2)
Heel PrU, n (%)	3 (75.0)	2 (100.0)	3 (50.0)
Average time to heal, days (weeks)	78.8 (11.3)	77.2 (11.0)	61.0 (8.7)
DFU, n (%) (weeks)	74.2 (10.6)	67.9 (9.7)	52.5 (7.5)
VLU, n (%) (weeks)	86.1 (12.3)	115 (16.5)	99 (14.2)
Heel PrU, n (%) (weeks)	73.5 (10.5)	57.4 (8.2)	44.1 (6.3)

Table II
Dressing usage and expenditures

	Q1 Sept-Nov. 2014	Q2 Dec. 2014-Feb. 2015	Q3 Mar-May 2015
Cellular and/or tissue-based graft units used (n)	144	84	58
CECM units used (n)	0	50	40
Total cost of cellular and/or tissue-based grafts ($US)	212,893	115,096	72,412
Avg. cellular and/or tissue-based graft cost/treated ulcer ($US)	3,326	1,370	664
Total cost of CECM units ($US)	0	1,363	1,253

on five fundamental factors necessary for wound healing: optimized perfusion (compression when needed), offloading properly, control of infection/bioburden, debridement of devitalized tissue, and balanced nutrition according to the specific needs of the patient.[14-18] Each of these fundamentals was addressed by the wound healing team through systematic use of the decision protocol. Once the fundamentals were addressed, and if the patient did not have a first or second degree burn or exposed tendon,[19] the patient could proceed to the treatment protocol.

Treatment protocol

Part two of the algorithm (Treatment Protocol) was used to guide treatment for each patient once the wound and patient were prepared. For the first three months after algorithm implementation, oxidized regenerated cellulose (ORC)/collagen dressings were used as first-line conventional treatment for all appropriate chronic wounds. Based on the needs of our chronic wound population and growing evidence implicating MMP imbalances as a critical factor in stalled wounds,[20] a decision was made to switch to CECM dressings as a first-line conventional treatment strategy after three months (beginning of quarter 2). Silicone fenestrated gauze or an antibacterial foam dressing bound with gentian violet and methylene blue (GV/MB) (Hydrofera Blue®; Hollister Incorporated, Libertyville, Illinois) was used as a cover over the CECM dressing, and paper tape was used to secure the cover dressing. The area was wrapped with a latex-free conforming stretch bandage and a light four inch self-adherent elastic wrap as needed.

Compression stockings and appropriate off-loading strategies (controlled ankle movement walker boot, offloading padding, and total contact cast) were used as needed. At weekly follow-up appointments, diet was reviewed, and wounds were debrided and irrigated as necessary. Changes in granulation tissue and wound dimensions were recorded, and wounds were photographed using a 16 megapixel digital camera system.[21] Wounds were reassessed at four, eight, and 12 weeks for progress.

If the wound size continued to contract after four to five weeks of conventional treatment, CECM dressings remained the primary dressing. If wound contraction stalled or wound size increased after four to five weeks, a cellular and/or tissue-based graft was chosen in lieu of CECM dressings to reach our resolution endpoint. The selection of cellular and/or tissue-based products was varied and included cryopreserved placental membrane, dehydrated human amnion/chorion membrane allograft, human fibroblast-derived skin substitute, living bi-layered skin substitute, and fetal bovine dermal scaffold materials.

Acceptable change in wound-base quality was defined as beefy red granulation tissue, limited or no hypergranulation, and no wound edge epibole. The wound was considered resolved when there was 100% re-epithelialization and no drainage.

Data analysis

Demographic, dressing usage, and outcomes data from September 15, 2014 to May 31, 2015 were retrospectively extracted from the electronic medical records, and entered into an Excel® (Microsoft Inc., Redmond, Washington) spreadsheet to calculate totals and averages. Endpoints measured were number of healed wounds, time to heal, and cost and units used of cellular and/or tissue-based grafts and CECM dressings. Data from the first quarter (three months) of protocol implementation were compared to the subsequent two quarters (six months) during which time the first-line dressing modification of the protocol was implemented.

RESULTS

Patient demographics and outcomes are listed by quarter in Table I. The total number of patients treated and average age were similar during all three quarters. The number of wounds treated increased by 70.3% (64 in Q1 to 109 wounds in Q3) and the number of clinic visits increased by 22.6% (274 in Q1 to 336 visits in Q3) between quarter one and three. During this same timeframe, the percentage of wounds healed increased by 95.5% (24/64 [37.5%] in Q1 to 80/109 [73.3%] in Q3), and the average time to heal each wound decreased by 22.6% (78.8 days in Q1 and 61.0 days in Q3).

Between quarters 1 and 3, cellular and/or tissue-based graft unit usage decreased by 59.7% (144 units in Q1 and 58 units in Q3), and expenditures on cellular and/or tissue-based grafts decreased by 66.0% ($212,893 in Q1 and $72,412 in Q3) (Table II, Figs. 2 and 3).

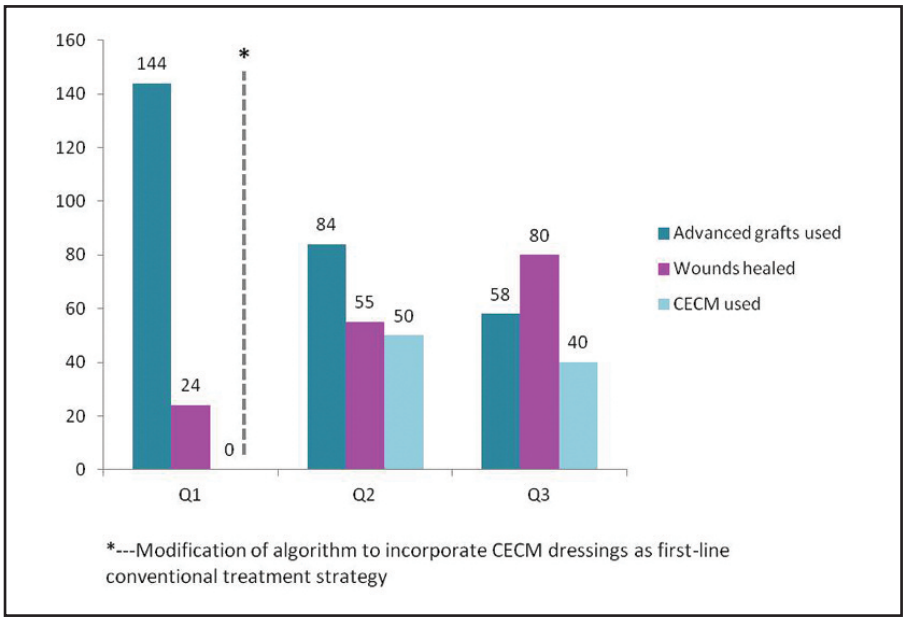

Figure 2. Cellular and/or tissue-based graft/CECM unit usage and wounds healed over time.

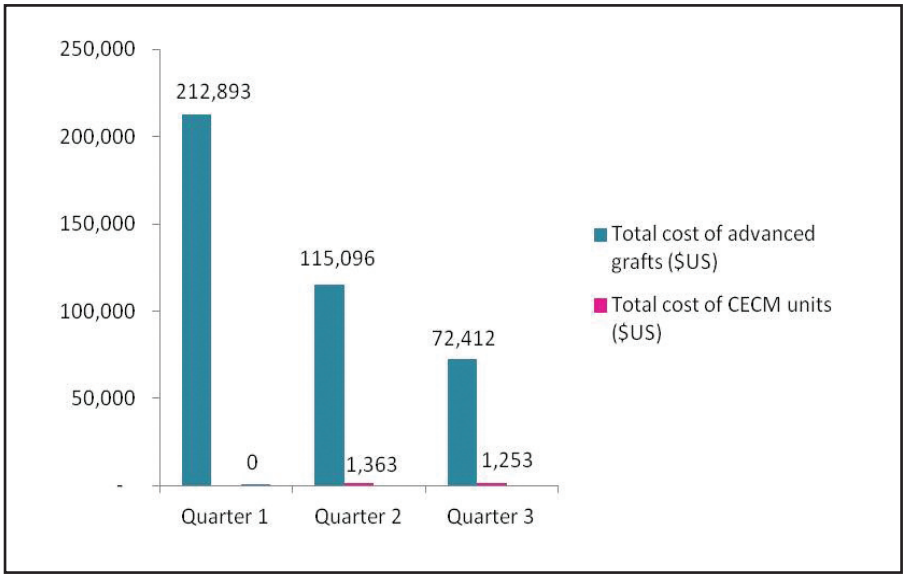

Figure 3. Cellular and/or tissue-based graft and CECM unit expenditures over time.

CASE STUDIES

Case Study 1: Diabetic foot ulcers in a patient with peripheral vascular disease

A 60-year-old male presented with diabetic foot ulcers on the hallux and second digit of his left foot (Figs. 4a and 4b). The man had type 2 diabetes with a medical history of neuropathy, syncopal events, sleep apnea, obesity, anemia, depression, peripheral vascular disease (PVD), coronary arteriosclerosis, acute osteomyelitis of the lower extremity (left), monoclonal paraproteinemia, and retinal detachment (legally blind). The wounds were ultrasonically debrided at initial presentation to remove eschar. Patient and wound preparation included attention to daily diet, noninvasive vascular diagnostic testing (arterial duplex ultrasound, CT-angiography), vascular intervention with stents, and mental/spiritual counseling.

After wound bed preparation, a CECM dressing was applied with a GV/MB foam dressing as a cover dressing. The foot was offloaded with a post-operative surgical shoe, and wounds were surgically debrided at each weekly dressing change. At week nine, a bi-layered skin substitute was applied to the wound (Fig. 4c) in an attempt to speed resolution. CECM dressings were continued after the bi-layered skin substitute, and a fetal bovine dermal repair scaffold (rich in type III collagen) was placed on week 12 to help speed restoration of the collagen-rich wound bed after the patient sustained a deep injury to the foot ulcers and set wound healing backward several weeks. CECM dressings were continued (Figs. 4d and 4e) until both ulcers were fully healed at 6 1/2 months (Fig. 4f).

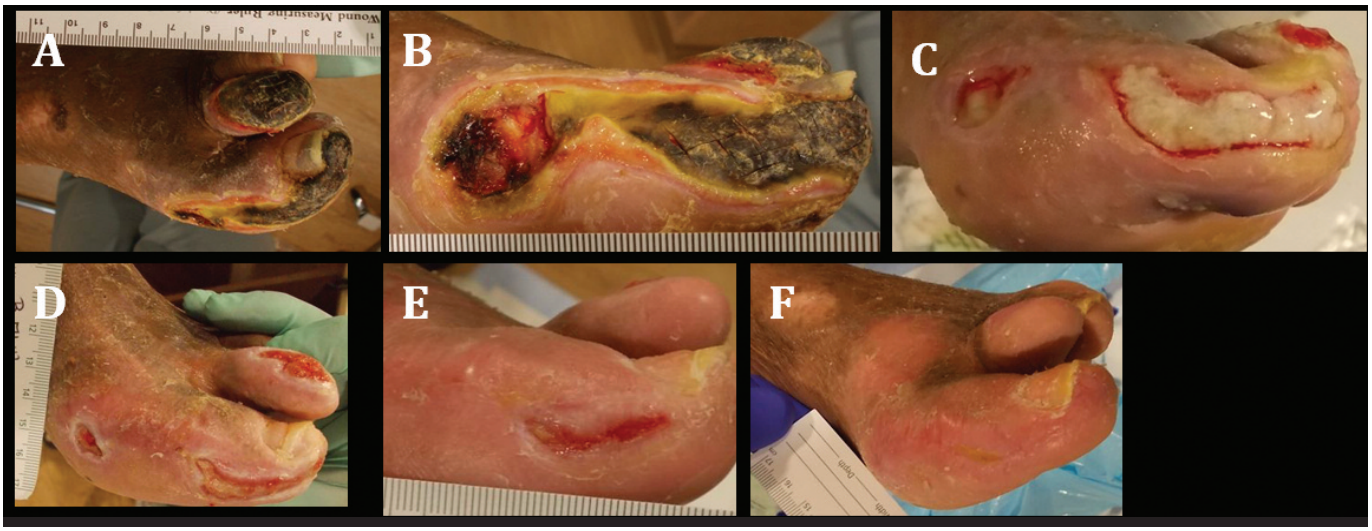

Figure 4. a) and b) At presentation, eschar-covered ulcers on the left hallux and second digit measured 9.5 x 2.0 cm and 4.5 x 3.5 cm, respectively. CECM dressings were initiated with a GV/MB foam cover dressing. c) Bi-layered skin substitute applied at nine weeks. CECM dressings were continued subsequently. d) DFUs after three months of CECM dressings and two skin substitute applications. e) Ulcers nearly re-epithelialized at five months. f) At 6 1/2 months, ulcers are completely healed.

Case Study 2: Bilateral diabetic foot ulcers in a patient on anti-coagulant therapy

A 64-year-old diabetic male presented with three diabetic foot ulcers under the metatarsal heads on the plantar aspects of both feet (Figs. 5a and 5b). Wounds had been present for four to five weeks. The patient was diabetic with a history of neuropathy, multiple type hyperlipidemia, PVD, hypertension, nicotine dependence, non-compliance issues, vitamin B-12 deficiency, coagulation therapy (treated with warfarin), depressive disorder, iron deficiency, coronary artery disease, pes cavus feet, varicose veins, and sleeplessness.

Wounds were mechanically and ultrasonically debrided. CECM dressings (2 x 2 cm) were sized and placed in all ulcers and GV/MB dressings (2.5 x 2.5 cm) were used as cover dressings. Both feet were offloaded with wedge offloading shoes. CECM dressings were applied once per week with weekly progression measured at each dressing change (Figs. 5c–5g). At each monthly evaluation, all ulcers achieved adequate wound healing progression (40 to 50% smaller) to continue with CECM dressings for the duration of therapy. The right foot ulcer was fully healed at eight weeks and the left foot ulcers were healed at six weeks.

Case Study 3: Post-amputation wound dehiscence in a diabetic patient

A 78-year-old male presented with a dehisced incision (Fig. 6a) following left hallux amputation 10 weeks prior. The patient was type 2 diabetic with a history of chronic congestive heart failure, atrial fibrillation, obesity, chronic obstructive pulmonary disease, hyperlipidemia, anemia, PVD, hypothyroidism, hypertension, age-related macular degeneration, benign prostatic hyperplasia, and insomnia. The wound had been treated with negative pressure wound therapy (NPWT) for two weeks prior to presentation. The patient wore

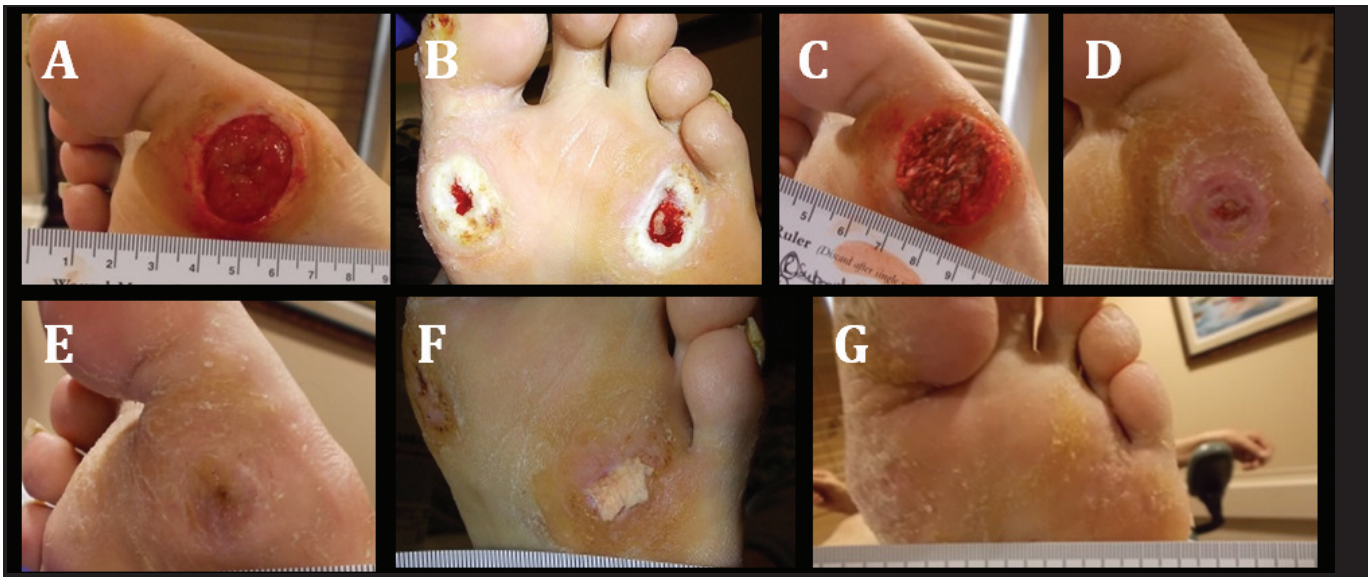

Figure 5. a) and b). Diabetic foot ulcers on right and left foot at presentation. c) Right foot ulcer edges are flattened after three weeks of CECM dressings. d) At seven weeks, right foot ulcer is nearly re-epithelialized. e) At eight weeks, right foot ulcer is healed. f) CECM dressing shown in left foot ulcer. g) Both left foot diabetic ulcers are 100% re-epithelialized after six weeks of CECM dressings.

Figure 6. a) and b). Post-amputation wound at presentation and after debridement. c) After two weeks of combined CECM dressings and NPWT. d) After eight weeks of CECM dressings and NPWT and two applications of cryopreserved placental membrane grafts. e) At 12 weeks with CECM dressings. f) At 16 weeks with CECM dressings. g) Wound is fully re-epithelialized at 22 weeks.

a post-surgical shoe and ambulated in a wheelchair.

Excisional and ultrasonic debridement were performed, (Fig. 6b) and CECM dressings with a polyvinyl alcohol GV/MB foam dressing cover were initiated in tandem with NPWT, underneath the NPWT foam dressing. CECM dressings were applied once per week throughout treatment. Fig. 6c shows the wound after two weeks. Cryopreserved placental membrane grafts were placed with NPWT at weeks four and five. CECM dressings were continued and the wound volume was markedly decreased at weeks eight (Fig. 6d) and 12 (Fig. 6e). At week 16, a human amniotic membrane allograft was placed over the remaining wound areas, and CECM dressings were continued (Fig. 6f) until complete closure at 22 weeks (Fig. 6g).

DISCUSSION

This retrospective analysis displayed a clear trend toward decreased expenditures, faster healing times, and a greater number of healed wounds following implementation and modification of an algorithm to incorporate CECM dressings as first-line treatment of chronic wounds. While there were substantial increases from quarter to quarter in the number of wounds treated, as well as clinic visits and percent of wounds closed, expenditures on cellular and/or tissue-based grafts decreased by $140,481 between the first and third quarter.

Although the incremental effect of each of the implemented changes is unknown, these authors propose multiple factors that likely contributed to improved outcomes and lower costs. During the first quarter of operation, the number of patients was greater than the number of wounds treated because several patients who did not have a wound were consulted by primary-care physicians to be seen by the wound center for general podiatry services like partial nail avulsions. After the wound healing center sent out a special reminder delineating the scope of practice, services offered, and days/hours of operation, staff members began to better direct appropriate patients to the center.

Also, once a dedicated wound center staff was assembled and educated regarding the algorithm for decision-making and treatment, wound management became consistent and could be tracked. The two-part algorithm was developed to incorporate pivotal wound healing concepts that have been shown over the past 13 years to contribute positively to wound management from dermal defect to complete closure. Evidence-based modalities, such as offloading boots, were consistently incorporated into the management strategies and appeared to influence outcomes over time.

Establishing a target healing timeline may have improved results as well. For venous leg ulcers, a 20–40% reduction in wound area within two to four weeks has been found to be predictive of healing,[22] whereas for diabetic foot ulcers, a reduction of >50% by week four is predictive of healing.[23-25] We added one week to our algorithm, making it a four to five week timeframe before switching to a new dressing/therapy, to allow for real world uncontrollable factors like patient compliance, missed appointments, or other random events. Setting such quality measures will be a necessity for wound center survival in the future scenario of value-based reimbursement.

CECM dressing characteristics may also have contributed to the improved outcomes and lower costs observed in Q2 and Q3. The dressings are made from propria submucosa of ovine forestomach tissue using proprietary processes to delaminate and decellularize the tissue.[13,26] They consist of natural, intact collagen, including types I, III, and IV, as well as secondary ECM components such as elastin, fibronectin, laminin, and glycosaminoglycans.[27] The matrix dressing retains the three-dimensional architecture present in tissue ECM[27] and has demonstrated broad spectrum matrix MMP reduction.[13]

The new CECM/GV-MB dressing combination was less expensive per dressing than previously used dressings, but the primary reason for the switch was that we observed faster healing rates with the use of CECM dressings compared to our experience with C/ORC dressings. Our outcomes may also have been influenced by the antibacterial effects of the GV/MB foam cover dressings, but the incremental effect of the cover dressings is unknown. In our experience, CECM provided the strength of a dermal template but was simple to apply like a standard collagen-based dressing. CECM dressings could be applied as little as once per week and remained in the wound bed until they were no longer visible, which could save costs compared to other collagen dressings that

require applications up to three times per week.

These authors know of just two case series that have evaluated the use of CECM in chronic wounds. Bohn et al. (2014) reported, in a retrospective analysis, that 23 of 23 venous stasis ulcers healed in an average of 7.3 weeks (range: 2 to 15 weeks) with the use of CECM dressings.[28] This is considerably faster than the average time to heal VLUs in our study (14.2 weeks). In another series of 19 participants with 24 ulcers of various etiologies, the mean wound area decrease at 12 weeks with the use of CECM dressings was 73.4%.[31] Of the 24 wounds, eight (33%) were closed after eight weeks of treatment and 12 (50%) were closed at 12 weeks. Of wounds that closed, mean time to complete closure was 6.8 weeks, which is similar to our closure rate for DFUs and faster than our closure rate for VLUs.[29] Reasons for longer and inconsistent times to closure for VLUs in our study could be due to the comparatively advanced age of our patient population, as well as a historic lack of a specific process to identify VLUs within the VA system and the tendency for patients with VLUs to be referred to a VA wound clinic late in the disease course.[30]

This analysis contains all the inherent limitations of a retrospective, uncontrolled, nonrandomized study. Data were extracted from the first nine months of operation, which was a somewhat erratic period as the wound center was becoming fully functional. Small "settling in" adjustments were made throughout the study period that were undocumented and could have influenced outcomes. CECM dressings were introduced into the algorithm in Q2, and it is not possible from the data to know if there was a carryover effect from other treatment strategies. Cover dressing use and cost were also not considered in the analysis. Additionally, "wound closure" was tracked over time in quarterly increments, and the patients treated during each quarter were not mutually exclusive; therefore, the number of wounds treated in Q1 that were resolved in Q2 or Q3 was not determined. Clinician bias also may have skewed data results with respect to selection for, or timing of, a cellular and/or tissue-based graft. Long-term controlled studies are needed to determine the actual incremental effect on clinical outcome and cost of each of the variables within the systematic algorithm.

CONCLUSION

This publication describes the first attempt at implementing an evidence-based wound management algorithm within our VA hospital, or any VA facility within our Veterans Integrated Service Network. Algorithm modifications incorporating an MMP-modulating CECM dressing showed improved clinical outcomes and reduced advanced graft expenditures in this VA population. Our aim in developing a comprehensive algorithm is that it could serve as a roadmap for other wound care center directors in and outside of the VA system who are looking to decrease the use of more expensive modalities while improving quality of care.

Healing wounds more efficiently on the front-end—through the use of progressive algorithms—to reduce overall costs on the back-end fits with the current health care emphasis on evidence-based, outcome driven health care delivery systems. This pilot study/algorithm is novel in the VA system because, compared to non-VA hospital-based outpatient wound care departments in the US, there remains great access to advanced wound dressings and therapies, and administrators have not yet been forced to think of cost containment at every level. The benefits of this approach are broad reaching and include saving US taxpayer dollars and enhancing military veteran quality of care. STI

AUTHORS' DISCLOSURES

Daniel Ferreras is a consultant for Hollister Incorporated.

All other authors have no conflicts of interest to disclose.

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Tel. +1 415 704 3160
Email: info@surgicaltechnology.com
Internet: www.surgicaltechnology.com

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