IJTR
The International Journal of Tissue Repair

RESEARCH ARTICLE

Real world evidence retrospective study to evaluate the safety and efficacy of an amniotic membrane allograft for lower extremity diabetic ulcers in a post-acute care setting

Ayesha Qadeer,[1] MPH | **Emaad Basith,**[1] MD | **Martha R Kelso,**[2] RN | **Saad Mohsin,**[1] MD | **Rashad Sayeed,**[3] DPM

[1]United WoundCare Institute; [2]Chief Executive Officer for Wound Care Plus, LLC, Kansas City, MO; Head of Research for United Health Partners, LLC, Naperville, IL, US

Correspondence: Ayesha Qadeer (aqadeer@unitedwounds.org)

Received: 22 October 2025 | Accepted: 30 October 2025

Funding: Sponsored by OneBiotech, LLC.

Keywords: Chronic wound | wound healing | cellular, acellular and matrix-like products (CAMPs) | lower extremity diabetic ulcer | amniotic membrane allograft

Abstract

Aims: To evaluate the reduction of LEDU wound size after amniotic membrane allograft (AmnioBurgeon (OneBiotech, LLC, USA) treatment.

Methods: Single center retrospective database review for patients treated with AmnioBurgeon for LEDUs. Wound area was measured prior to each allograft application and change in wound area over each application was evaluated over progression of therapy.

Results: In total, 24 patients with 28 LEDUs were treated weekly with AmnioBurgeon with average wound size of 17.4cm^2. During the treatment course, 14% of the wounds completely healed with a mean time to healing of 77 days. Overall, 64% of them achieved partial closure with at least 50% area reduction within 21 days on average. By week 4, 46% of wounds achieved ≥50% reduction in their size.

Conclusion: Amniotic membrane allograft is an effective treatment for LEDUs which were not successful in healing with standard of care.

Introduction

The physiological process of wound healing in ulcers that have stalled is a complex, multi-step process for restoring injured tissue.[1] When this process is interrupted, it can lead to either over-healing or the formation of a chronic wound.[2] By definition, a chronic wound is one that has not healed after receiving four weeks of standard care.[3] Such wounds often last for extended periods, from months to years, and are associated with a lower quality of life, pain, a greater chance of infection, and increased healthcare use. Individuals with multiple chronic illnesses and risk factors such as age, diabetes, poor circulation, renal failure, or immobility are particularly at risk for experiencing delayed wound healing.[2-6]

Chronic wounds pose a significant economic burden on the US health care system, with around 10.5 million Medicare beneficiaries and annual cost approaching $22.5 billion.[5] Lower Extremity Diabetic Ulcers (LEDU) is an example of the huge health and economic impact of chronic wounds. LEDUs are a common diabetic disease complication affecting more than 18 million people worldwide.[6] LEDUs accounts for ~80% of lower extremity amputations in patients with diabetes.[6] The 5-year mortality rate is 30% for patients with LEDU and can be as high as 70% if it results in significant amputation. In the US, the direct cost of treating LEDU costs $9–13 billion each year, accounting for one third of the cost of managing diabetes.[6] Overall, LEDU is a devastating problem affecting patients and the health care system due to recurrent infections, hospitalizations, amputations, loss of QOL and even mortality.

The underlying pathophysiology of LEDU is multifactorial; vascular, neurological, and biochemical aberrations being major players.[6] These include loss of sensation (neuropathy) accompanied by frequent pressure and mechanical stress on the foot, leading to small fissures in the skin. This is further aggravated by either trauma or inflammation. The result is a poor healing wound mainly due to compromised vascular (micro and macro) blood supply. Management of LEDU requires a multidisciplinary approach with collaboration between but not limited to primary care physicians, podiatrists, vascular surgeons, foot and ankle surgeons, infectious disease specialists, nutritionists, pharmacists, orthotists/pedorthists, and among others but still remains a challenge.[6] LEDU SOC includes wound debridement, infection control, moisture balance along with offloading pressure interventions.[2-6] Several inherited characteristics make LEDU a major burden. LEDUs are more prone to infection than other chronic wounds and resistant to healing, with a high recurrence rate.[4] Patient risk factors such as advanced age and underlying comorbidities such as peripheral neuropathy, ischemia and peripheral vascular disease along with patient non-adherence delay and regress wounds from reaching the healing stage.[7]

CAMPs

Advanced wound care therapies such as cellular, acellular and matrix-like products (CAMPs) have become an appealing treatment option for patients with chronic wounds. CAMPs products are commonly sourced from human tissue (allograft) or animal tissue (xenograft). LEDU management guidelines published by Society for Vascular Surgery, American Podiatric Medical Association, and the Society for Vascular Medicine recommended consideration of using CAMP treatment.[8] This was based on a randomized clinical trial investigating 256 patients in which Apligraf (OneBiotech, LLC, USA), an FDA-approved allograft from neonatal skin, has shown improvement in chronic wound healing.[7] Since then, additional CAMPs were tested in clinical trials.[9] Placental-derived allografts derived from amniotic fluid or sac, umbilical cord, or a combination of placental tissue are gaining attention.[10] Allograft tissue provides a fertile environment for wound healing as it provides cellular, mechanical, and biochemical support.[9,10] It releases analgesic, anti-inflammatory, anti-bacterial, and non-immunogenic properties that support the wound healing process.[9,10] Published clinical trials have shown better healing outcomes compared to SOC when placental allografts are added to treatment.[10-14] Amniotic membrane-derived grafts have been used in treatment such as burn, post-operative adhesion prevention, Moh's surgery, ophthalmology, dura matter covering, reanastomosis sites, and tympanoplasty.[15] Amniotic membranes are rich in biological components such as collagen, growth factors, and extracellular matrix proteins, all of which are vital to the wound healing process.[15] Previous studies showed that amniotic-derived allografts are proven to be effective in LEDU treatment.[11-17] Furthermore, amniotic-derived allograft is also more cost effective when incorporated into the treatment plan than SOC alone.[18]

However, due to variations in composition and in the preparation process of these allografts, the right choice needs to be made. In addition, determining the safety and treatment schedule, and identifying eligible patients who will benefit is of high importance. AmnioBurgeon is a resorbable, chorion-free human free amnion allograft derived from donated human birth tissue which has been approved for patients with LEDU. In this retrospective study, we sought to determine the safety and efficacy of this preparation in LEDU patients.

Patients and methods

Data source

For this retrospective study, The Institutional Review Board (IRB), UNIVO has determined that the study is exempt from IRB oversight requirements found at 45 CFR 46.104(d) federal regulations under category 4 (#STU25090176). The IRB has approved the request for a waiver of consent and a waiver of authorization for this study. The medical charts that were reviewed in this study included data from March 2025 to September 2025. All treatment records for patients meeting eligibility criteria and received applications of AmnioBurgeon were extracted from the database and de-identified. Atlas 360 electronic medical records were reviewed for patient demographics and history, clinical visit notes and laboratory results. Patients' characteristics included basic information as age, sex, weight, comorbidities and laboratory results related to diabetes such as Hemoglobin A1c (HbA1c).

Eligibility criteria for the study included: diagnosis of type 1 or type 2 diabetes, at least 18 years old, non-healing wound >4 weeks and wound size ≥0.25cm^2. Additional information included those related to treatment such as number

TABLE 1 | Eligibility criteria

Inclusion criteria	Exclusion criteria
• Age 18 years or older • Diagnosed with diabetic foot ulcer with type I or type II diabetes mellitus diagnosis • Wound ≥ 4 weeks without significant reduction (<50% in 4 weeks) in wound size • The target ulcer must be located on the foot with at least 50% of the ulcer below the malleolus	• Treated with immunosuppressants, corticosteroids, chemotherapy in last 30 days • Treated with other Cellular and tissue-based products in last 30 days • Active infection or cellulitis • Active course of antibiotics • Lack of baseline or follow-up wound measurements • Wounds with a surface area less than 0.25 cm^2 • Ulcers from other causes such as arterial ulcers, venous ulcer, trauma, surgical, burns

of AmnioBurgeon treatment applications received and duration and wound-related examinations, wound area (in cm^2) prior to treatment and over the course of treatment. Wound area was measured with a wound ruler. Furthermore, wound severity was assessed based on the Wagner Scale denoting the following:

- Grade 0: Skin intact but bony deformities lead to 'foot at risk'
- Grade 1: Superficial ulcer
- Grade 2: Deeper, full thickness extension
- Grade 3: Deep abscess formation or osteomyelitis
- Grade 4: Partial gangrene of forefoot
- Grade 5: Extensive gangrene.19

Wound duration, location, complexity, and infection based on clinical signs and symptoms were also documented.

Study subject

The study included medical charts of patients who were treated at United WoundCare Institute in (Naperville, IL). The patients were selected based on the eligibility criteria which is summarized in *Table 1*.

Outcome and follow-up

The primary goal of this study was to evaluate the change in wound area after receiving AmnioBurgeon treatment. Complete wound closure was defined as 100% re-epithelialization by the treating physician. 'Partial reduction' was defined as ≥50% reduction in wound area. 'No response' was defined as <25% reduction in the initial two weeks of treatment or increase in size. Percentage of wound area reduction, time to reduction, complete wound closure, and number of AmnioBurgeon applications required for reduction were also determined. Infections during treatment were assessed by signs and symptoms without a requirement of culture confirmation.

Statistical analyses

Statistical analyses were conducted using Python (version 3.9.21) and the following packages: Pandas (2.1.4), Numpy (1.26.4), Statsmodels (0.14.0), SciPy (1.11.4), Lifelines (0.28.0), Matplotlib (3.8.2), Seaborn (0.13.0), and the built-in datetime module. Some plots were generated using Google Sheets. Demographics and clinical variables were summarized. Descriptive summaries of continuous variables included the mean, standard deviation, median, and range. Categorical variables were summarized in frequencies and percentages.

A mixed-effects linear regression model accounting for repeated measures was performed to assess significance ($p<0.05$) in change of wound area before and after treatment, and between applications. Baseline wound areas were placed into three groups (<10cm^2, 10 to <25cm^2, ≥25cm^2). The Chi-squared test was performed to compare proportion of wounds achieving ≥50% area reduction after 28 days of treatment for the three baseline wound area groups. Kaplan-Meier analysis was performed to compare time to ≥ 50% wound area reduction for the three baseline wound area groups.

Results

Patients' demographics and wound characteristics

In this study, 28 LEDUs in 24 patients were treated with AmnioBurgeon after failing to heal with SOC treatment alone. The median age was 75.1 (range 55.8–95.4), and 29.1% were female (*Table 2*). At baseline, the median wound size was 8.9 cm^2 (range 2.2–140.0), with 18% of wounds ≥25 cm^2 and 4% ≥100 cm^2. The median wound duration prior to CAMPs treatment was 113 days (range 37–1,095) and most wounds were in Grade 1 (75%). Wounds were treated with CAMPs every 7.1±0.7 days based on provider assessment of patients progress on treatment. The median number

TABLE 2 | Patient demographics and wound characteristics

Number of patients	24
Age, years (Mean±SD, Median, Min, Max)	75.1±9.9, 75.1, 55.8, 95.4
Female (N, %)	7 (29.1%)
Number of wounds	28
Wound locations	
Feet, Left	9
Feet, Right	7
Feet-heel, Left	4
Feet-malleolus, Left	2
Feet-heel, Right	2
Feet-lateral, Left	1
Feet-bunion, Left	1
Feet-malleolus, Right	1
Feet-plantar, Left	1
Grade/Severity	
Grade 1	21
Grade 2	5
Grade 3	1
Grade 4	1
Wound size at baseline (cm^2) (Mean±SD, Median, Min, Max)	17.4±27.8, 8.9, 2.2, 140.0
Wound Size ≥25cm^2 (%)	5 (18%)
Wound Size ≥100cm^2 (%)	1 (4%)
Wound duration prior to amnio treatment (Days) (Mean±SD, Median, Min, Max)	185.5±230.3, 113.0, 37.0, 1095.0
Wound age, (Days) (Mean±SD, Median, Min, Max)	174.1±233.4, 104.0, 35.0, 105.8
Time from first visit to CTP treatment, (Days) (Mean±SD, Median, Min, Max)	11.5±16.2, 5.0, 0, 55.0
HbA1c* (n, Mean±SD, Median, Min, Max)	28, 6.0±1.1, 5.9, 4.4, 7.9
HbA1c > 6.5 (n, %)	7 (25%)

of CAMPs applications per wound was 7 (range 2-15). The median duration of CAMP treatment course was 42.5 days (7-97).

Wound healing efficacy outcome

AmnioBurgeon treatment in conjunction with sharp debridement, tissue cultures, moist wound healing, offloading measures, patient adherence, nutrition, smoking cessation and sufficient vascularization resulted in an overall favorable outcome in LEDUs which were previously unsuccessful with SOC alone (*Table 3*). Of the 28 wounds, 18 (64%) achieved more than ≥50% reduction in wound area. The median time to ≥50% reduction was 21 days (range 7-60) and required a median of 4 (range 2-10) CTP applications. A wound area reduction of at least 50% after 28 days of treatment is a strong predictor of potential complete wound closure, which was observed in 13 (46%) wounds. This

TABLE 3 | Wound healing efficacy outcomes

Completely healed wound (%)	4 (14%)
Complete healing time (days) (Mean±SD, Median, Min, Max)	78±20, 77, 56, 103
Number of CTP placement encounters for completely healed wound (Mean±SD, Median, Min, Max)	8.3±1.3, 8.0, 7.0, 10.0
Partial healed wound (>=50%)	18 (64%)
>=50% reduction by day 28 (%)	13 (46%)
Partial healed time (days) (Mean±SD, Median, Min, Max)	25±13, 21, 7, 60
Number of CTP placement encounters for partial healed wound (Mean±SD, Median, Min, Max)	4.6±2.0, 4.0, 2.0, 10.0
No response (<25% reduction or increased size) (%)	5(17%)
Duration of CTP placement (Mean±SD, Median, Min, Max)	41.4±24.9, 42.5, 7.0, 97.0
Number of CTP placement encounters (Mean±SD, Median, Min, Max)	6.6±3.3, 7.0, 2.0, 15.0
Time until max PAR** (Mean±SD, Median, Min, Max)	40.9±26.5, 38.5, 7.0, 103.0
Duration between CTP treatments (days) (Mean±SD, Median, Min, Max)	7.1±0.7, 7.0, 6.0, 9.0
Infections (n, %)	4 (14%)

result showed a substantial early response to the treatment. AmnioBurgeon treatment resulted in complete wound closure in 4 (14%) wounds. The median time to complete healing was 77 days (range 56-103) and required a median of 8 applications. 'No response' (< 25% reduction or increased size) was noted only in 5 (18%) wounds and was possibly due to risk factors and other underlying comorbidities such as advanced age, non-adherence, obesity and a history of recurring wounds.

Wounds were divided wound area size into three groups based on their baseline: <10 cm2, 10-<25 cm2, ≥ 25 cm2. After 28 days of treatment, there was no significant association between baseline wound size and the likelihood of achieving ≥50% reduction in wound area (*Figure 1*). Similarly, there is no statistically significant difference in the treatment time required for ≥50% reduction in wound area across the three groups. Infections were rare with only 4 (14%) wounds exhibiting signs and symptoms of infection and were discontinued CAMPs treatment.

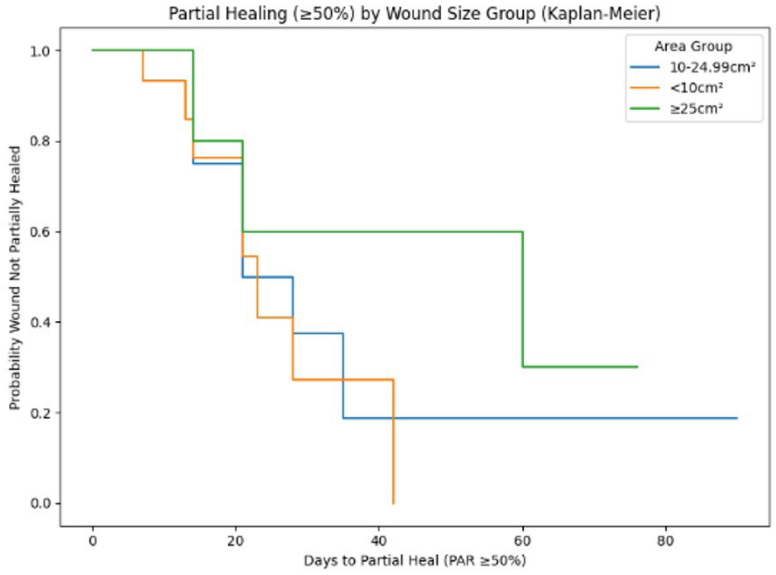

FIGURE 1 | Kaplan-Meier analysis; No Correlation between probability of partial healing and wound size .

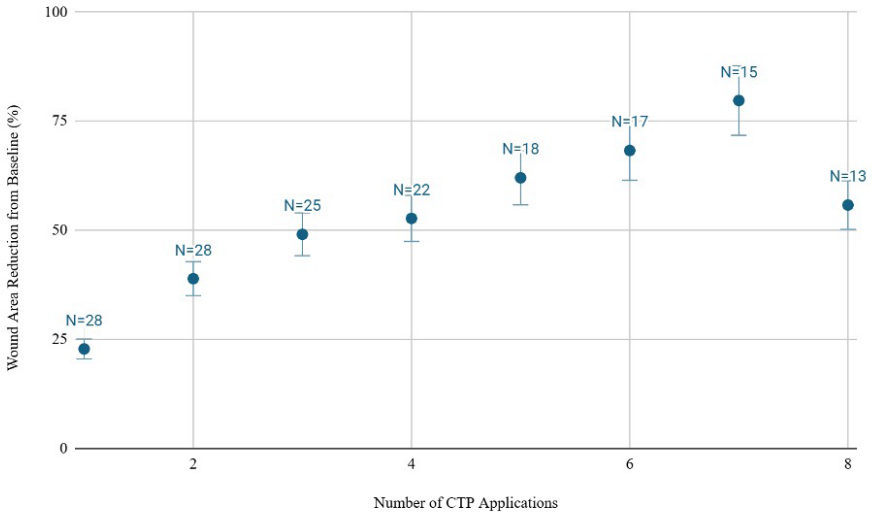

FIGURE 2 | Wound area reductions correlate with CTP application. Area reduction relative to initial wound area at first treatment. Measurement was performed before each CTP application.

To determine the best schedule and frequency of AmnioBurgeon treatment application, we studied the correlation between CAMPs application and wound size reduction (*Figure 2*). As expected, wound size reduction was correlated with CAMP application but not in a linear association. The most benefit was observed within four CAMPs applications, and the majority of wounds achieved partial reduction after four applications.

Discussion

LEDUs are a major healthcare problem affecting 40-60 million patients worldwide causing a high morbidity and mortality rate.[20] The 5-year mortality rate of patients with LEDUs ranges from 30% to 70% based on severity of amputation.[6] Patients with LEDUs also have a high morbidity rate, as it is a leading cause of lower extremity amputation with an incidence of 20% and high recurrence.[20] It is noteworthy to mention that LEDU-related amputations are preventable by 49 to 85% with early intervention and advanced therapies such as CAMPs treatment.[21] This supports the development of new preventive and treatment measures for LEDUs.

In addition to the SOC, skin substitute products including CAMPs/CTPs are increasingly incorporated into wound-healing treatments.[9,10] Poor healing is not the only challenge of LEDUs, infection, as prolonged hospitalization, and amputation are among other complications. Significantly, the post-acute care (PAC) patient population faces many challenges to healing with risk factors such as advanced age and other underlying comorbidities that delay wound healing.

CAMP treatments can provide a scaffold and protective layer for the wound, while stimulating the formation of new dermal tissue.[9,10] Multiple layers of evidence have demonstrated beneficial effects on wound healing, complication rates, and overall outcomes.[11-18] Studies comparing adjunctive treatment with cellular therapy and SOC compared to SOC alone have demonstrated improved outcomes with reduced amputations, emergency visits and hospitalizations.[21] In the first year following administration of CAMPs treatment, Tettelbach et al, found savings of $3,670 per LEDU patient and five-year net savings of $5,003.[22]

Many studies have shown better outcomes of LEDU treatment using these approaches compared to SOC alone, even in hard-to-heal wounds.[23] In a real-world evidence crossover study, in patients treated with human reticular acellular dermal matrices (HR-ADM), 83% achieved completed wound healing within an average time of 21 days compared to the SOC group.[23] The healing time was also significantly faster. These findings have been supported by other clinical studies that confirm higher closure rates, fewer complications, and lower recurrence.[11-17,24]

In this retrospective analysis, we studied the effect of AmnioBurgeon on wound healing outcomes in patients with LEDUs. We measured the effect of AmnioBurgeon across 28 wounds that were not successful with conservative treatment alone. AmnioBurgeon was found to result in complete wound healing in 14% of wounds and a wound size reduction of 50% or more at 4 weeks in 46% of patients. This is a strong predictor of complete healing at 12 weeks[25,26] and it serves as a valid endpoint in chronic wound management.[25,26]

In the studied cases, 18% had no response (<25% reduction or increase size). In addition to inherent poor wound

healing caused by the complications of diabetes, studies found several factors involved in healing-resistant wounds.[27] This includes the degree of ischemia as blood supply and perfusion is vital for wound healing process. Furthermore, loss of sensation (neuropathy) and being negligent of self-care practices can lead to more mechanical stress and pressure which will aggravate the ulcer.[27] In addition, severity of infection, causative microbiome and infectious agents also play a role.[27] Other studies identified blood biomarker to predict hard-to-heal wounds such as severity of of hyperglycemia, and levels of albumin and trace elements.[28] Additional biomarkers include inflammatory cytokines such as Chemokine (C-X-C motif) ligand 6 (CXCL6).[29] Furthermore, lack of adherence to therapy or incomplete treatment likely worsens outcomes. In our study, two out of five wounds that had not responded to treatment had received less than three applications of CAMP treatment. In four out of the five wounds that had not responded to treatment, patients had other risk factors such as advanced age and off-loading non-adherence and other comorbidities such as obesity and history of recurring wounds.

It is important to note that the baseline characteristics of our study population—particularly wound size and patient age—may have influenced healing outcomes. The median patient age in our study was 75 years, with a median baseline wound size of 8.9 cm², and 18% of wounds exceeding 25 cm². In contrast, other studies have included comparatively younger populations (mean age 55–60 years) and smaller baseline wounds (2–4 cm²), which may partly explain their higher reported healing rates.[24,30]

Study limitations
This study has several limitations. It was single-center retrospective study with a small sample size and no control group which could limit the generalizability of findings. Limited data on racial and ethnic diversity, variability in comorbidity conditions, and differences in patient adherence to therapy may also have influenced outcomes.

Conclusion
In this retrospective analysis, treatment with AmnioBurgeon demonstrated favorable outcomes in LEDUs that had failed to respond to standard care. Nearly two-thirds of treated wounds achieved ≥50% area reduction within 4 weeks, and complete healing occurred in a subset of cases despite advanced age and large baseline wound size. These findings support the clinical utility and safety of AmnioBurgeon as an adjunctive CAMP therapy for chronic, hard-to-heal diabetic ulcers. While outcomes were encouraging, interpretation is limited by the study's retrospective, single-center design, small sample size, and lack of control group. Further multicenter, prospective trials are warranted to validate efficacy, optimize treatment frequency, and identify patient characteristics most predictive of response.

Acknowledgments
Support in data collection, cleaning, validation and visualization: Mohsin Ansari; Hafsa Ahmed; Maham Khan; Maham Surtee; Naz Khan.

Conflicts of interest
The authors have no conflicts of interest to declare.

Data availability statement
Data is not publicly available.

Ethics approval and consent to participate
UNIVO IRB approval.

Author contributions
Ayesha Qadeer: Study design, data analysis and authorship; Emaad Basith: Medical expert and authorship; Martha R Kelso: Medical expert and authorship; Saad Mohsin: Medical expert and authorship; Rashad Sayeed: Study design, medical expert and authorship.

References
1. Deng X, Gould M, Ali MA. A review of current advancements for wound healing: Biomaterial applications and medical devices. J Biomed Mater Res B Appl Biomater. 2022;110(11):2542-2573. https://doi.org/10.1002/jbm.b.35086
2. Ozgok Kangal MK, Kopitnik NL. Physiology, Wound Healing. StatPearls. Treasure Island (FL) 2025. https://www.ncbi.nlm.nih.gov/books/NBK535406/ (accessed 30 October 2025)
3. Beckman JA, Creager MA. Vascular Complications of Diabetes. Circ Res. 2016;118(11):1771-1785. https://doi.org/10.1161/CIRCRESAHA.115.306884
4. Falanga V, Isseroff RR, Soulika AM, et al. Chronic wounds. Nat Rev Dis Primers. 2022;8(1):50. https://doi.org/10.1038/s41572-022-00377-3
5. Bowers S, Franco E. Chronic Wounds: Evaluation and Management. Am Fam Physician. 2020;101(3):159-166.
6. Armstrong DG, Tan TW, Boulton AJM, Bus SA. Diabetic Foot Ulcers: A Review. JAMA. 2023;330(1):62-75. https://

doi.org/10.1001/jama.2023.10578
7. Wolny D, Štěpánek L, Horáková D, Thomas J, Zapletalová J, Patel MS. Risk Factors for Non-Healing Wounds-A Single-Centre Study. J Clin Med. 2024;13(4):1003. Published 2024 Feb 9. https://doi.org/10.3390/jcm13041003
8. Hingorani A, LaMuraglia GM, Henke P, et al. The management of diabetic foot: A clinical practice guideline by the Society for Vascular Surgery in collaboration with the American Podiatric Medical Association and the Society for Vascular Medicine. J Vasc Surg. 2016;63(2 Suppl):3S-21S. https://doi.org/10.1016/j.jvs.2015.10.003
9. Vecin NM, Kirsner RS. Skin substitutes as treatment for chronic wounds: current and future directions. Front Med (Lausanne). 2023;10:1154567. Published 2023 Aug 29. https://doi.org/10.3389/fmed.2023.1154567
10. Protzman NM, Mao Y, Long D, et al. Placental-Derived Biomaterials and Their Application to Wound Healing: A Review. Bioengineering (Basel). 2023;10(7):829. https://doi.org/10.3390/bioengineering10070829
11. Serena TE, Yaakov R, Moore S, et al. A randomized controlled clinical trial of a hypothermically stored amniotic membrane for use in diabetic foot ulcers. J Comp Eff Res. 2020;9(1):23-34. https://doi.org/10.2217/cer-2019-0142
12. Zelen CM, Poka A, Andrews J. Prospective, randomized, blinded, comparative study of injectable micronized dehydrated amniotic/chorionic membrane allograft for plantar fasciitis--a feasibility study. Foot Ankle Int. 2013;34(10):1332-1339. https://doi.org/10.1177/1071100713502179
13. Zelen CM, Serena TE, Gould L, et al. Treatment of chronic diabetic lower extremity ulcers with advanced therapies: a prospective, randomised, controlled, multi-centre comparative study examining clinical efficacy and cost. Int Wound J. 2016;13(2):272-282. https://doi.org/10.1111/iwj.12566
14. Zelen CM, Serena TE, Snyder RJ. A prospective, randomised comparative study of weekly versus biweekly application of dehydrated human amnion/chorion membrane allograft in the management of diabetic foot ulcers. Int Wound J. 2014;11(2):122-128. https://doi.org/10.1111/iwj.12242
15. Schmiedova I, Dembickaja A, Kiselakova L, Nowakova B, Slama P. Using of Amniotic Membrane Derivatives for the Treatment of Chronic Wounds. Membranes (Basel). 2021;11(12):941. https://doi.org/10.3390/membranes11120941
16. Serena TE, Carter MJ, Le LT, Sabo MJ, DiMarco DT; EpiFix VLU Study Group. A multicenter, randomized, controlled clinical trial evaluating the use of dehydrated human amnion/chorion membrane allografts and multilayer compression therapy vs. multilayer compression therapy alone in the treatment of venous leg ulcers. Wound Repair Regen. 2014;22(6):688-693. https://doi.org/10.1111/wrr.12227
17. Penny H, Rifkah M, Weaver A, et al. Dehydrated human amnion/chorion tissue in difficult-to-heal DFUs: a case series. J Wound Care. 2015;24(3):104-111. https://doi.org/10.12968/jowc.2015.24.3.104
18. Carter MJ. Dehydrated human amnion and chorion allograft versus standard of care alone in treatment of Wagner 1 diabetic foot ulcers: a trial-based health economics study. J Med Econ. 2020;23(11):1273-1283. https://doi.org/10.1080/13696998.2020.1803888
19. Shah P, Inturi R, Anne D, et al. Wagner's Classification as a Tool for Treating Diabetic Foot Ulcers: Our Observations at a Suburban Teaching Hospital. Cureus. 2022;14(1):e21501. https://doi.org/10.7759/cureus.21501
20. McDermott K, Fang M, Boulton AJM, Selvin E, Hicks CW. Etiology, Epidemiology, and Disparities in the Burden of Diabetic Foot Ulcers. Diabetes Care. 2023;46(1):209-221. https://doi.org/10.2337/dci22-0043
21. Armstrong DG, Tettelbach WH, Chang TJ, et al. Observed impact of skin substitutes in lower extremity diabetic ulcers: lessons from the Medicare Database (2015-2018). J Wound Care. 2021;30(Sup7):S5-S16. https://doi.org/10.12968/jowc.2021.30.Sup7.S5
22. Tettelbach WH, Armstrong DG, Chang TJ, et al. Cost-effectiveness of dehydrated human amnion/chorion membrane allografts in lower extremity diabetic ulcer treatment. J Wound Care. 2022;31(Sup2):S10-S31. https://doi.org/10.12968/jowc.2022.31.Sup2.S10
23. Zelen CM, Orgill DP, Serena TE, et al. Human Reticular Acellular Dermal Matrix in the Healing of Chronic Diabetic Foot Ulcerations that Failed Standard Conservative Treatment: A Retrospective Crossover Study. Wounds. 2017;29(2):39-45.
24. DiDomenico LA, Orgill DP, Galiano RD, et al. Use of an aseptically processed, dehydrated human amnion and chorion membrane improves likelihood and rate of healing in chronic diabetic foot ulcers: A prospective, randomised, multi-centre clinical trial in 80 patients. Int Wound J. 2018;15(6):950-957. https://doi.org/10.1111/iwj.12954
25. Serena T, Yaakov S, Yaakov R, King E, Driver VR. Percentage area reduction at week 4 as a prognostic indicator of complete healing in patients treated with standard of care: a post hoc analysis. J Wound Care. 2024;33(Sup9):S36-S42. https://doi.org/10.12968/jowc.2024.0141
26. Sheehan P, Jones P, Caselli A, Giurini JM, Veves A. Percent change in wound area of diabetic foot ulcers over a 4-week period is a robust predictor of complete healing in a 12-week prospective trial. Diabetes Care. 2003;26(6):1879-1882. https://doi.org/10.2337/diacare.26.6.1879
27. Kumar A, Naik BN, Ojha VS, et al. Factors associated with severity and outcomes of diabetic foot ulcers: A single center hospital-based cross-sectional observational study in Eastern India. J Family Med Prim Care. 2025;14(4):1431-1436. https://doi.org/10.4103/jfmpc.jfmpc_1703_24
28. Lee SH, Kim SH, Kim KB, Kim HS, Lee YK. Factors Influencing Wound Healing in Diabetic Foot Patients. Medicina (Kaunas). 2024;60(5):723. https://doi.org/10.3390/medicina60050723
29. Qin Q, Haba D, Nakagami G. Which biomarkers predict hard-to-heal diabetic foot ulcers? A scoping review. Drug Discov Ther. 2024;17(6):368-377. https://doi.org/10.5582/ddt.2023.01086
30. Lavery LA, Fulmer J, Shebetka KA, et al. The efficacy and safety of Grafix(®) for the treatment of chronic diabetic foot ulcers: results of a multi-centre, controlled, randomised, blinded, clinical trial. Int Wound J. 2014;11(5):554-560. https://doi.org/10.1111/iwj.12329