Original Article

Efficacy of Platelet-Rich Fibrin in Non-Healing Ulcers: An Interventional Study

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Abstract

Background: Chronic non-healing ulcers are difficult to manage and may persist despite standard wound care. Platelet-rich fibrin (PRF) is an autologous biomaterial that may promote tissue repair through sustained growth-factor release. The objective is to evaluate the efficacy of PRF in chronic non-healing cutaneous ulcers of different etiologies. **Material and Methods:** This prospective single-arm interventional study included 30 patients with 44 ulcers; 42 ulcers with evaluable follow-up were analyzed. Autologous PRF was applied weekly for up to 6 weeks. Outcomes included complete re-epithelialization, serial ulcer-volume reduction, number of dressings, infection-related discontinuation, recurrence, and response according to ulcer etiology. **Results:** Complete re-epithelialization occurred in 38/42 ulcers (90.5%; 95% CI, 77.9%–96.2%) after a median of 3 dressings. All healed ulcers closed by the sixth dressing. Hansen disease-associated trophic ulcers achieved 95.8% healing. Healing status and number of dressings did not differ significantly across etiologies. Infection-related treatment abandonment occurred in 3 ulcers (7.1%), and recurrence was recorded in 6/39 evaluable ulcers (15.4%). **Conclusion:** Weekly autologous PRF was associated with rapid healing and a high re-epithelialization rate across varied chronic ulcer etiologies, although infection and recurrence remained important concerns.

Keywords: Platelet-rich fibrin; chronic ulcer; wound healing; re-epithelialization; Hansen disease.

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Introduction

Chronic non-healing ulcers are a major therapeutic challenge because they persist despite standard wound care and are associated with pain, recurrent infection, functional impairment, and substantial healthcare burden. They may arise from neuropathy, diabetes mellitus, vascular insufficiency, pressure, trauma, or chronic inflammatory and infectious conditions. Impaired progression through the normal phases of wound repair, together with persistent inflammation, protease excess, poor angiogenesis, cellular dysfunction, and microbial burden, contributes to delayed healing.[1,2]

Platelet-derived therapies have emerged as regenerative adjuncts for chronic wounds. Platelet-rich fibrin (PRF) is a second-generation autologous platelet concentrate prepared by centrifuging whole blood without anticoagulants or exogenous thrombin. It forms a three-dimensional fibrin matrix containing platelets, leukocytes, cytokines, and growth factors that may support angiogenesis, fibroblast proliferation, collagen synthesis, extracellular-matrix formation, and epithelial migration.[3–5] Because PRF is autologous, inexpensive, and easy to prepare, it is particularly attractive in resource-limited settings.

Experimental and clinical evidence suggests that PRF can enhance soft-tissue healing, accelerate epithelialization, and improve wound closure, although published studies remain heterogeneous in design and preparation technique.[6] Favorable outcomes have been reported in Hansen disease-associated trophic ulcers, with marked reductions in ulcer area and volume and complete closure after repeated applications.[7] Studies involving chronic ulcers of mixed etiologies have likewise shown progressive reduction in wound dimensions and high healing rates with serial PRF dressings.[8,9] However, most reports are limited by small samples, variable ulcer types, inconsistent outcome definitions, and short follow-up.

The present study was therefore undertaken to evaluate the efficacy of autologous PRF in chronic non-healing cutaneous ulcers of different etiologies. The primary objectives were to determine the proportion achieving complete re-epithelialization and to assess serial reduction in ulcer volume

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after weekly PRF application. Treatment exposure, infection-related discontinuation, recurrence, and response across etiologic groups were also examined.

Materials and Methods

Study design, setting, and ethics: This prospective, hospital-based, single-arm interventional study was conducted from 1 November 2024 to 31 October 2025 in the outpatient and inpatient services of the Departments of Dermatology, Venereology and Leprosy and Surgery at Jorhat Medical College and Hospital, Jorhat, Assam, India. The study protocol was approved by the Institutional Ethics Committee of Jorhat Medical College and Hospital. Written informed consent was obtained from all participants before enrollment.

Participants and recruitment: Patients presenting during the study period were assessed for eligibility and enrolled until the planned sample of 30 participants was reached. A non-healing ulcer was defined as a cutaneous ulcer persisting for more than 8 weeks despite conventional wound care. Eligible participants were older than 15 years, had a controlled or satisfactorily treated underlying disease, and agreed to participate.

Exclusion criteria were a bleeding diathesis or hematologic disorder; platelet count below 100,000/mm³; current antiplatelet or anticoagulant therapy, including aspirin, warfarin, or heparin; pregnancy or lactation; severe hypoproteinemia (serum protein <6 g/dL); an ulcer with exposed bone, muscle, or tendon; or refusal to provide consent. Thirty participants with 44 ulcers entered the study. Ulcers with evaluable follow-up data were included in the final analysis, and the ulcer was the unit of analysis.

Baseline evaluation: A detailed history and general, systemic, and cutaneous examination were performed at enrollment. Ulcer etiology, anatomical site, dimensions, depth, wound-bed characteristics, and surrounding skin findings were documented. Baseline investigations included hemoglobin, total and differential leukocyte counts, platelet count, random blood glucose, serum total protein and albumin, HIV and hepatitis B surface antigen screening, and pus culture and antimicrobial susceptibility testing when clinically indicated.

Preparation and application of platelet-rich fibrin: Autologous platelet-rich fibrin (PRF) was prepared under aseptic conditions using a single-spin technique. Venous blood was collected into sterile plain tubes without anticoagulant and centrifuged immediately at 3000 rpm (approximately 704 g at a 7-cm rotor radius) for 10 minutes. Centrifugation produced an upper platelet-poor plasma layer, a middle PRF clot, and a lower red-cell layer. The PRF clot was removed with sterile instruments, retaining a thin portion of the red-cell interface.

The ulcer was irrigated with normal saline, the surrounding skin was cleansed with povidone-iodine, and devitalized tissue was debrided when required. PRF was placed directly over the ulcer bed and covered with a non-adherent sterile dressing and roller bandage. Participants were advised to avoid weight bearing on the treated limb for 1-2 days when applicable. PRF was applied at baseline and repeated at weekly visits according to the healing response, with scheduled assessments through week 6.

Ulcer measurement and follow-up: Ulcer length and width were measured along the greatest perpendicular axes, and depth was measured at the deepest point. Ulcer area was calculated using the ellipse formula (length x width x 0.7854), and ulcer volume was calculated as area x depth. Measurements were recorded at baseline and immediately before each subsequent PRF application. Standardized clinical photographs were obtained at the same assessments.

At each weekly visit, the ulcer was assessed for necrotic tissue, granulation tissue, exudate, pain, clinical infection, and complete healing. The percentage reduction in volume after each treatment interval was calculated as [(previous volume - current volume) / previous volume] x 100. A negative value therefore represented an increase in volume. Complete re-epithelialization was defined as 100% epithelial coverage of the ulcer with no residual open area. Treatment was discontinued after complete re-epithelialization or when continued PRF application was not clinically appropriate. A final clinical review was scheduled 2 weeks after the last application; recurrence was recorded when breakdown occurred at a previously re-epithelialized site.

Outcomes: The efficacy outcomes were the proportion of ulcers achieving complete re-epithelialization and the recorded percentage reduction in ulcer volume after successive PRF dressings. Additional outcomes were the number of PRF dressings administered, infection-related treatment abandonment, and recurrence during follow-up. Outcomes were also compared across ulcer etiologies to address the prespecified objective of evaluating response in different types of non-healing ulcers.

Statistical analysis: Continuous variables were summarized using mean and standard deviation (SD) and, where appropriate, median, interquartile range (IQR), and range. Categorical variables were reported as n (%). The Wilson method was used to calculate 95% confidence intervals (CIs) for principal proportions. Cumulative complete re-epithelialization was summarized by the number of weekly PRF dressings.

Associations between ulcer etiology and categorical outcomes were evaluated using the Fisher-Freeman-Halton exact test because of sparse contingency-table cells; the corresponding Pearson chi-square statistic and degrees of freedom were also reported. The number of PRF dressings and dressing-specific percentage reductions were compared across etiologic groups using the Kruskal-Wallis H test. Session-specific numeric summaries included only ulcers with a recorded percentage value at that dressing; status entries denoting complete healing or treatment abandonment were not treated as numeric reductions. Missing observations were not imputed, and available-case denominators were stated for each outcome.

All tests were two-sided, and $p < 0.05$ was considered statistically significant. Analyses were performed using SPSS version 24.

Results

Thirty patients with 44 chronic cutaneous ulcers were enrolled.

Two ulcers were lost to follow-up, leaving 42 ulcers for final analysis. Because treatment response was recorded for each ulcer, all analyses were conducted at the ulcer level.

Study population and baseline ulcer characteristics

The median age was 50 years (interquartile range [IQR], 30-64.75), and 23 (54.8%) ulcers occurred in female patients. Hansen disease-associated trophic ulcers constituted the largest etiologic group, and the right foot was the most frequent anatomical site. Baseline demographic and ulcer characteristics are presented in [Table 1].

Table 1: Baseline demographic and ulcer characteristics (N = 42 ulcers)

Characteristic	Value	Characteristic	Value
Age, years: mean ± SD	48.64 ± 20.23	Baseline ulcer volume, mm³: mean ± SD	1204.43 ± 1548.82
Age, years: median (IQR)	50 (30-64.75)	Baseline ulcer volume, mm³: median (IQR)	616.90 (212.06-1458.79)
Age, years: range	16-80	Baseline ulcer volume, mm³: range	39.27-7938.24
Sex: female	23 (54.8%)	Sex: male	19 (45.2%)
Etiology	n (%)	Anatomical site	n (%)
Hansen disease	24 (57.1%)	Right foot	22 (52.4%)
Post-traumatic ulcer	5 (11.9%)	Left foot	7 (16.7%)
Pressure ulcer	4 (9.5%)	Left hand	3 (7.1%)
Diabetic foot ulcer	3 (7.1%)	Left ankle	3 (7.1%)
Arterial ulcer	3 (7.1%)	Right ankle	3 (7.1%)
Venous ulcer	2 (4.8%)	Right leg	3 (7.1%)
Necrolytic acral erythema	1 (2.4%)	Right hand	1 (2.4%)

Values are n (%) unless otherwise indicated. IQR, interquartile range; SD, standard deviation.

Treatment exposure and overall clinical response: Ulcers received a median of 3 weekly platelet-rich fibrin (PRF) dressings (IQR, 2-4). Complete re-epithelialization was achieved in 38 (90.5%) ulcers (95% confidence interval [CI], 77.9%-96.2%). The cumulative proportion healed increased with successive dressings, and all 38 healed ulcers reached the endpoint by the sixth dressing [Figure 1]. Infection-related treatment abandonment occurred in 3 (7.1%) ulcers, and recurrence was recorded in 6/39 (15.4%) evaluable ulcers [Table 2].

Table 2: Treatment exposure and overall clinical outcomes

Domain	Outcome measure	Result	95% CI
Treatment exposure	PRF dressings, mean ± SD	3.29 ± 1.42	-
Treatment exposure	PRF dressings, median (IQR)	3 (2-4)	-
Treatment exposure	PRF dressings, range	1-7	-
Clinical response	Complete re-epithelialization	38/42 (90.5%)	77.9%-96.2%
Clinical response	Not completely re-epithelialized	4/42 (9.5%)	3.8%-22.1%
Safety	Infection-related treatment abandonment	3/42 (7.1%)	2.5%-19.0%
Follow-up	Recurrence	6/39 (15.4%)	7.2%-29.7%

Confidence intervals for proportions were calculated using the Wilson method. The recurrence denominator comprises ulcers with an observed recurrence status.

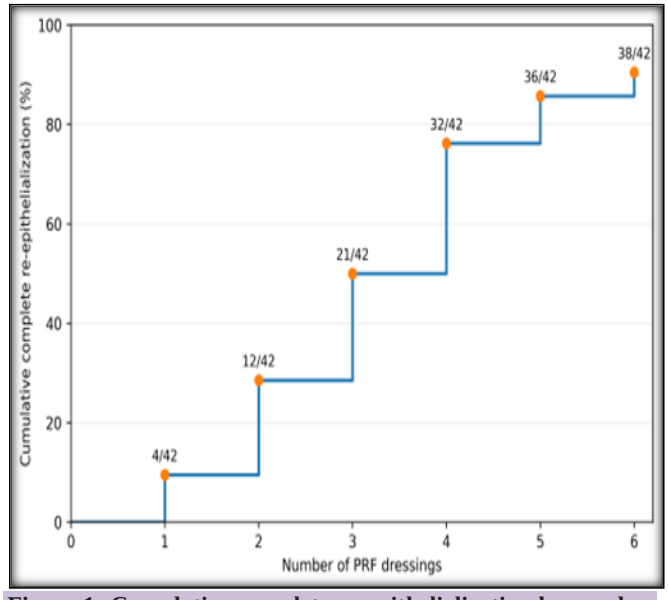

Figure 1: Cumulative complete re-epithelialization by number of weekly PRF dressings. Labels show the cumulative number healed among 42 analyzed ulcers.

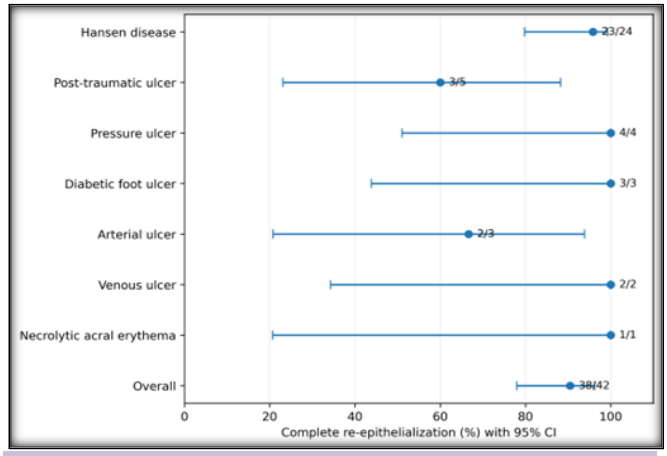

Figure 2. Complete re-epithelialization according to ulcer etiology. Points indicate proportions, error bars indicate Wilson 95% confidence intervals, and labels show n/N.

Clinical response according to ulcer etiology

Complete re-epithelialization ranged from 3/5 (60.0%) in post-traumatic ulcers to 100% in pressure ulcers, diabetic

foot ulcers, venous ulcers, and necrolytic acral erythema. Healing status was not significantly associated with ulcer etiology ($\chi^2[6] = 9.22$; Fisher-Freeman-Halton exact p = 0.149). The number of PRF dressings also did not differ significantly among etiologic groups (Kruskal-Wallis H,[6] = 7.25; p = 0.298). Etiology-specific outcomes are detailed in Table 3 and the healing estimates with 95% CIs are displayed in [Figure 2].

Table 3: Treatment outcomes according to ulcer etiology

Etiology	Ulcers, n (%)	Complete re-epithelialization, n/N (%)	Infection-related abandonment, n/N (%)	Recurrence, n/N (%)	PRF dressings, median (IQR)
Hansen disease	24 (57.1%)	23/24 (95.8%)	1/24 (4.2%)	3/23 (13.0%)	3 (2-4)
Post-traumatic ulcer	5 (11.9%)	3/5 (60.0%)	2/5 (40.0%)	0/3 (0.0%)	3 (3-4)
Pressure ulcer	4 (9.5%)	4/4 (100.0%)	0/4 (0.0%)	1/4 (25.0%)	3 (2.75-3.25)
Diabetic foot ulcer	3 (7.1%)	3/3 (100.0%)	0/3 (0.0%)	0/3 (0.0%)	5 (4-5)
Arterial ulcer	3 (7.1%)	2/3 (66.7%)	0/3 (0.0%)	1/3 (33.3%)	4 (4-5.5)
Venous ulcer	2 (4.8%)	2/2 (100.0%)	0/2 (0.0%)	1/2 (50.0%)	2.5 (1.75-3.25)
Necrolytic acral erythema	1 (2.4%)	1/1 (100.0%)	0/1 (0.0%)	0/1 (0.0%)	2 (2-2)
Overall comparison	-	$\chi^2(6) = 9.22$; exact p = 0.149	$\chi^2(6) = 9.46$; exact p = 0.236	$\chi^2(6) = 4.24$; exact p = 0.483	H(6) = 7.25; p = 0.298

Categorical comparisons show the Pearson chi-square statistic with Fisher-Freeman-Halton exact p-values. PRF dressing counts were compared using the Kruskal-Wallis H test. Recurrence percentages use the observed follow-up denominator within each etiologic group.

Ulcer-volume reduction after PRF dressing

A reduction in ulcer volume was recorded from the first PRF dressing onward. Between-etiology comparisons of the recorded percentage reduction were not statistically significant at any evaluable dressing (all p > 0.05). Session-specific estimates and test statistics are presented in [Table 4].

Table 4: Recorded percentage reduction in ulcer volume after successive PRF dressings

Dressing	Numeric n	Mean ± SD, %	Median (IQR), %	Range, %	Kruskal-Wallis H (df)	p value
1	38	64.86 ± 35.52	76.15 (54.37-88.61)	-87.60 to 95.19	8.44 (6)	0.208
2	29	52.21 ± 25.16	50.10 (33.33-76.01)	11.61 to 97.32	8.85 (5)	0.115
3	18	66.89 ± 20.66	72.39 (61.64-79.17)	12.49 to 93.16	8.38 (5)	0.136
4	7	48.60 ± 33.56	59.23 (15.55-78.40)	10.39 to 82.69	1.02 (2)	0.601
5	3	68.45 ± 5.45	69.64 (66.07-71.42)	62.50 to 73.21	1.50 (1)	0.221
6	1	60.01	60.01 (60.01-60.01)	60.01 to 60.01	-	-

Numeric n is the number of ulcers with a recorded percentage value at that dressing. Kruskal-Wallis tests compared etiologic groups contributing numeric values. No comparison was performed at dressing 6 because only one etiologic group contributed a numeric value.

Discussion

In this prospective single-arm study, autologous platelet-rich fibrin (PRF) was associated with substantial healing across chronic ulcers of varied etiologies. Complete re-epithelialization occurred in 38 of 42 ulcers (90.5%), typically after three weekly dressings, and all healed ulcers reached closure by the sixth dressing. Healing status and dressing requirements did not differ significantly by etiology. Hansen disease-associated trophic ulcers, which constituted more than half of the cohort, achieved a 95.8% closure rate. However, infection led to treatment abandonment in 7.1%, and recurrence occurred in 15.4% of evaluable ulcers, indicating that successful epithelialization does not eliminate the need for infection control, pressure relief, and continued etiologic management.

The overall response compares favourably with controlled evidence in venous ulcers. Somani and Rai randomized patients with chronic venous leg ulcers to PRF or saline dressings and reported progressive area reductions of 26.27%, 46.25%, 77.08%, and 85.51% after four weekly PRF applications. The corresponding final reduction with saline was 42.74%, and complete closure occurred in 55.6% of PRF-treated ulcers but in none of the controls.[10] Our higher complete-healing proportion may reflect longer treatment exposure, inclusion of several smaller ulcers, and the predominance of neuropathic trophic ulcers rather than exclusively venous disease.

Singampalli et al. similarly randomized 50 patients to weekly PRF or saline dressings for six weeks. Baseline wound areas were 14.95 and 13.28 cm², respectively; at six weeks, these had decreased to 1.59 cm² with PRF and 11.08 cm² with saline. Mean area reduction was 89.3% versus 16.5%, with a highly significant between-group difference.[11] These findings support a treatment effect beyond repeated cleansing and dressing alone. Our study extends this evidence by examining complete re-epithelialization, recurrence, and response across seven etiologic categories rather than limiting assessment to lower-limb area reduction.

Evidence from mixed-etiology cohorts also resembles our results. Dorjay and Sinha treated 18 ulcers caused by leprosy, neuropathy, venous disease, diabetes, trauma, and graft-site breakdown. Mean ulcer area was 8.44 cm², mean duration was 5.55 months, and complete healing required three to nine weekly applications, with a mean of five sessions; no treatment-

related adverse events were reported.[12] Our cohort was larger, received a lower median of three dressings, and achieved closure by six applications in all successfully treated ulcers. Differences in initial wound dimensions and etiologic composition may explain the shorter treatment exposure in our series.

The response among Hansen disease-associated ulcers is particularly relevant. Dorjay et al. studied trophic ulcers in patients with Hansen disease and reported a mean age of 44.3 years, mean ulcer duration of 7.4 months, and mean baseline area of 6.25 cm². Ulcer area decreased significantly after the third weekly PRF application, and all ulcers healed within six weeks.[13] Our 95.8% closure rate in Hansen disease-associated ulcers is concordant with these findings, although one ulcer did not heal and recurrence occurred in 13.0% of evaluable healed ulcers. This difference highlights the persistent influence of sensory loss, repetitive trauma, deformity, and inadequate off-loading after apparent closure.

Comparative evidence suggests that the fibrin matrix itself may provide clinically relevant advantages. Gehlawat et al. randomized patients with non-healing leg ulcers to PRF matrix, platelet-rich plasma, recombinant human epidermal growth factor, or collagen particles. PRF produced faster healing at eight weeks, the mean time to complete closure was approximately four to five weeks, and 79.2% of ulcers achieved complete healing by 12 weeks; patient acceptability was also reported as favourable.[14] The rapid cumulative closure in our study, with half of ulcers healed by the third dressing and more than three-quarters by the fourth, is consistent with their observed early response.

Yuvasri and Rai compared PRF with Unna's paste in chronic venous leg ulcers. PRF produced an approximately 86% mean reduction in ulcer area, both groups improved during follow-up, and the between-group difference was not statistically significant despite the larger numerical response with PRF.[15] Their findings suggest that PRF should be interpreted as an adjunct rather than a replacement for cause-specific therapy, particularly compression in venous disease. In our study, both venous ulcers healed, but the denominator was too small to determine whether PRF performs differently in venous disease than in neuropathic, diabetic, pressure, or arterial ulcers.

More recent real-world evidence also supports benefit across heterogeneous wounds. Sharma et al. applied weekly PRF to chronic ulcers of different etiologies, using an average of two applications and a maximum of three. Daily healing rates ranged from 1.19% to 3.84% by Pressure Ulcer Scale for Healing score and from 1.78% to 5.89% by wound area; three wounds achieved complete closure during follow-up of up to ten weeks.[16] Their small case series emphasized functional recovery and feasibility in rehabilitation practice. Our study adds a larger ulcer-level analysis, confidence intervals for healing and recurrence, and formal comparisons across etiologies.

The early volume reduction observed after the first PRF application supports a rapid biological response, but the wide dispersion—including one negative value—shows that not every ulcer improves immediately. Infection, inadequate debridement, ischemia, repeated trauma, or measurement variability may account for early enlargement in selected wounds. The absence of significant differences in serial volume reduction among etiologies should also be interpreted cautiously because later dressing-specific analyses contained progressively fewer ulcers as wounds healed or treatment was discontinued.

Infection-related abandonment occurred predominantly among post-traumatic ulcers and contributed to their lower closure rate. PRF supplies a regenerative scaffold but does not substitute for drainage, antimicrobial treatment, debridement, vascular correction, glycemic control, compression, or off-loading. Similarly, recurrence after epithelialization was most frequent proportionally in the small venous and arterial subgroups. These findings emphasize that wound closure is an intermediate outcome; durable healing depends on correction of the underlying mechanical, vascular, neurological, or metabolic abnormality.

The study's strengths include prospective assessment, standardized PRF preparation, serial three-dimensional ulcer measurement, explicit definition of complete re-epithelialization, and inclusion of ulcers commonly encountered in regional practice, particularly Hansen disease-associated trophic ulcers. Ulcer-level analysis also captured outcomes for patients with multiple lesions.

Several limitations require consideration. The absence of a control group prevents attribution of healing exclusively to PRF, and concurrent debridement, dressings, off-loading, and treatment of underlying disease may have contributed. The sample was small, etiologic subgroups were uneven, and multiple ulcers from some participants may not have been statistically independent. Ulcer volume was estimated from linear measurements rather than planimetry or three-dimensional imaging. Follow-up after closure was brief, limiting assessment of late recurrence. Moreover, dressing-specific percentage reductions were based on available observations and may be influenced by informative attrition because rapidly healed ulcers no longer contributed numeric measurements.

Conclusion

Weekly autologous PRF application was associated with rapid volume reduction and a high rate of complete re-epithelialization in chronic ulcers of varied etiologies, including Hansen disease-associated trophic ulcers. The procedure was feasible and required relatively few applications, but infection-related discontinuation and recurrence remained clinically important. Controlled studies with participant-level analysis, standardized co-interventions, objective wound imaging, and longer follow-up are needed to establish comparative effectiveness and durability.

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Conflicts of interest

There are no conflicts of interest.

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