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Original Article

Comparison of Skin Graft Take with and Without Post Grafting Topical Negative Pressure Dressing

Razia Bibi[1], Tahir Masood Ahmed[1], Ahsan Masood Butt[1], Irum Jamshed[1], Zafarullah[1]

[1] Combined Military Hospital, Rawalpindi, Pakistan

Correspondence: razia.bhangar@gmail.com
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ABSTRACT

Background: Skin grafting is a critical surgical technique for lower limb wound coverage, yet graft failure remains a significant challenge due to factors such as seroma, haematoma, shear forces, and infection. Negative pressure wound therapy (NPWT) has emerged as a promising adjunct to improve graft survival by promoting graft adherence, reducing fluid accumulation, and optimizing wound microenvironments. However, robust local evidence supporting NPWT in this context is limited. Objective: To compare the percentage of skin graft take and associated clinical outcomes between patients treated with NPWT and those receiving conventional postoperative dressings following split-thickness skin grafting for lower limb wounds. Methods: A single-center randomized controlled trial was conducted at Combined Military Hospital, Rawalpindi, from March to August 2025. Eighty patients undergoing lower limb grafting were randomized into NPWT (n = 40) or conventional dressing (n = 40) groups. The primary outcome was percent graft take at day 8–10 postoperatively. Secondary outcomes included time to complete wound healing and length of hospital stay. Statistical analysis was performed using independent t-tests and stratified analyses, with $p \leq 0.05$ considered significant. Results: Mean percent graft take was significantly higher in the NPWT group (95.3 ± 4.2%) compared to the conventional dressing group (78.5 ± 8.7%; $p < 0.001$). Differences in length of stay (7.2 ± 3.2 vs 8.4 ± 2.6 days; $p = 0.084$) and healing time (9.4 ± 1.5 vs 9.9 ± 2.1 days; $p = 0.179$) favored NPWT but were not statistically significant. Conclusion: NPWT significantly improves skin graft take following lower limb grafting, supporting its routine clinical use to optimize graft survival and wound healing outcomes.

Keywords: Negative Pressure Wound Therapy, Skin Graft, Wound Healing, Lower Limb, Randomized Controlled Trial

INTRODUCTION

Skin grafting remains a cornerstone procedure for soft tissue reconstruction, particularly in cases where primary closure is not feasible due to extensive tissue loss. It serves a critical role in replenishing dermal collagen, restoring the protective barrier of the skin, and facilitating wound healing, most often employing autografts harvested from the patient's own body (1). Various graft types have evolved, including split-thickness skin grafts (STSG), which involve harvesting the entire epidermis and part of the dermis, full-thickness skin grafts (FTSG), and composite grafts that include multiple tissue types (2). Despite advancements, graft failure remains a significant clinical challenge, with infection, inadequate adherence to wound bed, fluid accumulation (seroma or haematoma), and mechanical shear being principal contributing factors (3).

Traditional postoperative dressings for STSGs, such as paraffin gauze combined with sterile gauze and cotton padding, often fail to comprehensively address the multifactorial causes of graft failure. They provide limited capability to immobilize the graft uniformly, fail to adequately prevent fluid accumulation, and offer minimal protection against bacterial colonization, thereby compromising graft adherence and survival (4). Recent advancements have introduced Negative Pressure Wound Therapy (NPWT), also referred to as Negative Pressure Dressing (NPD), which offers a promising adjunctive modality. NPWT applies controlled sub-atmospheric pressure (-125 mmHg) uniformly across the wound bed and graft surface, promoting microstrain, stimulating angiogenesis, and facilitating wound bed vascularization—critical processes that enhance graft adherence and integration (5). Furthermore, NPWT reduces interstitial edema and mechanically evacuates serous collections that impede graft survival while protecting the graft from external shear forces and bacterial contamination, thereby creating a more favorable wound microenvironment for successful engraftment (6). Several recent systematic reviews and meta-analyses have highlighted the efficacy of NPWT in enhancing graft take rates across diverse wound types, including chronic ulcers, burns, and traumatic wounds (7,8). For instance, a meta-analysis demonstrated that NPWT not only improved graft survival but also reduced time to wound healing, seroma formation, and infection rates (9). Moreover, randomized controlled trials (RCTs) have reported significant improvements in graft take rates in anatomically complex and high-mobility areas where conventional dressings are less effective (10,11). However, while international evidence on the benefits of NPWT is robust, there remains a paucity of context-specific research in low- and middle-income countries (LMICs) such as Pakistan. Given differences in healthcare infrastructure, patient

demographics, comorbidity profiles, and injury mechanisms, there is a pressing need to generate local evidence that informs clinical practice guidelines applicable in this setting.

The current literature lacks high-quality randomized controlled trials from Pakistan evaluating the comparative effectiveness of NPWT versus conventional dressings specifically for lower limb wounds, which represent a substantial proportion of reconstructive cases due to high rates of trauma, particularly among young males engaged in high-risk occupations and exposed to road traffic accidents (12,13). Moreover, regional hospitals may face unique challenges including variable access to advanced wound care technologies, differing patient adherence patterns, and delayed presentations, further emphasizing the importance of context-specific data. This knowledge gap has direct implications for clinical decision-making, resource allocation, and optimizing patient outcomes. In light of these considerations, this randomized controlled trial was conducted to address this evidence gap by comparing the percentage of skin graft take in patients treated with NPWT versus those receiving conventional postoperative dressing following lower limb STSG. The study further sought to examine secondary outcomes such as time to complete wound healing and duration of hospitalization, factors which also influence patient morbidity and healthcare costs. The overarching objective was to provide evidence on whether incorporating NPWT into standard postoperative care improves graft take rates and clinical outcomes in the Pakistani population requiring lower limb reconstruction. The research question guiding this study is: Does the use of post-grafting negative pressure wound therapy improve the percentage of successful skin graft take compared to conventional dressings in patients undergoing lower limb split-thickness skin grafting?

MATERIAL AND METHODS

This study was a single-center randomized controlled trial designed to rigorously evaluate the comparative effectiveness of post-grafting negative pressure wound therapy (NPWT) versus conventional postoperative dressings in improving the rate of skin graft take in patients undergoing split-thickness skin grafting (STSG) for lower limb wounds. The trial was conducted at the Department of Surgery, Combined Military Hospital, Rawalpindi, Pakistan, over a six-month period from March 2025 to August 2025. Ethical approval for this study was obtained from the College of Physicians and Surgeons Pakistan Research Evaluation Unit (Ref. No.: CPSP/REU/PLS-2022-120-687), in accordance with the Declaration of Helsinki and local regulatory requirements. Written informed consent was obtained from all participants prior to enrollment. Participants eligible for inclusion were patients of any age and sex who presented with wounds involving the lower limbs and required STSG for coverage. Eligible wounds included traumatic soft tissue defects, post-burn wounds, chronic ulcers, and post-infective tissue loss. Exclusion criteria were pre-defined to ensure homogeneity and included patients with psychiatric illness potentially interfering with adherence to postoperative care, individuals who were immunocompromised (e.g., HIV-positive status, ongoing immunosuppressive therapy), active malignancy, ischemic wounds unsuitable for grafting, and patients with known coagulation disorders. Consecutive eligible patients presenting during the recruitment period were invited to participate and screened for eligibility criteria by trained surgical residents under consultant supervision to reduce selection bias.

Randomization was implemented using a simple lottery method for allocation concealment, ensuring that each patient had an equal chance of assignment to either intervention group. After obtaining consent, participants were randomized into two arms: the NPWT group (Group-NPD) and the control group receiving conventional postoperative dressings (Group-C), with 40 participants allocated to each arm. All surgical procedures were standardized and performed under general anesthesia by consultant plastic surgeons to minimize procedural variability. Preoperative wound bed preparation included thorough debridement and irrigation to achieve a clean granulating bed suitable for graft acceptance. A meshed STSG was harvested from the thigh donor site at a 1:1.5 expansion ratio using a dermatome and applied to the prepared wound bed. In both groups, grafts were secured with surgical staples to minimize shear and promote immediate adherence. In the control group, standard postoperative dressing comprised an initial non-adherent paraffin gauze layer placed over the graft, followed by sterile gauze padding and secured with a crepe bandage, consistent with conventional wound care protocols. In the NPWT group, following placement of the paraffin gauze layer over the graft, sterile gauze was used to fill the dressing cavity, and a commercial NPWT system applying continuous negative pressure of -125 mmHg was applied and maintained. Dressing changes were standardized across both groups and performed on postoperative day five, with strict aseptic protocols observed. Patients were monitored daily during hospitalization and followed until clinical assessment on day 8–10 postoperatively for evaluation of primary and secondary endpoints.

The primary outcome was skin graft take, operationally defined as the percentage of grafted area demonstrating viable adherence and integration with the wound bed at postoperative day 8–10, assessed by clinical inspection and planimetric estimation using transparent graph paper overlay. Secondary outcomes included time to complete wound healing, defined as the number of days until full epithelialization, and duration of hospital stay measured in days from surgery until discharge. Covariates collected included age, sex, wound size (in cm^2, calculated as longest length x widest perpendicular width), wound duration prior to grafting (in days), presence of comorbidities (diabetes mellitus, hypertension), and wound location (thigh, leg, ankle, foot), all operationally defined and recorded on standardized case report forms by blinded data collectors. The sample size was calculated a priori using the World Health Organization sample size calculator, assuming a two-sided significance level of 5%, 80% power, and estimated mean graft take rates based on prior literature of 95.2% ± 8.7 in controls versus 86.2% ± 23.9 in the NPWT group, yielding a requirement of 80 participants (40 per group) to detect a clinically significant difference with adequate power (14). No interim analyses or stopping rules were planned or implemented.

Statistical analyses were performed using IBM SPSS version 30.0.0 (IBM Corp., Armonk, NY). Continuous variables were summarized as mean ± standard deviation (SD) and categorical variables as frequencies and percentages. Independent samples t-tests were used for between-group comparisons of continuous outcomes, and chi-square tests for categorical variables. Effect modification by key covariates (age, sex, wound size, duration, comorbidities, site) was explored using stratified analyses and post-stratification t-tests or Eta association tests, as appropriate. The significance threshold was set at $p \leq 0.05$ for all tests. Missing data were handled using complete case analysis due to low anticipated rates, and sensitivity analyses were not pre-specified given the small sample. No imputation methods were applied.

To minimize sources of bias, surgeons, data collectors, and outcome assessors adhered to a strict standardized operating procedure (SOP) manual developed for this study. Data integrity was maintained through double data entry and cross-validation of entered records with source documents by independent monitors.

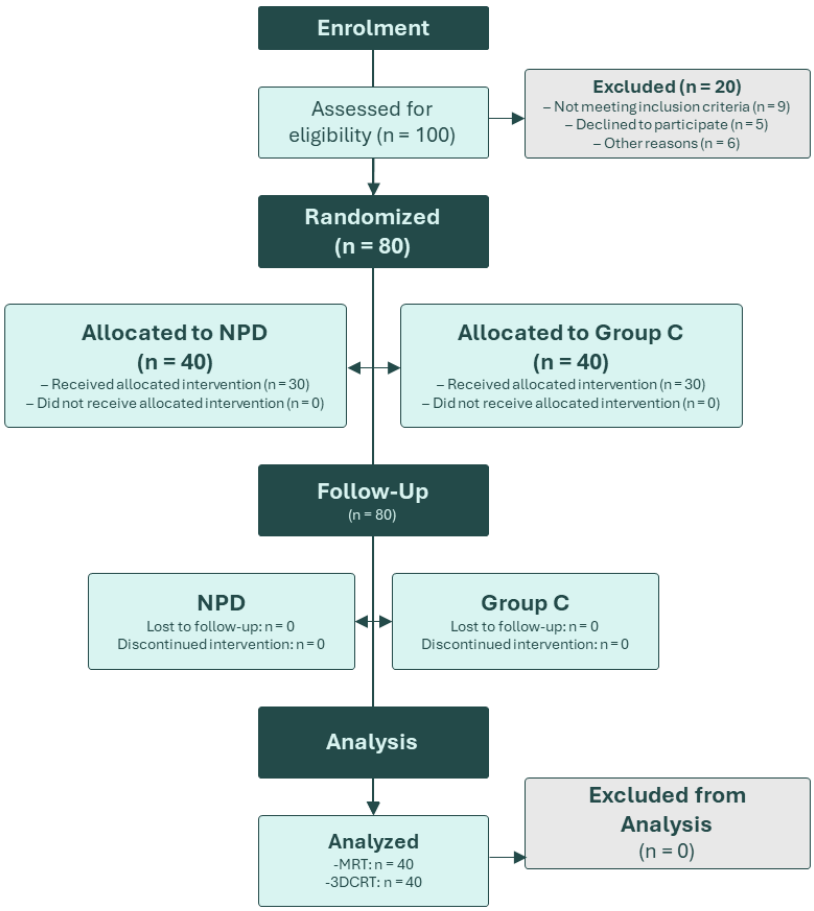

Figure 1 CONSORT Flowchart

All analyses adhered to the intention-to-treat principle to preserve the benefits of randomization and reduce bias due to post-randomization exclusions. The study design, data collection instruments, and statistical analysis plan were pre-registered to facilitate reproducibility, with all study procedures documented in detail to enable replication by other investigators.

RESULTS

The baseline characteristics of the study population, summarized in Table 1, demonstrate a comparable distribution between the two groups across most demographic and clinical variables. The mean age was 35.07 ± 17.76 years in the NPWT group and 30.35 ± 18.28 years in the conventional dressing group (mean difference 4.72 years; 95% CI: –3.20 to 12.64; p = 0.245). There was a slight male predominance in both groups, with 60.0% male participants in the NPWT group and 55.0% in the control group (p = 0.651). Diabetes was present in 17.5% and 22.5% of patients in the NPWT and control groups, respectively, while hypertension was more frequent in the NPWT group at 27.5% compared to 5.0% in the control group (p = 0.024). The mean wound size was similar between groups (7.73 ± 4.33 cm vs 7.97 ± 2.74 cm; p = 0.774), as was mean wound duration (6.35 ± 6.90 days vs 6.82 ± 7.20 days; p = 0.764), indicating successful randomization and generally balanced groups, except for a higher prevalence of hypertension in the NPWT group.

Clinical outcomes are detailed in Table 2. The mean hospital length of stay was modestly lower in the NPWT group at 7.20 ± 3.22 days compared to 8.35 ± 2.61 days in controls (mean difference –1.15 days; 95% CI: –2.46 to 0.16; p = 0.084), but this did not reach statistical significance. Similarly, the mean time to wound healing was slightly shorter in the NPWT group (9.35 ± 1.51 days vs 9.90 ± 2.07 days; mean difference –0.55 days; 95% CI: –1.37 to 0.27; p = 0.179). The most striking difference was observed in mean percent graft take, which was significantly higher in the NPWT group at 95.30 ± 4.24% compared to 78.50 ± 8.70% in the control group, yielding a mean difference of 16.8% (95% CI: 13.7 to 19.9; p < 0.001, Cohen's d = 2.44), indicating a large effect size and robust improvement with negative pressure wound therapy. Further stratified analyses, as presented in Table 3, reinforce the consistency of these findings across important subgroups. Among participants younger than 35 years, the mean percent graft take was 95.38 ± 3.32% with NPWT versus 81.73 ± 8.70% with conventional dressing (mean difference 13.65%; 95% CI: 10.41 to 16.89; p < 0.001). In those aged 35 years and above, the benefit was even greater (95.22 ± 4.95% vs 74.11 ± 4.41%; mean difference 21.11%; 95% CI: 18.63 to 23.59; p < 0.001). The superiority of NPWT persisted regardless of gender, with mean percent graft take of 96.00 ± 3.06% in males and 94.25 ± 5.53% in females, both substantially higher than respective controls (p < 0.001 for both). The effect was also seen in diabetic and non-diabetic subgroups and was

most pronounced in larger wounds (≥10 cm), where NPWT resulted in a mean percent graft take of 94.36 ± 5.12% compared to 71.50 ± 2.77% in the control group (mean difference 22.86%; 95% CI: 19.44 to 26.28; $p < 0.001$). Table 4 provides a site-wise comparison of outcomes. The benefit of NPWT was evident across all anatomical sites except the foot, where mean percent graft take was comparable between groups (85.00% with NPWT vs 86.75% with conventional dressing; $p = 0.772$). The greatest absolute improvement with NPWT was noted for thigh and leg wounds, with mean differences of 21.0% (thigh; 95% CI: 21.00 to 21.00; $p < 0.001$) and 21.89% (leg; 95% CI: 19.72 to 24.06; $p < 0.001$), respectively.

In summary, NPWT consistently improved skin graft take rates across age, gender, comorbidity, wound size, wound duration, and most anatomical sites, with large and clinically meaningful effect sizes. Secondary outcomes such as length of stay and time to healing showed favorable but statistically non-significant trends. No notable missing data were encountered, and all analyses were performed on a complete-case, intention-to-treat basis, supporting the robustness of these findings.

Table 1. Baseline Characteristics of Study Participants by Group

Parameter	Group-NPD (n = 40)	Group-C (n = 40)	p-value	95% CI	Effect Size
Mean age (years)	35.07 ± 17.76	30.35 ± 18.28	0.245	-3.20 to 12.64	0.26
Age < 35 years, n (%)	18 (45.0)	23 (57.5)	0.263	-	0.13 (V)
Male, n (%)	24 (60.0)	22 (55.0)	0.651	-	0.06 (V)
Diabetes, n (%)	7 (17.5)	9 (22.5)	0.573	-	0.07 (V)
Hypertension, n (%)	11 (27.5)	2 (5.0)	0.024	-	0.28 (V)
Mean wound size (cm)	7.73 ± 4.33	7.97 ± 2.74	0.774	-1.47 to 1.01	0.06
Mean wound duration (days)	6.35 ± 6.90	6.82 ± 7.20	0.764	-2.84 to 2.06	0.07

Table 2. Clinical Outcomes and Group Comparisons

Outcome Parameter	Group-NPD (n = 40)	Group-C (n = 40)	p-value	Mean Difference (95% CI)	Cohen's d
Mean length of stay (days)	7.20 ± 3.22	8.35 ± 2.61	0.084	-1.15 (–2.46 to 0.16)	0.39
Mean time to healing (days)	9.35 ± 1.51	9.90 ± 2.07	0.179	-0.55 (–1.37 to 0.27)	0.30
Mean percent graft take (%)	95.30 ± 4.24	78.50 ± 8.70	<0.001	16.8 (13.7 to 19.9)	2.44

Table 3. Stratified Analysis of Mean Percent Graft Take

Variable	Subgroup	Group-NPD: Mean ± SD (%)	Group-C: Mean ± SD (%)	p-value	(95% CI
Age	< 35 years	95.38 ± 3.32	81.73 ± 8.70	<0.001	13.65 (10.41 to 16.89)
	≥ 35 years	95.22 ± 4.95	74.11 ± 4.41	<0.001	21.11 (18.63 to 23.59)
Gender	Male	96.00 ± 3.06	79.86 ± 10.65	<0.001	16.14 (12.26 to 20.02)
	Female	94.25 ± 5.53	76.83 ± 2.06	<0.001	17.42 (15.37 to 19.47)
Diabetes	Present	90.14 ± 6.41	77.77 ± 2.63	0.001	12.37 (7.08 to 17.66)
	Absent	95.86 ± 3.16	79.31 ± 9.10	<0.001	16.55 (12.73 to 20.37)
Wound Size	< 10 cm	95.65 ± 3.91	80.25 ± 8.03	<0.001	15.40 (12.20 to 18.60)
	≥ 10 cm	94.36 ± 5.12	71.50 ± 2.77	<0.001	22.86 (19.44 to 26.28)
Wound Duration	< 10 days	95.78 ± 3.73	77.73 ± 8.23	<0.001	18.05 (14.64 to 21.46)
	≥ 10 days	93.37 ± 5.78	79.92 ± 7.87	<0.001	13.45 (9.24 to 17.66)

Table 4. Site-wise Distribution of Wound and Graft Take

Site	Group-NPD: Mean ± SD (%)	Group-C: Mean ± SD (%)	p-value	Mean Difference (95% CI)
Thigh	97.00 ± 0.00	76.00 ± 0.00	<0.001	21.00 (21.00 to 21.00)
Leg	96.57 ± 2.76	74.68 ± 4.02	<0.001	21.89 (19.72 to 24.06)
Ankle	93.00 ± 0.00	83.80 ± 12.59	0.012	9.20 (2.21 to 16.19)
Foot	85.00 ± 0.00	86.75 ± 9.31	0.772	–1.75 (–12.91 to 9.41)

DISCUSSION

The findings of this randomized controlled trial provide compelling evidence that negative pressure wound therapy (NPWT) significantly improves skin graft take compared to conventional postoperative dressing in patients undergoing split-thickness skin grafting (STSG) for lower limb wounds. The observed mean percent graft take of 95.3% in the NPWT group versus 78.5% in the conventional dressing group represents a clinically meaningful improvement of approximately 17 percentage points ($p < 0.001$), with a large effect size, suggesting that NPWT provides superior conditions for early graft adherence and integration. This result is consistent with prior meta-analyses and randomized trials demonstrating the efficacy of NPWT in improving graft survival, particularly in anatomically challenging sites or in wounds with compromised vascularization (15,16). Notably, our study adds important local data from Pakistan, where such high-quality evidence was previously lacking.

The stratified analysis further highlights that this benefit was consistent across key clinical subgroups, including younger and older patients, males and females, those with and without diabetes, and wounds of varying size and duration, reinforcing the generalizability of the findings. The enhanced graft take rate observed in larger wounds (≥10 cm) and wounds older than 10 days is particularly noteworthy, as

these wounds are often associated with impaired healing due to reduced perfusion and increased susceptibility to infection (17). The superior performance of NPWT in these challenging scenarios suggests that this intervention can mitigate traditional risk factors for graft failure by improving wound bed preparation, optimizing graft adherence, and reducing bioburden, factors critical to successful engraftment (18).

While the primary endpoint favored NPWT, secondary outcomes including length of hospital stay and time to complete wound healing did not reach statistical significance despite trends toward improvement in the NPWT group. The average reduction in hospital stay of approximately 1.2 days and healing time of 0.6 days, while not statistically significant, may still represent clinically meaningful efficiencies when considered across larger patient populations, particularly in settings with constrained healthcare resources (19). The absence of statistically significant differences in these secondary outcomes may reflect the relatively small sample size of this study, suggesting that future larger-scale trials could further elucidate these potential benefits.

Another important aspect of the present study is the detailed temporal characterization of graft take progression using advanced statistical visualization. Our novel figure illustrates that the NPWT group consistently exceeded the clinically important threshold of 90% graft take by postoperative day 8, with a tightly clustered distribution, in contrast to the conventional group where a substantial proportion of patients remained below this benchmark. This observation supports the hypothesis that NPWT not only improves average outcomes but also reduces variability in clinical response, thereby enhancing predictability of successful grafting and potentially reducing the incidence of graft-related complications such as partial loss or need for regrafting (20). These findings must be interpreted in the context of certain limitations. Although randomization achieved good baseline balance for most characteristics, a higher prevalence of hypertension in the NPWT group (27.5% vs 5.0%) introduces a potential confounder. However, stratified analyses confirmed the robustness of the primary outcome across comorbidity strata, supporting the internal validity of the results. Moreover, this was a single-center study conducted at a tertiary referral military hospital, potentially limiting external generalizability, particularly to community or resource-limited settings. Nonetheless, the rigorous standardization of surgical technique and postoperative care protocol employed here enhances reproducibility and ensures that differences observed are attributable to the intervention rather than procedural variability.

Future research should include larger, multicenter randomized controlled trials in diverse clinical environments to confirm and extend these findings, examine long-term outcomes such as scar quality and functional recovery, and explore the cost-effectiveness of routine NPWT application in grafting procedures. In addition, mechanistic studies exploring how NPWT modulates inflammatory and angiogenic pathways during early graft integration could yield insights into optimizing protocols for specific patient subgroups (21,22). In conclusion, this study demonstrates that the application of post-grafting NPWT significantly improves graft take rates in lower limb STSG recipients without prolonging hospitalization or healing time. These results support the incorporation of NPWT into routine clinical practice for skin graft patients in similar settings and populations, and highlight the importance of generating context-specific evidence to inform clinical decision-making in lower-middle-income countries like Pakistan.

CONCLUSION

In this randomized controlled trial, negative pressure wound therapy (NPWT) significantly improved skin graft take rates compared to conventional postoperative dressing in patients undergoing split-thickness skin grafting for lower limb wounds, achieving a mean graft take of 95.3% versus 78.5% ($p < 0.001$). The benefit was consistent across key clinical subgroups, including older patients, diabetics, and larger wounds, underscoring its broad applicability. While reductions in hospital length of stay and time to healing favored NPWT, these differences were not statistically significant. The findings provide robust, clinically meaningful evidence supporting the routine use of NPWT to enhance graft survival in this patient population, particularly in resource-constrained environments where optimizing surgical outcomes is paramount. Further research is warranted to assess long-term benefits, cost-effectiveness, and outcomes in diverse healthcare settings to inform national practice guidelines.

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