Comparison between Split Thickness Graft and Split Thickness Graft with Nano Fat in Healing of Diabetic Foot

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Abstract:

Background: Split-thickness skin grafts (STSG) use epidermis and partial dermis, applied as mesh or conventional grafts. Nanofat, rich in stem cells and growth factors, aids regeneration. Diabetic foot ulcers remain challenging, needing debridement, dressings, and infection control, with high amputation and mortality risks**.**

Objectives: To compare STSG versus STSG with nanofat for diabetic foot ulcers regarding esthetic and clinical outcomes.

Patients and methods: This study was conducted at the Plastic Surgery Department, Qena University Hospital, Qena University on 15 cases. Each ulcer was divided into two halves: one treated with STSG alone and the other with STSG plus nanofat, allowing direct intra-patient comparison. STSG involved thigh grafting with meshing and nylon fixation. In the STSG and nanofat group, emulsified lipoaspirates were injected and applied before grafting. Outcomes were assessed weekly using BWAT, scar scales, and Doppler. The Doppler probe handle and cable were covered with sterile disposable sleeves intraoperatively to maintain asepsis.

Results: The mean age was 59.3±7.5 years; 53.3% were female. Diabetes was present in 66.7% and hypertension in 26.7%. Ulcers occurred on the distal leg (46.7%), dorsum (33.3%), and plantar surface (20%), with mean duration 5.2 weeks and graft size 39.7 cm^2. Nanofat with STSG significantly improved healing time (2.16±0.21 vs. 2.74±0.5 weeks, p=0.0006), BWAT scores (15.67±5.87 vs. 22.2±8.25, p=0.0019), and POSAS outcomes from both patients (1.87±0.81 vs. 3±1.26, p=0.0135) and observers (1.33±1.25 vs. 3.13±1.36, p=0.0021).

Conclusion: Nanofat with split-thickness skin grafts improved diabetic foot ulcer healing, complications, and BWAT/POSAS scores while enhancing scar outcomes.

Keywords: Split Thickness Graft; Nanofat, Diabetic Foot; BWAT/POSAS scores.

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Introduction

Split-thickness skin grafts (STSG) include the full epidermis and part of the dermis, making them one of the most widely used grafting techniques. They are classified into mesh grafts, primarily applied in burns and trauma, and conventional STSG, which is commonly used for skin defects and ulcer healing due to its effectiveness and practicality **(Jang, 2024).** Their versatility allows them to be used alone or processed into mesh grafts of different expansion ratios **(Alsaif et al., 2023).**

Nanofat, derived from adipose tissue through mechanical emulsification and filtration of lipoaspirates, contains stem cells and growth factors that promote skin regeneration **(Ding et al., 2022).** It has been successfully applied in regenerative medicine for scar attenuation, skin rejuvenation, and chronic ulcer treatment, though the precise molecular mechanisms underlying its regenerative effects remain unclear **(Sanchez-Macedo et al., 2022).**

Diabetic foot ulcers (DFU) represent a major clinical challenge requiring multidisciplinary management. Standard care involves ulcer debridement, appropriate dressings, and infection control with antibiotics when needed **(Monteiro-Soares et al., 2020).** DFU is a leading cause of non-traumatic lower limb amputation and carries a significantly increased mortality risk **(Wang et al., 2022).**

The aim of this study is to compare the effectiveness of split-thickness skin graft (STSG) alone versus split-thickness skin graft combined with nano fat in promoting ulcer healing, improving tissue quality, and reducing complications in patients with diabetic foot ulcers, ultimately providing evidence-based recommendations for clinical practice.

Patients and methods

This randomized controlled trial was conducted at the Burn, Reconstruction, and Plastic Surgery Department, Qena University Hospital, South Valley University, The study was approved by the local Research Ethics Committee under the ethical code: **SVU-MED-SUR011-1-24-9-947**. The study included adults aged ≥18 years diagnosed with diabetic foot ulcers. Eligible patients had chronic non-healing ulcers persisting for more than four weeks and suitable for split-thickness skin grafting (STSG). All participants had stable glycemic control with HbA1c <8% within the last three months and adequate limb perfusion.

Patients were excluded if they had severe peripheral arterial disease unsuitable for surgery (e.g., diffuse multi-arterial occlusion, heavy calcification, or extensive atheromatous plaques), active infection or osteomyelitis at the ulcer site, or contraindications to surgery or anesthesia, or poor tolerance to grafting procedures. Additional exclusions included immunocompromised conditions such as HIV/AIDS or malignancy, pregnancy or breastfeeding, and poor compliance with medical treatment or follow-up.

The study enrolled 15 cases. Each ulcer was split into two halves of graft thickness and randomized by computer-generated tables: one half received STSG alone and the other STSG with nano-fat, allowing direct within-patient comparison of treatment efficacy.

Patients and methods

Lab tests and clinical evaluation

All patients had extensive history-taking and blood tests. Hematological tests included hemoglobin, red, white, and platelet counts. Prothrombin, partial thromboplastin, and international normalized ratio were used to assess coagulation. Blood samples were collected under aseptic circumstances, stored at 2–8 °C, and processed using HPLC, Variant II Turbo, and turbidimetric immunoassay with COBAS C501 to test glycemic control using

random blood sugar and HbA1c. All patients had renal and hepatic function tests. All patients got 1 g intravenous cephazoline to prevent perioperative infections **(Fig.1).**

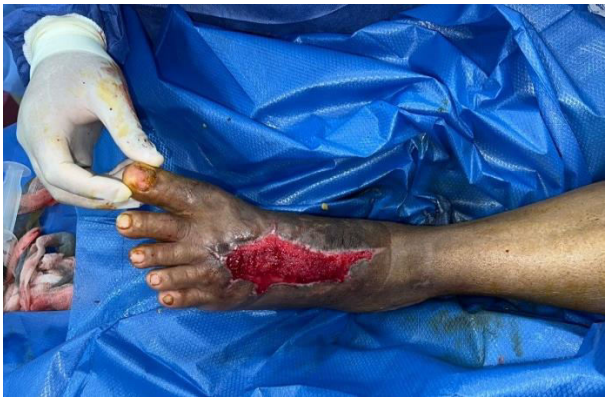

Figure (1**):** Preoperative assessment of the ulcer**.**

Intervention

Two treatments were used. The split-thickness skin graft (STSG) alone group retrieved 0.25–0.3 mm grafts using an electric dermatome after disinfecting the donor site on the thigh with betadine and saline. The donor site for all STSGs was the anterolateral aspect of the thigh, chosen for its reliable skin quality and accessibility. These grafts were meshed with dermacarrier at 1:1.5 and put over the ulcer bed without straining or wrinkling. Grafts were secured with interrupted 4-0 nylon anchoring sutures, placed 4–10 mm apart depending on ulcer size, ensuring firm fixation without tension or wrinkling. **(Guogienė et al., 2018).** Before application, nylon wraps were sterilized using standard autoclaving procedures to ensure asepsis prior to covering the graft.

Ulcer beds were meticulously prepared before grafting, including sharp debridement of necrotic tissue, irrigation with normal saline, and confirmation of a well-vascularized ulcer bed to optimize graft take.

Fat graft preparation in the STSG with nano fat group involved infusing the infraumbilical area with 20 cc of tumescent solution (1:200,000 adrenaline). Liposuction with a 3 mm cannula removed 20 cc of fat, which was rinsed with 20 cc of saline. After fluid removal, 30 Luer-to-Luer transfers between 2.4 mm and 1.2 mm connectors mechanically emulsified the fat. This disaggregated emulsion was processed through a Nano Transfer system to produce nano fat (0.6–0.4 mm fat pieces). A 1.2 mm cannula was used to inject 5–10 ml of nano fat into the ulcer base and surrounding margins in a “fanning out” pattern before grafting, and 5 ml was administered topically. Following harvesting, STSG was administered to the ulcer bed. After grafting, ulcers were dressed with Vaseline gauze followed by sterile gauze wraps and gentle compression bandaging to maintain graft adherence and prevent hematoma or seroma formation. Graft size for each ulcer half and operating time were recorded. A hand-held 8 MHz Doppler probe showed graft vascular viability intraoperatively, **(Fig.2).**

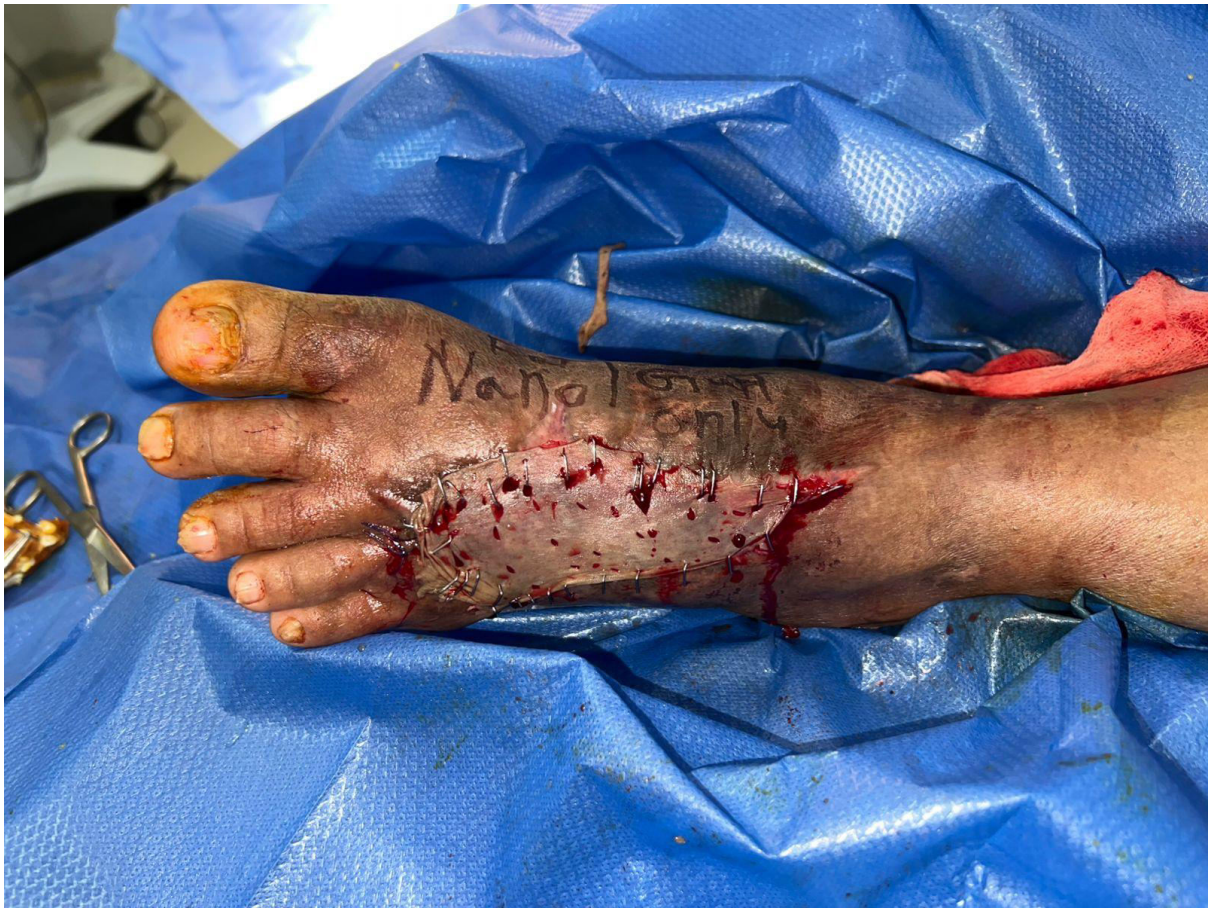

Fig.2. The ulcer was divided into 2 halves, one half was injected with nanofat followed by STSG, while the other half had only STSG applied.

Follow-up and Evaluation

Weekly visits were documented with photos to track ulcer progression. The Bates-Jensen Ulcer Assessment Tool (BWAT) evaluated 13 ulcer characteristics: size, depth, ulcer edges, detachment, necrotic tissue, exudate, edema, tissue hardening at the periphery, surrounding skin color, granulation tissue, and epithelialization. The total score ranged from 13 (best) to 65 (worst), with higher values indicating more severe ulcer impairment **(Macedo et al., 2021).** Each item was scored from 1 (best) to 5 (worst).

Clinical recommendations were followed to handle complications such infection, graft loss, and other adverse events throughout follow-up. Cosmetic and functional outcomes were assessed using the Patient and Observer Scar Assessment Scale at the final follow-up. Patient scale had six items (color, pliability, thickness, alleviation, itching, and pain), while observer scale had five (vascularization, pigmentation, pliability, thickness, and relief). For each parameter, 1 was best/normal and 10 was worst. Better outcomes were indicated by lower patient and observer scores of 6–60 and 5–50, respectively. Additionally, patients and observers rated scar appearance on a 1–10 scale, with 1 being the best and 10 being the worst **(Draaijers et al., 2004).**

Statistical analysis

Data were analyzed using SPSS version 20. Qualitative variables were expressed as numbers and percentages, while quantitative data were presented as mean ± SD.

Comparisons between groups were performed using Student's t-test for normally distributed data, Mann–Whitney test for non-parametric data, chi-square or Fisher's exact test for categorical variables. Associations were further assessed with univariate logistic and multivariate regression analyses. Statistical significance was set at $p < 0.05$, with smaller p-values indicating stronger significance.

Results

The study included 15 patients with a mean age of 59.33 ± 7.51 years; 53.3% were females and 46.7% males. Diabetes mellitus was present in 66.7% and hypertension in 26.7% of cases. Ulcers were located in the distal leg in 46.7%, dorsum of the foot in 33.3%, and plantar surface in 20%. The mean ulcer duration was 5.23 ± 0.55 weeks, with an average ulcer length of 8.65 ± 1.12 cm, width of 4.09 ± 0.53 cm, and a mean graft size of 39.65 ± 6.85 cm². **(Table.1).** The mean hemoglobin level was 12.31 ± 1.75 g/dL, mean serum albumin was 3.26 ± 0.30 g/dL, and mean HbA1c level was 7.05 ± 1.60 g/dL.**(Fig.3).**

Table 1. Demographic data among the included cases

Variables	All cases (N = 15)
Age (Years)	59.33 ± 7.51
Sex	
• **Male**	7 (46.67%)
• **Female**	8 (53.33%)
Comorbidities	
• **DM**	10 (66.67%)
• **HTN**	4 (26.67%)
Location	
• **Distal leg**	7 (46.67%)
• **Foot dorsum**	5 (33.33%)
• **Plantar foot**	3 (20%)
Ulcer characteristics	
• **Duration of ulcer (weeks)**	5.23 ± 0.55
• **Ulcer length (cm)**	8.65 ± 1.12
• **Ulcer width (cm)**	4.09 ± 0.53
• **Graft size (cm²)**	39.65 ± 6.85

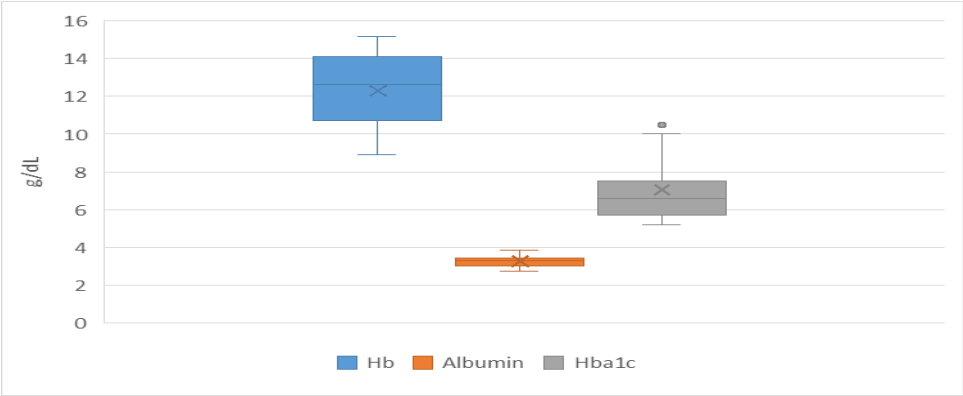

Fig.3. Laboratory investigations among the included cases:

The mean graft size was comparable between the two groups (19.76 ± 3.55 vs. 19.89 ± 3.32, P>0.05). The addition of nanofat to split-thickness skin grafts significantly improved outcomes. Healing time was shorter with nanofat (2.16 ± 0.21 vs. 2.74 ± 0.50 weeks, p = 0.0006). BWAT scores were lower (15.67 ± 5.87 vs. 22.2 ± 8.25, p = 0.0019), and POSAS scores showed better patient-reported (1.87 ± 0.81 vs. 3.00 ± 1.26, p = 0.0135) and observer-reported results (1.33 ± 1.25 vs. 3.13 ± 1.36, p = 0.0021). Complications were fewer with nanofat, though differences were not statistically significant (p > 0.05). (**Table.2).**

Table 2. Comparison between the treated sides regarding outcomes

Variables	Split thickness graft side (N = 15)	Split thickness graft and nanofat side (N = 15)	P. Value
Outcomes			
Time of complete healing (weeks)	2.74 ± 0.5	2.16 ± 0.21	0.0006* [MWU]
BWAT score	22.2 ± 8.25	15.67 ± 5.87	0.0019* [MWU]
POSAS score			
• **Patients score**	3 ± 1.26	1.87 ± 0.81	0.0135* [MWU]
• **Observer score**	3.13 ± 1.36	1.33 ± 1.25	0.0021* [MWU]
Complications rate			
• **Infection**	5 (33.33%)	1 (6.67%)	0.0679 [X]
• **Graft loss**	1 (6.67%)	0 (0%)	0.99 [f]
• **Necrosis**	2 (13.33%)	0 (0%)	0.4828 [f]
• **Hematoma**	1 (6.67%)	1 (6.67%)	0.99 [X]

Discussion

Our study showed that adding nanofat to split-thickness skin grafts accelerated healing, improved ulcer and scar quality, and lowered complication rates. These effects reflect nanofat's regenerative role in enhancing angiogenesis, reducing inflammation, and promoting collagen remodeling. Consistent with previous reports, our findings support nanofat as a valuable adjunct to skin grafting, offering functional and cosmetic benefits in chronic ulcer care.

Our study included 15 patients with a mean age of 59.33 ± 7.51 years, with females representing 53.33% and males 46.67%. Diabetes mellitus was present in 66.67% and hypertension in 26.67%. Lesions were most often located in the distal leg (46.67%), followed by the dorsum of the foot (33.33%) and the plantar surface (20%). The demographic profile reflects the typical risk pattern of diabetic foot ulcers, where older age, diabetes, and hypertension predispose to impaired vascularity and delayed healing **(Martin and Davis, 2023; Vahwere et al., 2023).** The distribution of lesions is consistent with high-pressure and poorly perfused areas, with plantar ulcers linked to neuropathy and gait abnormalities **(Packer et al., 2023).**

Yao et al. (2024) reported similar findings in a large cohort of 918 DFU patients among 85,872 type 2 diabetes cases, with a prevalence of 1.07%. Patients had a mean age of 61.86 ± 12.10 years, 68.2% were males and 31.8% females, and the most common age group was 50–59 years

(29.6%). Likewise, **Madanchi et al. (2013)** studied 873 patients with a mean age of 59.3 years, with 58.1% males and 41.9% females, also showing male predominance. **Packer et al. (2025)** reported higher prevalence of DFU in males (4.5%) than females (3.5%), with type 2 diabetes patients (6.4%) more affected than type 1 (5.5%).

In our study, ulcers had a mean duration of 5.23 ± 0.55 weeks, an average length of 8.65 ± 1.12 cm, width of 4.09 ± 0.53 cm, and mean graft size of 39.65 ± 6.85 cm^2. These findings highlight moderately sized, chronic ulcers. **Schipper et al. (2023)** and **Smuđ-Orehovec et al. (2018)** noted that STSG typically achieve ≥80% closure within 5–8 weeks in optimized cases. **Deng et al. (2019)** suggested that nano fat beneath grafts may enhance re-epithelialization and neovascularization, potentially accelerating healing. **Anderson et al. (2012)** reported similar outcomes, with 107 diabetic patients achieving mean healing in 5.1 weeks (range 3–16 weeks). **Farabi et al. (2024)** reviewed 71 patients treated with stem cells, where 64.7% achieved complete healing in 6.1 weeks. By contrast, J. J. Anderson et al. (2012) found longer healing (7.2 weeks) in 49 patients with larger ulcers (mean size 54.24 cm^2, range 15–124 cm^2).

Our study also found mean hemoglobin 12.31 ± 1.75 g/dL, serum albumin 3.26 ± 0.30 g/dL, and HbA1c 7.05 ± 1.60%. These values indicate preserved hematologic and nutritional status, which supports graft take and ulcer repair **(Lin et al., 2025; Cheng et al., 2021; Vlad et al., 2023). Shi et al. (2021),** in 494 and 231 DFU patients, reported mean hemoglobin 11.73 ± 2.25 and 12.47 ± 2.05 g/dL, serum albumin 3.36 ± 0.62 and 3.53 ± 0.55 g/dL, and HbA1c 9.1 ± 2.3% and 9.6 ± 2.6%, showing worse glycemic control than our patients. Jiang et al. (2024), in 105 DFU patients, found 59.05% with Hb ≤12.0 g/dL, 20.95% with moderate anemia (Hb 3.1–6.0 g/dL), and 1.90% with severe anemia (<6.0 g/dL), while only 18.10% had Hb ≥12.1 g/dL. **Cheng et al. (2021)** studied 174 DFU patients and reported mean hemoglobin 11.83 ± 2.57 g/dL, albumin 3.51 ± 0.57 g/dL, and HbA1c 8.62 ± 1.95%. **Xiang et al. (2019),** in 298 patients, found serum albumin declined with higher HbA1c, from 3.55 ± 0.40 g/dL at HbA1c ≤7% to 3.01 ± 0.47 g/dL at HbA1c >9%. **Akyüz et al. (2023)** studied 301 patients and found 44.5% had HbA1c ≥10.1%, 30.9% had 8.1–10%, and 24.6% had 6.5–8%. In disagreement, **Lin et al. (2025),** in a pooled analysis of 3,986 DFU patients, reported a significantly lower mean hemoglobin with a difference of 2.13 g/dL, which may reflect comorbidities, ulcer severity, or regional variations. **Lee et al. (2024),** in 46 DFU patients, found 91.3% had reduced hemoglobin and 36.9% reduced albumin.

Our study showed that adding nanofat to split-thickness skin grafts (STSG) significantly enhanced ulcer healing. The healing time was shorter with STSG plus nanofat (2.16 ± 0.21 weeks) than with STSG alone (2.74 ± 0.50 weeks, $p = 0.0006$). Ulcer quality, measured by BWAT, was better with nanofat (15.67 ± 5.87 vs. 22.2 ± 8.25, $p = 0.0019$). Scar quality was also improved, with lower POSAS scores for both patient-reported outcomes (1.87 ± 0.81 vs. 3.00 ± 1.26, $p = 0.0135$) and observer-reported outcomes (1.33 ± 1.25 vs. 3.13 ± 1.36, $p = 0.0021$). These findings reflect nanofat's regenerative mechanisms, as it provides stem/progenitor cells and extracellular matrix components that stimulate angiogenesis, reduce inflammation, and promote collagen remodeling **(La Padula et al., 2023**). In diabetic foot ulcer models, nanofat accelerated healing by increasing microvessel density and re-epithelialization **(Chen et al., 2019).** When combined with STSG, these effects enhance graft take, improve ulcer bed quality, and yield superior

scar outcomes **(Saif Eldein Elsayed et al., 2024; Terrasa et al., 2025).**

Our results agree with **ElSherbeny et al. (2023),** who conducted a self-controlled trial on 20 patients. They found that nanofat-treated donor sites healed in 13.30 ± 2.61 days (≈1.9 weeks), compared to 16.05 ± 2.43 days (≈2.29 weeks) in controls ($p < 0.001$). **Deng et al. (2019)** also showed significantly improved ulcer healing, where 15 patients treated with nanofat plus NPWT had a healing rate of 26.50% ± 9.51% after 10 days, compared to 12.02% ± 4.20% with NPWT alone ($p < 0.01$). Similarly, **Ramaut et al. (2024)** studied 13 female patients with scars, showing significantly better POSAS patient-reported texture at 1 month, improved color and appearance at 6 months ($p < .05$), and sustained observer improvements in texture (1–6 months), vascularization (3–12 months), pigmentation (6 months), and thickness (3–6 months). Overall scar appearance was rated superior at 3, 6, and 12 months ($p < .05$).

In terms of complications, our study found lower rates in the nanofat group, though not statistically significant. Infections occurred in 33.33% of STSG-only cases versus 6.67% with nanofat ($p = 0.0679$). Graft loss was 6.67% with STSG alone and none with nanofat ($p = 0.99$). Necrosis occurred in 13.33% with STSG only and none with nanofat ($p = 0.4828$). Hematoma was equal in both groups (6.67%). The lower complication rates in nanofat-treated ulcers may be explained by its antimicrobial and immunomodulatory effects, which reduce infection, improve tissue resilience, and enhance graft survival **(Deng et al., 2019; Sanchez-Macedo et al., 2022).**

These findings are supported by **ElSherbeny et al. (2023),** who reported only one case (5%) of donor site infection, equally affecting both STSG and nanofat-treated sites, with no significant difference ($p = 0.317$). **Kemaloğlu (2016)** followed patients for six months and found no infection in either STSG or STSG-plus-nanofat groups. Similarly, **Lamani et al. (2020)** studied 112 patients undergoing STSG and reported only one donor site infection, occurring in a diabetic patient, with no significant association between infection and diabetes ($p = 1$).

Our study have limitations as it is single center study, also sample size was relatively small.

Conclusion

The addition of nanofat to split-thickness skin grafts significantly enhances ulcer healing in patients with diabetic foot ulcers, leading to faster healing times, improved ulcer quality, and better scar appearance. The graft-plus-nanofat group showed shorter healing times, lower BWAT and POSAS scores, and a reduction in complications such as infections and graft loss, compared to the graft-only group.

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