Split-thickness skin graft together with site-specific offloading: accelerated and durable option for healing diabetic foot skin defect

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Background/purposes

Diabetic foot is a major health problem affecting a large portion of diabetic patients and needs multidisciplinary teamwork to achieve satisfactory results. Revascularization, surgical debridement, and soft tissue reconstruction are essential for complete cure. Split-thickness skin graft (STSG) is a widely accepted method for soft tissue coverage of open wounds; this technique has a significant role in burn wounds and plastic surgery reconstruction. Its use in the treatment of chronic diabetic foot ulcers is challenged by the high failure rates, particularly when used to cover plantar ulcers. Other reconstructive options are costly, demanding, and, therefore, not preferable in the setting of comorbid high-risk patients. This study assesses whether the addition of site-specific offloading would help prevent recurrent ulceration following the application of STSGs for the treatment of diabetic foot plantar ulcers.

Patients and methods

Adult patients with diabetic foot infection who underwent surgical debridement, plantar wound reconstruction with STSG, site-specific offloading, and completed a clinical follow-up of at least 1 year were selected for analysis.

Results

Forty-two patients underwent STSG. Out of them 38 (90.0%) patients had infection and 23 (54.8%) had gangrene. Successful revascularization was done in 27 (64.3%) patients before enrollment. Debridement and toe amputation were done in 16 (38.1%) and 17 (40.5%) patients, respectively. Transmetatarsal amputation was done in nine (21.4%) patients. The average wound size was 21 cm^2 and ranged from 6 to 120 cm^2. The median time to complete wound healing was 6 weeks. Thirty-four (81.0%) patients had complete healing by 2 months. We found a statistically significant relationship between compliance to offloading and healing at 3, 4, and 5 months of follow-up (P=0.001, 0.02, 0.02, respectively). During the 1-year follow-up period, 13 (30.95%) patients experienced ulcer recurrence. Ulcer recurrence was significantly higher among patients who were noncompliant to offloading (58.82 vs. 12%, P=0.0021).

Conclusions

STSG together with site-specific offloading can be considered a reliable option for achieving accelerated wound healing and prevention of recurrence in diabetic foot patients after proper wound preparation.

Keywords:
diabetic foot, diabetic foot ulcer, offloading, split-thickness skin graft, ulcer recurrence

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Introduction

Diabetic foot is a major problem affecting a large portion of diabetic patients. The pooled worldwide prevalence of diabetic foot ulceration (DFU) is 6.3% [95% confidence interval (CI): 5.4–7.3%), while the prevalence in Egypt is 6.2% (95% CI: 4.1–8.2%) [1].

Management of diabetic foot complications is costly. In addition to direct health-care costs, indirect costs are significant in terms of the disability and medically related absenteeism [2]. In one study, the mean annual NHS cost of DFU care was an estimated £7800 [3]. In the United States, the average annual spending per patient with DFU was estimated at $26 844 [4]. In India, the average cost for management of an episode of foot complications was estimated at $3526 [5].

Following revascularization, whenever indicated, and after adequate debridement and control of infection,

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the wound becomes prepared with a floor of healthy granulation tissue [6]. The wound may be put on frequent dressings and site-specific offloading aiming at achieving healing by secondary intention. Healing can be aided by adjunctive wound care measures, such as negative pressure wound therapy, hyperbaric oxygen therapy, bioengineered skin substitutes, growth factors, and shockwave therapy [7]. Healing by secondary intention is the simplest way of management; however, the risk for recurrent infection and the substantial direct and indirect cost of prolonged hospitalization and outpatient wound care are potential limitations [8]. Alternatively, soft tissue reconstruction may be considered to achieve early wound closure, thus minimizing the risk for recurrent infection, shortening the time to healing, and reducing the overall cost. Soft tissue reconstructive procedures include skin grafting, fasciocutaneous/fasciomyocutaneous advancement, rotational or free flaps [9].

Split-thickness skin grafting (STSG) is a time-tested method for soft tissue reconstruction [10]. However, its use in the treatment of chronic DFUs is challenged by high failure rates, particularly in neuropathic patients with plantar ulcers. Other reconstructive options are costly and demanding in the setting of comorbid high-risk patient population. It is estimated that 17–60% of DFU patients will experience a recurrent ulcer following healing of the primary ulcer [11]. Currently, there is evidence to support the use of different offloading modalities to accelerate healing and prevent recurrence of DFUs [12].

Currently, most health-care facilities struggle to provide an efficient medical service; while making the maximum use of the available health and economic resources, the substantial economic burden of the diabetic foot cannot be overlooked [2]. This emphasizes the need for a sustained benefit of any form of interventions performed to help healing of UFUs.

Patients and methods

This is a prospective single-arm trial conducted to assess whether the addition of site-specific offloading to STSG in the treatment of diabetic foot would result in a more sustained clinical outcome, in terms of lower reintervention and ulcer recurrence rates. During the period between January 2020 through January 2021, patients were recruited from the Vascular Surgery Outpatient Clinic, Kasr Al-Ainy School of Medicine and the Diabetic Foot Clinic, National Institute of Diabetes and Endocrinology (NIDE). Forty-two patients with debrided plantar DFUs and/or unhealed minor foot amputation stumps met the following inclusion criteria:

(1) Patients over 18 years old.
(2) Patients with nonischemic diabetic foot lesions.
(3) Patients with ischemic diabetic foot lesions following successful revascularization.
(4) The presence of healthy granulation tissue in the floor of the ulcer.

Exclusion criteria

(1) Infected ulcers according to Infectious Diseases Society of America (IDSA) and International Working Group on the Diabetic Foot (IWGDF) perfusion, extent/size, depth/tissue loss, infection, and sensation (PEDIS) classifications of diabetic foot infection [13].
(2) Ulcers with exposed bone and/or osteomyelitis.
(3) ABI less than 0.80 and ankle systolic pressure less than 100 mmHg.
(4) The presence of comorbidities such as heart failure, chronic kidney disease, recent myocardial infarction, and decompensated liver cirrhosis.

All procedures performed in this study were in accordance with the ethical standards. Written informed consent was obtained from all participants. Baseline demographic and clinical data were recorded. Surgical techniques were as per standard institutional protocols. Split-skin grafts were harvested from the anteromedial aspect of the proximal ipsilateral thigh, 'pie-crusted' using stab incision with a scalpel to allow for fluid egress, and applied to the ulcer using staples or absorbable sutures. A multilayer dressing composed of paraffin gauze, saline soaked gauze, sterile dry dressing, and a crepe bandage was applied to the recipient site and the DFUs. Offloading knee-high removable walkers were prescribed for all patients. They were instructed to use the walkers during all weight-bearing activities, with the aid of crutches during the early period of acclimatization to the off-loading device. Patients were discharged home the same day of the procedure, and were invited to follow-up visits at the fifth and tenth postoperative days and weekly thereafter for 1 month, and then at monthly basis. At each follow-up visit, recipient sites were assessed for the reduction in wound area, signs of infection, necrosis, or ulcer recurrence. The duration of wound healing was reported. Compliance to offloading was ensured at each follow-up visit. Patients were considered compliant to the use of offloading devices if the patient/relatives reported the use of removable cast walkers during all weight-bearing episodes except during short walking distance (e.g. to use the bathroom at night). Patients were considered noncompliant to the use of offloading devices if the patient/relatives reported a complete abstinence from the use of walkers or its use only for walking short distances during the day, but no use outdoor. After complete healing, ulcer recurrence is defined as the development of full thickness loss on the grafted area after being healed.

Statistical methods

Data management and statistical analysis were done using SPSS, version 25 (IBM, Armonk, New York, USA). Quantitative data were assessed for normality using the Shapiro–Wilk test and direct data visualization methods. Then, quantitative data were summarized as means and SDs or medians and ranges. Categorical data were summarized as numbers and percentages. Post-hoc comparisons were Bonferroni adjusted. Kaplan–Meier curve was used to estimate median time to healing. Log-rank test was used for comparing time to healing curves according to different variables. Fisher's exact test was used to determine the relation between compliance to offloading and healing, the relation between compliance to offloading and ulcer recurrence, as well as the relation between the site of original ulcer and ulcer recurrence. All statistical tests were two-sided. P values of less than 0.05 were considered significant.

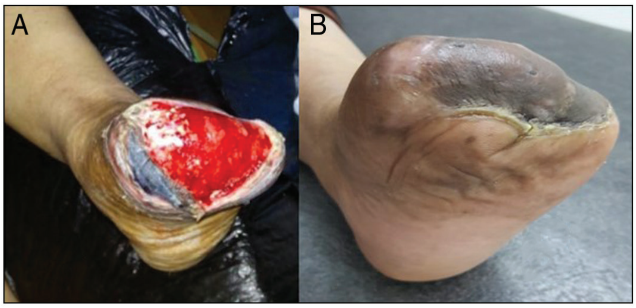
Results

In all, 42 patients with debrided plantar DFUs and/or unhealed minor foot amputation stumps who received STSGs and site-specific offloading were followed up for a minimum of 1 year (Figs 1–3).

The mean age of the studied patients was 58 years. There was male predominance; 27 (64.3%) patients were males. Hypertension, ischemic heart disease, smoking habit, and dyslipidemia were found in 31 (73.8%), 21 (50%), 21 (50%), and 21 (50%) patients, respectively. All patients had diabetes mellitus. Baseline demographic and clinical characteristics are shown in Table 1.

Regarding the initial foot insult, 38 (90.0%) patients had infection and 23 (54.8%) had gangrene. Twenty-seven (64.3%) patients had successful revascularization before enrollment in the current study. Before inclusion in the current study, debridement and toe amputation were done in 16 (38.1%) and 17 (40.5%) patients, respectively. Transmetatarsal amputation was done in nine (21.4%) patients. The resultant skin defect was located in the plantar forefoot in 20 (47.6%) patients, in the plantar midfoot in 19 (45.2%) patients, and in the heel in three (7.1%) patients. Following adequate wound bed preparation, patients were enrolled into the study. The median wound size was 21 cm^2 and ranged from 6 to 120 cm^2.

Figure 1



(a) A forefoot amputation stump with an adequately prepared wound bed and (b) the same patient following complete take of STSG at 5 weeks. STSG, split-thickness skin graft.

At 1 month, complete wound healing was achieved in four (9.5%) patients. Reduction of the wound area by more than 50% occurred in 36 (85.7%) patients. Two (4.8%) patients had recipient site infection and were candidates for readmission and debridement. Donor-site infection did not occur. Thirty-two (76.2%) patients were compliant to the use of removable walkers.

At 2 months, 34 (81%) patients had their ulcers healed completely. Five (11.9%) patients had more than 50% reduction in wound area. Graft failure occurred in three (7.1%) patients. At this point, patients who were compliant to the use of removable walkers dropped to 27 (64.3%), which was the same at 3 months.

At 4 months, 38 (90.5%) patients had complete wound healing. At this point, patients compliant to the use

Figure 2

Heel ulcer; (a) with adequately prepared bed and (b) 1 month following STSG. STSG, split-thickness skin graft.

Figure 3

Heel ulcer: (a) wound bed preparation, (b) 4 weeks following STSG, and (c) 2 months following STSG. STSG, split-thickness skin graft.

Table 1 Baseline demographic and clinical data

Age (years)	
Mean±SD	58±9
Sex [*n* (%)]	
Males	27 (64.3)
Females	15 (35.7)
Smoking [*n* (%)]	21 (50.0)
CVS [*n* (%)]	3 (7.1)
Ischemic heart disease [*n* (%)]	21 (50.0)
Hyperlipidemia [*n* (%)]	21 (50.0)
Hypertension [*n* (%)]	31 (73.8)
Diabetes mellitus [*n* (%)]	42(100)
Gangrene [*n* (%)]	23 (54.8)
Infection [*n* (%)]	38 (90.5)
Revascularization [*n* (%)]	27 (64.3)
Surgical intervention [*n* (%)]	
Debridement	16 (38.1)
Toe amputation	17 (40.5)
TMA	9 (21.4)
Wound size (in cm^2)	
Median (range)	21 (6–120)

of removable walkers dropped to 25 (59.5%). Patients compliant to the use of walkers remained compliant until the end of the follow-up period.

Wound healing at different time points is shown in Table 2.

Kaplan–Meier curve for time to healing

Time to healing for the studied patients was estimated using the Kaplan–Meier curve (Fig. 4). It revealed a median time to healing of 6 weeks (95% CI: 5.48–6.52). The mean time to healing was 5.8 weeks.

Kaplan–Meier curves for time to healing according to different variables

Figures 5 and 6 show Kaplan–Meier curves for time to healing according to sex, smoking, ischemic heart disease, hyperlipidemia, and hypertension with no significant differences; log-rank *P* values were 0.989, 0.834, 0.474, 0.219, and 0.963, respectively.

Table 2 Healing at different points of time

	n (%)
At 1 month	4 (9.5)
At 2 months	34 (81.0)
At 4 months	38 (90.5)

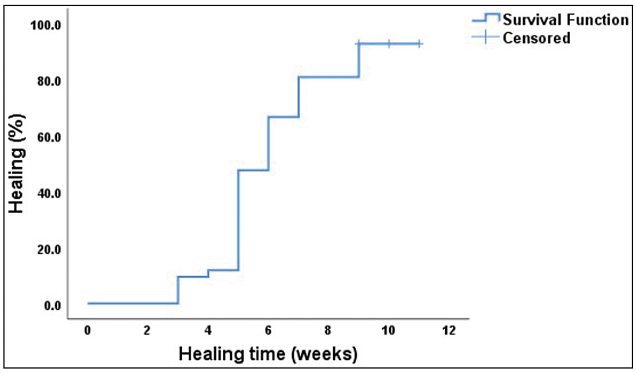
We found a positive correlation between compliance to offloading devices and healing.

There was a statistically significant relationship between compliance to offloading and healing at 3, 4, and 5 months of follow-up (*P*=0.001, 0.02, 0.02, respectively) (Table 3).

During the 1-year follow-up period, 13 (30.95%) patients experienced DFU recurrence following complete healing. Subgroup analysis showed that ulcer recurrence occurred in only three (12%) patients who were compliant to offloading throughout the entire follow-up period. On the other hand, ulcer recurrence occurred in 10 (58.82%) out of 17 patients who were noncompliant to offloading. Ulcer recurrence was significantly higher among patients who were noncompliant to offloading (*P*=0.0021) (Table 4). Another finding was that patients who were incompliant to the use of offloading devices experienced an overall earlier recurrence (seven patients had recurrence by the end of the sixth month) than offloading-compliant patients (all had the recurrence after 10 months of the initial wound healing).

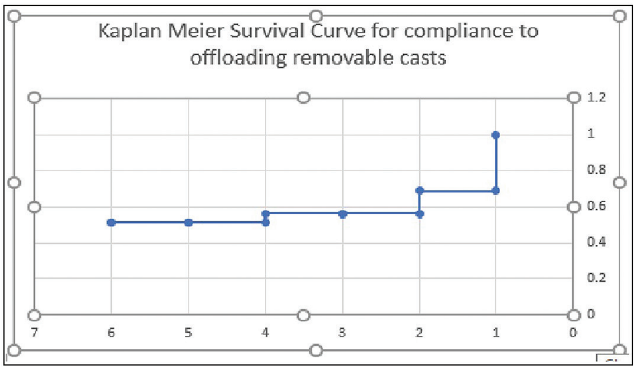
Subgroup analysis showed that ulcer recurrence occurred in five (25%) out of 20 patients, who had initial ulcer located in the forefoot, in six (31.58%) out of 19 patients who had initial ulcer in the midfoot, and in two (66.67%) out of three patients who had the initial ulcer located at the heel. Although ulcer recurrence was much more prevalent among patients with initial ulcer located in the hindfoot, the correlation between site of the initial foot ulcer and ulcer recurrence was not statistically significant (*P*=0.35).

Figure 4



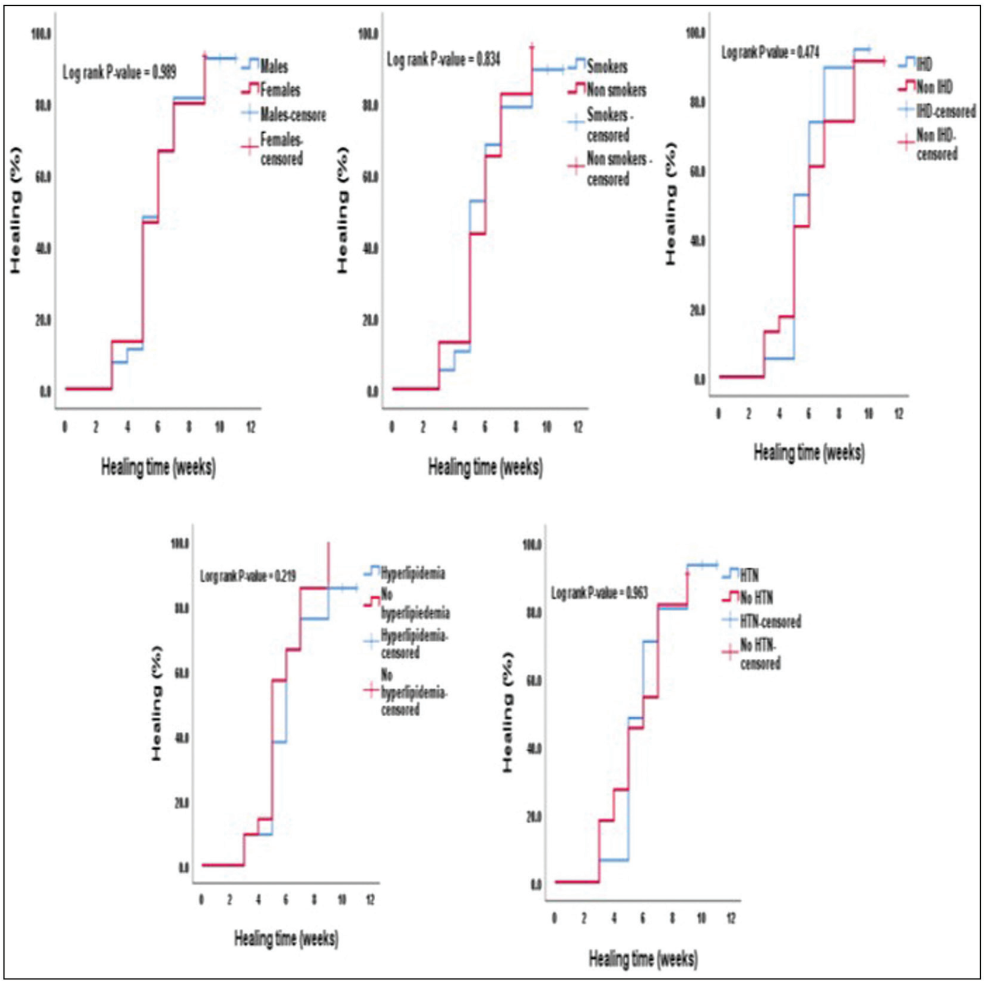
Kaplan–Meier curve of time to healing.

Figure 6



Kaplan–Meier curve for compliance to offloading.

Figure 5



Kaplan–Meier curves for time to healing according to different variables.

Discussion

Successful wound healing is a complex phenomenon, necessitating an overlapping, highly coordinated sequence of cellular and biochemical events including the arrest of hemorrhage, followed by inflammatory response, formation of granulation tissue, reepithelization, and finally remodeling. The presence of diabetes results, among several other mechanisms, in impaired angiogenesis, further complicates the wound-healing process and contributes to chronicity of DFUs [14].

The simplest method of management of diabetic foot is ulcer debridement and follow-up with appropriate dressing, awaiting secondary intention healing [15]. The unstable nature of the resultant scar, the substantial risk for recurrent infection, and direct and indirect cost

Table 3 Association between patients' compliance to offloading and healing

	Compliant patients		Noncompliant patients		*P* value
	No healing	Healing	No healing	Healing	
1 month	28	4	10	0	0.55
2 months	4	23	4	11	0.40
3 months	2	25	9	8	0.001
4 months	0	25	4	13	0.02
5 months	0	25	4	13	0.02
6 months	0	25	3	14	0.059

Table 4 Association between patients' compliance to offloading and ulcer recurrence

	Recurrence (*N*)	Recurrence	Total	*P* value
Compliant	22	3	25	0.0021
Noncompliant	7	10	17	
Total	29	13	42	

of prolonged hospitalization and outpatient wound care are the drawbacks of this strategy [8]. Alternatively, soft tissue reconstruction may be considered to achieve early wound closure, thus minimizing the risk for recurrent infection and reducing the time to healing, with potential overall cost reduction.

After adequate wound preparation, definitive soft tissue reconstruction can be performed. Soft tissue coverage of a foot ulcer in a diabetic patient is a challenging conundrum. Among myriad of simple and rather more complex procedures, the selected procedure should be tailored to each patient's circumstances to obtain as much durable results as possible [16]. STSGs offer a rapid solution for wound closure. In a meta-analysis, Yammine and Assi [17] reported the outcomes of STSGs on diabetic leg and foot ulcers of a pooled sample of 757 patients with 759 ulcers. They reported a pooled ulcer healing rate of 85.5% (95% CI: 0.766–0.925, I^2=90%). The mean time to complete healing was 5.35 ± 2.25 weeks, with an estimated pooled recurrence rate of 4.2% (95% CI: 0.009–0.096, I^2=76%) within a mean follow-up duration of 2 years. These results are by far much better than the results reported following standard wound dressings, even with the addition of adjunctive measures such as NPWT or hyperbaric oxygen therapy, with even a more sustained clinical benefit. Margolis *et al.* [18,19] reported a 3-month healing rate of 24.2–47% and 30.9–68% healing rate by 5 months after standard care.

Currently, there is high-quality evidence that supports the use of removable offloading devices to heal diabetic foot plantar as well as non-plantar ulcers. Although the best available evidence is for the use of nonremovable knee-high offloading devices, studies persistently show that removable walkers are associated with better patient compliance [12]. A removable knee-high device redistributes peak pressures in a similar manner as a nonremovable knee-high device. It redistributes the pressure more effectively than a removable ankle-high offloading device [20].

In the current study, we reported a healing rate of 90%, which is greater than heeling rates reported with traditional wound care protocols. It is slightly higher than healing rates reported by previous studies. We suppose that this increased likelihood of healing is related to patients' compliance to the offloading protocol.

Following complete healing of a DFU, the risk of recurrence is high, particularly in the presence of foot deformity and/or loss of protective sensation. By reviewing 19 studies on incidence rates for ulcer recurrence, Armstrong *et al.* [21] estimated that 40% of patients would have a recurrence within 1 year after ulcer healing, almost 60% within 3 years, and 65% within 5 years. Several studies have reported different risk factors associated with ulcer recurrence including loss of proprioception, younger age, peripheral vascular disease, osteomyelitis, high levels of C-reactive protein, presence of foot deformity, and high plantar peak pressure [21–23]. In the current study, we found that compliance to site-specific offloading offered protection against reulceration, thus providing more durable healing.

Yet, by the end of the follow-up period, and despite the continuous efforts exerted with patients and their families, almost one-third of patients were not compliant to the daily use of offloading walker. Several methods were proposed for improving compliance that included providing more style and color options, providing shoes suitable for indoor and outdoor use, and improving patient and clinician education on proper footwear [20].

Some variables that may have an impact on ulcer recurrence such as the duration of diabetes, glycemic control, and obesity were not considered, conferring the potential limitation of the current study.

Conclusions

STSG can be considered a reliable option for achieving wound healing in nonischemic diabetic foot patients and ischemic diabetic foot patients after successful revascularization and proper wound preparation. Patient compliance to offloading devices is positively correlated to ulcer healing and results in a more sustained clinical benefit. The synergism between skin coverage using STSGs and offloading may be associated with reduced overall cost of management, particularly when patients are encouraged to use offloading devices following complete wound healing.

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Nil

Conflicts of interest

There are no conflicts of interest.

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