REVIEW ARTICLE

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Split thickness skin grafts for the treatment of non-healing foot and leg ulcers in patients with diabetes: a retrospective review

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We retrospectively reviewed 107 diabetic patients who received a split thickness skin graft (STSG) for treatment of a non-healing diabetic foot or leg ulcer to describe healing times based on patient characteristics, comorbidities or complications. The minimum follow-up was 6 months from the time of STSG application. The mean time to healing among all patients was 5.1 weeks (3 to 16 weeks). The mean healing time for patients with complications was 12.0 weeks (10 to 16 weeks) while the mean healing time for those without complications was 4.9 weeks (3 to 10 weeks). Overall complication rate was 2.8%. Patients with a STSG take of less than 95% had a mean healing time of 7.9 weeks compared to 4.8 weeks for those with a STSG take of 100% ($p < 0.001$). The use of autologous STSG for treatment of non-healing diabetic foot and leg wounds is a viable method for soft tissue closure and may present a low complication rate and a satisfactory rate of healing.

Keywords: *Diabetic foot*; *skin grafts*; *diabetic ulcer*; *infection*; *neuropathy*

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Foot and leg ulcers are the leading cause of hospitalization in patients with diabetes mellitus and precede approximately 70–80% of all diabetic-related amputations (1, 2). Timely healing and closure is critical to reducing the cost and morbidity associated with chronic diabetic lower extremity wounds (3–5). Split thickness skin grafts (STSG) are a well-known and widely accepted method for soft tissue coverage of open wounds (6). Historically, this technique has had a significant role in burn wounds and plastic surgery reconstruction, but has also been used successfully in the treatment of chronic diabetic foot ulcers (7–9). There are a vast number of wound care products and synthetic grafts available to the clinician today, but STSG remain the gold standard and may be considered a first-line treatment for lower extremity wounds associated with diabetes. Despite its common indications, there have been few large studies assessing the use of STSG as a modality for treatment of diabetic foot and leg wounds. Furthermore, few papers have examined the effect of individual patient risk factors on the healing time of STSG in the diabetic population. The aim of this retrospective review was to study the clinical use of STSG in a diabetic population and also identify any risk factors that may affect healing time or lead to complications.

Patients and methods

Following approval by our institutional review board, the medical charts of patients who received STSG for treatment of foot and leg ulcers between 2002 and 2010 were identified and retrospectively reviewed. Inclusion criteria included those patients who had a documented history of diabetes mellitus and an ulceration of the foot or leg distal to the tibial tuberosity. Patients were excluded from the study if they did not have a history of diabetes mellitus and/or less than 6 months follow up from the time of the application of the STSG. Patients with weight-bearing plantar ulcers were also excluded. A total of 183 patients received STSG treatment by the primary author during the selected time frame.

Seventy-six patients were excluded based on the above exclusion criteria. One hundred seven ($n = 107$) met the inclusion criteria and were included in the study. Information regarding comorbidities and potential risk factors for healing was also collected from each patient's medical record including age, history of smoking, history of alcohol use, history of intravenous (IV) drug use, wound size, rheumatoid arthritis, end-stage renal disease, cardiac disease (coronary artery disease or congestive heart failure), peripheral vascular disease (PVD), history of fracture and history of Charcot neuroarthropathy.

Prior to application of the STSG, all patients underwent conservative local wound care with or without negative-pressure wound therapy in an attempt to promote a uniform granular wound bed with minimal wound exudate, fibrin, or slough. STSG application was delayed if there were any local signs of infection, malodor, purulent drainage, or edema. No STSG were applied directly over exposed bone, joint capsule or tendon. Any patient with questionable peripheral vascular status was referred to vascular surgery for workup and cleared prior to surgery. All STSG were performed in an operating room setting under either general or local regional anesthesia. Surgical preparation of the wound was achieved by sharp or mechanical debridement of all non-viable tissue from the wound bed and wound edges in a sterile environment. The wound was copiously irrigated with at least 1000 mL of normal saline and local hemostasis was achieved by a combination of direct pressure and/or topical thrombin. The wound was measured and the dimensions documented. All donor sites for patients in this study were from the anterior aspect of the ipsilateral thigh (Fig. 1).

Marcaine 0.5% plain was infiltrated in the subcutaneous tissue surrounding the donor site and the appropriately sized area was prepped with sterile mineral oil to enhance gliding of the dermatome. The donor STSG site was then harvested utilizing a power dermatome set to 0.018 inch thickness and a width of two to four inches. For larger recipient areas, additional passes of the dermatome were made as needed in the same manner. The donor site was dressed with povidone-iodine soaked non-adherent gauze and sterile dry dressing. The STSG was then meshed in a 1:1.5 ratio and applied directly to the wound bed taking care to smooth any wrinkles and allow maximum apposition of the graft with the wound surface (Fig. 2). The STSG was secured with staples around the edges under minimal tension and a non-adherent dressing was placed directly over the graft surface. In order to minimize graft migration and limit shear forces, a bolster dressing consisting of the foam portion of a surgical scrub brush and multiple layers of cast padding were secured firmly over the STSG (Fig. 3). All patients were placed in a bulky splint until after the first post-operative visit. The patients were followed clinically at two weeks post-operatively and then on a weekly basis for dressing changes and to assess healing progress. One week follow-up intervals were chosen in order to allow a quantifiable degree of healing to occur between clinic visits. Dressing changes consisted of re-application of the bolster dressing roll gauze with continuation of the short leg cast or boot. Once healed, patients were seen in the outpatient clinic every four weeks until a minimum of 6 months follow up from the time of STSG application (Figs 4A–4G).

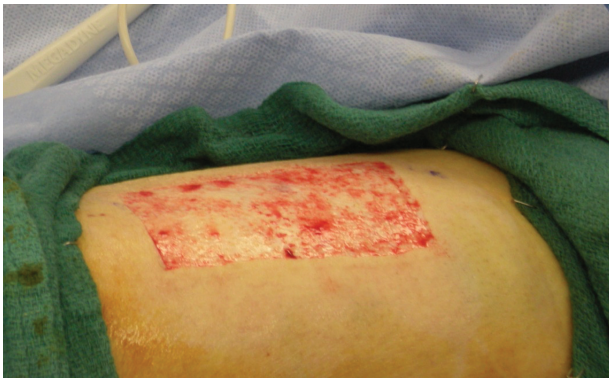

Fig. 1. Donor site from anterior thigh following harvesting of STSG.

The frequencies and mean time to healing were calculated for all variables of interest. Each variable was analyzed for healing time using a two-sample independent t-test. Analysis of variance (ANOVA) tests were also used to compare healing times. P values of less than 0.05 were considered significant.

Results

A total of 107 consecutive diabetic patients met the inclusion criteria for this study ranging in age from 28 to 88 years (average age, 59.1). All 107 patients were

Fig. 2. Graft site with STSG meshed, smoothed, and secured STSG covered with non-adherent dressing in place with staples.

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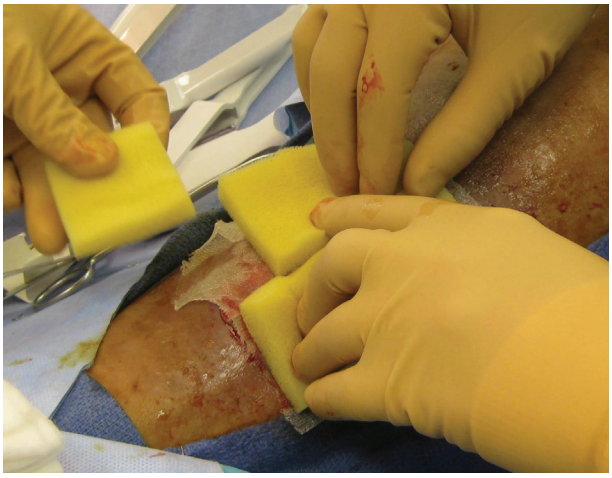

Fig. 3. STSG bolstered with foam portion of a sterile scrub brush.

available for follow up at 6 months. One-hundred-and-seven STSG were applied in total, with 29/107 (27.1%) to the right foot, 28/107 (26.2%) to the left foot, 25/107 (23.4%) to the right leg and 25/107 (23.4%) to the left leg. Six patients (5.6%) were current smokers, two (1.9%) admitted to current chewing tobacco use, and three patients (2.8%) admitted to IV drug abuse. Seven patients (6.5%) had rheumatoid arthritis. Nine patients (8.4%) had end-stage renal disease, defined as a glomerular filtration rate <15 mL/min, with all nine patients receiving ongoing dialysis treatment. Three patients (2.8%) had a significant history of cardiac disease which included a diagnosis of coronary artery disease and/or congestive heart failure. Seven patients (6.5%) had a documented history of peripheral vascular disease which included at least one abnormal non-invasive vascular test (ankle-brachial index, transcutaneous oximetry, Doppler wave-forms, segmental pressures, and pulse volume recordings) and/or non-palpable pedal pulses on examination. All patients with PVD received a workup by vascular surgery prior to application of STSG and were deemed to have sufficient blood supply for healing. In addition, all patients included in the study were deemed to have adequate blood flow to heal a STSG before undergoing the procedure. Twenty-six patients (24.3%) had a history of hypertension. One patient (0.9%) had a history of Charcot neuroarthropathy and received a STSG. Sixty patients (56.1%) had no other comorbidities besides diabetes mellitus, 29 patients (27.1%) had one comorbidity, and 18 patients (16.8%) had two or more comorbidities in addition to diabetes. Among all patients, the average starting wound size prior to graft treatment was 69.3 cm^2. Approximately half the patients (53/107 patients, or 49.5%) had a starting wound area of less than 50 cm^2, 37/107 (34.6%) had a wound area of 50 to

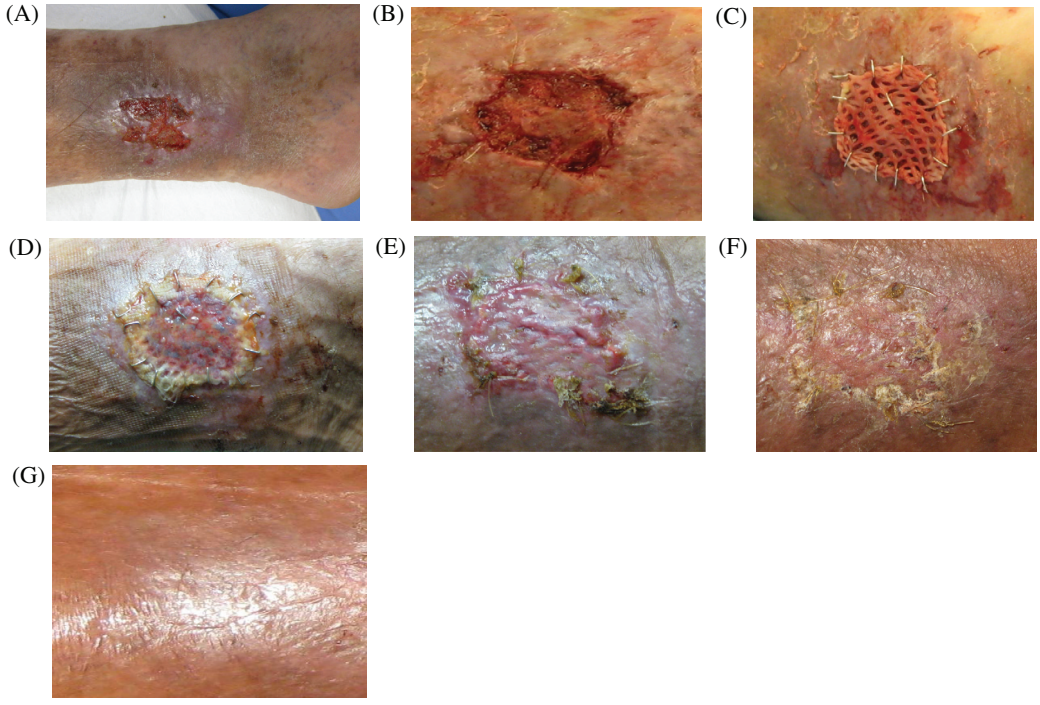

Fig. 4. Fifty-eight year old male with type 2 diabetes mellitus treated for ulceration on the lateral aspect of his ankle. His ulceration showed no improvement following conservative treatment with compressive dressings and local wound care. Multiple applications of human fibroblast-derived dermal substitute were also performed with no improvement. After 6 months of treatment, he was taken to the operating room for an autogenous STSG. (A) Pre-debridement, (B) Post-Debridement, (C) Postoperative day 0, (D) Postoperative day 10, (E) 4 weeks postoperative, (F) 8 weeks postoperative, (G) 6 months postoperative.

Graph 1. Distribution of time to complete wound healing among $n = 107$ patients.

100 cm^2, and 17/107 (15.9%) had a wound area greater than 100 cm^2.

The number of weeks to complete wound healing ranged from 3 to 16 weeks with an average healing time of 5.1 weeks. The vast majority of patients (97/107, or 90.1%) were completely healed by 6 weeks post-operatively while only four patients (3.7%) required 10 weeks or more to completely heal (Graph 1). Our analysis demonstrated that none of the comorbidities or risk factor variables had an independent effect on time to complete wound healing (Table 1). Similarly, age, wound location and wound size each appeared to have had no effect on time to heal (Table 2). The patients who had 100% graft take had a shorter healing time than those with graft take of less than 95% ($p < 0.001$) (Table 3). Those patients with 100% STSG take had a mean healing time of 4.8 weeks compared to 7.9 weeks for those patients with less than 95% STSG take (Graph 2).

Table 1. Time to complete wound healing ($n = 107$)

Risk factor	N	%	Mean weeks to healing	*p*
Smoking	6	5.6	6.0	0.183
Alcohol use	5	4.7	5.6	0.504
Intravenous drug use	3	2.8	5.0	0.916
Rheumatoid arthritis	7	6.5	5.0	0.869
End stage renal disease	9	8.4	6.1	0.415
Cardiac disease	3	2.8	4.0	0.254
Peripheral vascular disease	7	6.5	5.7	0.325
Charcot neuroarthropathy	1	0.9	4.0	****
Hypertension	26	24.3	5.2	0.281
Underlying fracture	1	0.9	10.0	****
Chewing tobacco	2	1.9	4.5	0.614

****Sample size too small for calculation of *p* value.

The range of STSG take percentage among all groups was between 40 and 100% with a mean take, overall, of 97%.

Only three of the patients (2.8%) had a complication with the original STSG. In two patients (1.9%), the STSG dressing was removed too early and both patients required re-grafting and eventually healed. The other patient had underlying osteomyelitis and required revisional resection of the bone and re-grafting which also eventually healed completely. No patient experienced a donor site complication. Patients with complications had a mean time to complete wound healing of 12.0 weeks compared to 4.9 weeks for patients without complications (Table 4).

Discussion

Despite success with STSG in surgery and wound care, there remain relatively few studies addressing its use in diabetic lower extremity wounds. In our study of diabetic patients, the mean time to complete wound healing was

Table 2. Time to complete wound healing for patient age, wound size, and wound location

	n	%	Mean weeks to healing	*P* value
Age ≥65	41	38.3	5.4	0.179
Age <65	66	61.7	4.9	
Wound size <50 cm^2	53	49.5	5.2	0.111
Wound size 50–100 cm^2	37	34.6	4.7	
Wound size >100 cm^2	17	15.9	5.7	
Right foot	29	27.1	4.7	0.319
Right leg	25	23.4	5.4	
Left foot	28	26.2	4.9	
Left leg	25	23.4	5.4	

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Table 3. Percent of STSG take and time to complete wound healing

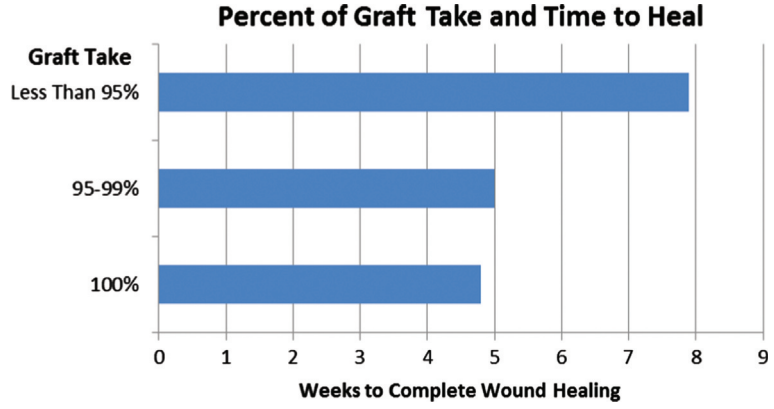
Percent take of graft	*N*	Mean weeks to complete healing	*p*
100%	79	4.8	*< 0.001*
95–99%	18	5.0	
<95%	*10*	*7.9**	

*Represents statistical significance from other values.

5.1 weeks with a range of 3–16 weeks. This average is comparable to that of other studies of wound healing in diabetic populations. Recently, Ramanujam et al. retrospectively reviewed 83 diabetic patients treated with STSGs for diabetic foot and ankle wounds and reported a median time to healing of 6.9 weeks among those patients without complications (10). Mahmoud et al. prospectively studied patients with STSG versus conservative wound care for diabetic foot wounds and found a statistically significant reduction in mean hospital stay and healing time for those patients treated with STSG (11). They noted that 62% of all STSG patients had healed by week eight. Puttirutvong et al. compared the healing rates of meshed vs non-meshed STSG in 42 patients and found no significant difference (12). The mean healing time for the meshed group was 19.84 and 20.36 days for the non-meshed group. Most STSG studies in non-diabetic studies report healing times between 2 and 4 weeks.

Impaired healing in diabetic patients is well-studied and can be attributed to multiple factors including impaired macro and microcirculation, peripheral neuropathy, endothelial dysfunction, and poor glycemic control (14–16). One shortcoming of our study is that we did not quantitatively analyze preoperative glycemic control. However, Ramanujam et al. did not find a statistically significant difference in preoperative hemoglobin A1C levels and healing time, despite high average preoperative hemoglobin A1C values in their patients (10). Conversely, a study by Marston found a direct correlation between hyperglycemia and wound healing. In this study, we found that the specific preoperative risk factors showed no effect on healing time (13). Likewise, age, wound size, and wound location did not seem to have a significant effect on healing time. Surprisingly, there was no significant effect of wound size on difference in healing time. The mean time to healing for those with wound size >100 cm^2 was 5.7 weeks compared to 4.7 weeks for wounds 50 to 100 cm^2 and 5.2 weeks for wounds <50 cm^2. Thus, those patients with a wound size between 50 and 100 cm^2 actually healed faster, on average, than those with a wound size of <50 cm^2.

Patients in our study with complications took longer to heal by more than 7 weeks on average than those without complications. Of the three patients who had complications, two had healing times of 10 weeks and the other had a healing time of 16 weeks. The mean healing time for those patients with complications was 12.0 weeks versus 4.9 weeks for those without complications. Only one patient among those without complications had a healing time longer than 7 weeks. Two patients in our study had the STSG pulled off at 2 weeks by the nursing facility. Both patients required re-grafting and healed without further complications by week 10. The other patient had osteomyelitis of the underlying bone which required resection. This patient eventually went on to heal the wound with aggressive local wound care and re-grafting by week 16. It stands to reason that postoperative complications such as infection, noncompliance, seroma, swelling and STSG pressure delay healing time by disruption of the graft and interfering with the healing process. Likewise, patients who must undergo revisional surgery would also be expected to have a delay in healing time. The overall complication rate in our study was only 2.6%. This is in contrast to several other studies that have reported higher rates of complications. Ramanujam et al. reported a post-graft complication rate of 35% with 16 patients experiencing an infection (10).



Graph 2. Percent graft take and mean healing time

Table 4. Patients with complications ($n = 3$)

Complication	Number of weeks to complete healing
STSG pulled off early	10
STSG pulled off early	10
Underlying osteomyelitis with exposed bone	16

They similarly noted a significant increase in time to complete wound healing in those patients who experienced complications. Similarly, Mahmoud et al. reported that 38% of their diabetic patients who received a STSG failed to heal by post-operative week eight (11).

The patients in our study who had less than 95% graft take had an average healing time of more than 3 weeks slower than those with a graft take of 100% (7.9 weeks vs 4.8 weeks), and almost 3 weeks slower than those with a graft take between 95 and 99% (7.9 weeks vs 5 weeks). Skin graft healing and incorporation is a complex biological process involving various stages of adherence, nourishment, revascularization, and final incorporation (6). Once harvested, the skin graft is deprived of its native nutrients and blood supply and can only survive by adherence to the wound bed and diffusion of nutrients from the underlying vascular supply until revascularization occurs. It stands to reason that any mechanical or biological disruption of this process puts the graft at risk for failure or prolonged healing. In our study, we took measures to prevent disruption to the graft by securing it place with staples and applying a bolster dressing to minimize shearing or compressive forces. Care was also taken to prepare the wound bed prior to graft placement in a manner that wound maximize the probability of incorporation. The vast majority of our patients (90.7%) had greater than 95% graft take and, of those, 73.8% had 100% graft take. Only 10 patients (9.3%) had less than 95% graft take, but this group took longer to heal. Clearly, the amount of graft take is an indication of the underlying healing process. STSG with poor graft take can naturally be expected to take significantly longer to heal.

Our study is only descriptive in nature, therefore other statistical methods such as tests for association and regression analysis would likely provide better information regarding the effects of each variable of interest as well as their additive effects on STSG healing times. On the same note, this study does not take into account possible interactions among the variables themselves which can influence the results. A major limitation of our study was the small sample size. Only having one patient with Charcot neuroarthropathy, for example, was inadequate for analysis with respect to healing time. A larger population size would have allowed more statistically meaningful analysis of our data. In addition, our study was retrospective in design which prevented inclusion of some data (e.g. type of diabetes and preoperative hemoglobin A1C levels) which might have been useful. A prospective, multicenter study is needed to more accurately investigate and determine the effects of certain risk factors and comorbidities on STSG wound healing time in the diabetic population.

Conclusion

Our study demonstrated a very low complication rate of 2.8% and an average wound healing time of 5.1 weeks for all patients who received a STSG for treatment of a diabetic foot or leg ulcer. None of the patient characteristics or comorbidities in this study appeared to affect STSG healing times, but we did find an average increase in healing time among patients with complications (12.0 weeks) versus those without complications (4.9 weeks). Finally, in our group of subjects, those patients with decreased graft take had prolonged healing times. This underscores the importance of optimizing the STSG for incorporation by minimizing any mechanical or biological barriers to healing. We conclude that autologous STSG are a safe and reliable alternative for the treatment of non-healing diabetic foot and leg wounds.

Conflict of interest and funding

The authors have received no funding or benefits from industry to conduct this literature review.

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