CHAPTER **47**

SPLIT THICKNESS SKIN GRAFTS FOR THE TREATMENT OF NONHEALING FOOT AND LEG ULCERS IN PATIENTS WITH DIABETES: A Retrospective Review

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INTRODUCTION

Foot and leg ulcers are the leading cause of hospitalization in patients with diabetes and precede approximately 70-80% of all diabetic-related amputations (1-2). Timely healing and closure are critical to reducing the cost and morbidity associated with chronic diabetic foot 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). Despite its clinical popularity, there have been few large studies assessing the use of STSGs as a modality for treatment of diabetic foot and leg wounds. The purpose of this study was to retrospectively review a large group of diabetic patients treated with STSG for foot and leg wounds and identify any risk factors associated with delayed healing time or complications.

PATIENTS AND METHODS

Following institutional review board approval, 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 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 107 patients 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 and included the following variables of interest: age, history of smoking, history of alcohol use, history of intravenous drug use, wound size, presence of rheumatoid arthritis, end-stage renal disease, cardiac disease (coronary artery disease or congestive heart failure), peripheral vascular disease, history of fracture, and history of Charcot neuroarthropathy.

Prior to application of the STSG, all patients underwent treatment with either aggressive local wound therapy or 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 was 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 STSGs were performed in an operating room setting under either general anesthesia or a regional anesthetic block with intravenous sedation. Surgical preparation of the wound was achieved by sharp or mechanical debridement of all nonviable 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 thigh of the ipsilateral leg (Figure 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

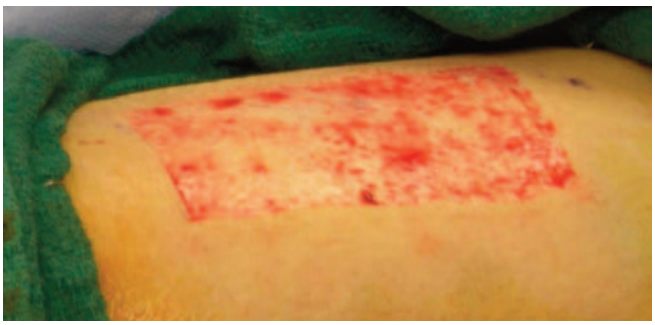

Figure 1. Donor site from anterior thigh following harvesting of split-thickness skin graft.

of the dermatome. The donor site STSG was then harvested utilizing a power dermatome set to 0.018 inch thickness and a width of 2 to 4 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 nonadherent gauze and a 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 (Figure 2). The STSG was secured with staples around the edges under minimal tension and a bolster dressing applied to prevent graft motion or migration. All patients remained nonweightbearing in a short leg cast until clinically healed, which was defined as complete epithelialization of the wound. The patients were followed clinically at 2 weeks postoperative and then on a weekly basis for dressing changes and to assess healing progress. Once healed, patients were seen in the clinic every 4 weeks until a minimum of 6 months follow up from the time of STSG application.

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, both one-way and two-way were also used to compare healing times of multiple variables within a group. *P* values 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 59.1 years). All 107 patients were available for follow up at 6 months. A total of 107 STSGs were applied, with 29 (27.1%) to the right foot, 28 (26.2%) to the left foot, 25 (23.4%) to the right leg and 24 (22.4%) to the left leg. Six patients (4.7%) were current smokers, 2 (1.9%) admitted to current chewing tobacco use, and 3 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 GFR <15 ml/min, with all 9 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 (ABI, TCPO2, Doppler wave-forms, segmental pressures, and pulse volume recordings) and/or nonpalpable 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.

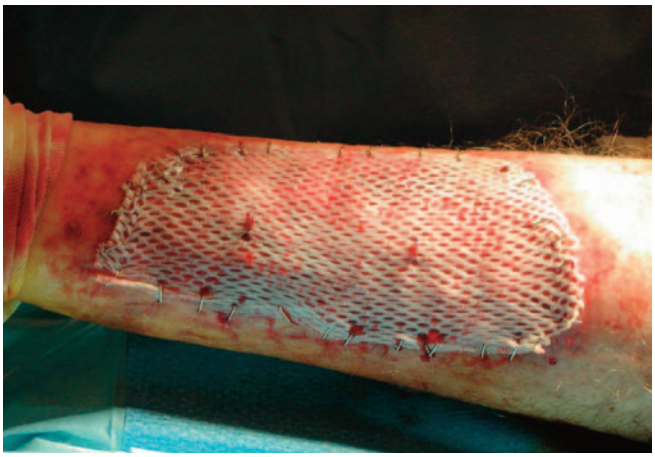

Figure 2. Graft site with split-thickness skin graft meshed, smoothed, and secured in place with staples.

Twenty-six patients (24.3%) had a history of hypertension. One patient (0.9%) had a history of Charcot neuroarthropathy and received a STSG to the affected Charcot foot. Sixty patients (56.1%) had no other comorbidities besides diabetes mellitus, 29 patients (27%) had 1 comorbidity, and 18 patients (16.8%) had 2 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 patients, or 49.5%) had a starting wound area of less than 50 cm^2, 37 (34.6%) had a wound area of 50 to 100 cm^2, and 17 (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 majority of patients (97/107) were completely healed by 6 weeks postoperative while only 4 patients required 10 weeks or more to completely heal (Figure 3). No significant differences in time to complete wound healing were found for any of the comorbidity or risk factor variables (Table 1). Similarly, there was no statistically significant association between time to heal and age, wound location, or wound size (Table 2). There was, however, a statistically significant inverse correlation between percent of graft take and time to heal. The patients who had 100% graft take had a significantly shorter healing time than those with graft take of less than 95% ($P < 0.001$) (Table 3). Those patients with 100% graft take had a mean healing time of 4.8 weeks compared to 7.9 weeks for those patients with less than 95% graft take (Figure 4). The range of graft take percentage among all groups was between 40 to 100% with a mean take, overall, of 97 percent.

Only 3 patients (2.8%) had a complication with the

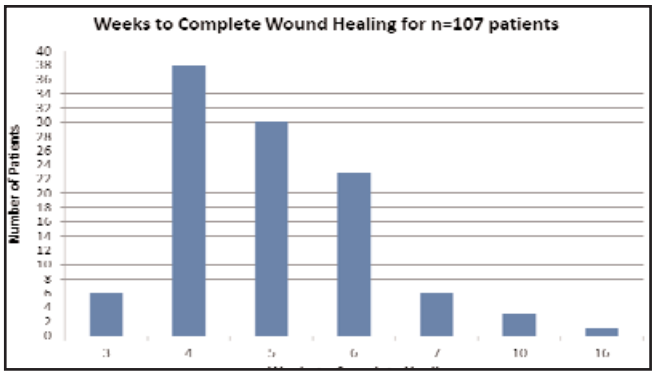

Figure 3. Distribution of time to complete wound healing in 107 patients.

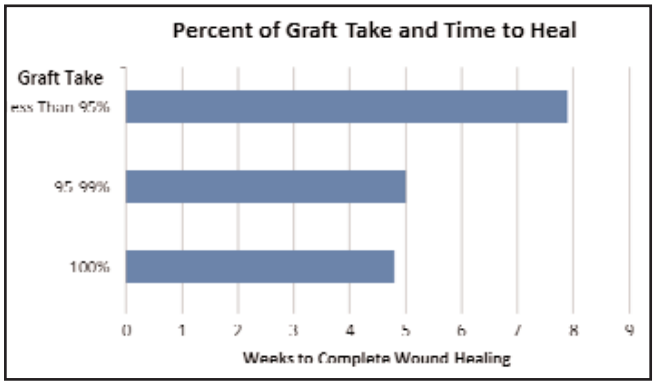

Figure 4. Percent graft take and mean healing time.

original skin graft. In 2 patients, the nursing facility pulled off the skin graft too early. These patients both required regrafting and eventually healed. The other patient had underlying osteomyelitis and required revisional resection of the bone and regrafting, 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 which showed a trend toward significance (P = 0.071) (Tables 4 and 5). Although the number of patients with complications may represent a clinically significant difference, the sample size (n = 3) does not meet the equality of variance test needed to obtain a reliable statistical correlation.

DISCUSSION

Despite success with STSGs 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 5.1 weeks with a range of 3 to 16 weeks. This average is comparable to that of other studies of wound healing in diabetic populations. Recently, Ramanujam et al (10) retrospectively reviewed 83 diabetic patients treated with

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
EtOH	5	4.7%	5.6	0.504
IV Drug Use	3	2.8%	5.0	0.916
RA	7	6.5%	5.0	0.869
ESRD	9	8.4%	6.1	0.415
Cardiac (CAD or CHF)	3	2.8%	4.0	0.254
PVD	7	6.5%	5.7	0.325
Charcot	1	0.9%	4.0	*
HTN	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.

Table 2

TIME TO COMPLETE WOUND HEALING FOR *P* ATIENT AGE, WOUND SIZE, AND WOUND LOCATION

	n	%	Mean Weeks to Healing	*P*
Age ≥65 years	41	38.3%	5.4	0.179
Age <65 years	66	61.7%	4.9	
Wound size <50 cm2	53	49.5%	5.2	0.111
Wound size 50-100 cm2	37	34.6%	4.7	
Wound size >100 cm2	17	15.9%	5.7	
Right foot	29	27.1%	4.7	0.319
Right leg	25	23.3%	5.4	
Left foot	28	26.2	4.9	
Left leg	25	23.3%	5.4	

Table 3

PERCENT OF GRAFT 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*	

*Statistically significant

STSGs for diabetic foot and ankle wounds and reported a median time to healing of 6.9 weeks among those patients without complications. Mahmoud et al (11) 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. They noted that 62% of all STSG patients had healed by week 8. Puttirutvong et al (12) compared the healing rates of meshed versus nonmeshed STSGs in 42 patients and found no significant difference. The mean healing time for the meshed group was 19.84 days and 20.36 days for the nonmeshed group. Most STSG studies in nondiabetic studies report healing times between 2 to 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 (13-16). We did not quantitatively analyze preoperative glycemic control in our study. However, Ramanujam et al (10) 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. Conversely, a study by Marston (13) found a direct correlation between hyperglycemia and wound healing. In this study, we were unable to establish a significant association between any of the preoperative risk factors and delayed healing time. Similarly, we did not find a statistical correlation between healing time and age, wound size, or wound location. Surprisingly, there was no significant difference in healing time among those with large wounds versus those with smaller wounds ($P = 0.111$). 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 to 100 cm^2 actually healed faster, on average, than those with a wound size of <50 cm^2.

Table 4

PATIENTS WITH COMPLICATIONS (N = 3)

Complication	Number of Weeks to Complete Healing
SNF pulled graft off early	10
SNF pulled graft off early	10
Underlying osteomyelitis with exposed bone	16

Table 5

TIME TO WOUND HEALING AMONG PATIENTS WITH AND WITHOUT COMPLICATIONS

Complications	n	Average Time to Complete Healing	*P*
No	104	4.9 weeks	0.071
Yes	3	12.0 weeks	

Our study did not find a statistically significant increase in healing time for those patients with postoperative complications although there was a trend toward significance ($P = 0.71$). The lack of significance is most likely due to the small sample size (n = 3) of patients with complications since those with complications took longer to heal by more than 7 weeks on average than those without complications. Of the 3 patients who had complications, 2 had healing times of 10 weeks and 1 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 1 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 regrafting 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 regrafting by week 16.

It stands to reason that postoperative complications such as infection, noncompliance, seroma, swelling, graft pressure, etc. 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 (10) reported a postgraft complication rate of 35% with 16 patients experiencing an infection. They similarly noted a significant increase in time to complete wound healing in those patients who experienced complications. Similarly, Mahmoud et al (11) reported that 38% of their diabetic patients who received a STSG failed to heal by postoperative week 8.

We found a statistically significant inverse correlation between healing time and percentage of graft take. Those patients with less than 95% graft take had a significantly longer healing time than those with greater than 95% graft take ($P < 0.001$). 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 versus 4.8 weeks), and almost 3 weeks slower than those with a graft take between 95 to 99% (7.9 weeks versus 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 in 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 would maximize the probability of incorporation. The 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 significantly longer to heal. Clearly, the amount of graft take is an indication of the underlying healing process and is, therefore, a predictor of wound healing time. STSGs with poor graft take can be expected to take significantly longer to heal.

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. There was no difference between any patient characteristic or comorbidity that statistically correlated with prolonged healing time, but we did find an average increase in healing time among patients with complications (12.0 weeks) versus those without complications (4.9 weeks), though this finding was not statistically significant ($P = 0.71$). Finally, we found a statistical significance between percent of graft take and healing time such that those patients with decreased graft take were at higher risk for prolonged healing ($P < 0.001$). This underscores the importance of optimizing the STSG for incorporation by minimizing any mechanical or biological barriers to healing. We conclude that autologous STSGs are a safe and reliable alternative for the treatment of nonhealing diabetic foot and leg wounds.

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