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# *Strategies to Promote Healing of Split Thickness Skin Grafts: An Integrative Review*

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## ■ ABSTRACT

Skin grafts are commonly used to promote healing of shallow wounds and burns, and wound care nurses play an important role in management of wounds treated with grafting. The purpose of this article was to review recent findings regarding strategies to promote healing of split-thickness skin grafts including topical phenytoin or platelet-rich plasma prior to graft application, fibrin sealant, or negative pressure wound therapy to stabilize a graft and to promote close adherence of the graft to the underlying wound bed and adjunctive therapies such as laser.

**KEY WORDS:** dressings, evidence-based practice, fixation, nursing care, split thickness skin graft, wound care

## ■ Introduction

Skin grafts are a common method of closing skin defects and have been used since the early 1500s by the Germans and Hindus.[1,2] Skin grafts are either split thickness or full thickness. Split-thickness skin grafts (STSGs) contain the epidermis and varying levels of dermis[3] in order to resurface large areas.[4] Full-thickness skin grafts contain the epidermis and full-thickness dermis; they are primarily used for facial reconstruction because these grafts prevent contraction and better cosmetic results as compared to STSG.[4] Healing rates are typically better for STSGs than for full-thickness skin grafts, because initial graft survival is dependent on osmotic transfer of oxygen and nutrients from the underlying wound bed; thinner grafts are easier to support and more likely to heal.[1]

Split-thickness skin grafts may be used for primary closure of a wound, as adjunctive treatment for wounds that have closed partially in response to other therapies, or to promote healing of donor sites created by other plastic surgery procedures.[5] There is increasing use of STSGs for diabetic foot and leg ulcers, because grafting has been found to shorten healing time and reduce complications.[6,7] Split-thickness skin grafts are the preferred approach in situations where there are large surface areas to be covered, and in burn wound care, where the success rate is close to 100%.[8] These grafts also may be used to provide coverage for soft tissue injuries, management of nontraumatic defects like vitiligo, and face resurfacing for patients with xeroderma pigmentosum.[3,9,10]

Despite their widespread use, STSGs frequently fail. Studies have identified a number of factors that affect healing, including patient age, wound size, anatomic location, wound bed factors such as vascularity and bacterial bioburden, mobility of the graft site, and management of the graft site.[11] The success of the STSG procedure depends not only on the complete integration of the graft with the recipient bed but also on reepithelialization of the skin graft donor site.[12] Optimal management of the donor site is important to achieve wound healing and prevent complications such as infection or pain. Delayed healing of the donor site is a complication that can cause the patient more pain and inconvenience than either the skin graft or the condition for which the graft was performed.[13] Mismanagement of the donor site can lead to drying of the wound, increased time to healing, and deeper scarring.[14]

Recent studies indicate that increased weight-to-hip ratio, obesity, and metabolic syndrome are strongly associated with graft failure. A weight-to-hip ratio greater than 1 has been associated with partial or total graft loss.[15] Research reveals a relationship between infection and graft failure, and newer evidence suggests that patients who receive prophylactic antibiotics have reduced risk of graft failure.[16] Colonization of the wound bed without

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apparent infection also may adversely affect healing; a study at the Copenhagen Wound Healing Center demonstrated a significant difference in healing rates for STSGs applied to venous leg ulcers colonized with *Pseudomonas aeruginosa* versus STSGs applied to noncolonized ulcers (33.3% vs 73.1% healing at 12 weeks; $P = .001$), despite aggressive treatment of the colonized ulcers.[17] In this study, smoking was also associated with failure to heal.

Other factors known to influence STSG survival include vascularity of the graft site, and maintenance of close adherence between the graft and the wound bed to promote diffusion of oxygen and nutrients from the wound bed into the grafted skin.[5] In addition, it is critical to prevent shearing of the graft against the underlying wound bed; shear forces disrupt ingrowth of new vessels and increase the risk of graft failure. As a result of these influences, postgraft management should include measures to ensure tight adherence of the graft to the underlying wound bed. Care must be taken to stabilize the graft and prevent shearing; this is typically accomplished by the application of bolster or compression dressings or use of negative pressure wound therapy (NPWT) to maintain adherence of the graft to the wound bed, and limiting range of motion when the graft is adjacent to a joint.[5]

## ■ Emerging Interventions to Promote STSG Healing

Strategies to promote STSG healing can be classified as those designed to improve wound bed preparation, those designed to provide effective graft fixation and to prevent shearing of the graft against the wound bed, and those used as adjunctive therapy. Younes and colleagues[18] studied the impact of topical phenytoin on STSG healing in a group of 16 patients with diabetic foot ulcers. They applied topical phenytoin (10% w/w ointment) for 2 to 8 weeks prior to grafting, along with standard wound bed preparation including debridement of necrotic tissue. Graft survival was 100% in 12 out of 16 patients (75%), 80% to 90% in 3 out of 16 subjects (18%), and 60% in 1 patient (6%). No local or systemic adverse side effects were observed.[18] Although this study lacked a control group, the authors concluded that phenytoin ointment might enhance STSG survival in diabetic foot ulcers. More studies including studies with control or comparison groups are needed to determine the efficacy of phenytoin on STSG survival.

### *Platelet-Rich Plasma to Enhance Wound Bed Preparation*

Researchers have also investigated the effects of adjunctive treatment with platelet-rich plasma (PRP) on healing of STSGs. For example, a retrospective observational cohort study was conducted involving 13 patients with medical comorbidities and complex soft-tissue defects who were treated with a combination of STSG and PRP (Accelerate Platelet Concentrating System; Exactech, Inc, Gainesville, Florida).[19] Participants were managed in an inpatient setting with complete bed rest, and a multidisciplinary approach was used to treat comorbid medical conditions and optimize the potential for healing.[19] The graft site was treated with PRP produced from 55 mL of the patient's own blood obtained during surgery. Four patients also received adjunctive negative pressure therapy for 4 days following application of the STSG; in these patients, NPWT was used as opposed to a standard bolster dressing because their wounds were larger and had irregular surfaces. The remaining patients had a simple stapled bolster dressing. The mean time to 90% or more healing of the STSGs was $16 \pm 4.2$ days. The results of this study suggest that the addition of PRP to the graft site may reduce the time to 90% or more healing in patients with well-controlled medical comorbidities. This may be attributable to multiple growth factors provided by the PRP.[19]

In another study, platelet gel (PG), STSGs, and fibrin glue were used in combination to promote healing of recalcitrant lower extremity ulcers.[20] Fifteen patients with 17 ulcers of various etiologies were enrolled. Skin ulcers were debrided and the wounds were covered with a moist saline dressing. Three to 14 days later, the wound bed was sprayed with PG, a thin STSG with multiple fenestrations was applied, fibrin glue was sprayed over the skin graft, and the leg was immobilized. Most skin grafts (13/17; 76%) took well. Minor areas of skin graft loss (<5%) were observed in 4 patients, all of which healed spontaneously. The interval between skin graft application and complete wound healing ranged from 3 weeks to 2 months. No recurrence of ulcers was noted during the 3- to 18-month follow-up period. No adverse reactions were observed. This study suggests that the use of PG may promote healing of STSGs; however, there was no control group and controlled trials are needed before any practice recommendations can be made.[20]

## ■ Effects of Early Patient Mobilization on Graft Adherence and Healing

Clinicians have frequently limited patient activity following STSG application, in an attempt to reduce the risk of shearing forces that could cause graft failure. However, immobility is associated with a number of outcomes that may paradoxically increase the risk of morbidity and graft failure. A retrospective review of 48 patients undergoing STSGs to the lower extremity in Australia showed that early mobilization resulted in a reduced length of hospital stay, diminished deconditioning effects, and overall reduction in morbidity rate.[21] In a related study, Tallon and colleagues[22] evaluated the effects of early mobilization on both graft survival and patient morbidity. Forty-two patients were randomly allocated to strict bed rest for 2 or 7 days, based on departmental routines.[22] During the period of strict bed rest, patients were allowed bathroom privileges only; at the conclusion of the bed rest period, patients could return to their usual activities. Three outcomes measures were evaluated: graft loss, infection, and bleeding. In addition, the

number of follow-up visits was tracked as a surrogate measure for time to healing, because patients returned to clinic until satisfactory healing had occurred. All grafts were evaluated and redressed at 7 days; sutures were removed at day 14, and subsequent appointments were arranged if the patient experienced infection, bleeding, or poor graft take. All 42 patients were followed to study completion. The defect size ranged from 210 to 2025 $mm^2$ (mean = 915 $mm^2$) in the 2-day group and 180 to 2250 $mm^2$ (mean = 716 $mm^2$) in the 7-day group. No significant differences were noted in graft survival, and no postoperative venous thrombosis occurred in either group. Six (6) patients experienced significant bleeding events; only 1 graft loss was associated with bleeding. Infection was a common complication, occurring in 44% of the 2-day bed rest patients and in 31% of the 7-day bed rest patients; 2 graft losses were attributed to wound infection. Overall, the results suggest that a shorter period of bed rest (2 days) for patients undergoing STSG for lower extremity ulcers may reduce morbidity rate without compromising graft survival.[22]

### Graft Stabilization/Fixation

Successful skin grafting requires stabilization and compression of the graft site to maintain close adherence between the STSG and underlying wound bed. Stabilization also prevents shearing forces that interfere with ingrowth of vessels and graft take. Bolster dressings or NPWT devices are commonly employed in the postoperative period to accomplish these goals.

In a case-controlled retrospective study, STSG patients were treated with either a hydrocolloid dressing ($n$ = 31) or a bolster dressing and splinting ($n$ = 31).[23] Treatment duration for the hydrocolloid group was significantly less than that for the bolster dressing and splinting group (8.32 ± 1.82 days vs 13.55 ± 5.30 days; $P < .001$). No significant differences were observed between the groups with regard to age, sex, or graft size. The hydrocolloid group included 1 case with a complication (stitch abscess), whereas the bolster and splinting group included 8 cases with partial skin loss. These findings suggest that the use of a hydrocolloid dressing as opposed to a bolster dressing and splinting may enhance graft survival as measured by shorter treatment time and lower complication rates.[23]

The use of fibrin sealant has also been shown to promote graft adherence and healing. Foster and colleagues[24] compared the impact of fibrin sealant containing 4 IU/mL thrombin to staples on graft adherence in 138 burn patients requiring wound excision and skin grafting. Patients had burn wounds measuring 40% of total body surface area or less with 2 comparable test sites measuring between 1% and 4% total body surface area each. The primary outcome measures were wound closure at day 28 assessed via planimetry and review of photographs taken on day 28 by 3 independent blinded evaluators. Secondary efficacy measures included hematoma/seroma on day 1, engraftment on day 5, and wound closure on day 14. Complete wound closure at day 28 occurred in 70.3% of the fibrin sealant treated sites and 65.8% of stapled sites, suggesting that fibrin sealant is at least as efficacious as staples in promoting complete wound closure by day 28. The subjects in the fibrin sealant group scored significantly better than subjects in the staple group for all investigator-assessed outcomes, including quality of graft adherence ($P < .0001$), preference for method of fixation ($P < .0001$), satisfaction with graft fixation ($P < .0001$), and overall quality of healing ($P < .0001$). Likewise, all patient-assessed outcomes were better among the fibrin sealant subjects, including anxiety about pain ($P < .0001$) and treatment preference ($P < .0001$). No serious adverse occurred among patients treated with the fibrin sealant. These findings suggest that fibrin sealant may be a safe and effective option for attachment of skin grafts, with outcomes as good as or better than staple fixation.[24] However, further studies are needed in order to more definitively determine its efficacy and safety.

### Honey Dressings and NPWT to Promote Graft Fixation and Wound Healing

In recent years there has been a renewed interest in active leptospermum honey dressings as one approach to wound management. In addition to its antimicrobial and immunological effects, medicinal honey has also been shown to have adhesive or sealant properties.[25] To evaluate the use of honey for STSG fixation, 11 patients who underwent STSGs for wounds of different etiologies were studied.[26] Medical grade honey was used for the fixation of the skin graft; specifically, a modern synthetic material was impregnated with decontaminated and regulated honey (HoneySoft; MediProf, Moerkapelle, The Netherlands) that was used to stabilize the graft. No graft loss was seen during either the first dressing or the last assessment of the grafted areas. No complications such as graft loss, infection, or graft rejection were seen. These results suggest that honey may be one option for STSG fixation.[26] However, this was a small study with no control group and randomized controlled trials are needed before definitive recommendations can be made.

Negative pressure wound therapy is another intervention that has evaluated for stabilization and promotion of wound healing in patients with STSGs. Petkar and colleagues[27] compared STSG healing, using NPWT to grafts managed with standard care. The study involved 30 patients with burn wounds who required 40 STSGs; NPWT was used on 21 of the grafts, and the remaining 19 served as controls. After the STSG was applied and secured with staplers or catgut sutures as necessary, the control group grafts were dressed with Vaseline gauze, cotton pads, and cotton bandage (for limbs) or an elastic adhesive bandage (for trunk). Patient profiles and average graft size were comparable between the 2 groups. The NPWT was described as "well tolerated" by all patients. Graft take at 9 days ranged from 90% to 100% (mean = 96.7%) in the NPWT group versus 70% to 100% (mean = 87.5%) in the control group. The mean number of days for which dressings were

required on the graft site was 8 ± 1.48 in the NPWT group and 11 ± 2.2 in the control group ($P < .001$). Results of this study suggest that NPWT may improve graft take in burn patients.[27] Another retrospective study compared STSG survival in patients managed with NPWT using reticulated open cell foam to patients managed with conventional therapy.[28] Conventional therapy involved a cotton bolster dressing, a sterile compressive dressing, or a stainless steel gauze dressing used for at least 5 days. Outcomes measures included overall graft take, duration of graft take, need for repeated grafts, and complications. Significantly fewer repeated STSGs occurred in the NPWT (3.5% vs 16%; $P = .006$). In addition, fewer complications were associated with graft failure (seroma, hematoma, and infection) in the NPWT group as compared to the conventional therapy group at 8 to 9 months. These results suggest that NPWT is an effective option for stabilizing an STSG and may improve graft survival as measured by a reduction in the number of repeated STSGs and graft failure complications.[28]

A third study evaluated the impact of a NPWT system using vacuum-assisted closure (VAC) in management of complicated wounds in the head and neck region.[29] The VAC system (Kinetic Concepts Inc, San Antonio, Texas) was used in 12 patients with 13 grafts. Nine subjects had exposed calvaria necessitating bony coverage. All STSGs demonstrated 100% viability after 5 to 7 days of the VAC system used as a bolster dressing, and all wounds healed successfully without complications.[29] These results suggest that VAC may also be a valuable tool in the management of STSGs for complicated head and neck wounds.

### *Adjunctive Therapies*

Recently, STSG has been used for treatment of conditions such as vitiligo. Al-Mutairi and coworkers[30] evaluated long-term results of combination therapy involving STSG and a 308-nm excimer laser for the treatment of vitiligo.[30] Seventeen patients with stable focal or segmental vitiligo who were unresponsive to nonsurgical modalities were treated with STSGs and 32 sessions of 308-nm excimer laser, beginning 2 weeks after surgery. Final evaluation completed 12 months revealed cosmetically acceptable results in all 17 patients; none of the patients developed depigmentation of the transplanted skin. This study did not include a control group so no conclusions can be reached regarding the specific effects of the laser therapy.

Application of STSGs to visible and exposed body surfaces, such as the face and extremities, is associated with postgraft color changes. In a randomized controlled trial, basic fibroblast growth factor (bFGF) was shown to promote postoperative color uniformity in wounds treated with STSG.[31] In this trial, one group of patients received skin grafting plus bFGF spray daily and the other group received skin grafting alone. Clinical and objective assessments of the scars were conducted 12 to 18 months following complete healing based on the Vancouver Scar Scale. There was less of a color differential in comparison with the surrounding skin in grafts treated with bFGF for all parameters ($P < .01$).[31] However, it should be noted that these findings about STSG combined with bFGF are from a single study and therefore should be interpreted with caution. There is a need for more studies to confirm the effectiveness of STSG combined with bFGF.

Fraccalvieri and associates[32] reported results of 7 cases of heel ulcerations with chronic osteomyelitis treated with partial tangential calcanectomy and application of Integra Dermal Regeneration Template followed by STSG. Negative pressure wound therapy was also used to promote healing.[32] Specifically, NPWT was used for 14 days following application of the Integra; when the silicone layer of the Integra dressing was removed 14 days following surgery, an STSG was applied to the neodermis and NPWT was utilized for another 5 days to stabilize the graft and promote healing. All wounds healed and no patients required amputation. In these patients, the combined use of partial calcanectomy, Integra, Dermal Regeneration Template, STSG, and NPWT provided long-term healing; nevertheless, controlled trials are needed to validate these findings.[32]

## Conclusion

Wound clinicians play an important role in managing patients with wounds that require STGS and therefore should be aware of emerging evidence regarding strategies to promote healing. Current evidence suggests that topical phenytoin and PRP may be used prior to graft application to improve healing rates, and NPWT and fibrin sealant may be used to promote graft adherence. In addition, recent evidence suggests that prolonged activity restriction may not be necessary or beneficial for patients with lower extremity wounds managed by STSG. Further study is needed to validate these findings, and wound clinicians must critically review research reports in order to maintain evidence-based practice.

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