Single-stage Reconstruction for Soft Tissue Defects: A Case Series

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Abstract

Various techniques for obtaining expedient aesthetic coverage of soft tissue defects with limited donor site morbidity have been developed, including the use of a dermal regeneration template (DRT) as the first step in a two-stage surgical approach. Use of DRT in reconstruction has increased as a result of reports suggesting improved cosmetic results and reduced scarring compared to split-thickness skin grafts (STSG), but this approach requires a return to the operating room. To evaluate outcomes of a single-stage procedure, a prospective evaluation of patients with complicated soft tissue defects measuring <200 cm^2 was conducted. Following trauma or resection of a tumor, 20 patients underwent single-stage reconstruction with surgical debridement and application of a single-layered DRT and a meshed STSG. Negative pressure wound therapy (NPWT) was applied as a bolster with continuous -125 mm Hg pressure for 5 days. After 5 days, traditional dressings were applied and patients were followed until healed with a minimum follow-up of 5 months to a maximum follow-up of 19 months. Participants included 20 patients (14 men, six women; average age 60 years old [range: 27–92 years]; average wound size 104.5 cm^2 [range: 40.0–180.0 cm^2]). Wounds were located on the lower extremities (10 patients), upper extremities (seven patients), and trunk (three patients). Average graft take was 98.3% with an average take time of 5.6 days (SD 0.50). No significant differences in graft take rates between male and female patients, smokers and nonsmokers, and patients with and without diabetes mellitus were observed. Wound location also did not affect graft take rates. No wound breakdown, adverse events, or re-operation occurred during follow-up. In this case series, single-stage reconstruction using DRT, STSG, and NPWT was used with good outcomes and second-stage reconstruction surgery was avoided. Prospective, randomized, controlled clinical studies to compare the various surgical and wound care approaches to closing these tissue defects are warranted.

Keywords: negative pressure wound therapy, wound closure technique, skin transplantation, case series, single-stage reconstruction

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Aesthetic coverage of soft tissue defects is an ongoing challenge in plastic surgery. Thorough evaluation of wound characteristics and patient comorbidities is critical for achieving optimal goals of wound healing, which may include obtaining durable coverage, minimizing donor site morbidity, and maximizing function.[1,2] The introduction of advanced wound care technologies, including negative pressure wound therapy (NPWT) utilizing reticulated open-cell foam, has resulted in a decreased requirement for complex surgical procedures (eg, orthopedic), particularly microsurgical free tissue transfers.[3,4] In a study of 296 consecutive open tibia-fibula fractures over a 12-year period, Parrett et al[3] found that local wound care for grade III fractures, including skin grafts, delayed primary closures, and secondary intention closures increased from 22% to 39% for reconstructions between 1992 and 2003. The authors concluded the observed trend toward less complex reconstructive procedures was related to, among other factors, the use of improved wound care technology, including NPWT.[3]

Reconstruction techniques of lesser complexity that often follow the use of NPWT include local flaps or skin grafting. However, skin grafting over exposed bone, cartilage, or tendon generally is not recommended due to historically low graft take rates.[5] In addition, outcomes related to long-term elasticity and appearance following split-thickness skin graft (STSG) are not optimal. The STSGs are prone to contraction, and meshed grafts (1:1.5, 1:2, or 1:3) may have a pebble or cobblestone appearance when re-epithelialized compared to unmeshed or sheet grafts.[5-8]

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Key Points

- To obtain optimal aesthetic outcomes, a two-stage surgical procedure to close smaller tissue defects may be required.
- The authors used a one-stage approach to close 20 wounds (average size 104.5 cm^2) involving a dermal regeneration template (DRT), split-thickness skin graft, and negative pressure wound therapy as a bolster dressing.
- Graft take was good (average 98.3%), and no second surgical procedures were needed.
- Studies to examine optimal strategies for surgical closure of small (and larger) defects are needed.

A dermal regeneration template (DRT) has been used for a two-stage approach in reconstruction of complicated lower extremity wounds and soft tissue defects, such as those resulting from radical skin cancer removal or trauma.[9-13] DRT is applied as a bilaminate membrane consisting of a porous acellular collagen-glycosaminoglycan dermal layer bonded to a thin silicon layer. Results of a three-patient case series focusing on small area defects showed that, with normal progression, the artificial dermal scaffold is replaced by neodermis tissue with function and histology similar to normal human dermis.[14] Histological studies[12] demonstrate the same four phases of dermal regeneration observed in wound healing and skin graft take with use of DRT: imbibition, fibroblast migration, neovascularization, and remodeling and maturation. A prospective randomized trial by Heimbach et al[10] showed less hypertrophic scarring and greater patient satisfaction with DRT compared to autograft, allograft, xenograft or a synthetic dressing in 106 patients with 139 burn sites, although the median DRT graft take was 80% compared to 90% for autograft sites. The authors concluded that DRT with STSG provides a permanent cover at least as satisfactory as control skin grafting techniques and requires a thinner donor graft, which results in faster healing of donor sites.

Despite the paucity of well-designed, controlled studies evaluating use of DRT, several case series have reported benefits of DRT in burn and reconstructive surgery, including volume stability over time,[15] improved functional and cosmetic outcomes without donor-site morbidity factors,[10,12,13] and minimized scar contraction, all as compared to STSGs.[16] A retrospective analysis[15] of 30 patients who received DRT in augmentation rhinoplasty concluded that DRT volume remained stable throughout the follow-up period of at least 12 months. In 39 patients who received DRT grafts for burn scar contractures (n = 19) or acute surgery for burn patients (n = 20), long-term results suggested improved cosmetic (eg, minimal scarring) and functional (eg, good range of motion) results in treatment of burns in the acute and late surgery stages compared to STSGs.[13] In a consecutive case series[12] of 20 consecutive wounds with 30 anatomical site reconstructions utilizing DRT, patients reported increased range of movement and improved appearance compared to preoperative states.

Without adjunctive therapies, Greenwood et al[17] determined through clinical blood flow evaluation and confocal microscopy of wounds in a single burn patient who presented with 80% total body surface area burn that neovascularization of the DRT takes approximately 2 weeks in the acute burn setting and can take 4 to 5 weeks in reconstructive cases. However, these study results[17] are limited by a population size of only one patient and therefore cannot necessarily be extrapolated to all patients.

Once the dermal layer is integrated, traditional protocol requires an ultra-thin STSG or epidermal autograft be placed over the new dermis after atraumatic removal of the silicone layer from the new dermal layer. However, poor graft take and loss due to infection remain a concern for at-risk patients.[18,19] In a consecutive case series, Moiemen et al[12] showed that earlier split skin grafting at 2 to 3 weeks following DRT application often resulted in graft loss, and this was shown to be histologically related to poor vascularization. Applying NPWT over DRT's dermal layer may enhance contact between the layer and wound bed and provide a protective barrier over the graft. Previous case series[20,21] have suggested application of NPWT over DRT may reduce the time between DRT and second-stage STSG. Molnar et al[21] reported on simultaneous application of DRT and NPWT over eight complex wounds with exposed bone, joint, tendon, or bowel, resulting in a 96% graft take of DRT and second-stage skin grafting performed at 4 to 11 days post DRT application. The authors concluded that the observed take rate and time to vascularization was better than that reported by others.[21] In an additional series,[20] 10 soft tissue defects initially debrided and then treated with NPWT and DRT could be skin grafted 7 to 10 days post-DRT, resulting in STSG take rates between 75% and 100%. The authors concluded that combined use of NPWT over DRT may improve outcomes in difficult anatomical areas and/or outpatient settings. These results perhaps could be explained by the continuous removal of fluid between the graft and recipient bed by way of negative pressure, which may enhance surface-to-surface contact. A randomized, double-masked, controlled trial[22] suggests that improved surface contact appears to facilitate plasmatic imbibition and revascularization that can lead to significant improvement in overall graft survival.

In an effort to decrease costs of care and length of hospital stay and eliminate the return to the operating room for a second-stage reconstruction, a prospective evaluation was conducted of a single-stage approach in closing small soft tissue defects using single-layer DRT and STSG in combination with NPWT. It was theorized that in smaller wounds the waiting period between first- and second-stage DRT/STSG

application could be successfully eliminated with adjunctive use of NPWT. The purpose of this study was to assess the take rate and integration of DRT with synchronous application of DRT, STSG, and NPWT.

Methods and Procedures

Approval to perform the study was obtained by the internal review boards at Loma Linda University Medical Center (Loma Linda, CA) and Southwest Washington Medical Center (Vancouver, WA). Twenty (20) consecutive patients with complicated soft tissue defects <200 cm^2 in area due to trauma following resection of a tumor or debridement of an ulcer were prospectively enrolled in the study from one study site between September 2008 and February 2010. Exclusion criteria included the presence of necrotic tissue, positive margins for cancer, or peripheral vascular disease (PVD). No other comorbidities were addressed. Written informed consent was obtained before enrollment in the study. Data regarding patient variables (age, gender, presence of diabetes mellitus, and smoking habit) and wound location were collected.

All patients underwent single-stage reconstruction with application of a 1:1 meshed, unexpanded DRT (Integra®, Integra LifeSciences Corp, Plainsboro, NJ) to a debrided and granulating wound. The silicon layer was separated from the dermal matrix layer if the double layer matrix was used. During the course of the trial, a single-layer, meshed DRT was introduced by the manufacturer and was used in the study. The new single-layer product was the same as the dermal matrix layer of the initial double-matrix layer product used. Seven of the 20 patients received the single-layer product.

A meshed (1:1.5) split-thickness autograft (0.0254-mm dermatome setting) was placed directly over the DRT and covered by a thin, porous nonadherent dressing (Adaptic®, Johnson & Johnson, Somerville, NJ). NPWT (V.A.C.® Therapy, KCI Licensing Inc., San Antonio, TX) was applied immediately after as a bolster. The reticulated, open-cell foam dressing (V.A.C.® GranuFoam™ Dressing, KCI Licensing Inc, San Antonio, TX) was cut slightly larger than the size of the graft, and negative pressure was applied continuously at -125 mm Hg for 5 days. Patients were discharged on the day of surgery or the following day and treated as outpatients for dressing changes and follow-up. NPWT was discontinued on postoperative day 5 and replaced with gauze and a nonadherent dressing (Adaptic, Johnson & Johnson, Somerville, NJ), changed daily for 7 to 10 days until complete graft take was observed. Nutrition and mobility were optimized during treatment. All patients were taking multivitamins, vitamin C (1,000 mg, twice a day), L-arginine, and B complex daily. Vitamins were started at the time of consultation and continued for 4 weeks after surgery; at each follow-up visit, patients were asked if they were still taking their vitamins and other products. Patients were not asked to limit mobility unless an underlying fracture that needed mobilization was present; NPWT served as a splint for the graft. Physical therapy was consulted only if patient had underlying long bone fractures that required therapy.

Graft take was assessed by a single surgeon (based on observation, experience, and how much graft was present or absent) at the 1-month follow-up and was deemed successful if take was >80%. All patient variables and wound outcomes were entered into a Microsoft® Excel (Microsoft Corporation, Redmond, WA) spreadsheet. Wilcoxon Rank Sum and Kruskal-Walli tests were performed using SAS® version 9.1.3 (SAS Institute Inc, Cary, NC) to determine whether patient gender, age, diabetes status, smoking status, or wound location affected graft take. PVD information was collected to qualify patient inclusion.

Results

Twenty patients (14 men and six women) with 20 wounds were enrolled in the study. Average age was 60 years old (range: 27–92 years), and average wound size was 104.5 cm^2 (range: 40.0–80.0 cm^2). Wounds were located on the lower extremities (10 patients), upper extremities (seven patients), and trunk (three patients) (see Table 1).

All patients were treated initially for 5 days with NPWT post other procedures and followed for dressing changes for an additional 2 to 3 weeks until complete wound closure. Graft take was 85% in one patient, 90% in two patients, and 100% in the remaining 17 patients. Average graft take was 98.3% with an average take time of 5.6 days (SD 0.05). All DRTs took successfully, but time to neovascularization was not measured. No significant differences in graft take rates were noted between male and female patients, smokers and nonsmokers, and patients with and without diabetes. Wound location also did not affect graft take rate.

Patients with <100% graft take had partial skin loss and required prolonged wound care. Each of these wounds was fully healed within 6 weeks without a need for re-operation. No adverse events were reported. Follow-up averaged 12 months (range: 5–19 months) with no wound breakdown observed (see Figures 1 and 2). A reduction or complete elimination of contour irregularities was anecdotally observed with simultaneous use of DRT and STSG, compared to the authors' experience with STSG alone.

Discussion

The results of this study suggest that single-stage grafting with DRT, STSG, and NPWT is a safe alternative to the two-stage approach for grafting and was effective in this patient series. In this study, no second procedures were needed, eliminating the need for additional anesthesia and operating room costs. Application of DRT to create a thicker, cosmetically appealing skin graft supports a primary reconstructive goal of replacing like tissue with like. This one-stage technique may be particularly beneficial over areas of the body where exposed skin is common and coverage with clothing may not be suitable depending on climate.

Table 1. Patient demographics

Patient #	Age	Gender	Diabetes mellitus	Smoker	Wound location	Source	Size (cm^2)	Follow-up time (days)	Graft take (%)
1	78	F	NO	NO	Lower extremity	Trauma	180	577	90
2	65	M	NO	YES	Lower extremity	Ulcer	120	487	85
3	39	M	NO	YES	Lower extremity	Trauma	60	516	100
4	29	M	NO	NO	Upper extremity	Trauma	140	486	100
5	85	M	NO	NO	Trunk	Cancer	180	393	100
6	77	F	YES	NO	Lower extremity	Cancer	100	334	100
7	71	M	NO	NO	Lower extremity	Cancer	50	487	90
8	92	F	YES	NO	Upper extremity	Cancer	50	304	100
9	59	M	NO	NO	Lower extremity	Cancer	60	426	100
10	36	M	NO	NO	Lower extremity	Trauma	140	395	100
11	54	F	NO	NO	Upper extremity	Trauma	120	365	100
12	47	M	NO	NO	Trunk	Trauma	120	396	100
13	78	F	NO	NO	Lower extremity	Trauma	140	334	100
14	62	M	NO	NO	Lower extremity	Cancer	120	273	100
15	54	M	NO	NO	Upper extremity	Cancer	180	304	100
16	65	M	NO	NO	Upper extremity	Cancer	80	212	100
17	89	F	NO	NO	Trunk	Cancer	50	243	100
18	28	M	NO	NO	Upper extremity	Trauma	40	243	100
19	54	M	NO	NO	Upper extremity	Cancer	120	243	100
20	39	M	NO	YES	Lower extremity	Trauma	40	150	100

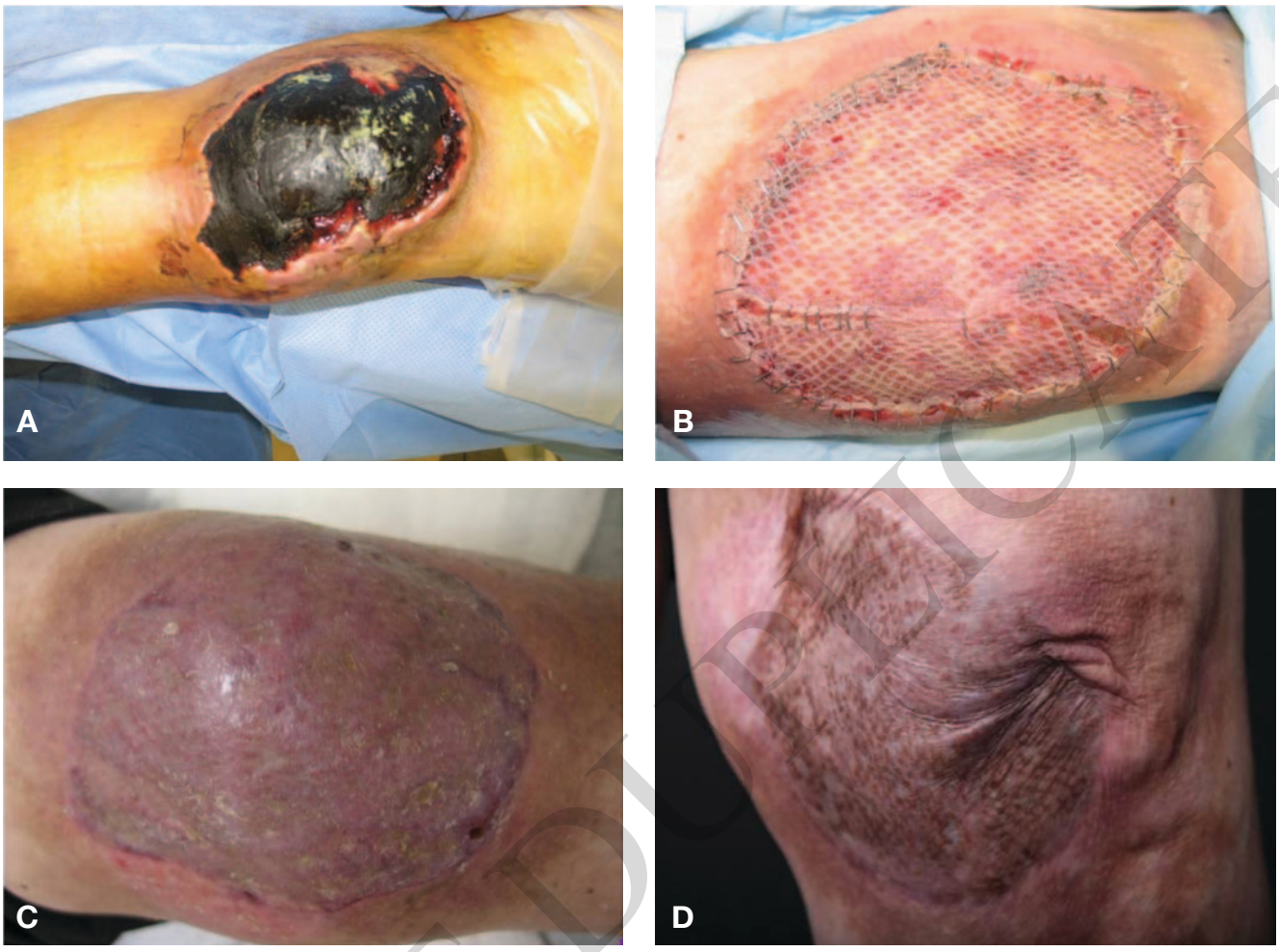

Figure 1. Patient 1: a) A 78-year-old woman was admitted with left knee skin necrosis following a traumatic fall. Medical history included cardiomyopathy and atrial fibrillation. Current medications included coumadin, antihypertensives, and beta blockers; b) single-stage intra-operative procedure.; c) 7 weeks postoperative follow-up; d) 2 years post procedure.

Previous, smaller case studies[23-25] describing successful single-stage application of similar DRT originally prompted investigation of this technique. One case report[23] described treatment of a 25-year-old man with DRT in combination with NPWT and a STSG. The combined treatment resulted in complete graft take. Additionally, Burd et al[25] described a series of 10 patients who underwent circular excisions for facial cancers successfully repaired using a single-stage DRT approach. All wounds were fully healed within 6 weeks, either by wound contraction or in conjunction with re-epithelialization. The authors concluded that single-stage reconstruction can "reduce operating time with no delay for frozen section, flap raising, or graft harvesting."[25] Several small case series[26,27] have been published about the successful single-step use of an alternate brand collagen-elastin matrix as well.

Neovascularization of the DRT can be impaired by seromas, hematomas, or infection. It has been suggested based on observations of a single-patient study[17] of a person who presented with 80% total body surface area burn that the first steps of DRT neovascularization follow the increase of bone-marrow-derived progenitor cells that penetrate the DRT surface in the wound bed exudate, which is in contrast to STSG inosculation (ie, acquiring nourishment via a connection between new blood vessels in the wound bed and existing graft vessels). Greenwood et al[17] observed blood flow using a VivaScope™ (Lucid, Inc, Rochester, NY); the STSG was applied to his hands, while the DRT was applied to his remaining wounds. Results showed blood flow in the STSG on day 4 post-application, whereas blood flow was not seen in the DRT until day 23 post-application. These results suggest that different processes exist for establishing circulation in skin grafts and DRTs, and that inosculation offers a rapid circulatory return to skin grafts, whereas DRT revascularization is by neo-angiogenesis, takes longer, and is initially characterized by more rapid, higher-volume flow through larger vessels.

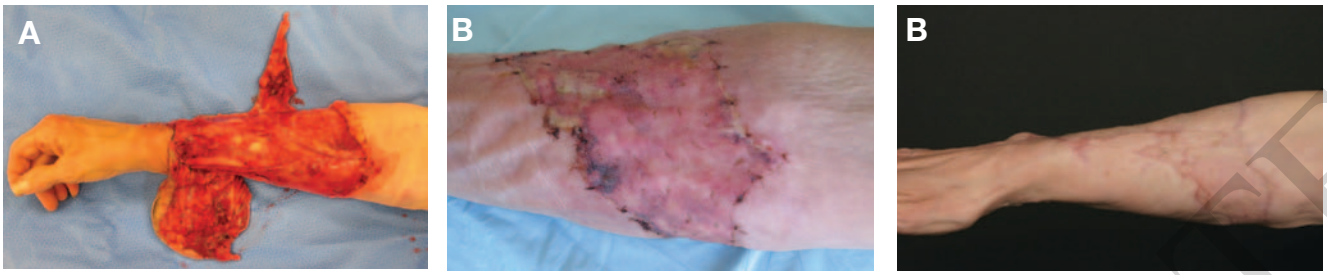

Figure 2. Patient 11: a) A 54-year-old woman presented with soft tissue loss of the forearm with some circumferential involvement following a rollover car accident. Past medical history was negative for chronic health conditions, and she was not taking medications; b) wound 10 days following reconstruction and single-stage DRT artificial skin grafting bolstered with NPWT; c) 1-year follow-up.

Adjunctive NPWT appears to have a positive effect on both of these processes. For example, a small series[20] of 10 patients treated with adjunctive NPWT over the dermal layer of DRT allowed for skin grafting within 7 to 10 days, with a mean of 8 days. Using an in vitro model, Baldwin et al[28] showed endothelial cells were switched to a migratory and proliferative phenotype with application of NPWT over DRT, identifying a potential pro-angiogenic mechanism by which NPWT may accelerate integration of DRT. In a consecutive case series,[29,30] NPWT also has been shown to positively affect autograft survival as measured by a reduction in secondary procedures and number of repeated STSGs.

Use of the NPWT system reduces edema. This reduction in edema was initially observed in a large, consecutive case series[31] in which NPWT was applied to more than 300 wounds (ie, acute, subacute, and chronic wounds). Other clinical studies, including a randomized controlled trial,[29,32-34] have shown that the system also removes infectious materials (ie, wound exudate that contains organisms that may cause infection) from beneath the grafts, and because NPWT is a closed system it may help protect the grafts from outside contaminants. In addition, known microdeformational effects of NPWT at the cellular level (eg, cell migration and proliferation, leading to granulation tissue formation) have been found in computer modeling and in vitro studies,[35-37] which may facilitate wound healing in general.[31-33] Such research suggests these mechanisms of action may help facilitate neovascularization of the DRT.[19,21,28] For example, in a randomized clinical study, Jeschke et al[19] compared the use of conventional therapy and DRT (n = 6) to NPWT plus fibrin glue with DRT in patients (n = 6) with large tissue defects. Results showed that the DRT take rate was 98.2% in the fibrin plus NPWT group versus 78.8% in the conventional DRT therapy group (P <0.003). The authors hypothesized that the effect on neovascularization is "mainly the negative-pressure treatment that improves vascularization."[19] Molnar et al[21] used NPWT as an adjunct to optimize vascularization and adherence of DRT in eight patients with complex wounds. The mean time for vascularization of DRT was 7.25 days (range: 4–11 days) with an average take rate of 96%.[17] In all cases, a nonadherent material (eg, Adaptic®, Johnson & Johnson, New Brunswick, NJ) should be used between the NPWT dressing and the DRT.[30,33,38]

Authors of the current study hypothesized that the outcomes of the synchronized technique are good because epithelialization occurs while neovascularization of the dermal layer is taking place. A potential explanation for this hypothesis may be the effect of a continuous, firm contact between the undersurfaces of the grafts and recipient bed caused by the force of negative pressure. This theory could be supported by Grant et al's[39] observation in porcine models that more intimately opposing the DRT to the wound bed enhances biocompatibility of DRT and the recipient bed. This study used sequential protocol modifications to remove dead space beneath the DRT (ie, by grafting the DRT onto the panniculus carnosus muscle layer), which allowed for more direct contact between the DRT and wound bed and resulted in improved graft take rates (from close to 0 to a mean of 96%).

Relevant contraindications for DRT and/or STSG placement over a wound should be considered at all times. Wounds that are heavily contaminated with bacteria and chronic wounds with thick exudate or thick fibrotic tissue should be surgically debrided and converted into smaller, acute wounds.[31,33] It is important to adhere to well-established principles of debridement and surgical technique, regardless of adjuvant products used, to optimize outcomes and minimize morbidity.[31,33] The current study authors' experience with grafting small wounds has been successful following these principles. The question arises as to whether this technique can be used for wounds with larger exposed surface areas. To date, a single staging has not been attempted in larger wounds because patients with larger surface area deficits are generally in more critical condition and require additional medical care. Although the traditional two-stage process should be followed for these patients, more studies are necessary to determine what role DRT and NPWT could play in enhancing coverage over the exposed area to minimize fluid loss and stabilize wounds in patients recovering from an acute injury.

Limitations

The results of this study are limited by the small sample size, as well as a lack of control group and histological data. Larger, prospective controlled clinical studies are needed to compare the outcome of this technique to two-stage procedures that do and do not include placement of the DRT followed by STSG in 3 to 6 weeks. Efficacy information on use of DRT remains limited and also should be included in any future studies.

Conclusion

The findings of a small prospective case series suggest that single-stage grafting involving DRT, STSG, and NPWT was safe and an effective alternative to the two-stage approach for grafting in this patient population with defects measuring <200 cm^2. No wound breakdown or re-operation occurred during the average 12-month follow-up time and this technique has become standard practice in the authors' institutions. Controlled clinical studies to compare the efficacy, effectiveness, and cost-effectiveness of DRT and non-DRT use, as well as DRT with and without NPWT for single-stage reconstruction, are warranted. n

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