Complex lower extremity wounds treated with skin grafts and NPWT: a retrospective review

• **Objective:** To evaluate a single centre experience with the use of NPWT for securing split-thickness skin grafts in the management of specifically lower extremity chronic wounds, including revascularised arterial wounds, amputations, diabetic and venous leg ulcers.

• **Method:** A seven-year retrospective review of a prospectively maintained database of all the patients who underwent primary split-thickness skin grafts (STSGs) with immediate postoperative NPWT for at least 96 hours was carried out. The percentage graft take after removal of NPWT device and clinical follow-up date were reviewed.

• **Results:** A total of 59 skin grafts procedures had adequate follow up to be reviewed. This included 39% post-debridement/ amputation wounds in patients who presented with diabetic foot infection/ gangrene, 31% venous leg ulcers, and 31% other post-surgical wounds (arterial ulcers that had undergone revascularisation). The mean percentage graft survival after removal of V.A.C. was 94%; 63% of cases had complete graft survival, 25% had 90–99% survival, and 8.5% had 80–89% survival. Outpatient follow up ranged from 2 weeks to 5 years (mean of 10 months). Fifteen per cent of patients were lost to follow up, and, of the remaining patients, 76% remained completely healed, 10% remained partially healed, and 14% lost the entire STSG.

• **Conclusion:** Patients with STSGs secured with NPWT required fewer repeated grafting procedures, had very high initial graft survival with complete recipient bed coverage, and had good long-term wound closure rates compared with historical controls. While retrospective reviews, such as this, support NPWT as a good method of STSG affixation, the paucity of reviews with other study designs does not allow for good historic comparison, so a well-enrolled prospective trial would be of use.

• **Declaration of interest:** Dr J.C. Lantis is a member of the speakers' bureau, has been a site principal investigator of four multicentre trials and has been a consultant for KCI Inc. The same author has no equity in the company and has no financial benefit from positive results for the company's product(s). No external funding was sought nor obtained for this study.

split-thickness skin grafts; negative wound pressure therapy; lower extremity wounds

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Negative pressure wound therapy (NPWT) has been increasingly used in the fixation of split-thickness skin grafts (STSGs). However, there is a lack of strong objective evidence regarding its superiority to conventional dressing methods. Classically, skin grafts are immobilised in place using a tie-over bolster dressing, maintained *in situ* for 5–7 days.[1] Despite being successful in the majority of cases, an inadequate graft bed, haematoma, fluid collection, movement, infection and technical errors can contribute to graft loss.[1–5]

It is difficult to find data on the success of STSG secured with traditional methods in the chronic wound environment, with the majority of the previous data documented in the burns literature.[4–6] According to various investigators, in very homogenous patient cohorts, skin grafting is associated with a relatively high failure rate in chronic wounds, especially in patients with vascular impairment, either venous or arterial in nature.[7,8] In the authors' experience, graft take in contoured anatomical positions or mobile lower extremity surfaces is more problematic.

NPWT is an attractive approach, seeming to overcome some of the factors responsible for failure of skin grafts. In a number of independent reports, it has been associated with a high rate of graft take in exuding, irregular or mobile recipient beds and in difficult anatomic locations or irradiated fields.[9–14] Despite the widespread clinical application of NPWT in recent years, the published data supporting its use for securing skin grafts are limited to case series and retrospective reviews.[11–17] There are few prospective randomised studies focusing on NPWT in skin grafted wounds,[18,19] which all suffer from small sample size, heterogeneity of patients, non-comparable study groups and poor randomisation.

Clinical research with wound healing technology is challenging due to the heterogeneity of the wounds treated by clinicians, inability to compare

Fig 1. Intraoperative pictures (from debridement to application of V.A.C.) of a patient in our series with a large VLU who had complete initial graft survival, and whose wound remained completely closed 13 months after grafting

the outcome measures, and the difficulty of blinding the treatment arms. The 10 patients that we presented in 2004 represent the only attempt at a multicentre randomised trial to evaluate the efficacy on NPWT in affixing STSGs to the lower extremity wound, specifically venous leg ulcers (VLUs).[20] This failed due to poor enrolment. Therefore, in the absence of large prospective randomised studies on the effects of NPWT therapy in the healing of skin grafted wounds, clinicians often have to rely on personal experience and retrospective reviews. The best attempt at this may be Korber et al.'s work — a retrospective analysis of 54 patients having 74 procedures, which were not randomised.[16] The majority of patients (85%) had VLUs, those treated with NPWT (n=28) had a 93% take while those treated with a bolster technique (n=46) had a 67% take.[16]

The current study describes the versatility of Vacuum Assisted Closure system (V.A.C., KCI Inc.) in securing STSGs in the management of the three major categories of chronic lower extremity wounds. Compared with previous reports, these patients all had complex lower extremity diabetic, arterial or venous insufficiency ulcers that were refractory to non-operative management. It also represents the largest group of patients in this category to be treated with active NPWT, and has a longer mean follow-up at 10 months than any other similar study.

Method

Using an IRB approved surgical database, we performed a retrospective review of all patients who underwent skin grafting and immediate fixation with NPWT at our institution over a 7-year period, from January 2004 to January 2011. Patient demographics, indications for procedures, wound locations, operative reports and postoperative follow-up data were reviewed. All wounds were on the lower extremity and included post-debridement/amputation wounds in patients who presented with diabetic foot infection/gangrene, VLUs, and other post-surgical wounds.

Wounds were only grafted after all necrotic slough, excessive drainage and gross infection were cleared using various other adjunctive wound-care techniques. In all cases there was evidence of healthy granulation tissue of the ulcer bed. All patients had ankle brachial pressure indices greater than 0.7, while those with diabetes had no specific controls for their haemoglobin A1c. In addition, wound bioburden surveillance was not routinely performed in this cohort. A significant proportion of the diabetic foot wounds (85%) had their wound bed prepared with V.A.C. therapy, especially those undergoing open transmetatarsal amputation (TMA) and calcanectomy.

The operative procedure (Fig 1) was notable for all patients receiving a single dose of prophylactic antibiotics within 1 hour prior to skin grafting. The recipient bed was mechanically debrided and prepared with pulse irrigation when appropriate. Preoperative qualitative and/or quantitative cultures were not taken.

STSG were harvested from the ipsilateral thigh with a dermatome at 15 thousandths of an inch and meshed to a ratio of 1:1.5. The NPWT system used was the V.A.C. system. A non-adherent petroleum-based dressing (Adaptic, Ethicon Surgical, Johnson & Johnson) was placed directly over the STSG before the open pre-foam was applied to reduce graft adherence to the foam, which would have made dressing removal very difficult, risking graft loss. The non-adherent layer and the foam were both cut to the wound size and placed on the wound in that order. Negative pressure was maintained at 125mmHg continuously for 96 hours in all cases, and all but three patients were kept in the inpatient setting for that period. The graft take was recorded subjectively (expressed as percentage of re-epithelialisation evaluated by gross inspection) after removal of V.A.C. dressing, 4 days after the grafting procedure. Follow-up graft take was recorded routinely at 2 and 4 weeks. The procedure was the same for all patients.

Postoperative care included strict bedrest and subcutaneous unfractionated heparin given three times a day at 5000 units to prevent deep venous thrombosis. The attending physician always removed the initial NPWT, being careful not to disturb the STSG. Staples were removed prior to discharge. Patients were discharged to skilled nursing facilities or to home nursing, with a dressing of topical triple antibiotic ointment and bismuth/petroleum-impregnated gauze, to be changed daily for DFUs or post-surgical amputation wounds, and twice a week with multilayer wrap for VLU patients.

Results

Over the study period, a total of 71 STSGs were performed, 59 of which had adequate medical records available for review. Patients ranged 25–80 years of age. All the wounds were located in lower extremities. There were 39% (n=23) post-debridement/amputation wounds in patients who presented with diabetic foot infection/gangrene, 31% (n=18) VLUs and 31% (n=18) other post-surgical wounds. This last group included ischaemic lower extremity ulcers (after revascularisation), post-fasciotomy and post-traumatic wounds.

The mean percentage graft surface area that survived and was incorporated as wound coverage after the V.A.C. therapy was removed, was 94% (mean 93% in the diabetic group (30–100%), 92% in the VLUs group (80–100%) and 96% among the others (80–100%)). In 63% (n=37) of cases there was 100% graft survival, 25% (n=15) had 90–99% graft survival, and 8.5% (n=5) had 80–89% graft survival. Of the remaining two cases, one patient had a diabetic wound with 30% survival, and the other had a VLU with complete graft loss when the graft was inadvertently removed with the overlying dressing (not the NPWT dressing). The latter patient was re-grafted during the same admission and subsequently had 100% graft survival.

Eighty per cent or more of cases in each wound sub-category had 90% or greater graft survival. There were no cases of graft-site infection. Three cases were managed as outpatients with portable NPWT devices (Freedom VAC) and they all had 100% graft survival. Ninety-three per cent (n=55) of cases were cleared for discharge within two or three days of removal of the NPWT. The remaining 9% (n=5) were cleared after 4–6 days after removal of the NPWT, when the clinician was satisfied that the STSG was continuing to heal and epithelialise.

Outpatient follow-up ranged from 2 weeks to 5 years (mean 10 months), and 15% (n=9) of patients were lost to follow-up. All nine of these patients made it to at least their 1-month follow-up visit, therefore, are included in the above analysis. At the time of data collection, of the remaining patients, 76% (n=38/50) of cases had wounds that remained completely closed, 10% (n=5/50) had wounds that remained partially closed and 14% (n=7/50) lost the entire STSG.

Factors associated with eventual graft loss, both complete and partial, were diabetic plantar foot ulcers in which the patient did not wear appropriate offloading (33%, n=4/12), open TMA with poor offloading (33%, n=4/12), and lack of concordance with compression garment therapy in patients with VLUs (33%, n=4/12).

Discussion

The classic method of graft fixation consists of a tie-over bolster dressing maintained *in situ* for approximately 5–7 days.[1] Surprisingly, there is almost no prospectively collected data on the outcomes of standard bolster dressings. In the senior author's experience, primary dressings have ranged from mineral oil-soaked cotton batting to saline-soaked gauze rolls, none of which has a body of clinical evidence to support their use. In addition, these methods, as well as others, are subject to inadequately prepared graft bed, haematoma or seroma collection, movement, infection and technical errors, which can all contribute to skin graft loss.

In 1952, Arthur Raffel devised a negative pressure technique to reduce these complications under the mastectomy skin flaps, which was further modified by Silvis et al.[21] Morykwas et al. first described the beneficial use of the NPWT for wound healing in 1997.[22] In the same year, Argenta and Morykwas described using a NPWT device as a bolster for skin grafts.[9] Since these early reports, there has been rapid adoption of NPWT in fixing STSGs. There is not much difference in the postoperative management of the NPWT versus traditionally bolstered STSG. The main nursing concern is around the seal of the NPWT and making sure NPWT is maintained at all times.

The clinical evidence for the efficacy of the V.A.C. therapy in skin grafted wounds, however, mostly comprises retrospective case series. In 1998, Blackburn et al. reported a greater than 95% graft take by coupling of skin grafting with negative pressure dressings (-125mmHg for 3 days) for closure of large complex wounds.[15] Scherer et al. did a retrospective analysis of a heterogeneous group of patients, comparing continuous NPWT therapy (-125mmHg for 4 days) (n=34) with conventional bolster dressings (n=27) in traumatic or thermal wounds and found no difference in percentage of skin graft survival or hospital stay between the two groups. However, the NPWT group required significantly fewer repeated STSGs than the non-NPWT group (3% vs 19%, p=0.04).[11] In another retrospective review, in a group of dermatology patients largely with venous ulcers, Korber et al. demonstrated an improved rate of graft take with NPWT (-125mmHg for 5–7 days).[16] Subsequently, Senchenkov et al. reported a high rate of skin graft take (>95%) in preoperatively irradiated wounds using V.A.C. application (-75mmHg for 5 days).[12] In a retrospective analysis of STSG take in radial forearm flap donor sites in 45 patients, Vidrine et al. demonstrated a significantly higher rate of skin graft healing in the group with NPWT versus traditional bolsters. At 4 weeks those with NPWT had 92% healing versus 81% healing. The rate of graft loss was 10% vs 28% (Table 1).[23]

There are few published randomised prospective studies on the effect of V.A.C. therapy on take of skin

Table 1. A summary of previous reports on using NPWT for securing skin grafts

Author	N	Wound type	Outcome	Comments	Study type
Blackburn et al.[15]	3	Large complex	95% take		Retrospective
Scherer et al.[11]	34 (NPWT) vs 27 (control)	Traumatic/thermal	3% regraft in NPWT group	19% regraft in control group	Retrospective
Körber et al.[16]	28 (NPWT) vs 46 (control)	Largely venous	93% take	100% take in patients with DM and the elderly	Retrospective
Vidrine et al.[23]	20 (NPWT) vs 25 (control)	Radial forearm flap donor site	92% take, 0% graft loss	81% take, 28% graft loss with traditional bolster	Retrospective
Moisidis et al.[19]	20 (NPWT) vs 20 (control)	Heterogeneous (majority trauma, 50% acute wounds)	Improved qualitative graft take in NPWT	No difference in quantitative graft take	Prospective
Chio & Agrawal[18]	27 (NPWT) vs 27 (control)	Radial forearm flap donor site		No difference in graft failure/wound complications	Prospective
Lantis & Gendics[20]	5	Venous	100% take		Prospective

grafts. In a heterogeneous group of 20 patients, most of whom were trauma cases, and 50% were acute wounds, Moisidis et al. did an randomised crossover study, in which, after grafting, each wound half was randomised to receive either a standard bolster dressing or a NPWT dressing.[19] The quantitative graft take (based on degree of epithelialisation) was not significantly different between the groups; however, the subjective graft take at 2 weeks' follow-up was found to be significantly better with the use of NPWT.

As described above, we previously presented a small randomised controlled trial evaluating skin graft survival secured to VLUs with NPWT (n=5), compared with traditional bolster dressing (n=5).[20] This trial was terminated because of poor accrual and resistance to randomisation to the non-NPWT group, but 100% graft survival was noted in the NPWT group compared with an average of 84% in the non-NPWT group at 7 days after grafting (p=0.31); at 3 months after grafting, all wounds in the NPWT group remained fully healed versus 60% in the standard of care arm.

Interestingly, in a recent randomised, prospective, controlled study of skin grafts in radial forearm donor sites, Chio and Agrawal found no significant difference in graft failure and wound complications between the negative pressure dressing versus static pressure dressing groups.[18] However, as these are acute wounds, these data has little correlation to the chronic vascular wound in which we are interested.

This study reports our single-centre experience with a rather homogenous cohort of complex lower extremity wounds treated with skin grafting and V.A.C. therapy. Historically, coexisting vascular disease, either arterial or venous, has been associated with a high rate of skin graft failure (up to 80% in one report).[7] A significant number of our patients were diabetic and the majority had underlying vascular disease, either venous or arterial in nature. Post-amputation wounds or diabetes were common causes of ulceration and subsequently skin grafting. Despite the associated comorbidities and complexity of the wounds in our cohort, we observed a high rate of graft take of 94% and a high percentage of the completely healed wounds at an average follow-up of 10 months. We did not find a significant difference in the graft take between the diabetic, VLUs and other wound types. Also, unlike other authors, age did not play a role in graft take.

This therapy adds a cost of $240 to our hospital charges as the NPWT is charged at $60/day and these patients had the therapy for 4 days. In our population, this would not add to length of stay (LOS) as social services and home nursing service availability dictates our patients' LOS more than the NPWT. However, one potential cost advantage that is difficult to assess is the theoretical cost decrease due to the decreased operative time of NPWT affixation versus bolster fixation.

The observed effect of NPWT on healing of skin grafted wounds may be explained by several mechanisms.[24] These may include macrodeformation, removal of periwound fluid, and the maintenance of a moist wound environment. Negative pressure results in approximation of the wound edges (macrodeformation), allowing for earlier closure by secondary intention, and stimulating the cellular cascade of neo-epithelialisation.[25]

The importance of maintaining a moist environment in the promotion of wound healing and proliferation of skin grafts has been investigated previously.[26–28] By minimising the water evaporation and evacuating the wound fluid with its accompanying electrolytes and proteins, V.A.C. seems to prevent desiccation of the wound surface and keep the osmotic and oncotic gradients of the wound environment theoretically stable. Removal of the wound exudate was also seen to reduce the amount of seroma or haematoma between the wound surface and the graft that would otherwise jeopardise its survival.

Another beneficial function of V.A.C. in skin grafting is providing an equal distribution of the negative pressure over the wound surface, allowing for uniform opposition between the graft and the wound bed, hence reducing the disruption of neovascularisation of the STSG that can occur with excessive sheering between the STSG and the recipient bed. This is particularly true in difficult anatomical positions or moving parts of the body.

Moreover, the mechanical effects of microdeformations at the foam-wound interface have been shown to induce cellular proliferation and angiogenesis *in vivo*,[25] an effect similar to proliferative and angiogenic response to tissue expansion.[29] Laboratory and clinical studies of NPWT versus wet-to-moist dressings have demonstrated a four-fold increase in local wound blood flow (with a negative pressure of 125mmHg), a four-fold decrease in the bacterial load of infected wounds, and a statistically significant 63–103% increase in the formation of wound granulation tissue.[22,30]

Conclusion

NPWT using a V.A.C. device seems to be a promising approach in securing STSGs. In our and others' experience, STSG secured with NPWT have required fewer repeated grafting procedures, have had very high initial graft survival with complete recipient bed coverage, and been associated with good long-term wound closure rates. The patients in our series in general had more significant chronic conditions than those reported in other series, and we had a longer follow- up. While retrospective reviews such as this support NPWT as a good method of STSG affixation, the paucity of reviews of other methods does not allow for good historic comparison. Therefore, ideally a well-enrolled prospective trial would be of use. However, given the wide adoption this technique, even without scientifically rigorous data, the initiation of such a trial is very unlikely. ■

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