Effective use of negative pressure wound therapy provides quick wound-bed preparation and complete graft take in the management of chronic venous ulcers

Onur Egemen, Ozay Ozkaya, Muhammed Besir Ozturk, Tolga Aksan, Çağdaş Orman, Mithat Akan

ABSTRACT
Venous ulcers are characterised by longstanding and recurrent loss of skin integrity. Once occurred, healing is slow and recurrence is high because of inappropriate conditions of the wound bed. This study involves 20 patients with chronic venous ulcers at least 6 weeks of duration treated with negative pressure wound therapy (NPWT). Patients underwent a radical debridement of all devitalised tissues in the first operation. After adequate haemostasis, silver-impregnated polyurethane foam was applied. Once the wounds were determined to be clean and adequate granulation tissue formation was achieved, split-thickness skin grafts were applied. Black polyurethane foam was applied over them. All wounds completely healed without the need for further debridement or regrafting. The mean number of silver-impregnated foam dressing changes prior to grafting was 2.9 (one to eight changes). The mean number of NPWT foam changes was 2.6 after skin grafting (two to five changes). Two patients who did not use conservative treatments for chronic venous insufficiency (CVI) after discharge from the hospital had recurrence of venous ulcers in the follow-up period. Application of NPWT provides quick wound-bed preparation and complete graft take in venous ulcer treatment.

Key words: Chronic venous insufficiency • Chronic wound • Negative pressure wound therapy • Skin graft • Venous ulcer

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Venous ulcers are characterised by a long-standing and recurrent loss of skin integrity. They have irregular borders, are surrounded by a brown hyperpigmentation, and are classically located at the lateral or medial malleolus of a swollen leg (1,2). They are expensive to treat and adversely impact patients’ quality of life (1–3). The condition restricts an individual’s social function and work life and affects up to 1% of the adults in developed countries (4–6). In people over the age of 65, this rate increases to 4% (7).

Ulcereation is a severe clinical manifestation of chronic venous insufficiency (CVI). The prevalence of CVI ranges from 2% to 7% in the population, and CVI is responsible for about 70% of chronic ulcers of the lower limb (7, 8). CVI triggers a cascade of events leading to blood reflux from deep to superficial veins via perforating vessels, and consequently chronic venous hypertension develops (9,10). Venous hypertension interferes with the capillary haemodynamic balance and disrupts the skin’s microcirculation. Increased pressure in the venous end of the capillaries allows the large molecules and cells to escape into the interstitial fluid (11). Extracapillary fibrinogen forms pericapillary cuffs to act as a barrier and inhibits dermal collagen production (12). Red and white blood cell accumulation and plugging of the capillaries lead to tissue ischaemia (12,13). Leucocytes secrete transforming growth factor (TGF)-β1 to activate fibroblasts; however, TGF-β1 is bounded by α2-macroglobulin, which leaks from the vessels because of venous hypertension (14). Moreover, it is shown that matrix metalloproteases are highly elevated in CVI. All these unfavourable factors lead to tissue breakdown and create a non-healing environment (15,16).

Once occurred, healing rates may be as slow as 22% at 12 weeks, and recurrence rates may be as high as 69% in 12 months because of inappropriate conditions of the wound bed (17,18). Treatment of venous ulcers should start with efforts to decrease venous hypertension and regulate venous flow such as extremity elevation, compression bandaging, Unna boot application and vascular surgical intervention (19–30). Various techniques, wound dressing products, devices, cultured cells and growth factors have been proposed to improve healing and decrease the recurrence of venous ulcers (3,19,20,30–38).

This study describes the effective use of negative pressure wound therapy (NPWT) for the treatment of recalcitrant and large venous ulcers in a series of 20 patients. NPWT was applied for the preparation of the wound bed prior to grafting and for improving the take of meshed grafts later as well.

### PATIENTS AND METHODS

From August 2009 to December 2010, 20 patients with chronic venous ulcers of at least 6 weeks of duration were treated with NPWT in the Okmeydani Training and Research Hospital Plastic and Reconstructive Surgery Clinic (Table 1). Detailed written informed consent was obtained from all subjects. There were 18 male and 2 female patients with a mean age of 54.1 years. Bedridden patients, patients with diabetics or ischaemic ulcers, patients with arterial insufficiency of the lower extremity (ankle/brachial index <0.9), obese patients, and patients with existing deep venous thrombosis were not included in the study. Wound dimensions ranged between 4 × 5 cm and 25 × 35 cm.

All patients received standardised conservative treatment for their leg ulcers upon admission (elevation, compressing bandaging and dressings). To document the presence of venous insufficiency, patients underwent a continuous wave Doppler evaluation of deep veins and perforators of both legs. Calf circumference was measured upon admission and on every dressing change at the mid-point of a line drawn between the lateral malleolus and fibular head. Multiple incisional biopsies for pathological examination and tissue samples for bacterial culture were obtained. IV antibiotics (cefazolin) were started empirically. Antibiotic regimens were changed considering the culture results. Vancomycin was administered for meticilline-resistant *Staphylococcus aureus* (MRSA) and Ciprofloxacin was administered for *P. aeruginosa* in appropriate doses upon the results of antibiogram tests.

Patients underwent a radical debridement of all chronic and infected granulation tissue in the first operation. All necrotic and unhealthy materials were excised tangentially down to clean and bleeding tissues. After adequate haemostasis, silver-impregnated polyurethane foam (Granufoam Silver, KCI, San Antonio, TX)

### Key Points

- Venous ulcers are characterised by a long-standing and recurrent loss of skin integrity.
- Ulceration is a severe clinical manifestation of chronic venous insufficiency (CVI).
- Treatment of venous ulcers should start with efforts to decrease venous hypertension and regulate venous flow such as extremity elevation, compression bandaging, Unna boot application and vascular surgical intervention.
- This study describes the effective use of negative pressure wound therapy (NPWT) for the treatment of recalcitrant and large venous ulcers in a series of 20 patients. NPWT was applied for the preparation of the wound bed prior to grafting and for improving the take of meshed grafts later as well.

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NPWT in the management of venous ulcers

Table 1  Patient characteristics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Duration of the VI (years)</th>
<th>Duration of the existing ulcer (months)</th>
<th>Ulcer dimensions (cm)</th>
<th>Calf circumference on admittance (cm)</th>
<th>Calf circumference in grafting operation (cm)</th>
<th>Complication</th>
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VI, venous insufficiency.

was applied and the pump was set to a continuous negative pressure of 125 mm Hg. Dressings were changed on alternate days, and the amounts of discharge and calf circumference were noted (Figures 1–4). Once the wounds were determined to be clean by clinical assessment and adequate granulation tissue formation was achieved, meshed split-thickness skin grafts were applied. The grafts were fixed with skin staples, and standard black polyurethane foam (Granufoam, KCI, San Antonio, TX) was applied over them with a continuous negative pressure of 75 mm Hg. The NPWT dressings were changed on the 3rd day and every other following day. NPWT application was discontinued when it was considered that the grafts had completely taken (Figures 5–9).

The patients were examined on monthly follow-up visits after discharge and their accordance with the preventive methods were checked.

RESULTS

Patients were followed between 6 and 22 months (mean: 17.4 months).

The mean duration of venous insufficiency in the selected patient group was 25.6 (2–50 years) years, and the mean duration of the existing ulcer was 91.1 months (2–246 months) (Table 1).

The mean calf circumference was measured as 39.1 cm (33–46 cm) on admittance. The mean calf circumference rapidly decreased to 34.1 cm (27–41 cm) after NPWT application to prepare the wound for grafting (Table 1).
While 16 wounds were infected with *P. aeruginosa*, 7 wounds had a mixed infection of *P. aeruginosa* and MRSA. *S. aureus* was the only microorganism isolated from two patients (Table 2).

Pathologic examination of tissue biopsies showed chronic inflammation with layers of fibrin deposits surrounding capillaries and increased number of dermal capillaries. There was no sign of malignant differentiation in any case.

Only one silver-impregnated foam application for 2 days was enough in three patients for preparing the wound for skin grafting. The mean number of silver-impregnated foam dressing changes prior to grafting was 2.9 (one to eight changes). The mean number of NPWT foam changes was 2.6 after skin grafting (two to five changes) (Table 2). The mean duration of hospital stay was 16.9 days (10–43 days).
NPWT in the management of venous ulcers

Figure 8. The graft seemed completely taken on postoperative 5th day.

Figure 9. The appearance of the patient 1-year after grafting.

All wounds completely healed without the need for further debridement or regrafting. The NPWT dressings were well tolerated by the patients. None of the patients complained about the pain limiting the application of negative pressure.

Two patients who did not use conservative treatments for CVI after discharge from the hospital had recurrence of venous ulcers in the follow-up period.

DISCUSSION
Topical application of negative pressure has been shown to improve wound healing in a number of settings from acute traumatic injuries to chronic and infected wounds (39–41). Moreover, it has been used to prepare wound beds for grafting or flap closure (42).

Controlled experiments in animals indicated that the reduction of the interstitial fluid by means of NPWT significantly enhances the wound healing and oedema. In our opinion, NPWT has substantial contribution in the rapid decrease of the calf circumference in our patients. It is assumed that the reduction of interstitial oedema facilitates the local blood circulation and thus reduces the mechanical limitation of the capillary flow (43). In addition, increased granulation tissue, decreased bacterial levels and increased cell growth have been noticed in NPWT-treated wounds (44,45).

Chronic venous ulcers are commonly colonised by bacteria such as *P. aeruginosa* and *S. aureus* (46). Chronic infection prolongs healing and may increase ulcer size over time. Decreasing the bacterial counts is of paramount importance in the wound-bed preparation for skin grafting. Using an acute wound swine model that was treated with NPWT, Morkywas et al. showed a marked decrease in bacterial counts of quantitative cultures (43). Gerry et al. presented two infected venous ulcer cases where they used silver-impregnated NPWT foam effectively in wound-bed preparation for grafting (47). They placed the silver-impregnated foam to secure the grafts as well. Despite its advantages in treating contaminated wounds, silver has been shown to be cytotoxic to human keratinocytes (48).

Table 2 Isolated microorganism and number of dressing changes

<table>
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<tr>
<th>Patient</th>
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<th>Number of dressing changes after grafting</th>
<th>Days of hospital stay</th>
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<td>3</td>
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Key Points
- Topical application of negative pressure has been shown to improve wound healing in a number of settings from acute traumatic injuries to chronic and infected wounds.
- In our opinion, NPWT has substantial contribution in the rapid decrease of the calf circumference in our patients.
- Decreasing the bacterial counts is of paramount importance in the wound-bed preparation for skin grafting.
Key Points

- This study describes the effective and efficient use of NPWT in the treatment of chronic and recalcitrant venous ulcers.
- Although chronically colonized wounds are often refractory to definitive treatment, we achieved 100% wound closure with split-thickness skin grafts in 20 patients.
- Application of NPWT provided quick wound-bed preparation and complete graft take in venous ulcer treatment.
- Further controlled and randomized trials are needed to show the benefits of NPWT in the treatment of venous ulcers.

NPWT has been shown to increase the graft take and graft quality by changing the passive process of inosculation into an active one and removing the blood and exudates that may prevent the graft from adhering (42,44). In their recent study of patients with chronic leg ulcers, Körber et al. showed complete healing in 92.9% of meshed grafts in which they had applied negative pressure to secure the grafts in spite of 67.4% graft take in the control group (49). However, they reported significantly lower graft take rates (71.4%) in patients with venous ulcers. Although our study does not contain a control group, we showed that 100% graft take can be accomplished in patients with venous ulcers. Thanks to the NPWT, the graft is adhered to its bed strictly by the negative pressure, and interstitial oedema resulting from the venous insufficiency is effectively removed.

Despite NPWT dressings and devices being more expensive than other wound-care products, cost-benefit analyses show lower treatment costs. In their randomized controlled trial, Vuerstack et al. showed significant shorter wound-preparation time and faster complete healing compared with the control group (50). They emphasised that higher treatment costs of the control group were created by higher personnel costs and longer hospitalisation time due to slower healing.

CONCLUSION

This study describes the effective and efficient use of NPWT in the treatment of chronic and recalcitrant venous ulcers. Although chronically colonized wounds are often refractory to definitive treatment, we achieved 100% wound closure with split-thickness skin grafts in 20 patients. Application of NPWT provided quick wound-bed preparation and complete graft take in venous ulcer treatment. Further controlled and randomized trials are needed to show the benefits of NPWT in the treatment of venous ulcers.

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