Comparison of Negative Pressure Wound Therapy With and Without Instillation of Saline in the Management of Infected Wounds

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Abstract

Background
Negative pressure wound therapy (NPWT) with instillation and dwell time (NPWTi-d) includes periodic instillation of topical solution into the wound followed by a negative pressure. Our objective was to evaluate potential differences in wound outcomes in patients receiving NPWT and those receiving NPWTi-d using saline.

Methods
An analysis was performed using two previously published independent studies from a single investigator and hospital to compare patient characteristics and clinical outcomes of infected wounds from 74 NPWT-treated patients with 42 NPWTi-d-treated patients.

Results
Patient demographics and comorbidities, wound etiologies, and anatomical locations of wounds were similar between groups, although a significantly higher percentage of NPWT-treated patients had end-stage renal disease (P = 0.0119). Compared with patients treated with standard NPWT, NPWTi-d-treated patients had a significantly lower number of operations (P = 0.0048), shorter length of hospital stay (P = 0.0443), shorter time to final surgical procedure (P = 0.0001), higher percentage of closed wounds (P = 0.0004), and a higher percentage of wounds that remained closed at one month (P = 0.0001).

Conclusions
The results of this analysis suggest that management of infected wounds with NPWTi-d using saline leads to favorable wound outcomes when compared to those managed with NPWT.

Introduction
Increased patient morbidity and mortality, length of hospital stay, and costs are associated with
infection in both acute and chronic wounds [1]. Wound infection management strategies include the use of antibiotics and the removal of infectious materials. While numerous advanced wound care products assist in the management of wound infection, negative pressure wound therapy (NPWT) utilizes negative pressure to remove exudate and infectious materials from wounds. The resulting negative pressure draws wound edges together and promotes angiogenesis and granulation tissue formation in the wound bed [2-5].

NPWT has evolved to include the periodic instillation of topical wound solutions directly over the wound bed, followed by removal using negative pressure. This NPWT with instillation and dwell time (NPWTi-d) utilizes the same properties of NPWT with the added benefit of wound cleansing [6]. NPWTi-d has been reported to promote wound cleansing, granulation tissue development, and healing in wounds that did not respond to traditional NPWT [7-9]. The comparative effectiveness of NPWTi-d using normal saline, a recommended first-line NPWTi-d solution, versus standard NPWT has not been adequately assessed in previous studies [10-12]. Our objective was to evaluate potential differences in wound outcomes in patients at an institution receiving NPWT and those receiving NPWTi-d with saline.

Materials And Methods

An analysis was performed using two independent previously published studies from a single investigator and hospital to compare patient characteristics and clinical outcomes of infected wounds from 74 NPWT-treated patients from the article’s retrospective control cohort (control group) with 42 NPWTi-d-treated patients from the article’s per protocol population (study group) [13,14]. As previously described, all patients underwent excisional debridement in the operating room and received parenteral or oral antibiotics [13,14]. The control group received continuous negative pressure at -125 mmHg using NPWT (INFOV.A.C.™ Therapy System, KCI, San Antonio, TX) [13]. The study group received NPWTi-d (V.A.C. VERAFLÒ™ Therapy, KCI, San Antonio, TX) with instillation of 0.9% saline with a dwell time of 20 minutes followed by two hours of negative pressure (-125 mmHg) [14]. Outcomes assessed included the number of operations, time to final surgery, length of hospital stay, wound closure, and percentage of wounds that remained closed at one month. Wound closure was defined as coverage of wound through delayed primary closure, skin graft, or flap. Statistical significance was determined using a t-test for continuous variables or Fisher’s exact test for categorical values. Results were considered statistically significant at a P-value ≤0.05.

Results

The mean age of patients in the control group (n = 74) and the study group (n = 42) was 58.0 ± 13.0 years and 60.7 ± 15.1 years, respectively (Table 1). Patient demographics, comorbidities, wound etiologies, and anatomical locations of wounds were similar between groups, although a significantly higher percentage of NPWT-treated patients had end-stage renal disease (P = 0.0119) (Tables 1, 2).
| Characteristics               | Control Group (n = 74) | Study Group (n = 42) | P-value |
|-------------------------------|------------------------|----------------------|---------|
| Age, years (mean ± SD)        | 58.0 ± 13.0            | 60.7 ± 15.1          | 0.3202  |
| BMI, kg/m² (mean ± SD)        | 32 ± 9.1               | 29.1 ± 8.2           | 0.0913  |
| Gender, n (%)                 |                        |                      | 0.2429  |
| Male                          | 38 (51.0)              | 27 (64.0)            |         |
| Female                        | 36 (49.0)              | 15 (36.0)            |         |
| Race, n (%)                   |                        |                      | 0.0995  |
| African American              | 21 (28.0)              | 19 (51.4)            |         |
| Caucasian                     | 39 (53.0)              | 17 (45.9)            |         |
| Hispanic                      | 2 (6.0)                | 0 (0)                |         |
| Asian                         | 1 (3.0)                | 1 (2.7)              |         |
| Other race                    | 6 (8.0)                | 0 (0)                |         |
| Comorbidities, n (%)          |                        |                      |         |
| ESRD                          | 22 (30.0)              | 4 (9.5)              | 0.0119  |
| PVD                           | 27 (36.0)              | 9 (21.4)             | 0.1004  |
| History of cancer             | 6 (8.0)                | 6 (14.3)             | 0.3477  |

TABLE 1: Patient demographics and comorbidities

BMI = body mass index; ESRD = end-stage renal disease; PVD = peripheral vascular disease; SD = standard deviation
| Characteristic          | Control Group (n = 74) | Study Group (n = 42) |
|------------------------|------------------------|----------------------|
| **Wound type, n (%)**  |                        |                      |
| Ischemic               | 17 (23.0)              | 6 (14.3)             |
| Neuropathic            | 16 (22.0)              | 14 (33.3)            |
| Decubitus              | 16 (22.0)              | 4 (9.5)              |
| Surgical               | 17 (23.0)              | 13 (31)              |
| Venous insufficiency   | 3 (4.0)                | 2 (4.8)              |
| Traumatic              | 4 (5.0)                | 1 (2.4)              |
| Other                  | 3 (4.0)                | 1 (4.8)              |
| **Anatomical location, n (%)** |                      |                      |
| Forefoot               | 12 (16.0)              | 10 (23.8)            |
| Midfoot                | 12 (16.0)              | 2 (4.8)              |
| Hindfoot               | 22 (30.0)              | 3 (7.1)              |
| TMA site               | 1 (1.0)                | 6 (14.3)             |
| Ankle                  | 7 (9.0)                | 7 (16.7)             |
| Lower leg              | 7 (9.0)                | 5 (11.9)             |
| BKA/AKA                | 1 (1.0)                | 1 (2.4)              |
| Knee                   | 1 (1.0)                | 3 (7.1)              |
| Thigh                  | 3 (4.0)                | 0 (0)                |
| Back/buttock           | 2 (3.0)                | 3 (7.1)              |
| Abdomen                | 5 (7.0)                | 2 (4.8)              |
| Arm                    | 1 (1.0)                | 0 (0)                |

**TABLE 2: Wound type and anatomical location**

AKA = above-knee amputation; BKA = below-knee amputation; TMA = transmetatarsal amputation

Compared with the control group patients, the study group patients had a significantly lower number of operations (P = 0.0048), shorter length of hospital stay (P = 0.0445), and shorter time to final surgical procedure (P = 0.0001). Additionally, higher percentage of closed wounds (P = 0.0004) and higher percentage of wounds that remained closed at one month (P = 0.0001) were observed in the study group (Table 3).
| Characteristic                              | Control Group (n = 74) | Study Group (n = 42) | P-value |
|--------------------------------------------|------------------------|----------------------|---------|
| Number of operations (mean ± SD)           | 3.0 ± 0.9              | 2.5 ± 0.9            | 0.0048  |
| Length of hospital stay, days (mean ± SD)  | 14.9 ± 9.2             | 11.7 ± 6.0           | 0.0443  |
| Time to final procedure, days (mean ± SD)  | 9.2 ± 5.2              | 5.6 ± 3.6            | 0.0001  |
| Wound closure/coverage, n (%)              | 46 (62)                | 39 (92.9)            | 0.0004  |
| Wounds remained closed at one month, n (%) | 28 (37.8)              | 32 (82.1)            | 0.0001  |

### TABLE 3: Clinical outcomes
SD = standard deviation

**Discussion**

Wound infection can create a barrier to healing and increase patient morbidity and healthcare costs [1]. While treatment includes the use of bacteria-specific antibiotics, advanced wound therapies play an important role in wound management during treatment. NPWT can help manage wounds through the use of negative pressure to remove exudate and infectious materials. NPWT use in infected wounds has been reported as safe for patients [15,16]. Product advancements have led to the addition of wound cleansing to NPWT, which may provide an additional wound management option to patients with infected wounds. This study examined differences in wound outcomes in patients with infected wounds at one institution receiving either NPWT or NPWTi-d using saline.

NPWT uses macrostrain and microstrain resulting from negative pressure to draw wound edges together, remove infectious materials and exudate, reduce edema, and promote angiogenesis and granulation tissue formation in the wound bed [2-5]. NPWTi-d utilizes these same properties with the added benefit of wound cleansing with the instillation of topical wound solutions [6]. However, while the clinical benefit of NPWTi-d use has been shown, limited published evidence exists for NPWTi-d use in infected wounds.

In this study, significantly lower number of operations, shorter length of hospital stay, shortened time to final procedure, higher percentage of closed wounds, and higher percentage of wounds that remained closed at the one-month follow-up visit were reported in the NPWTi-d group. These results are similar to those reported by Gabriel et al. and Omar et al. [11,12]. However, patients received either saline or a polyhexanide instillation solution in the Gabriel et al. study. Additionally, while a shorter hospital stay and time to wound closure were observed in the NPWTi-d group in the Omar et al. study, these were not statistically significant compared to the NPWT group [12]. The results of this analysis suggest that management of infected wounds with NPWTi-d using saline leads to favorable wound outcomes when compared to those managed with NPWT.

The retrospective nature and the analysis of only two previously published studies are limitations to this work. Limited data exist for the use of NPWTi-d in infected wounds [13,14]. The publications that were available for comparison used polyhexanide and saline instillation solutions with limited numbers of patients in each. Instead of a meta-analysis, we opted to assess patients treated by one clinician at one hospital using to provide a more direct
comparison. Caution should be used when interpreting the conclusions of this study due to the limited scope of the analysis. Future, large-scale, controlled cohort studies are warranted to further assess the potential benefits associated with NPWTi-d use in the management of infected wounds.

**Conclusions**

The results indicate that wound cleansing combined with NPWT may provide an additional clinical benefit in the management of infected wounds. However, due to the limited analysis, conclusions should be interpreted with caution. Future studies assessing the potential benefits of NPWTi-d use in the management of infected wounds are necessary.

**Additional Information**

**Disclosures**

**Human subjects:** All authors have confirmed that this study did not involve human participants or tissue. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** PJ Kim and CE Attinger are consultants for KCI. R Silverman and L Griffin are employees of 3M. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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