Abstract: Introduction. Subatmospheric pressure wound therapy (SAWT) is commonly used to manage infected wounds. However, this practice remains controversial because the safety and efficacy of the technique has not been carefully documented. Methods. The authors assessed the safety and efficacy of a sealed gauze dressing with wall suction applied (GSUC) compared to vacuum assisted-closure (VAC), both soaked with topical antimicrobials. Subjects included 31 hospitalized patients with acutely infected wounds compared with 56 patients with noninfected wounds. Results. There were significant reductions in wound surface area and volume in both infected and noninfected groups; there was no significant difference in the rate of change observed in the GSUC vs the VAC arms of the study. In the infected group, the reduction in wound surface area was 4.4% per day for GSUC and 4.8% per day for VAC. Wound volume was 7.8% per day for GSUC, and 9.7% per day for VAC ($P < 0.001$ for all). Evidence of wound infection in all patients, regardless of treatment group, resolved by 96 hours of onset of treatment, and there were no complications specifically related to the use of a sealed dressing over infected wounds. Conclusion. Gauze dressing with wall suction and VAC therapy can be used in selected acute, infected wounds and both methods of treatment appear to be similarly effective for reducing wound surface area and volume.

Key words: subatmospheric pressure wound therapy, vacuum-assisted closure, gauze dressing with suction, infection

The application of a suction pump device for the treatment of suppurative wounds was first described in the 1980’s by several authors from the former Soviet Union in a series of articles now known as the “Kremlin papers.” In the early 1990’s, Western European surgeons adopted subatmospheric pressure wound therapy (SAWT) for the treatment...
of open wounds, and by 1997 the technique was introduced in the United States and commercialized as the vacuum-assisted closure (VAC) device (KCI, San Antonio, TX). Although SAWT for infected wounds is still controversial, and is even considered contraindicated by some authors, the VAC system is now commonly used for treatment of colonized and infected wounds. Despite this, clinical trials documenting the effectiveness and safety of SAWT in the treatment of infected wounds have been lacking.

The patients described in this report are part of a larger investigation used to compare the effectiveness of 2 types of SAWT in a variety of hospitalized patients with acute wounds: the standard VAC system vs wall suction applied to sealed gauze dressings (GSUC). Although these methods of SAWT are generally similar, GSUC usually employs more frequent dressing changes and pressure settings in the range of 75 mm Hg to 80 mm Hg. The authors did not think it would be useful or practical to require the treatment details be identical in both arms of the trial; instead they opted to use the currently available best practice standards for each technique. This allowed outcomes to be compared for these 2 interventions as they are most often used in real-world clinical circumstances. The initial analysis showed GSUC was not inferior to VAC with respect to changes in wound volume and surface area, but was less costly and less painful than VAC.

Comparative effectiveness research often leaves open the question of whether or not one of the alternative interventions is more beneficial for a subset of the population. Stratified randomization schemes can help answer these questions in a prospective fashion. Thus, infection status was used as a stratification factor in the randomization scheme to ensure balance of the treatment groups.
with respect to infection, and to facilitate subgroup analysis. The primary objectives were to document any complications associated with the use of SAWT for infected wounds, and to compare the efficacy of VAC and GSUC as measured by changes in wound size. It was hypothesized that both GSUC and VAC could be used safely with selected infected wounds, and that both treatment methods would result in similar changes in wound surface area and volume for infected wounds. The secondary objective of the analysis was to assess the pain associated with each type of dressing. Anecdotally it was observed that the GSUC dressings seemed to cause less pain than VAC, and this was confirmed by initial analysis. It was expected that GSUC might be less painful than VAC for infected wounds, and that, overall, dressing changes for infected wounds would be more painful than for noninfected wounds, regardless of the type of dressing used.

**Methods**

The original GSUC trial was prospective, randomized, and designed according to CONSORT guidelines (Figure 1). Participants were men and women age 18 years or older who were admitted to the University of Chicago Medical Center with acute wounds resulting from trauma, dehiscence, or surgery between October 2006 and May 2008. Table 1 illustrates exclusion criteria. All eligible patients were offered the opportunity to participate in the study. Upon enrollment into the study, each patient was assessed for the presence of a wound infection. Patients with grossly necrotic wounds or systemic sepsis caused by wound infection were initially excluded, but were considered eligible after the wound was adequately debrided, and the patient’s septic state had resolved. Wound infection was defined as the presence of an abscess with purulent material, with or without associated cellulitis, and a positive rapid slide quantitative Gram stain showing > 10⁵ colony forming units per gram of tissue. Tissue from the initial wound biopsy was retained for culture to guide antimicrobial therapy. Once patients were allocated to either the infected or the noninfected wound category, a stratified randomization scheme was used to assign VAC or GSUC therapy in a 1:1 ratio.

In the VAC arm, GranuFoam (KCI, San Antonio, TX) black sponge was applied to wounds and sealed with an occlusive plastic cover. Continuous suction at 75 mm Hg to 125 mm Hg was initiated and the dressing was changed every 48 hours, as recommended by VAC therapy guidelines. In the GSUC arm, a gauze dressing (Kerlix 4.5 inch roll, Covidien, Mansfield, MA) moistened with 0.9% normal saline was applied to the wounds. A red rubber catheter (Bard Medical, Covington, GA) was placed in the center of the dressing, and the dressing was then sealed with an occlusive cover (Ioban 2 Antimicrobial Incise Drape, 3M, St. Paul, MN). Continuous wall suction at 75 mm Hg to 80 mm Hg was applied and the dressings were changed daily, as recommended for optimal wound healing in the original descriptions of this technique.

Patients with infected wounds were managed the same as the noninfected cohort described in the original GSUC trial, except that in addition, the VAC or GSUC dressing was soaked with quarter-strength Dakin’s solution (Century Pharmaceuticals, Indianapolis, IN) 3 times a day for 30 minutes while suction was on hold. After 48 hours of treatment with Dakin’s solution, a second wound biopsy and rapid slide quantitative gram stain were performed. If > 10⁵ colony-forming units per gram of tissue were still present, a mixture of liquid sulfamylon and nystatin (mafenide acetate [5%] 50 gms and nystatin powder 15 gms [100,000 units per gram] in 1 liter water as prepared
by the inpatient pharmacy) irrigation was substituted for the Dakin’s solution. On the other hand, if the second wound biopsy < 10^5 colony forming units per gram of tissue, wound irrigation was discontinued. Another wound biopsy and quantitative rapid slide gram stain were performed at 96 hours from the start of treatment with GSUC or VAC. The study protocol specified that SAWT would be considered to have failed if > 10^5 colony-forming units per gram of tissue remained at 96 hours, and SAWT would be discontinued in that event. Patients received systemic antimicrobial drugs at the discretion of the primary physicians as clinically indicated.

The outcomes used to assess safety included development of an enlarging or necrotizing wound, evidence of systemic sepsis (fevers, leukocytosis, and/or hemodynamic changes), or any other clinical complication thought to be related to treatment with SAWT. The outcomes used to assess efficacy were changes in wound surface area and volume. The dimensions of each wound were documented at each dressing change. Wound size was calculated as described by Xakellis and Frantz:23

\[ \text{wound surface area} = \text{length} \times \text{width} \times 0.783; \]
\[ \text{wound volume} = \text{area} \times \text{depth} \times 0.327. \]

Pain associated with each type of dressing change was assessed using self-reported pain levels. Patients were asked to rate their pain level according to the 0-10 linear analog scale immediately prior to, during, and after removal of the dressing. The Sum of Pain Intensity Differences (SPID) was used to facilitate comparison of pain levels between groups. The SPID score was calculated using the following formula: (pain during dressing change) – (pain before dressing change) + (pain after dressing change) – (pain during dressing change) = SPID score.24

**Statistical Methods**

Comparisons of demographics and clinical characteristics between groups were performed using Pearson’s chi-square test for categorical variables and two-sample t test for continuous variables. Nonparametric tests were used as needed. The percent change in wound volume and surface area over time was compared between treatment groups using a linear mixed model. Of particular interest was comparison of the rate of change (slope) in the 2 treatment groups; this was accomplished by testing the treatment-by-time interaction in the model and constructing the 95% confidence interval (CI). A noninferiority margin of 5% per day was used. Separate models were fit based on the presence or absence of infection.

The SPID values are reported as least square means (LS means). A general linear model was used to analyze the association between SPID scores and the different variables, including the interaction between dressing type and infection, to determine whether the presence of infection altered the effect of dressing type on SPID, and vice versa. All tests were performed at a significance level of 0.05 and data were analyzed using STATA software (StataCorp LP, College Station, TX).

**Results**

**Primary Outcomes.** An intention to treat analysis was performed for all outcomes. There were 18 patients (40%) with initially infected wounds in the GSUC arm vs 13 patients (31%) in the VAC arm (P = 0.38). There was no statistically significant difference in the anatomical distribution of the wounds between the GSUC and VAC arms (P = 0.59). A majority of the patients in both the infected and noninfected groups had wounds on the trunk. A subgroup analysis was used to compare the efficacy of GSUC and VAC for the management of infected wounds. However, due to the limited number of observations after day 7—most patients were discharged from the hospital or underwent operative treatment for their wounds—these analyses included data only through the first week (Figure 2 and Figure 3).

**Safety:** None of the patients in either treatment group developed complications related to SAWT, evidence of systemic sepsis during the study period, or progressing or necrotizing wound infections under the dressings. At 48 hours, > 10^5 colony-forming units per gram of tissue

**Keypoints**

- In the VAC arm, GranuFoam (KCI, San Antonio, TX) black sponge was applied to wounds and sealed with an occlusive plastic cover. Continuous suction at 75 mm Hg to 125 mm Hg was initiated and the dressing was changed every 48 hours.
- In the GSUC arm, a gauze dressing (Kerlix 4.5 inch roll, Covidien, Mansfield, MA) moistened with 0.9% normal saline was placed in the center of the dressing, and the dressing was then sealed with an occlusive cover (Ioban 2 Antimicrobial Incise Drape, 3M, St. Paul, MN). Continuous wall suction at 75 mm Hg to 80 mm Hg was applied and the dressings were changed daily.
were present in 8 of 18 (44%) patients in the GSUC arm and in 6 of 13 (46%) patients in the VAC arm. However, at 96 hours, there were < $10^5$ colony-forming units per gram of tissue in all of the tissue biopsies.

**Efficacy.** Among the infected group, there was a statistically significant reduction in wound surface area in both treatment arms. The average rate of change was a decrease of 4.4% per day for GSUC and 4.8% per day for VAC ($P < 0.001$ for both). However, the rate of change between the arms was not significantly different ($P = 0.73$ for the treatment-by-time interaction), with the estimated difference (VAC - GSUC) being -0.3%, 95% CI (-2.3, 1.6). There also was a statistically significant reduction in wound volume in both treatment arms. This represented a mean decrease of 7.8% per day for GSUC and 9.7% per day for VAC ($P < 0.001$ for both). As with surface area, the rate of volume reduction was not significantly different between the 2 arms based on the treatment-by-time interaction ($P = 0.22$). The estimated VAC - GSUC difference was -2.0%, 95% CI (-5.1, 1.2).

Among the noninfected group, there was also a statistically significant reduction in wound surface area in both treatment arms. The average rate of change was a decrease of 4.7% per day for GSUC and 5.0% per day for VAC ($P < 0.001$ for both). However, the rate of change between the arms was not significantly different based on the treatment-by-time interaction ($P = 0.77$), with the estimated difference VAC - GSUC being -0.3%, 95% CI (-2.1, 1.6). There also was a statistically significant reduction in wound volume in both treatment arms. This was a mean decrease of 8.9% per day for GSUC and 9.7% per day for VAC ($P < 0.001$ for both). As with surface area, the rate of volume reduction was not significantly different between the 2 treatment arms ($P = 0.58$ for the treatment-by-time inter-

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**Figure 2. Percent change from baseline in wound surface area.** Among the infected and noninfected groups, there was a statistically significant reduction in wound surface area in both VAC and GSUC groups. However, the rate of change between the treatment groups was not significantly different for the infected group ($P = 0.73$) and the noninfected group ($P = 0.77$). Mean values with error bars representing ± 1 SEM are presented.

**Figure 3. Percent change from baseline in wound volume.** Among the infected and noninfected groups, there was a statistically significant reduction in wound volume in both VAC and GSUC groups. However, the rate of change between the treatment groups was not significantly different for the infected group ($P = 0.22$) and the noninfected group ($P = 0.58$). Mean values with error bars representing ± 1 SEM are presented.
The estimated VAC - GSUC difference was -0.8%, 95% CI (-3.6, 2.0).

**Secondary Outcome: Pain Associated with Dressing Change.** Overall, patients in the GSUC arm reported less pain (SPID = 0.50, 95% CI -0.11 to 1.11) compared to patients in the VAC arm (SPID = 1.73, 95% CI 0.91 to 2.54, \( P = 0.019 \)). For patients with infected wounds, average SPID was 0.50 in the GSUC arm compared to 2.16 for patients in the VAC arm. This difference approached statistical significance (\( P = 0.056 \)). However, the presence of infection did not significantly alter the effect of dressing type on SPID (\( P = 0.41 \) for the treatment by infection status interaction) (Table 3).

**Microbiological Analysis of Wounds.** A diverse group
of organisms was cultured from the wounds, including Gram-positive and Gram-negative bacteria, combinations of multiple organisms, and fungus. In the GSUC arm, there were 3 patients (17%) with a Gram-positive infection, 4 patients (22%) with a Gram-negative infection, 9 patients (50%) with a polymicrobial infection, 1 patient (6%) with a fungal infection, and 1 patient (6%) from whom no organisms were recovered. All of the Gram-positive organisms were methicillin-resistant Staphylococcus aureus (MRSA), and vancomycin-resistant Enterococcus was present in 2 patients (11%). In the VAC arm, there were 4 patients (31%) with a Gram-positive infection (all MRSA), one patient (8%) with a Gram-negative infection, 6 patients (46%) with a polymicrobial infection, and 2 patients from whom no organisms were recovered (15%). Thirteen out of 18 patients (72%) in the GSUC arm, and 11 out of 13 patients (85%) in the VAC arm, received systemic antimicrobial therapy. Based on clinical indications, and the judgment of the primary treating physicians, broad-spectrum antimicrobial therapy was initiated before the culture results were available for 12 patients in the GSUC arm, and 11 patients in the VAC arm. Furthermore, systemic antimicrobial therapy was initiated prior to obtaining cultures in 3 patients (2 in the VAC arm and 1 in the GSUC arm). Ultimately, no organisms were isolated from these cultures. Decisions about the specific drugs used, dosages, and duration of treatment were made by the primary attending physicians.

**Failure of Intervention.** Subatmospheric wound therapy failed in 2 of the 31 patients in the subgroup with infected wounds (6.5%), both of whom were in the VAC arm of the trial. One of the patients had an infected perineal wound where the VAC seal could not be maintained after 4 days; this patient successfully crossed over to GSUC treatment. Another patient had an infected abdominal and flank wound after evacuation of a retroperitoneal hematoma; the VAC seal could not be maintained because of excessive fluid drainage. This patient also successfully crossed over to GSUC therapy after 4 days. Data collected after patients crossed over to the other arm of the study was not included in the analysis of the results.

**Discussion**

The physicians who originated SAWT used a suction tube attached to hemispherical chamber that was applied to a wound. Their management of infected wounds also included irrigation with antimicrobial solutions. They thought this resulted in fewer complications and improved healing. More recently, the VAC system, which applies suction to a wound through an open, polyurethane cell sponge, has become the preferred technique for SAWT. Although SAWT was initially described for management of infected wounds, use of the VAC system for colonized or infected wounds remains controversial, and current manufacturer guidelines suggest using the VAC with caution under these circumstances.

Several groups have tried to understand how SAWT facilitates wound closure, and a number of potential mechanisms have been suggested including increased local blood flow, reduced edema, maintenance of a moist wound environment, and stimulation of cell proliferation through various signaling actions. No consensus has emerged about the mechanism of action for SAWT. Similarly, no consensus has emerged about the safety and efficacy of SAWT dressings for infected wounds. Some authors have proposed that SAWT dressings are capable of removing infectious material from wounds and decreasing tissue bacterial burden. Other clinical studies have shown that SAWT may increase the bacterial burden, perhaps because the occlusive dressing promotes bacterial proliferation and/or the production of bacterial toxins. It is also possible that SAWT fundamentally changes the way bacteria interact with wounds. This may allow healing to occur even in the presence of > 10⁵ organisms per gram of tissue. Much of the concern about using SAWT dressings with infected wounds is based on case reports and expert opinion. At least 1 report has linked the use of SAWT in infected wounds to toxic shock syndrome and death. Although it is difficult to ignore these warnings, other investigations have been successful using SAWT therapy for infected wounds in several different settings including surgical site infections, infected sternal wounds, infected facial wounds, the infected open abdomen, open fractures, and complicated saphenous vein donor sites.

Recognizing that the use of SAWT for infected wounds is potentially dangerous, the authors attempted to minimize any associated risk by limiting the study population to patients without evidence of systemic sepsis or grossly necrotic wounds. In addition, patients with untreated osteomyelitis or peripheral arterial occlusive disease were excluded. Gabriel et al studied SAWT and suggested the technique can be safe for infected or colonized wounds as long as there are no systemic signs of infection, all necrotic tissue and debris has been removed from the wound, purulent fluid collections and abscesses have been appropriately drained, and the wound is not complicated by ischemia. The protocol in this study also required daily
Key Points

- Recognizing that the use of SAWT for infected wounds is potentially dangerous, the authors attempted to minimize any associated risk by limiting the study population to patients without evidence of systemic sepsis or grossly necrotic wounds.
- Patients with untreated osteomyelitis or peripheral arterial occlusive disease were excluded.

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examination of the wounds to ensure that there was no progression of the infection. Furthermore, 77% of the patients received intravenous antimicrobial drugs.17 Lastly, surveillance cultures were performed at 48 hours and 96 hours. At 48 hours, organisms were still present in rapid slide preparations from 45% of all patients with initially positive cultures. However, no organisms were seen, and no growth occurred from any of the samples collected at 96 hours.

The trial described here used SAWT as a platform to deliver topical antimicrobial agents. This idea was introduced by Iusupov et al in 1987 and Fleischman et al in 1998. A combination of VAC and instillation therapy, introduced in 2003, is a refinement of this technique and allows antimicrobials introduced through the suction tubing to percolate through the foam to the wound surface. Drugs with United States Food and Drug Administration approval for use with VAC plus instillation therapy include Dakin’s solution, sulfamylon, silver nitrate, and benzalkonium chloride.

This study used both gauze and foam dressings to deliver 0.25% Dakin’s solution or liquid sulfamylon with nystatin. The active ingredient in Dakin’s solution is chlorine, which kills most forms of bacteria and viruses, and is also active against fungus; it also dissolves necrotic tissue debris, and helps keep wounds moist. Adverse reactions include hypersensitivity reaction and impaired wound healing at higher concentrations. Liquid sulfamylon is bacteriostatic for a wide range of organisms, and nystatin powder has antifungal properties. Adverse reactions include skin irritation, hypersensitivity, coagulopathy, hemolytic anemia, metabolic acidosis, myelosuppression, and porphyria. Clinical studies have demonstrated that VAC instillation therapy can be associated with reduced length of hospital stay, earlier resolution of clinical infection, and earlier wound closure compared to treatment with standard wet-to-dry dressings. However, these studies did not assess changes in wound size in response to treatment, and, to our knowledge, no study has quantified the rate of change in wound surface area and volume in infected wounds treated with SAWT in human subjects. Furthermore, most contemporary authors evaluated instillation therapy using only foam dressings. The authors found that both GSUC and VAC reduced wound surface area and volume in acutely infected wounds, though the treatment effect was slightly less than in noninfected wounds. There are a number of well-documented reasons why infections impede wound healing, such as stimulating inflammation, releasing bacterial endotoxins, cytokines and metalloproteinases, and reducing wound tensile strength. Both GSUC and VAC performed similarly well in managing acutely infected wounds using the authors’ instillation technique. This suggests that the type of interface over a wound, whether it be a black sponge or gauze, may not be a critical variable affecting the outcome when SAWT is used to treat acute, infected wounds in the manner described here.

Study limitations. Finally, there was a trend towards lower SPID scores in the infected patients treated with GSUC dressings compared to those treated with VAC dressings, but this failed to reach statistical significance, and did not differ significantly from the treatment effect observed in the noninfected group. At least 2 factors may have contributed to this situation: 1) the sample size of patients with infected wounds was quite small, and 2) by microbiological analysis, the wound infections resolved after 96 hours of treatment; thus any effect on SPID caused by infection was diminished over time. Both of these factors limited the ability of the study to detect differences in SPID between the subgroups.

Conclusion

Subatmospheric pressure wound therapy with antimicrobial irrigation can be safely used for selected infected wounds in an inpatient setting. Both GSUC and VAC effectively reduce wound surface area and volume in infected wounds, and GSUC therapy is not inferior to VAC. Regardless of the technique used, the authors suggest that SAWT be limited to wounds that have been adequately prepared by debridement to reduce the bacterial burden and eliminate necrotic tissue. The authors suggest frequent dressing changes and wound biopsies for surveillance cultures. If SAWT is to be used for infected wounds, concurrent systemic antimicrobial drugs and antimicrobial irrigation may also be indicated. Furthermore, there should be a low threshold to discontinue SAWT if there is any clinical evidence of a progressive wound infection. The authors do not have carefully documented experience with SAWT for infections that fail to resolve after 96 hours, and do
not recommend generalizing the data reported here for the treatment of chronic wound infections. Finally, corroborating data from larger population studies is needed before SAWT can be more widely recommended for management of infected wounds.

References


