



A commentary by Thomas G. Harris, MD, and Casey Pyle, DO, is linked to the online version of this article at jbjs.org.

Wound-Healing Following Negative-Pressure Wound Therapy with Use of a Locally Developed AquaVac System as Compared with the Vacuum-Assisted Closure (VAC) System

Hansel Gould B. Cocjin, MD, DPBO, Jair Kimri P. Jingco, MD, FPOA, Franklin Delano C. Tumaneng, MD, FPOA, FPCS, and Jose Maria R. Coruña, MD, FPOA, FPCS

Investigation performed at CLMMRH, Bacolod City, Philippines

Background: Negative-pressure wound therapy (NPWT) gained widespread clinical use after its introduction in the 1990s because of its many beneficial effects on the wound environment. However, high treatment costs have limited its use in third-world countries. The present study compares a low-cost, locally developed NPWT system with a commercially available system in terms of efficacy, reliability, ease of application, and safety.

Methods: This prospective, randomized controlled trial involved 36 patients who were managed with NPWT with either a low-cost, locally developed system (AquaVac) or a commercially available Vacuum-Assisted Closure Advanced Therapy System (VAC ATS; KCI). The low-cost NPWT system described consists of a converted aquarium pump as a reusable vacuum source and a dressing system that can be found in the hospital supply room: food plastic wrap as an occlusive drape, surgical gauze as wound filler, nasogastric tubes as tubing, and used intravenous (IV) bottles as effluent canisters. The purpose of the study was to compare the 2 systems in terms of (1) time to apply the dressing, (2) exudate levels, (3) amount of granulation tissue, (4) wound size reduction, (5) average cost of treatment, (6) visual analog scale (VAS) pain scores, and (7) complications.

Results: The experimental low-cost system had a small but statistically insignificant advantage over the commercially available system in terms of application time, pain during dressing changes, and wound contraction percentage. The 2 systems were comparable in terms of the amount of exudate, granulation tissue coverage, and VAS scores during the course of treatment. No wound or periwound complications were observed. The systems were significantly different in terms of cost, with the AquaVac system being 7 times less expensive than the VAC ATS system (\$63.75 compared with \$491.38 USD).

Conclusions: The low-cost AquaVac system was shown to be comparable with the commercial VAC ATS system, suggesting that it is an effective and safe alternative method for NPWT in resource-challenged settings.

Level of Evidence: Therapeutic Level I. See Instructions for Authors for a complete description of levels of evidence.

Negative-pressure wound therapy (NPWT) involves the application of subatmospheric pressure into a closed, sealed system of dressing¹⁻³. Since its introduction in the 1990s, it has rapidly become an important tool in wound management. However, NPWT's cost has limited its use, especially in third-world countries⁴⁻⁶. Worse, many patients

Disclosure: The study grant was provided by the Philippine Council for Health Research and Development (PCHRD) in cooperation with the Department of Science and Technology VI (DOST VI) and Western Visayas Health Research and Development Consortium (WVHRDC). The funding source did not play a role in the investigation. The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (<http://links.lww.com/JBJS/F531>).

with devastating soft-tissue injuries live in resource-challenged environments, further compounding the problem⁷⁻⁹.

The mechanisms of NPWT include macrodeformation of the wound, with the wound edges being brought closer together. Microdeformation of the wound surface produces a 5% to 20% strain across the healing tissues, which promotes cell division and proliferation, growth factor production, and angiogenesis. Extraction of edema fluid and exudate from the extracellular space improves recovery of damaged tissues. The maintenance of a warm and moist environment prevents desiccation of the wound and enhances the formation of granulation tissue¹⁰⁻¹².

NPWT improves the outcomes of wound care, significantly shortening the duration of hospitalization¹³⁻¹⁵. Previous studies have demonstrated no significant differences between foam-based and gauze-based dressings¹⁶⁻¹⁸. In previous studies, a homemade foam-based NPWT system has been found to be cost-effective and economically viable in comparison with the commercially available vacuum-assisted closure (VAC) system^{19,20}. A plethora of NPWT modifications have been tried in

an attempt to reduce cost without compromising efficacy and safety²¹⁻²⁶. These modifications of the NPWT system were not inferior to the patented VAC system²⁷⁻³¹. A bedside suction machine also has been utilized to apply negative pressure intermittently³²⁻³⁴; however, that machine can be intolerably loud and overheats quickly, necessitating intermittent use.

Regimens combining NPWT with repetitive debridement, irrigation, and antibiotics have been shown to reduce the bacterial load and the rate of infection³⁵⁻³⁷. The use of NPWT decreased time to wound closure, the length of hospitalization, and the number of surgical procedures. The locally developed AquaVac system was developed with adherence to the principles of NPWT. This system consists of an inexpensive, reusable vacuum source (a converted aquarium pump equipped with a pressure gauge and pressure regulator) and a dressing system that can be easily found in the hospital supply room (including food plastic wrap as an occlusive drape, surgical gauze as wound filler, nasogastric tubes as tubing, and used intravenous [IV] bottles as effluent canisters). This system ensures that a surgical unit does not

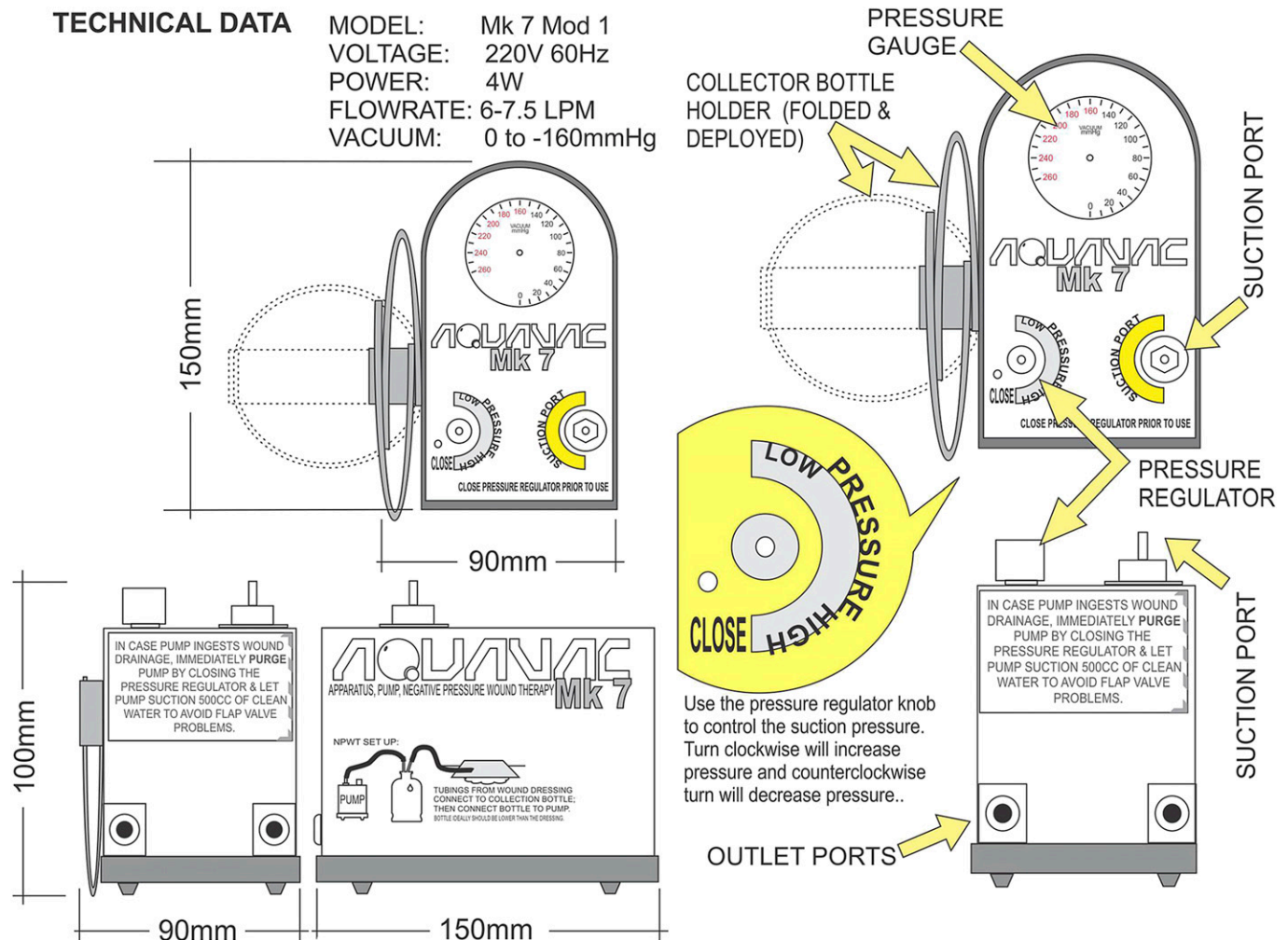


Fig. 1
The AquaVac system machine.

have to be dependent on a supply of expensive and model-specific NPWT dressings.

Materials and Methods

The present prospective, randomized controlled trial was conducted in a tertiary hospital in Bacolod City, Philippines, and was approved by the hospital's research ethics review committee. The study involved 36 patients who were managed with NPWT with either a low-cost, locally developed system (AquaVac) or a commercially available system (Vacuum-Assisted Closure Advanced Therapy System [VAC ATS]; KCI) for 7 days. All patients were admitted from March 1, 2018, to October 31, 2018, for the treatment of acute traumatic injuries to the upper or lower limbs with substantial soft-tissue involvement and skin loss that was not amenable to primary closure. Patients who had surgical contraindications because of medical conditions, chronic wounds, implant exposure, and multiple injuries or polytrauma were excluded from the study. All patients who were included were randomly allocated into treatment groups utilizing the random "fish bowl" method with 50% chance. (Specifically, 100 rolled papers were placed inside a container, 50 of which were marked as AquaVac group and the other 50 were marked as VAC ATS group. A random rolled paper was picked to determine the treatment group and then was returned to the container to maintain the 50% chance.)

Interobserver variability was assessed by having a third, blinded person evaluate outcomes by verifying the results and measurements. The wounds were measured with use of a clear 5 × 5-mm grid sheet and photographed. The dressing materials for the low-cost NPWT (AquaVac) group were sterilized in the institution's central supply section. The AquaVac system machine and dressing setups are shown in Figures 1 and 2. The VAC ATS machine and dressing materials were used according to their specifications. In both groups, a splint was applied to the extremity for immobilization, and continuous negative pressure (−120 to −125 mm Hg) was applied³⁸. The outcome measures were collected from the patient charts and were recorded by the principal investigators. The outcome measures included (1) dressing application time (time recorded), (2) exudate levels (amount measured in the canister), (3) area of wound bed covered by healthy tissue (measured with use of a 5 × 5-mm grid), (4) size reduction (determined by comparing the measurements before and after application of NPWT), (5) cost (average costs for all the materials used per patient), (6) visual analog scale (VAS) pain scores (recorded as scheduled monitoring), and (7) the presence of complications such as infection (noted at the end of the treatment or dressing change).

Statistical analysis was performed with use of SPSS software (version 20; IBM). Descriptive statistics (frequencies, percentages, cross-tabulations) were used for summarizing the data for each group. The statistical tools used were the independent t test (with the Levene test for equality of variances), Pearson product moment correlation coefficient, and Spearman rank correlation coefficient.

Results

From March 1 to October 31, 2018, a total of 38 eligible patients were seen; 2 were excluded (1 did not meet the inclusion criteria, and the other declined to participate). The remaining 36 patients were included in the study and were randomly allocated into 1 of the 2 treatment groups. No patient was lost to follow-up or withdrew from the study (Fig. 3).

The majority of patients were male, were 18 to 34 years of age, and had avulsion-type soft-tissue injuries due to road traffic accidents, mostly involving the leg. The 2 groups did not differ in terms of age, sex, mechanism of injury, and extremity involved.

The AquaVac dressing was faster to apply (5.5 minutes) than the VAC ATS dressing (7.5 minutes), but the difference was not significant ($t = 1.730$, degrees of freedom [df] = 34, $p = 0.093$) (Table I). There was moderate and significant correlation between wound size and the time needed to apply the dressing in the VAC ATS group ($r = 0.636$, $p = 0.006$) but not in the AquaVac group ($r = 0.277$, p value = 0.250). That is, in the VAC ATS group, the bigger the size of the wound, the longer the time it took to apply the dressing. In the AquaVac group, however, the wound size did not influence the time that it took to apply the dressing.

With regard to exudate levels, the 2 groups did not differ significantly from each other, with the average amounts in the

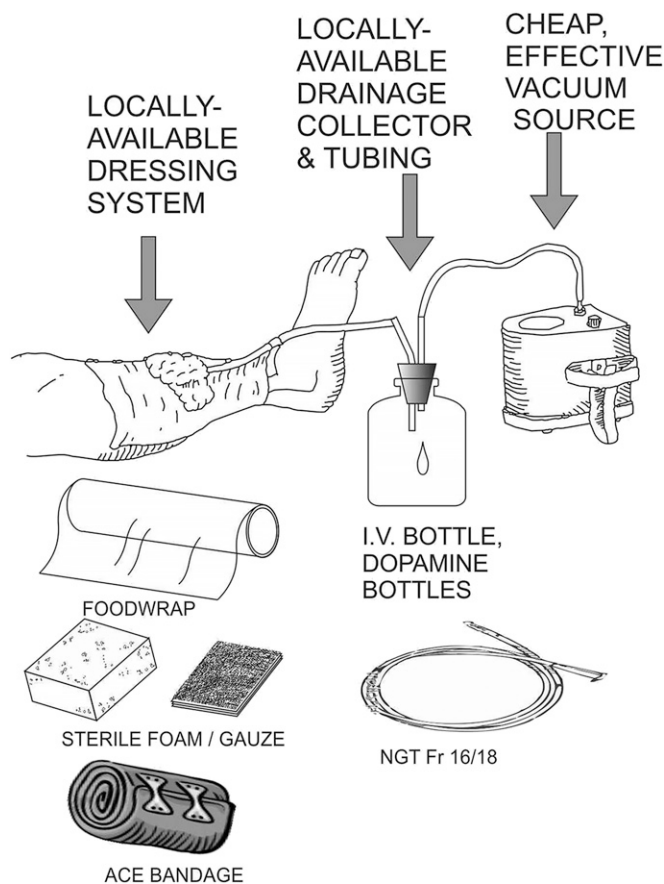


Fig. 2
The AquaVac system dressing set-up.

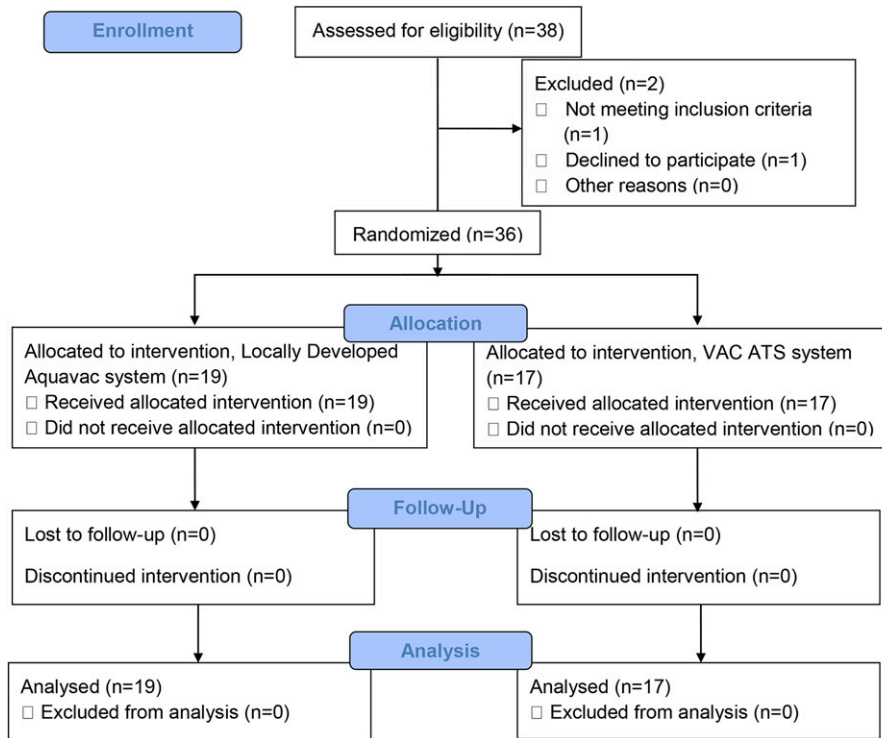


Fig. 3
CONSORT (Consolidated Standards of Reporting Trials) flow diagram.

VAC ATS and AquaVac groups being 198 and 161 mL, respectively. There was a significant correlation between the exudate level and wound size in both the VAC ATS group ($r = 0.898, p = 0.000001$) and the AquaVac group ($r = 0.601, p = 0.006$), implying that the bigger the size of the wound, the higher the amount of the exudate.

In all wounds, a large part of the wound bed area was covered by healthy granulation tissue in both the VAC ATS and AquaVac groups (98.01% and 97.16%, respectively). The average reduction in wound size was greater in the AquaVac group than in the VAC ATS group (19.50% compared with the 14.99%, respectively). The results related to the amount of granulation tissue and reduction of wound size were not significantly different between the 2 treatment groups (Table II). Representative photographs of wounds involving the leg, foot, and forearm in the 2 groups are shown in Figures 4 and 5. Wound photographs for all 36 patients who were enrolled in the study are shown in the Appendix.

Patients in both groups reported mild pain during the duration of NPWT treatment (VAS score, 3 to 4). The VAS scores on Day 7 (during dressing changes) showed that majority of patients (9 patients; 52.9%) in the VAC ATS group reported moderate pain (VAS score, 5 to 7), whereas the majority of patients in the AquaVac group (10 patients; 52.6%) reported mild pain (VAS score, 1 to 2). However, the cross-tabulation showed no significant difference at the 0.05 level (Table III). There was a significant correlation between pain and wound size on Days 1 to 7 in both the VAC ATS group ($r_s = 0.494, p = 0.044$) and the AquaVac group ($r = 0.790, p = 0.00006$). On Day 7, the correlation between pain and wound size was significant in both the VAC ATS group ($r_s = 0.641, p = 0.006$) and the AquaVac group ($r = 0.615, p = 0.005$), suggesting that, even when the wound had reduced in size, the intensity of the pain was still directly related to the wound size.

There were no deep infections involving wounds or periwound complications in either of the 2 groups. No pump in

TABLE I Independent Sample Tests for Time Required to Apply Dressing*

| Levene Test for Equality of Variances | | T Test for Equality of Means | | | | |
|---------------------------------------|---------------------------|------------------------------|----|--------------------|-----------------------|------------------------------------|
| F | Significance of Variances | T | df | P Value (2-Tailed) | Mean Difference (min) | Standard Error of Difference (min) |
| 0.752 | 0.392 | 1.730 | 34 | 0.093 | 1.98427 | 1.14677 |

*The AquaVac dressing was faster to apply (5.5 minutes) than the VAC ATS dressing (7.5 minutes), but the difference was not significant ($t = 1.730, df = 34, p = 0.093$). *df* = degrees of freedom.

TABLE II Amount of Exudate, Granulation Tissue, and Wound Size Reduction*

| Variable | Treatment Group | Mean | Standard Deviation | Mean Difference | T | df | P Value (2-Tailed) |
|---|-----------------|---------|--------------------|-----------------|--------|--------|--------------------|
| Approximate amount of exudate (mL) | VAC ATS | 197.647 | 181.160 | 36.858 | 0.696 | 34 | 0.491 |
| | AquaVac | 160.790 | 135.567 | | | | |
| Percentage of granulation tissue | VAC ATS | 98.012 | 4.209 | 0.853 | 0.532 | 34 | 0.598 |
| | AquaVac | 97.159 | 5.279 | | | | |
| Wound size (granulated) after NPWT (cm ²) | VAC ATS | 159.635 | 137.159 | 68.901 | 2.018 | 17.714 | 0.059 |
| | AquaVac | 90.735 | 33.551 | | | | |
| Wound size (not granulated) after NPWT (cm ²) | VAC ATS | 2.750 | 6.177 | 0.090 | 0.046 | 34 | 0.963 |
| | AquaVac | 2.660 | 5.500 | | | | |
| Wound size before NPWT (cm ²) | VAC ATS | 188.647 | 158.694 | 73.831 | 1.867 | 17.791 | 0.079 |
| | AquaVac | 114.816 | 39.679 | | | | |
| Wound size after NPWT (cm ²) | VAC ATS | 162.427 | 139.843 | 69.032 | 1.979 | 17.847 | 0.063 |
| | AquaVac | 93.395 | 35.514 | | | | |
| Wound size reduction (cm ²) | VAC ATS | 26.221 | 19.858 | 4.800 | 0.896 | 34 | 0.377 |
| | AquaVac | 21.421 | 11.657 | | | | |
| Wound size reduction (%) | VAC ATS | 14.987 | 3.549 | -4.515 | -1.839 | 22.893 | 0.079 |
| | AquaVac | 19.501 | 10.022 | | | | |

*The results related to the amount of exudate, granulation tissue, and wound size reduction showed no significant difference between the 2 treatment groups at the 0.05 level. df = degrees of freedom.



Fig. 4
Representative wound photographs of the leg, foot, and forearm of patients in the AquaVac group before and after application of NPWT.



Fig. 5
Representative wound photographs of the leg, foot, and forearm of patients in the VAC ATS group before and after application of NPWT.

either group failed or malfunctioned during the 7-day treatment period.

The average cost for a 7-day NPWT treatment regimen was \$491.38 USD per patient for the VAC ATS group (including the local price for the pump rental, dressing, and canister) and

\$63.75 USD per patient for the AquaVac group (with the pump being considered single-use; if the pump were to be used several times, the costs would be considerably lower). The cost analysis showed that the AquaVac system was at least 7 times cheaper than the VAC ATS system.

TABLE III Average VAS Scores Measured on Days 1 to 7 and Day 7*†

| Level of Pain‡ | VAC ATS Group (N = 17) | AquaVac Group (N = 19) | Total (N = 36) |
|-----------------|------------------------|------------------------|----------------|
| Days 1-7 | | | |
| None (1-2) | 5 (29.4%) | 8 (42.1%) | 13 (36.1%) |
| Mild (3-4) | 10 (58.8%) | 9 (47.4%) | 19 (52.8%) |
| Moderate (5-7) | 2 (11.8%) | 2 (10.5%) | 4 (11.1%) |
| Severe (8-10) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Total | 17 (100.0%) | 19 (100.0%) | 36 (100.0%) |
| Day 7 | | | |
| None (1-2) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) |
| Mild (3-4) | 4 (23.5%) | 10 (52.6%) | 14 (38.9%) |
| Moderate (5-7) | 9 (52.9%) | 7 (36.8%) | 16 (44.4%) |
| Severe (8-10) | 4 (23.5%) | 2 (10.5%) | 6 (16.7%) |
| Total | 17 (100.0%) | 19 (100.0%) | 36 (100.0%) |

*Cross-tabulation shows that there was no significant difference between columns of the same row at the 0.05 level. †The values are given as the number of patients, with the percentage in parentheses. ‡The VAS pain scores associated with each pain category are shown in parentheses.

Discussion

The present study showed that the low-cost AquaVac NPWT system was not inferior to the commercial VAC ATS system. There were no significant differences between the systems in terms of application time, exudate levels, wound size reduction, and granulation tissue formation. These results agree with the findings of previous studies regarding granulation formation, edema control, and facilitation of wound closure^{11,39-43}. Adequate surgical debridement until viable tissues are present in the wound base is needed. Both systems were comparable in terms of reducing the edema and wound exudate, which agrees with previous findings⁴⁴⁻⁴⁶. The study involved a 7-day continuous application of NPWT and demonstrated no significant difference between the 2 groups in terms of the reduction of wound size. These observations were promising and demonstrated a positive response of the wound, with reduction of the wound surface area, in agreement with previous studies⁴⁷⁻⁴⁹.

While there were differences between the groups in terms of pressure fluctuations during the first 72 hours of treatment, these fluctuations may have been due to the fact that the converted aquarium pump's pressure had to be regulated manually, whereas the VAC ATS pump had an automated pressure regulation system and thus had no fluctuations.

The low-cost AquaVac NPWT system consists of (1) a vacuum source and (2) modified dressings. The vacuum source is a modified aquarium aerator pump. An oscillating coil moves a magnetic lever back and forth, which in turn operates a bellows or diaphragmatic pump. This mechanism is quiet, can continuously operate for days or weeks without overheating, and consumes a small amount of electricity (4 W). A pressure regulator and pressure gauge were added to enable the user to manually regulate the suction from 0 to -160 mm Hg. The pump cost \$60.00 USD to modify. While inexpensive enough to be disposable, the pump can be reused up to 20 times. In comparison, the average cost of commercially available NPWT pumps range from \$2,500 to \$6,000 USD. These modified pumps are assembled with use of basic industrial tools and semi-skilled labor.

The second component of the system is the modified dressing. Food wrap (e.g., Cling Wrap [Glad] or Saran Wrap [SC Johnson]) is used as an occlusive drape, sterile surgical gauze is used for wound filler, Vaseline (Unilever)-impregnated gauze (e.g., Bactigras [Smith & Nephew]) is used as a barrier dressing for exposed tendons or bone, nasogastric tubes are used as tubing, and empty IV bottles are used as effluent canisters. All of these materials can be easily found in the operating room (anesthesiologists routinely use food wrap for temperature regulation in limbs of pediatric patients), and 1 dressing change costs only \$3.65 USD. In comparison, 1 VAC dressing set costs \$57.69 USD and a disposable canister costs \$52.88 USD, for a total of \$110.57 USD.

The use of food wrap (Cling Wrap, Saran Wrap) as an occlusive dressing may not be ideal but is adequate for this

purpose. Its lack of adhesive produces some air leakage, leading to minor pressure fluctuations shortly after application. The seal is tenuous in the area where the tubing exits the occlusive drape. Sealing this area with surgical tape usually solves the problem. The presence of body hair and dry, scaly skin also present problems with the seal, but not so much as to cause inadequate pressure. Applying petroleum jelly (e.g., Vaseline) on the periwound skin helps in sealing the dressing. The presence of external fixator pins also presents a challenge; utilizing multiple sheets and tape around the pins helps. The key is an adequate flow rate of the pump. If the suction flow is greater than the air leakage (which, in this case, it is), the seal and pressure are maintained.

Improvising canisters from IV bottles is fairly straightforward. A rubber stopper with 2 metal tubes is used; 1-cc syringe barrels also work. In fact, even soda or beer bottles can be used, and they can be easily steam-autoclaved.

Adequate surgical debridement was done when necessary. Once the wounds had a good granulating bed and were amenable to skin, the 2 NPWT dressing systems were used as skin-graft bolsters.

The AquaVac group had lower pain scores during dressing changes than the VAC ATS. This may be due to the granulation tissue ingrowth into the foam used by VAC ATS system.

The limitations of the present study included the low number of patients and the 7-day treatment period. The potential for selection bias was addressed through randomization, and the potential for detection bias was addressed by having third blinded person verify and measure the variables.

Patient comfort is one of the benefits associated with the use of NPWT⁵⁰. There was no significant difference between the 2 treatment groups, and VAS pain scores were highly correlated with wound size, indicating that greater wound size was associated with greater pain. In the present study, we did not observe any cases of infection or periwound complications. This observation agrees with the findings of previous studies⁵¹⁻⁵⁵.

Traditionally, the use of NPWT has been thought to be associated with higher costs. Today, however, the use of NPWT is more practical and inexpensive as the costs of NPWT are offset by a lower number of operations, less-time-consuming dressing changes, and shorter hospital stays⁵⁶⁻⁵⁹. Our cost analysis indicated that the locally developed AquaVac system was approximately 7 times cheaper than the VAC ATS system. Our findings suggest that potential savings can be achieved, while maintaining the quality of wound care needed by the patients, especially in areas with limited resources⁶⁰⁻⁶².


Conclusions

The present study showed that the 7-day results associated with the low-cost AquaVac NPWT system were not inferior to those associated with the commercially available VAC ATS system. There were no significant differences between the

systems in terms of application time, exudate levels, wound size reduction, and granulation tissue formation. In addition, although the difference was not significant, the VAS pain scores were lower in the AquaVac group during dressing changes at Day 7. Other notable findings were that wound size was highly correlated with the amount of wound exudate and the VAS scores.

The main difference between the 2 NPWT systems is the cost: the AquaVac system is at least 7 times cheaper than the commercial VAC ATS system. Such an economical method for delivering NPWT—which is noninferior to the gold standard—greatly impacts surgical units in developing countries, where most patients needing such treatments are those who can scarcely afford it. With such a system in place, cost becomes far less of an issue, and the decision on whether to use NPWT rests on whether the wound requires the benefits of NPWT or not. However, it should be noted that any NPWT system should not be used as a substitute for adequate surgical debridement and, where indicated, prompt definitive closure.

Appendix

 Supporting material provided by the authors is posted with the online version of this article as a data supplement at [jbjs.org \(http://links.lww.com/JBJS/F532\)](http://links.lww.com/JBJS/F532). ■

Hansel Gould B. Cocjin, MD, DPBO¹
Jair Kimri P. Jingco, MD, FPOA¹
Franklin Delano C. Tumaneng, MD, FPOA, FPCS¹
Jose Maria R. Coruña, MD, FPOA, FPCS¹

¹Department of Orthopaedics & Traumatology, Corazon Locsin Montelibano Memorial Regional Hospital (CLMMRH), Bacolod City, Philippines

Email address for H.G.B. Cocjin: hanselgouldcocjin@gmail.com

ORCID iD for H.G.B. Cocjin: [0000-0001-6010-431X](https://orcid.org/0000-0001-6010-431X)
ORCID iD for J.K.P. Jingco: [0000-0003-4124-4282](https://orcid.org/0000-0003-4124-4282)
ORCID iD for F.D.C. Tumaneng: [0000-0002-2207-2238](https://orcid.org/0000-0002-2207-2238)
ORCID iD for J.M.R. Coruña: [0000-0003-3578-1903](https://orcid.org/0000-0003-3578-1903)

References

1. Simman R, Phavixay L. Split-thickness skin grafts remain the gold standard for the closure of large acute and chronic wounds. *J Am Col Certif Wound Spec*. 2011 Sep;3(3):55-9.
2. Wu SC, Skratsky MK, Andersen CA. The evolution of negative pressure wound therapy [NPWT]: a review of science, available devices, and evolution in the usage of NPWT. *Surg Technol Int*. 2013 Sep;23:40-50.
3. Argenta LC, Morykwas MJ. Vacuum-assisted closure: a new method for wound control and treatment: clinical experience. *Ann Plast Surg*. 1997 Jun;38(6):563-76; discussion 577.
4. Cocjin HGB, Jingco JKP, Coruña JMR. Efficacy and cost of negative pressure wound therapy (NPWT) dressing versus tie-over bolster dressing on integrating split-thickness skin grafts. *Philippine J Surg Specialties*. 2018 Jan-Jun;73(1):19-27.
5. Yin Y, Zhang R, Li S, Guo J, Hou Z, Zhang Y. Negative-pressure therapy versus conventional therapy on split-thickness skin graft: a systematic review and meta-analysis. *Int J Surg*. 2018 Feb;50:43-8. Epub 2017 Dec 29.
6. Sarovath A, Chardokmaiprai C, Kruavit A. Vacuum-assisted closure: a reliable method to secure skin graft. *Thai J Surg*. 2005;26:32-8.
7. Vikatmaa P, Juutilainen V, Kuukasjärvi P, Malmivaara A. Negative pressure wound therapy: a systematic review on effectiveness and safety. *Eur J Vasc Endovasc Surg*. 2008 Oct;36(4):438-48. Epub 2008 Aug 3.
8. Brandon T. A portable, disposable system for negative-pressure wound therapy. *Br J Nurs*. 2015 Jan 22;24(2):98;100-6.
9. Matiasek J, Djedovic G, Mattesich M, Morandi E, Pauzenberger R, Pikula R, Verstappen R, Pierer G, Koller R, Rieger UM. The combined use of NPWT and instillation using an octenidine based wound rinsing solution: a case study. *J Wound Care*. 2014 Nov;23(11):590; 592-6.
10. Putnis S, Khan WS, Wong JM. Negative pressure wound therapy - a review of its uses in orthopaedic trauma. *Open Orthop J*. 2014 Jun 27;8:142-7.
11. Armstrong DG, Lavery LA; Diabetic Foot Study Consortium. Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial. *Lancet*. 2005 Nov 12;366(9498):1704-10.
12. Glass GE, Murphy GF, Esmaili A, Lai LM, Nanchahal J. Systematic review of molecular mechanism of action of negative-pressure wound therapy. *Br J Surg*. 2014 Dec;101(13):1627-36. Epub 2014 Oct 8.
13. Cirocchi R, Birindelli A, Biffi WL, Mutafchijyski V, Popivanov G, Chiara O, Tughnoli G, Di Saverio S. What is the effectiveness of the negative pressure wound therapy (NPWT) in patients treated with open abdomen technique? A systematic review and meta-analysis. *J Trauma Acute Care Surg*. 2016 Sep;81(3):575-84.
14. Stannard JP, Volgas DA, McGwire G 3rd, Stewart RL, Obremsky W, Moore T, Anglen JO. Incisional negative pressure wound therapy after high-risk lower extremity fractures. *J Orthop Trauma*. 2012 Jan;26(1):37-42.
15. Arti H, Khorami M, Ebrahimi-Nejad V. Comparison of negative pressure wound therapy (NPWT) & conventional wound dressings in the open fracture wounds. *Pak J Med Sci*. 2016 Jan-Feb;32(1):65-9.
16. Albert NM, Rock R, Sammon MA, Bena JF, Morrison SL, Whitman A, Kato I, Landis-Erdman JC. Do patient and nurse outcome differences exist between 2 negative pressure wound therapy systems? *J Wound Ostomy Continence Nurs*. 2012 May-Jun;39(3):259-66.
17. Dunn R, Hurd T, Chadwick P, Cote J, Cockwill J, Mole T, Smith J. Factors associated with positive outcomes in 131 patients treated with gauze-based negative pressure wound therapy. *Int J Surg*. 2011;9(3):258-62. Epub 2010 Dec 25.
18. Dunn RM, Ignatz R, Mole T, Cockwill J, Smith JM. Assessment of gauze-based negative pressure wound therapy in the split-thickness skin graft clinical pathway-an observational study. *Eplasty*. 2011 Mar 16;11:e14.
19. Llanos S, Danilla S, Barraza C, Armijo E, Piñeros JL, Quintas M, Searle S, Calderon W. Effectiveness of negative pressure closure in the integration of split thickness skin grafts: a randomized, double-masked, controlled trial. *Ann Surg*. 2006 Nov;244(5):700-5.
20. Shalom A, Eran H, Westreich M, Friedman T. Our experience with a "home-made" vacuum-assisted closure system. *Isr Med Assoc J*. 2008 Aug-Sep;10(8-9):613-6.
21. Hudson DA, Adams KG, Van Huyssteen A, Martin R, Huddleston EM. Simplified negative pressure wound therapy: clinical evaluation of an ultraportable, no-canister system. *Int Wound J*. 2015 Apr;12(2):195-201. Epub 2013 May 7.
22. Hurd T, Trueman P, Rossington A. Use of a portable, single-use negative pressure wound therapy device in home care patients with low to moderately exuding wounds: a case series. *Ostomy Wound Manage*. 2014 Mar;60(3):30-6.
23. Strugala V, Martin R. Meta-analysis of comparative trials evaluating a prophylactic single-use negative pressure wound therapy system for the prevention of surgical site complications. *Surg Infect (Larchmt)*. 2017 Oct;18(7):810-9. Epub 2017 Sep 8.
24. Saraiya HA, Shah MN. Use of indigenously made negative-pressure wound therapy system for patients with diabetic foot. *Adv Skin Wound Care*. 2013 Feb;26(2):74-7.
25. Gabriel A, Thimmappa B, Rubano C, Storm-Dickerson T. Evaluation of an ultra-lightweight, single-patient-use negative pressure wound therapy system over dermal regeneration template and skin grafts. *Int Wound J*. 2013 Aug;10(4):418-24. Epub 2012 Jun 11.
26. Mody GN, Zurovcik DR, Joharifard S, Kansayisa G, Uwimana G, Baganizi E, Ntakiyiruta G, Mugenzi D, Riviello R. Biomechanical and safety testing of a simplified negative-pressure wound therapy device. *Plast Reconstr Surg*. 2015 Apr;135(4):1140-6.
27. Hurd T, Rossington A, Trueman P, Smith J. A retrospective comparison of the performance of two negative pressure wound therapy systems in the management of wounds of mixed etiology. *Adv Wound Care (New Rochelle)*. 2017 Jan 1;6(1):33-7.
28. Rahmanian-Schwarz A, Willkomm LM, Gonsler P, Hirt B, Schaller HE. A novel option in negative pressure wound therapy (NPWT) for chronic and acute wound care. *Burns*. 2012 Jun;38(4):573-7. Epub 2011 Nov 17.

- 29.** Zurovcik DR, Mody GN, Riviello R, Slocum A. Simplified negative pressure wound therapy device for application in low-resource settings. *J Orthop Trauma*. 2015 Oct;29(Suppl 10):S33-6.
- 30.** Yıldız Ş, Uzun G, Mutluoglu M, Memis A. GATA negative pressure wound therapy system. *J Am Coll Clin Wound Spec*. 2014 Sep 16;5(2):45-7. eCollection 2013 Aug.
- 31.** Ranjeet N, Dy AU Jr. Modified negative pressure wound therapy (modified NPWT): an experience of 128 cases. *Nepal J Med Sci*. 2012;1(2):108-14.
- 32.** Estillore KM, Quevedo GL, Bonifacio LR. Improvised suction apparatus for closure of large soft tissue deficit. *Malays Orthop J*. 2013 Jul;7(2):29-33.
- 33.** Karlakki S, Brem M, Giannini S, Khanduja V, Stannard J, Martin R. Negative pressure wound therapy for management of the surgical incision in orthopaedic surgery: a review of evidence and mechanisms for an emerging indication. *Bone Joint Res*. 2013 Dec 18;2(12):276-84.
- 34.** Sullivan N, Snyder DL, Tipton K, Uhl S, Schoelles KM. Negative pressure wound therapy devices. Technology assessment report. 2009 Jul 29. https://www.ecri.org/Resources/EPC_Sample_Reports/Negative_Pressure_Wound_Therapy_Devices.pdf. Accessed 2019 Aug 7.
- 35.** Jentzsch T, Osterhoff G, Zwolak P, Seifert B, Neuhaus V, Simmen HP, Jukema GN. Bacterial reduction and shift with NPWT after surgical debridements: a retrospective cohort study. *Arch Orthop Trauma Surg*. 2017 Jan;137(1):55-62. Epub 2016 Dec 17.
- 36.** Felte R, Gallagher KE, Tinkoff GH, Cipolle M. A case review series of Christiana Care Health System's experience with negative pressure wound therapy instillation. *Cureus*. 2016 Nov 7;8(11):e866.
- 37.** Arvesen K, Nielsen CB, Fogh K. Accelerated wound healing with combined NPWT and IPC: a case series. *Br J Community Nurs*. 2017 Mar;22(Sup3)(Suppl 3):S41-5.
- 38.** Evangelista MS, Kim EK, Evans GRD, Wirth GA. Management of skin grafts using negative pressure therapy: the effect of varied pressure on skin graft incorporation. *Wounds*. 2013 Apr;25(4):89-93.
- 39.** Tevanov I, Enescu DM, Bălănescu R, Sterian G, Ulici A. Negative pressure wound therapy (NPWT) to treat complex defect of the leg after electrical burn. *Chirurgia (Bucur)*. 2016 Mar-Apr;111(2):175-9.
- 40.** Nain PS, Uppal SK, Garg R, Bajaj K, Garg S. Role of negative pressure wound therapy in healing of diabetic foot ulcers. *J Surg Tech Case Rep*. 2011 Jan;3(1):17-22.
- 41.** Sepúlveda G, Espíndola M, Maureira M, Sepúlveda E, Ignacio Fernández J, Oliva C, Sanhueza A, Vial M, Manterola C. [Negative-pressure wound therapy versus standard wound dressing in the treatment of diabetic foot amputation. A randomised controlled trial]. *Cir Esp*. 2009 Sep;86(3):171-7. Epub 2009 Jul 18. Spanish.
- 42.** Morykwas MJ, Argenta LC, Shelton-Brown EI, McGuirt W. Vacuum-assisted closure: a new method for wound control and treatment: animal studies and basic foundation. *Ann Plast Surg*. 1997 Jun;38(6):553-62.
- 43.** DeFranzo AJ, Argenta LC, Marks MW, Molnar JA, David LR, Webb LX, Ward WG, Teasdall RG. The use of vacuum-assisted closure therapy for the treatment of lower-extremity wounds with exposed bone. *Plast Reconstr Surg*. 2001 Oct;108(5):1184-91.
- 44.** Ford CN, Reinhard ER, Yeh D, Syrek D, De Las Morenas A, Bergman SB, Williams S, Hamori CA. Interim analysis of a prospective, randomized trial of vacuum-assisted closure versus the HealthPoint system in the management of pressure ulcers. *Ann Plast Surg*. 2002 Jul;49(1):55-61; discussion 61.
- 45.** Mouës CM, Vos MC, van den Bemd GJ, Stijnen T, Hovius SE. Bacterial load in relation to vacuum-assisted closure wound therapy: a prospective randomized trial. *Wound Repair Regen*. 2004 Jan-Feb;12(1):11-7.
- 46.** Joseph E, Hamori CA, Bergman S, Roaf E, Swann NF, Anastasi GW. A prospective randomized trial of vacuum-assisted closure versus standard therapy of chronic nonhealing wounds. *Wounds*. 2000;12(3):60-7.
- 47.** McCallon SK, Knight CA, Valiulus JP, Cunningham MW, McCulloch JM, Farinas LP. Vacuum-assisted closure versus saline-moistened gauze in the healing of postoperative diabetic foot wounds. *Ostomy Wound Manage*. 2000 Aug;46(8):28-32; 34.
- 48.** Etöz A, Özgenel Y, Özcan M. The use of negative pressure wound therapy on diabetic foot ulcers: a preliminary controlled trial. *Wounds*. 2004 Aug;16(8):264-9.
- 49.** Witkowski W, Jawien A, Witkiewicz W, Zon B. Initial multi-centre observations upon the effect of a new topical negative pressure device upon patient and clinician experience and the treatment of wounds. *Int Wound J*. 2009 Apr;6(2):167-74.
- 50.** Braakenburg A, Obdeijn MC, Feitz R, van Rooij IALM, van Griethuysen AJ, Klinckenbijl JHG. The clinical efficacy and cost effectiveness of the vacuum-assisted closure technique in the management of acute and chronic wounds: a randomized controlled trial. *Plast Reconstr Surg*. 2006 Aug;118(2):390-7; discussion 398-400.
- 51.** Glass GE, Murphy GRF, Nanchahal J. Does negative-pressure wound therapy influence subjacent bacterial growth? A systematic review. *J Plast Reconstr Aesthet Surg*. 2017 Aug;70(8):1028-37. Epub 2017 May 22.
- 52.** Hasse B, Husmann L, Zinkernagel A, Weber R, Lachat M, Mayer D. Vascular graft infections. *Swiss Med Wkly*. 2013 Jan 24;143:w13754.
- 53.** Parrett BM, Talbot SG, Pribaz JJ, Lee BT. A review of local and regional flaps for distal leg reconstruction. *J Reconstr Microsurg*. 2009 Sep;25(7):445-55. Epub 2009 Jul 10.
- 54.** Pollak AN. Use of negative pressure wound therapy with reticulated open cell foam for lower extremity trauma. *J Orthop Trauma*. 2008 Nov-Dec;22(10)(Suppl):S142-5.
- 55.** Armstrong DG, Marston WA, Reyzelman AM, Kirsner RS. Comparative effectiveness of mechanically and electrically powered negative pressure wound therapy devices: a multicenter randomized controlled trial. *Wound Repair Regen*. 2012 May-Jun;20(3):332-41.
- 56.** Mouës CM, van den Bemd GJ, Meerding WJ, Hovius SE. An economic evaluation of the use of TNP on full-thickness wounds. *J Wound Care*. 2005 May;14(5):224-7.
- 57.** Hussain A, Singh K, Singh M. Cost effectiveness of vacuum-assisted closure and its modifications: a review. *ISRN Plastic Surgery*. 2013;595789.
- 58.** Apelqvist J, Armstrong DG, Lavery LA, Boulton AJM. Resource utilization and economic costs of care based on a randomized trial of vacuum-assisted closure therapy in the treatment of diabetic foot wounds. *Am J Surg*. 2008 Jun;195(6):782-8. Epub 2008 Mar 26.
- 59.** Othman D. Negative pressure wound therapy literature review of efficacy, cost effectiveness, and impact on patients' quality of life in chronic wound management and its implementation in the United Kingdom. *Plast Surg Int*. 2012;2012:374398. Epub 2012 May 30.
- 60.** Eisenhardt SU, Schmidt Y, Thiele JR, Iblher N, Penna V, Torio-Padron N, Stark GB, Bannasch H. Negative pressure wound therapy reduces the ischaemia/reperfusion-associated inflammatory response in free muscle flaps. *J Plast Reconstr Aesthet Surg*. 2012 May;65(5):640-9. Epub 2011 Dec 3.
- 61.** Glass GE, Jain A. Pretibial lacerations: experience from a lower limb trauma centre and systematic review. *J Plast Reconstr Aesthet Surg*. 2014 Dec;67(12):1694-702. Epub 2014 Aug 20.
- 62.** Perez D, Bramkamp M, Exe C, von Ruden C, Ziegler A. Modern wound care for the poor: a randomized clinical trial comparing the vacuum system with conventional saline-soaked gauze dressings. *Am J Surg*. 2010 Jan;199(1):14-20. Epub 2009 Apr 10.