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Comparison of Vacuum Sealing Drainage and Traditional Therapy for Treatment of Diabetic Foot Ulcers: A Meta-Analysis

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ABSTRACT

Vacuum sealing drainage (VSD) is a noninvasive adjunctive therapy to help patients with diabetic foot ulcers by reducing edema and promoting wound healing and formation of granulation tissue. Multiple databases were searched for relevant studies, and full-text articles comparing VSD and conventional therapy were reviewed. Meta-analyses were conducted with Review Manager 5.0 software to estimate the results of the selected articles. Forest plots, sensitivity analysis, and bias analysis were also performed on the included articles. In total, 10 studies satisfied the inclusion criteria and were selected in this study. The meta-analysis suggested that the duration of therapy, decrease of wound size, and efficacy rate showed statistically significant differences between the 2 groups (mean difference = −12.86; 95% confidence interval [CI] −12.86 to −8.52; $p < .00001$; mean difference = 8.71; 95% CI 3.25 to 14.17; $p = .002$; relative risk = 1.41; 95% CI 1.22 to 1.62; $p < .00001$, respectively) although the complication rate between the 2 groups was comparable (relative risk = 0.83; 95% CI 0.60 to 1.16; $p = .28$). Publication bias was not assessed because only a few articles were included. In conclusion, VSD is a more effective therapy and is associated with a greater decrease in wound size and shorter time to wound healing, compared to the conventional method.

Diabetic foot ulcers (DFUs) are the most common, complex, and serious disabling health problem of patients with chronic diabetes mellitus (1–3). Studies reported that the prevalence of DFUs is ~15% among diabetics, and patients with DFUs have ~60% longer hospital stays compared with those without ulcers (4,5). Chronic wounds are difficult to treat and slow to heal (6). Ulcers require intensive local wound care, even for the most superficial ones, but poor healing responses result in prolonged disability, and individuals with diabetes have a significant risk of nontraumatic foot amputations (7,8).

Appropriate prevention practices and interventions could decrease the prevalence of foot complications and lower-limb amputations among patients with diabetes. Multiple treatments involve debridement, revascularization, and treatment of infection if indicated (9), but for physicians, DFUs are still a significant challenge (10,11).

The optimal therapy for DFUs remains ill defined. Several different studies have reported many different methods that establish good circulation in limbs and regional tissues. Saline-moistened gauze has been regarded as the standard method, but it is difficult to continuously maintain a moist wound environment. Various advanced technologies have been developed, including advanced moist wound therapy (12), growth factors (13,14), electric stimulation (15), and bioengineered tissue or skin substitutes (16), but the results have been lackluster, and some methods are not even better than basic care (17–19).

Recently, vacuum systems in improving tissue circulation on wound healing have been highly recommended to treat DFUs. Negative-pressure wound dressings have emerged for these complex wounds (20). This therapy is a noninvasive system and creates a continuous or intermittent negative pressure environment through a pump. The alternating negative pressure produced by the pump could increase blood circulation and enhance the transport of oxygen and nutrients to ulcers, which could accelerate wound healing (21–23). In addition, the therapy creates a moist environment and wound closure to reduce edema and promote the formation of granulation tissue. With the negative pressure on the ulcers, bacterial burden and chronic interstitial wound fluid would be reduced, and the wound environment is manipulated (24). Vacuum sealing drainage (VSD) is a well-tolerated method with few contraindications or complications, which makes the therapy popular in DFU treatment. Clinical evidence recommends the use of VSD; however, the randomized trials are weakly powered, and the overall evidence is low (25). The aim of this study was to evaluate the safety and efficacy of VSD compared to traditional therapy for the treatment of DFUs.

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Materials and Methods

Search Strategy

Related studies on treatment of diabetic foot by VSD and traditional therapy were searched in multiple databases, including PubMed, Springer, EMBASE, and the Cochrane library, up until October 2017. The systematic review and meta-analysis were undertaken with articles reporting on randomized controlled trials. The reference lists of each article were manually searched to obtain a comprehensive collection. The articles were efficiently searched with the following terms and string: (1) "vacuum sealing drainage" OR "vacuum assisted closure" OR "VAC" OR "VSD" OR "negative pressure wound therapy" OR "NPWT"; (2) "diabetic foot" OR "diabetic feet" OR "diabetic wound" OR "foot ulcer." These 2 strings were assembled with the connection symbol "AND" to search the articles related in the databases. All meta-analyses were limited to studies performed on human subjects.

Citation Selection

All the articles were reviewed independently and intensively for further selection. The following eligibility criteria must be met for inclusion in this study:

(1) A randomized controlled trial or a controlled clinical trial;
(2) Diabetic patients with chronic foot ulcers and surgical foot wounds;
(3) Studies comparing the outcomes of VSD and traditional therapy; and
(4) Availability of full text.

Exclusion criteria were as follows:

(1) Nonrandomized study;
(2) Studies on other diseases; and
(3) Studies lacking comparable results or not showing corresponding outcomes.

Two investigators (J.-T.W., H.-C.G.) checked whether the study met the criteria presented together and finally selected the articles. The full texts of the studies were then obtained if the studies were found to be relevant.

Data Extraction

Two authors (J.-T.W., H.-C.G.) read the full articles independently and assessed the quality of each included study. The information from every included study consisted of the first author's name, year of publication, year of onset, sample size (VSD/control), age range, and outcome parameters. Disagreements were resolved through discussion or a third reviewer's (G.C.) judgment.

Quality Assessment

We performed bias analysis to assess the quality of each included study with the Cochrane Collaboration tool including 7 domains: (1) random sequence generation, (2) allocation concealment, (3) blinding of participants and personnel, (4) blinding of outcome assessment, (5) incomplete outcome data, (6) selective reporting, and (7) other biases.

Statistical Analysis

Comparisons were performed with Review Manager 5.0 software (The Cochrane Collaboration, London, UK) to estimate difference in outcomes between VSD and traditional therapy, and STATA 10.0 software (StataCorp, College Station, TX) was used to estimate publication bias. The levels of heterogeneity were presented in these studies. The random-effects model was adopted when moderate or high heterogeneity was present; otherwise the fixed-effects model was chosen. In the included studies, relative risk (RR) for binary variables and mean difference (MD) for continuous outcomes with 95% confidence intervals (CIs) were calculated. Heterogeneity was assessed using Q statistics in this study. A p value <.05 was considered statistically significant.

Results

Description of Search Results

A total of 857 records were initially retrieved in these electronic databases until 2017 after primary selection, and finally 10 articles (26–35) satisfied the inclusion criteria. The remaining 847 articles were excluded because of duplication, irrelevant studies, inappropriate data, review articles, merely a case report, diseases other than diabetic foot wounds, or lack of a full text. The flowchart for the screening process is illustrated in Fig. 1. Among these 10 articles, 5 compared duration of therapy, 2 studied decrease of wound size, 7 studied efficacy, and 3 studied complications.

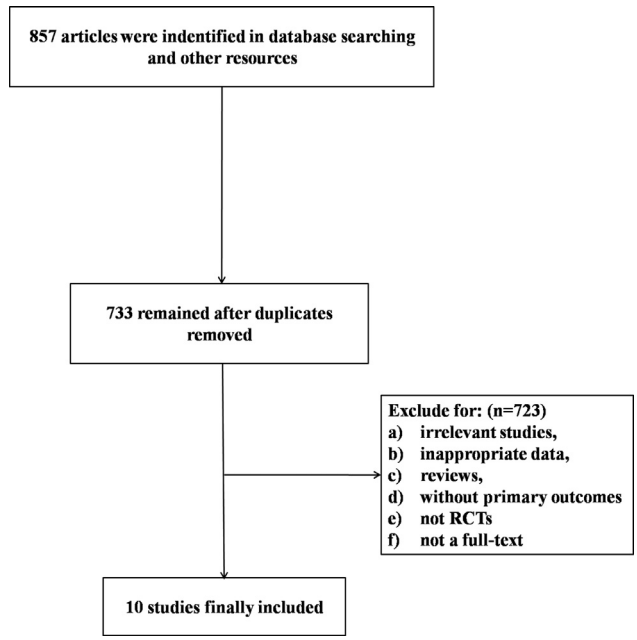

Fig. 1. Flow diagram of the study selection and screening process.

Characteristics of the Included Studies

The detailed characteristics of the included studies are given in Table 1. The name of the first author, year of publication, year of onset, age range of patients, sample size (VSD/control), sex distribution (male/female), and outcome parameters are presented in the Table. The articles were published from 2000 to 2015. The sample size of the 10 studies ranged from 18 to 335, and a total of 818 patients with diabetes were included. The mean age ranged from 18 to 75 years. All the statistical analysis used the random effects model owing to the variance of each study.

Quality Assessment

We evaluated the risk of bias of the articles with the criteria in the Review Manager 5.3 Tutorial. The risk of bias in this study is shown in Table 2.

Results of Meta-Analysis

Meta-Analysis of Duration of Therapy

Five of the 10 articles included in this study compared the duration of therapy in the VSD group and the traditional therapy group. Fig. 2 presents the forest plot for duration in different groups. All 5 studies showed that the duration of therapy in the VSD group was much shorter than that of the control group. Moreover, the combined results showed a statistically significant difference between the VSD group and the traditional therapy group (MD = −12.86; 95% CI −12.86 to −8.52; $p < .00001$; p for heterogeneity = .50; $I^2 = 0\%$).

Meta-Analysis of Wound Size Reduction

Two included studies compared wound size reduction after therapy, and both studies showed a statistically significant difference between the 2 groups. Moreover, as shown in Fig. 3, the meta-analysis indicated that wound size reduction in the VSD group was greater than that of

Table 1
Detailed characteristics of the included studies

Study	Year of Onset	Age Range, years	Sample Size (VSD/Control)	Sex Distribution (Male/Female)	Outcome Measurements
Akbari et al (26), 2007	NR	VSD: 58.2 ± 8.07; control: 57.6 ± 8.02	9/9	3/15	Efficacy
Armstrong et al (27), 2005	NR	VSD: 57.2 ± 13.4; control: 60.1 ± 12.2	77/85	132/30	Efficacy, complications
Blume et al (28), 2008	August 2002 to August 2005	VSD: 58 ± 12; control: 59 ± 12	169/166	263/72	Duration of therapy, efficacy, complications
Sepulveda et al (29), 2009	August 2006 to July 2007	VSD: 61.5 ± 10; control: 62.1 ± 8	12/12	19/5	Duration of therapy
McCallon et al (30), 2000	NR	18 to 75	23/26	NR	Duration of therapy
Nain et al (31), 2011	NR	VSD: 61.33 ± 7.63; control: 55.40 ± 11.54	15/15	25/5	Efficacy
Ravari et al (32), 2013	NR	NR	10/13	15/8	Efficacy, complications
Shi et al (33), 2015	June 2013 to December 2014	VSD: 61.5 ± 8.6; control: 60.3 ± 9.6	22/19	28/13	Duration of therapy
Yan et al (34), 2015	January 2006 to March 2014	18 to 68	44/32	56/20	Duration of therapy, efficacy
Zhu et al (35), 2014	January 2012 to June 2014	48 to 65	30/30	32/28	Efficacy

Abbreviations: NR, not recorded; VSD, vacuum sealing drainage.

Table 2
Risk of bias

Studies	Akbari et al (26), 2007	Armstrong et al (27), 2005	Blume et al (28), 2008	Sepulveda et al (29), 2009	McCallon et al (30), 2000	Nain et al (31), 2011	Ravari et al (32), 2013	Shi et al (33), 2015	Yan et al (34), 2015	Zhu et al (35), 2014
Random sequence generation	Low	None	Low	Low	Low	Low	Low	Low	Low	Low
Allocation concealment	Low	Low	Low	High	Low	Low	Low	High	Low	None
Blinding of participants and personnel	High	High	High	High	High	High	High	High	High	High
Blinding of outcome assessment	Low	Low	Low	None	Low	Low	High	Low	Low	Low
Incomplete outcome data	Low	Low	Low	Low	Low	Low	Low	Low	Low	Low
Selective reporting	None	Low	None	High	None	Low	Low	Low	Low	Low
Other bias	Low	Low	Low	None	None	Low	None	None	None	Low

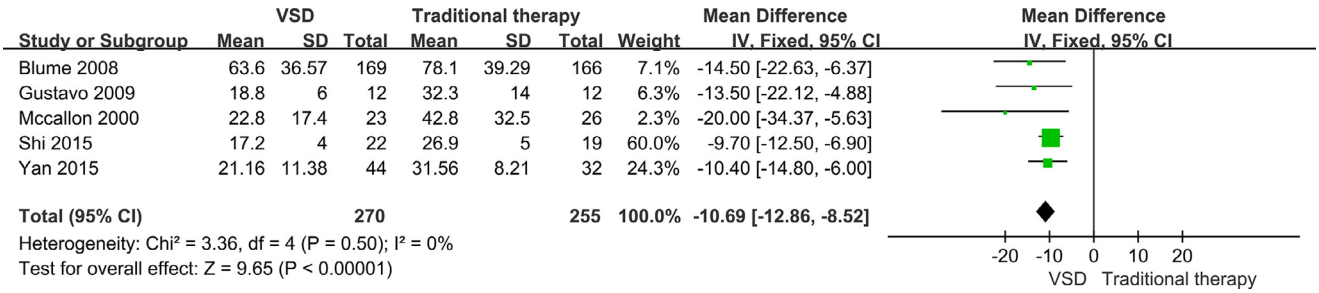

Fig. 2. Forest plot for the duration of therapy between the vacuum sealing drainage group and the conventional therapy group.

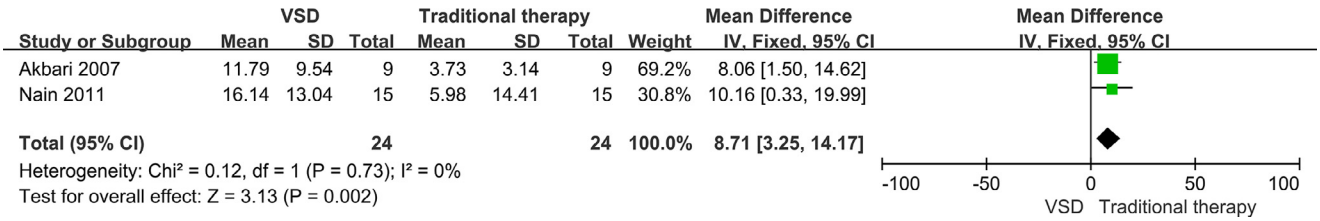

Fig. 3. Forest plot for wound size reduction between the vacuum sealing drainage group and the conventional therapy group.

the traditional therapy group (MD = 8.71; 95% CI 3.25 to 14.17; $p = .002$; p for heterogeneity = .73; $I^2 = 0\%$).

Meta-Analysis of Efficacy

Among the 10 included studies, 7 studied the efficacy rate in the VSD group and the traditional therapy group. The forest plot (Fig. 4) showed that 3 studies reported a statistically significant difference in efficacy, whereas the other 4 studies showed no difference. The overall results showed a statistically significant difference in the efficacy rate between the VSD group and the traditional therapy group, with a higher rate of efficacy in the VSD group (RR = 1.41; 95% CI 1.22 to 1.62; $p < .00001$; p for heterogeneity = .25; $I^2 = 24\%$).

Meta-Analysis of Complication Rate

Three studies compared the complication rate of the 2 groups. All 3 studies showed no statistically significant difference between the VSD group and the control group, as shown in Fig. 5, and the combined meta-analysis revealed that the complication rate was comparable between the groups (RR = 0.83; 95% CI 0.60 to 1.16; $p = .28$; p for heterogeneity = .21; $I^2 = 36\%$).

Bias Analysis

Publication bias was not assessed, although high heterogeneities were observed, because of the limited number of articles included (36).

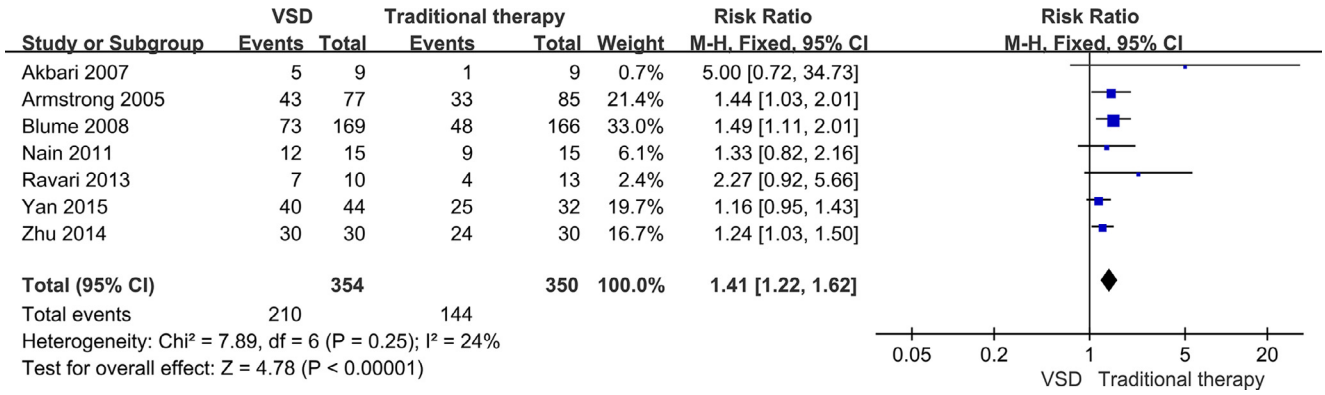

Fig. 4. Forest plot for efficacy in the vacuum sealing drainage group and the conventional therapy group.

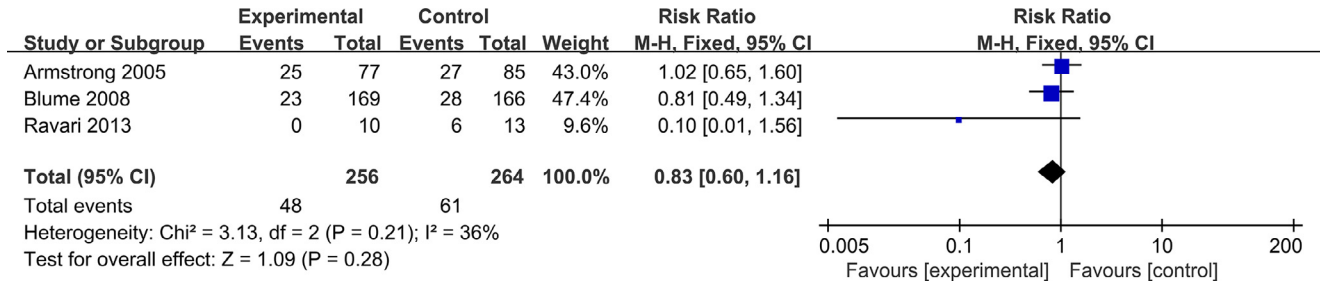

Fig. 5. Forest plot for the complication rate in the vacuum sealing drainage group and the conventional therapy group.

Discussion

The incidence of diabetes has rapidly increased worldwide, and surgery for patients with DFU, which is a significant risk and accounts for >50% of all nontraumatic amputations, has become more common (37). The complications are a major cause of hospitalization for diabetic patients, and the treatment success largely depends on chronicity, compliance, and method of therapy (38). Although conventional preventive methods and physiotherapy have good influences on ulcers, a high incidence of amputations in individuals with diabetes is observed. For patients with diabetes, wound healing has been altered through impaired neutrophil chemotaxis and phagocytosis, degradation of structural proteins, and decrease of microperfusion. It has been reported that VSD therapy has been proven effective in animal models, and several pieces of mechanistic evidence have supported the conclusion that negative-pressure therapy is quite applicable for diabetic foot wounds (39). Within a negative-pressure wound environment, blood flow is transiently increased, granulation tissue formation is more robust, and bacterial clearance is enhanced. All of the previously stated effects contribute to wound healing in diabetic patients, and the wound could benefit from the improvements.

It has been proven that VSD is a safe and effective method for patients with DFUs and, in several aspects, is more efficacious than traditional treatments. The efficacy rate is the most intuitive index to evaluate a therapeutic method. In our study, the efficacy of VSD is much higher than that of conventional treatment. Granulation tissue appeared earlier in VSD therapy. The closure of wound is influenced by both physiological impairments and susceptibility of wound to infection. With the treatment of VSD, all DFUs showed good changes including reduction of wound size and development of granulation tissue (40). This study suggested that compared with the control group, the mean ulcer surface after treatment with the VSD group showed a significant decrease, which means that VSD has a greater improvement ratio for foot ulcer surface area than conventional therapy. Also, with the rapid ulcer closure and granulation tissue formation, the time needed to heal DFUs was significantly reduced. It is not a surprise that the meta-analysis results in our study indicated that the hospital stay duration of the VSD group was much shorter than that of the control group.

Diabetes could affect the flow of blood, and the poor circulation of the skin may cause ulcers and infections, which heal slowly, and in some cases, amputation may be needed (41), but if proper interventions are applied, wound healing should decrease the complications of DFUs. The complications of DFUs mainly include infection, osteomyelitis, cellulitis, and amputation. The results of the meta-analysis in this study showed no significant difference in ulcer-related complications.

Although we obtained positive results, this study had some potential weaknesses. First, blinding of participants and personnel was difficult to achieve because of the large size of the device for VSD. Second, several studies had a small number of wounds, which could be another source of bias. Finally, the parameters in this study represented only some aspects of the method, and future studies may focus on the cost effectiveness and effect on quality of life.

In conclusion, our results indicate that VSD more effectively heals DFUs than conventional therapy. VSD could effectively promote arterial circulation and nutrition delivery. VSD shortens hospital stay, causes greater wound size reduction, and has a higher efficacy rate than conventional treatment, although the complication rates of the 2 groups were not significantly different. According to the results we have obtained, we recommend VSD as a preferred treatment for patients with DFUs.

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