

Original Article

Comparisons of negative pressure wound therapy and ultrasonic debridement for diabetic foot ulcers: a network meta-analysis

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Abstract: Objective: a network meta-analysis was performed to compare the strength and weakness of negative pressure wound therapy (NPWT) with ultrasound debridement (UD) as for diabetic foot ulcers (DFU). Methods: PubMed, Ovid EMBASE, Web of Science, Cochrane library databases, and Chinese Biomedical Literature Database were searched till February 2015. Clinical compared studies of negative pressure wound therapy and ultrasound debridement were enrolled. The primary efficacy outcomes included healed ulcers, reduction of ulcer areas and time to closure. Secondary amputation including major and minor amputations was used to assess the safety profile. Results: Out of 715 studies, 32 were selected which enrolled 2880 diabetic patients. The pooled analysis revealed that NPWT including vacuum assisted closure (VAC) and vacuum sealing drainage (VSD) were as efficacious as ultrasound debridement improving healed ulcers, odds ratio, 0.86; 95% CI 0.28 to 2.6 and 1.2; 95% CI 0.38 to 4, respectively. However, both were better to standard wound care in wound healing patients. Compared with the standard wound care treated diabetic foot ulcers, NPWT and UD resulted in a significantly superior efficacy in time to wound closure and decrement in area of wound. No significances were observed between NPWT and UD groups in both indicators. Fewer patients tended to receive amputation in NPWT and UD groups compared to standard wound care group. Conclusions: The results of the network meta-analysis indicated that negative pressure wound therapy was similar to ultrasound debridement for diabetic foot ulcers, but better than standard wound care both in efficacy and safety profile.

Keywords: Negative pressure wound therapy, ultrasound debridement, diabetic foot, network meta-analysis

Introduction

Diabetic foot ulcer (DFU)-an umbrella term for foot problems-is the most common, complex and costly sequelae of diabetes mellitus (DM) [1]. As reported, foot ulceration is affecting 15% or more of people with DM at some time in their lives [2]. According to Hunt's study [3], the prevalence of foot ulcers ranges from 4 to 10 percent among patients with diabetes, and the lifetime incidence is estimated to be 10 to 25 percent. At present, the standard therapy for diabetic foot ulcers includes glucose control, management of infection, debridement, off-loading high pressure, and use of dressings. However, the treatment outcomes are far from satisfaction, whatever the efficacy or the complications [4, 5]. Negative pressure wound ther-

apy (NPWT) is an ultramodern noninvasive adjunctive therapy system that applies controlled negative pressure using vacuum sealing drainage (VSD) or vacuum-assisted closure (VAC) device to help promote wound healing by removing fluid from open wounds through a sealed dressing and tubing which is connected to a collection container [6, 7]. Some clinical studies have suggested that negative pressure wound therapy is beneficial as an adjunctive treatment for diabetic foot ulcers compared with traditional wound therapy [8-10]. Withal, ultrasound therapy is a noncontact wound therapy to promote healing through the cleansing and debridement of wounds. Actually, therapeutic ultrasound has been used for years by physical therapists for the treatment of a variety of musculoskeletal disorders, using devices

that operate in the 1 to 3 MHz range [11]. The current trend is toward using low-frequency ultrasound devices that operate in the kilohertz range. In recent years, clinical evidence including randomized [12] or non-randomized studies [13] of improved healing of chronic wounds treated with ultrasound has been accumulating. Because of the lack of head-to-head comparisons between two interventions, using network meta-analysis, we endeavor to put forward a study to compare the efficacy and safety of negative pressure wound therapy and ultrasound therapy through standard wound care therapy in healing of diabetic foot ulcers.

Methods

Search strategy

A bibliographic search of medical literature until January 2015 was performed using databases as PubMed, Ovid EMBASE and Web of Science, Cochrane library. The search string (“negative pressure wound therapy” OR “vacuum assisted closure” OR “vacuum sealing drainage”) OR (“ultrasound” OR “ultrasonic”) AND (“diabetic foot” OR “diabetic wound” OR “diabetic ulcer”) were used to search for relevant articles. Chinese biomedicine literatures databases were also searched. Reference lists of included studies and review articles were manually searched. The network meta-analysis was limited to studies conducted in human.

Inclusion and exclusion criteria

Clinical randomized or non-randomizes, controlled reporting relevant outcome measures like efficacy and safety were selected. The study was eligible for inclusion if 1) the study was on diabetes patients; 2) compared studies; 3) outcome measures were including healed ulcers, time to wound closure, decrement in area of wound and secondary amputations. The study was excluded if 1) single arm design; 2) primary endpoints were missing; 4) dual submissions.

Intervention

Negative pressure wound therapy including vacuum assisted closure (VAC) and vacuum sealing drainage (VSD), ultrasound debridement, and standard wound care were as treatments.

Outcomes

The primary outcome was healed ulcers (success of treatment definition: as full epithelialization). Other outcomes included time to wound closure, decrement in ulcer area. Secondary amputations were used to assess the safety of different treatments.

Data extraction

Two investigators independently assessed the quality of trials and any disagreement was resolved through discussion with the third author. The Modified Jadad score was used to evaluate the quality analysis of methodology, including randomization, blinding and withdrawal from study. The Jadad scale scores from 1 to 7. We classified the quality of studies into 3: low quality of 1-2; middle quality of 3-4; high quality of 5-7.

Missing data

The standard deviation of four studies providing mean value including time to wound closure and decrement were missing. Generally, three ways of solutions could address this issue: 1) remove the missing data from our analysis; 2) similar studies could be reference; 3) through calculating if we know the confidence interval or other relevant information. Here, due to primary studies recording both indicators were limited, and confidence interval deficiency, we choose the second choice.

Network meta-analysis

Network meta-analyses were to compare direct and indirect evidence of class or agents using the Bayesian Markov-chain Monte Carlo method. Traditional meta-analyses compare one intervention with another at a time and combine evidence directly from head-to head clinical trials if such trials exist. A network meta-analysis combines effect sizes for all possible pairwise comparisons (direct and indirect), regardless of whether they have been compared in trials.

Statistical analysis

The statistical analysis was performed using software R (X64, 3.1.2, packages including gemtc and rjags). The output of the data was in

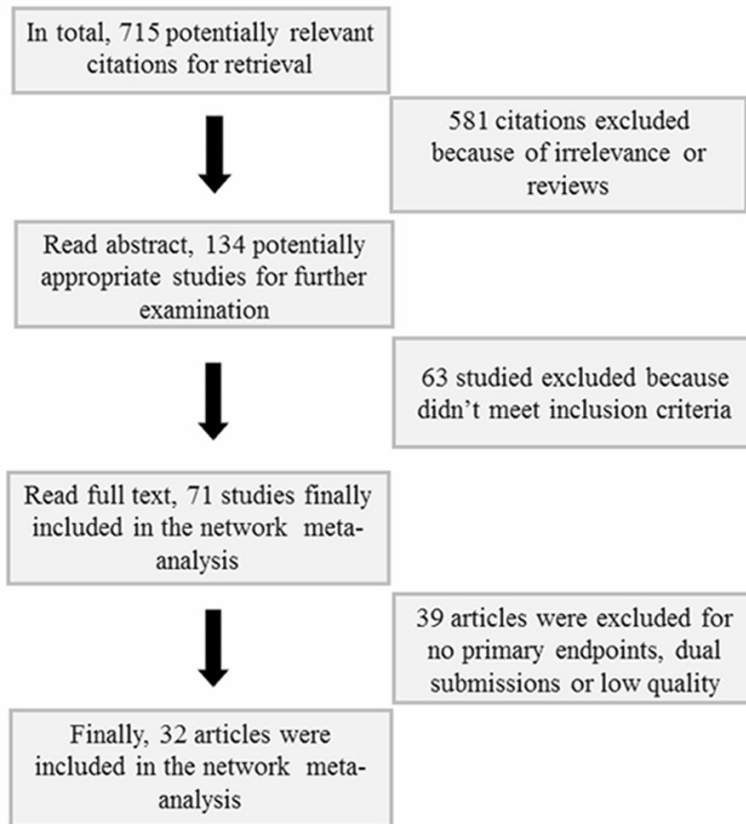


Figure 1. Flow diagram of studies selection.

the form of forest plot. The population varied in studies that we had selected for example the age of the subject varied from one study to another, so we took random effect model rather than fixed effect model. The comparison of the effects between two groups was expressed in terms of odds ratio (OR) or standard mean difference (SMD) and its 95% confidence interval (95% CI). In order to avoid risk of bias, we had included only the clinical controlled studies and excluded observational and follow up studies.

Results

Descriptions of studies

A total of 715 relative studies published till February 2015 was obtained by electronic databases searches. Of these, 581 were excluded on the basis of title and abstract. From these remaining 134 articles identified, 63 were rejected because of beyond our inclusion criteria. After reading 71 full text, 39 were excluded for data redundancy, extension study, no primary or secondary endpoints, etc. Finally,

32 [8-10, 12, 14-41] articles met all entry criteria and were included in the network meta-analysis. Among these all chosen studies, 12 of studies published in English, 19 of Chinese. The screening process is illustrated in **Figure 1**.

The characteristics of the included studies are given in **Table 1**. Of the 32 studies, a total of 2880 diabetes patients were included. In three of these studies, foot ulcers were characterized using the Texas Diabetic Wound Classification System or the Wagner Scale. Quality of each study was listed in **Table 1**. All the statistical analysis adopted random effect model due to the variance of each study.

Healed ulcers

20 studies recorded completely healed ulcers. Random effect model was adopted, and the pooled analysis revealed

that NPWT including VAC and VSD as well as UD significantly improved the proportion of diabetic foot ulcer healing compared with standard wound care, odds ratio and 95% confidence interval, 2.8 [1.9, 4.2]; 3.9 [2.3, 7] and 3.2 [1.2, 9.1], respectively. No significance was observed between VAC and VSD compared to UD, odds ratio and 95% confidence interval, 0.86 [0.28, 2.6] and 1.2 [0.38, 4] (**Figure 2**).

Time to wound closure

15 studies assessed the time to closure of ulcers. The result demonstrated that mean time to wound closure of VAC and VSD as well as UD were significantly shorter compared with standard wound care group, standard mean difference and 95% confidence interval, -18 [-29, -6.6]; -22 [-38, -6.3] and -23 [-46, 0.2], respectively. But the difference between UD and standard wound care was not very significant. On the other hand, VAC or VSD were as efficient as UD, standard mean difference and 95% confidence interval, 5.2 [-20, 31] and 1.1 [-27, 29], separately (**Figure 3**).

NPWT versus ultrasonic debridement for DFU

Table 1. Characteristics of selected studies

Study	Setting	Original country	Participants	Intervention	Duration	Indicators	N	Arms	Baseline	Quality
Prabhdeep 2011	Randomized, compared	India	20-75 years DM	NPWT/standard wound care	8 w	Wound size, time to wound closure	30	2	Comparable	Middle
O. Karatepe 2011	Randomized, compared	Turkey	Diabetic foot ulcers	VAC therapy/standard wound care	8 m	SF-36 scale	67	2	Comparable	Middle
PETER A 2008	Randomized controlled	US	Diabetic adults >18 years	NPWT/standard wound care	9 m	Complete ulcer closure, complications	603	2	Comparable	High
David G 2005	Randomized controlled	US	Diabetic adults >18 years	NPWT/standard wound care	16 w	Wounds healed	162	2	Comparable	High
Gustavo 2009	Randomized controlled	Chile	Diabetic adults >18 years	NPWT/standard wound care	Unclear	Wound granulation	24	2	Comparable	High
Asghar 2007	Randomized controlled	Iran	Diabetic foot ulcers	VCT/conventional therapy	3 w	Ulcer surface area	18	2	Comparable	Middle
Abdullah 2004	Preliminary controlled	Turkey	Diabetic patients	NPWT group and control group	Unclear	Surface area	24	2	Comparable	Middle
Mark T 2003	Compared study	US	Diabetic patients	VCT/conventional therapy	2 w	Wound volume and depth and area	10	2	Comparable	Middle
Hassan 2013	Compared study	Iran	Diabetic patients	NPWT/standard wound care	5 w	Wound size	23	2	Comparable	Middle
Ali M 2014	Compared study	India	Diabetic patients	NPWT/standard wound care	8 w	Wounds healed	56	2	Comparable	Middle
William 2005	Compared study	US	Diabetic patients	NPWT/standard wound care	12 w	Time to wound closure	122	2	Comparable	Middle
McCallon 2000	Randomized controlled	US	Diabetic patients	NPWT/standard wound care	Unclear	Decrease of wound size, Time to wound closure	10	2	Comparable	Low
Han 2012	Compared study	China	Diabetic patients	NPWT/UD/NPWT+UD	1 w	Decrease of wound size	82	3	Comparable	Middle
Huang 2013	Compared study	China	Diabetic patients	NPWT+UD/standard wound care	Unclear	Wounds healed	80	2	Comparable	Middle
Xin 2014	Compared study	China	Diabetic patients	UD/standard wound care	Unclear	Decrease of wound size	18	2	Comparable	Low
He 2015	Compared study	China	diabetic patients	NPWT+UD/NPWT	12 w	Wounds healed	47	2	Comparable	Middle
Lu 2014	Compared study	China	Diabetic patients	UD/standard wound care	Unclear	Wounds healed, time to wound closure	62	2	Comparable	Middle
Zhu 2014	Compared study	China	Diabetic patients	VSD/standard wound care	4 w	Wounds healed, time to wound closure	60	2	Comparable	Middle
Wu 2014	Compared study	China	Diabetic patients with infection	VSD/standard wound care	Unclear	Wounds healed	60	2	Comparable	Middle
Huang 2014	Compared study	China	Diabetic patients	VSD/standard wound care	5 d	Wounds healed	76	2	Comparable	Middle
Chen 2014	Compared study	China	Diabetic patients	VSD/standard wound care	2 w	Wounds healed	100	2	Comparable	Middle
Liu 2014	Compared study	China	Diabetic patients	VAC/standard wound care	3 m	Wounds healed	100	2	Comparable	Middle
Guan 2014	Compared study	China	Diabetic patients	VAC/standard wound care	1 w	Wounds healed, Time to wound closure	536	2	Comparable	Middle
Li 2013	Compared study	China	Diabetic patients	VSD/standard wound care	1 w	Time to wound closure	20	2	Comparable	Low
Huang 2013	Compared study	China	Diabetic patients	VAC/standard wound care	12 w	Wounds healed, Time to wound closure	294	2	Comparable	Middle
Yu 2013	Compared study	China	Diabetic patients	VSD/standard wound care	Unclear	Wounds healed, Time to wound closure	43	2	Comparable	Middle
Yu 2013	Compared study	China	Diabetic patients	VAC/standard wound care	Unclear	Wounds healed, Time to wound closure	75	2	Comparable	Middle
Zhu 2013	Compared study	China	Diabetic patients	VSD/standard wound care	4 w	Wounds healed	66	2	Comparable	Middle
Hu 2013	Compared study	China	Diabetic patients	VAC/standard wound care	Unclear	Wounds healed	74	2	Comparable	Middle
Hong 2013	Compared study	China	Diabetic patients	VSD/standard wound care	Unclear	Wounds healed, amputation	78	2	Comparable	Middle
Li 2012	Compared study	China	Diabetic patients	VAC/standard wound care	Unclear	Time to wound closure	46	2	Comparable	Low
Xu 2012	Compared study	China	Diabetic patients	VSD/standard wound care	Unclear	Time to wound closure, amputation	84	2	Comparable	Middle

NPWT versus ultrasonic debridement for DFU

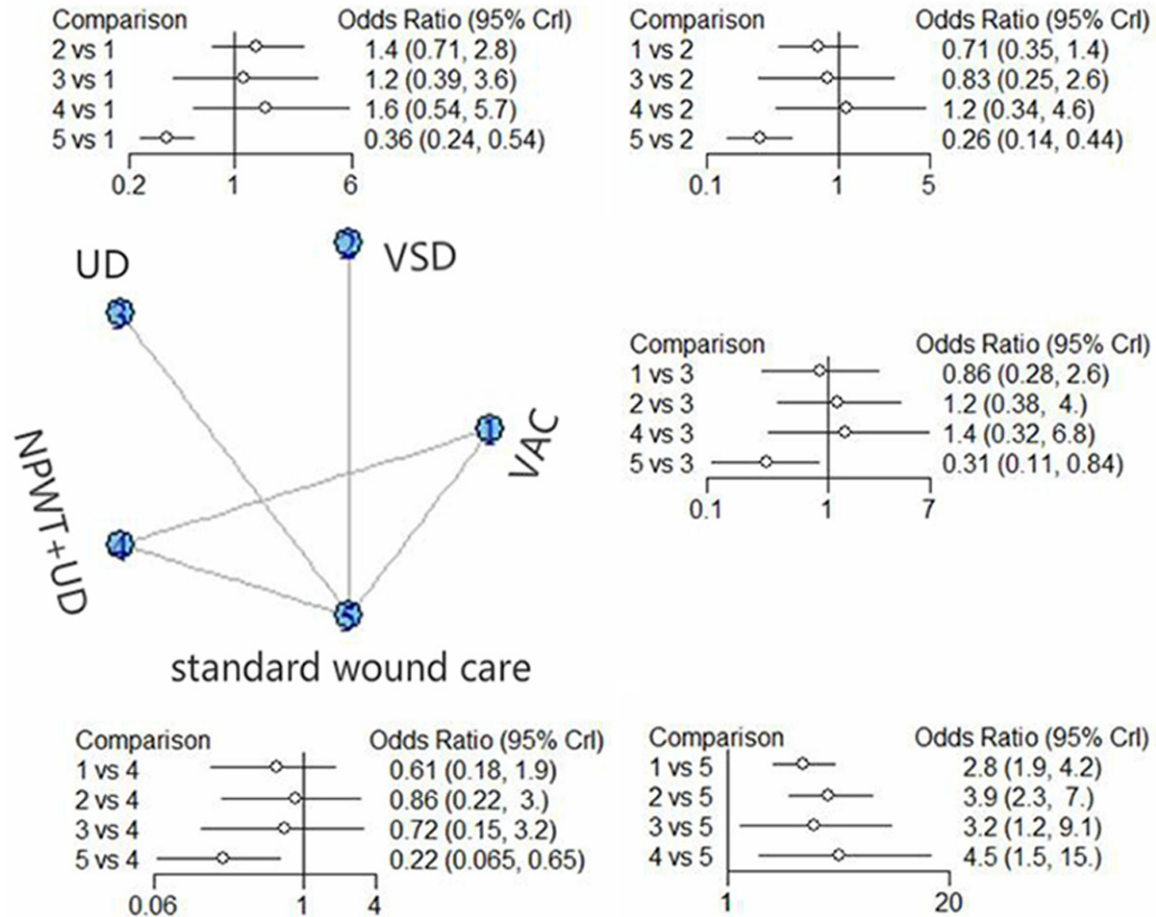


Figure 2. Forest plots with the random effect model comparing healed ulcers in different treatments. Risk ratio and 95% CI for each study are plotted on the graph.

Decrement in ulcer area

Decrement in ulcer area was described in 10 studies. In the random effects mode, there were significant differences in ulcer area reduction from baseline in VAC and VSD groups compared with standard wound care group, standard mean difference and 95% confidence interval, -18 [-29, -6.7] and -22 [-38, -6.1]. UD could decrease the ulcer area compared to standard wound care, however, the significance was not observed. When compared with UD, we did not find any significance in VAC and VSD groups, standard mean difference and 95% confidence interval, 4.9 [-21, 31] and 0.93 [-27, 29] (Figure 4).

Secondary amputations

Amputation contains major amputation defined as amputations above the ankle joint and minor amputation distal to the ankle joint. Only 7

studies represented data of secondary amputations in this network meta-analysis. The incidence of secondary amputation in the NPWT group (including VAC and VSD) and the standard wound care group were 3.2 percent (12/376) and 11.1 percent (43/386). In the forest plot, compared to standard wound care, secondary amputations was less in VAC and VSD groups, odds ratio and 95% confidence interval, 0.21 [0.026, 0.8]; 0.14 [0.0053, 1.4] (Figure 5).

Discussion

The present network meta-analysis was conducted to compare the strengths and weakness profile of negative pressure wound therapy and ultrasound debridement as an adjunctive treatment for diabetic foot ulcers. 32 clinical studies were identified and the data was pooled and analyzed. Healed ulcers, decrement of ulcer areas, time to closure, Secondary am-

NPWT versus ultrasonic debridement for DFU

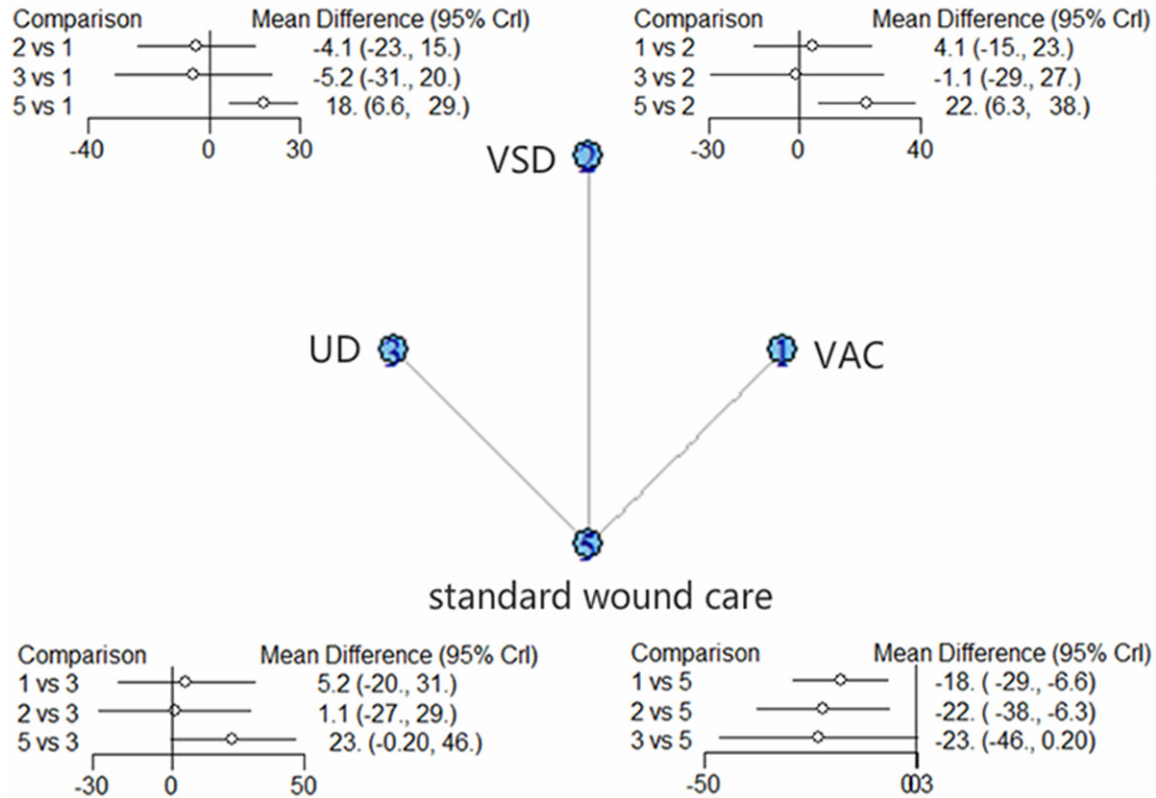


Figure 3. Forest plots with the random effect model comparing time to wound closure in different treatments. Standard mean difference and 95% CI for each study are plotted on the graph.

putation were compared within all groups. Overall, there was no significant difference between negative pressure wound therapy and ultrasound debridement both in efficacy and safety, but both better to standard wound care.

To our knowledge, this study is the first network meta-analysis to evaluate negative pressure wound therapy and ultrasound debridement in patients with diabetic foot ulcers, and also the first to distinguish VAC from VSD for diabetic foot ulcers. The International Working Group of the Diabetic Foot conducted two systematic reviews [42, 43] on negative pressure wound therapy treatment for diabetic foot ulcers and obtains the conclusion that negative-pressure wound therapy is possibly partially effective for diabetic foot ulcers. Whereas previous studies demonstrated that ultrasound therapy was shown to be clinically effective in healing of diabetic foot ulcers or common wound types compared to traditional wound care [12, 44]. We are wondering which treatment could be more effective for DFU, so through conducting this

network meta-analysis, final conclusions are obtained.

Endpoints such as ulcer healing, time to wound closure, decrement of wound area and amputations may be the most clinically relevant outcomes. Complete wound closure was defined as 100% re-epithelialization without drainage. Assessments were based on data from wound investigations and photographs done by the treating clinician. Other indicators like formation of granulation, wound infection and adverse events are also essential. Due to missing information of some articles, they were not included in our analysis. Secondary amputations are the most serious complications of diabetic foot ulcers, and severely impair the quality of life. Our results revealed that negative pressure wound therapy could reduce the incidence of secondary amputations compared with standard wound therapy.

In summary, negative-pressure wound therapy appears to be as effective as ultrasound debridement for diabetic foot ulcers compared

NPWT versus ultrasonic debridement for DFU

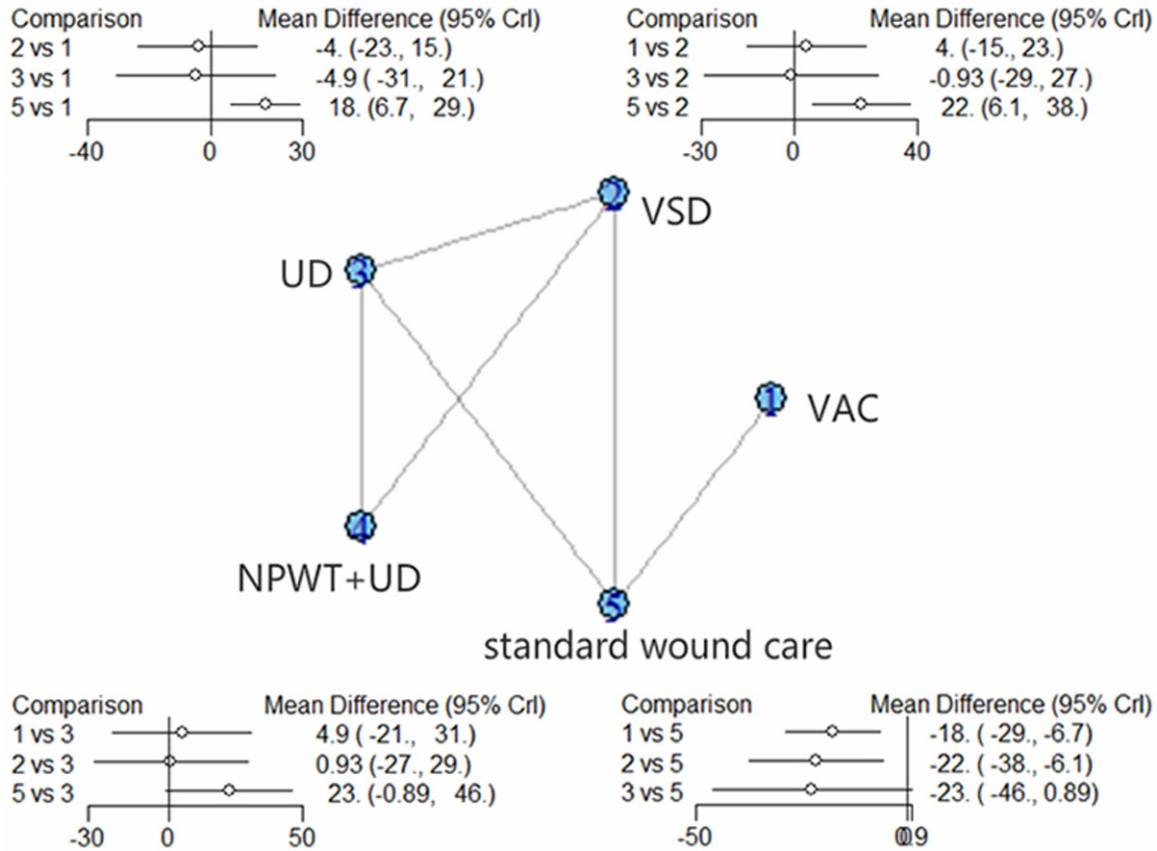


Figure 4. Forest plots with the random effect model comparing decrement of wound area in different treatments. Standard mean difference and 95% CI for each study are plotted on the graph.

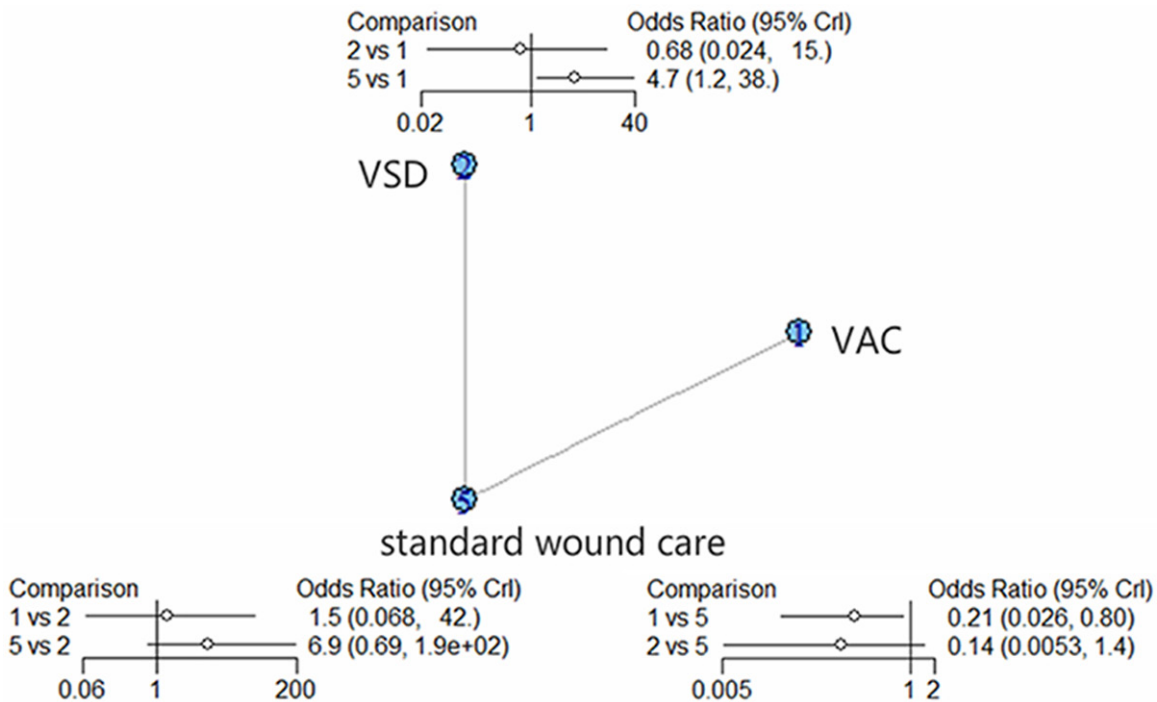


Figure 5. Forest plots with the random effect model comparing secondary amputations in different treatments. Risk ratio and 95% CI for each study are plotted on the graph.

with standard wound therapy. Despite of the limitation of studies on ultrasound therapy for diabetic foot, future well-designed clinical trials that should overcome the existing limitations are still needed to provide more convincing evidence for clinical practice.

Disclosure of conflict of interest

None.

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References

[1] Singh N, Armstrong DG and Lipsky BA. Preventing foot ulcers in patients with diabetes. *JAMA* 2005; 293: 217-228.

[2] Reiber GE. The epidemiology of diabetic foot problems. *Diabet Med* 1996; 13 Suppl 1: S6-11.

[3] Khanolkar MP, Bain SC and Stephens JW. The diabetic foot. *QJM* 2008; 101: 685-695.

[4] Cavanagh PR, Lipsky BA, Bradbury AW and Botek G. Treatment for diabetic foot ulcers. *Lancet* 2005; 366: 1725-1735.

[5] Cavanagh PR and Bus SA. Off-loading the diabetic foot for ulcer prevention and healing. *Plast Reconstr Surg* 2011; 127 Suppl 1: 248S-256S.

[6] Moisisidis E, Heath T, Boorer C, Ho K and Deva AK. A prospective, blinded, randomized, controlled clinical trial of topical negative pressure use in skin grafting. *Plast Reconstr Surg* 2004; 114: 917-922.

[7] Schwien T, Gilbert J and Lang C. Pressure ulcer prevalence and the role of negative pressure wound therapy in home health quality outcomes. *Ostomy Wound Manage* 2005; 51: 47-60.

[8] Armstrong DG and Lavery LA. Negative pressure wound therapy after partial diabetic foot amputation: a multicentre, randomised controlled trial. *Lancet* 2005; 366: 1704-1710.

[9] Blume PA, Walters J, Payne W, Ayala J and Lantis J. Comparison of negative pressure wound therapy using vacuum-assisted closure with advanced moist wound therapy in the treatment of diabetic foot ulcers: a multicenter randomized controlled trial. *Diabetes Care* 2008; 31: 631-636.

[10] Nain PS, Uppal SK, Garg R, Bajaj K and Garg S. Role of negative pressure wound therapy in

healing of diabetic foot ulcers. *J Surg Tech Case Rep* 2011; 3: 17-22.

[11] Baker KG, Robertson VJ and Duck FA. A review of therapeutic ultrasound: biophysical effects. *Phys Ther* 2001; 81: 1351-1358.

[12] Ennis W, Foremann P, Mozen N, Massey J, Conner-Kerr T and Meneses P. Ultrasound therapy for recalcitrant diabetic foot ulcers: results of a randomized, double-blind, controlled, multicenter study. *Ostomy Wound Manage* 2005; 51: 24-39.

[13] Kavros SJ and Schenck EC. Use of noncontact low-frequency ultrasound in the treatment of chronic foot and leg ulcerations: a 51-patient analysis. *J Am Podiatr Med Assoc* 2007; 97: 95-101.

[14] Akbari A, Moodi H, Ghiasi F, Sagheb HM and Rashidi H. Effects of vacuum-compression therapy on healing of diabetic foot ulcers: randomized controlled trial. *J Rehabil Res Dev* 2007; 44: 631-636.

[15] Eginton MT, Brown KR, Seabrook GR, Towne JB and Cambria RA. A prospective randomized evaluation of negative-pressure wound dressings for diabetic foot wounds. *Ann Vasc Surg* 2003; 17: 645-649.

[16] Etoz A, Ozgenel Y and Ozcan M. The use of negative pressure wound therapy on diabetic foot ulcers: a preliminary controlled trial. *Wounds-A Compendium of Clinical Research and Practice* 2004; 16: 264-269.

[17] Karatepe O, Eken I, Acet E, Unal O, Mert M, Koc B, Karahan S, Filizcan U, Ugurlucan M and Aksoy M. Vacuum assisted closure improves the quality of life in patients with diabetic foot. *Acta Chir Belg* 2011; 111: 298-302.

[18] Lone AM, Zaroo MI, Laway BA, Pala NA, Bashir SA and Rasool A. Vacuum-assisted closure versus conventional dressings in the management of diabetic foot ulcers: a prospective case-control study. *Diabet Foot Ankle* 2014; 5:

[19] McCallon SK, Knight CA, Valiulus JP, Cunningham MW, McCulloch JM and Farinas LP. Vacuum-assisted closure versus saline-moistened gauze in the healing of postoperative diabetic foot wounds. *Ostomy Wound Manage* 2000; 46: 28-32, 34.

[20] Ravari H, Modaghegh MH, Kazemzadeh GH, Johari HG, Vatanchi AM, Sangaki A and Shahrodi MV. Comparison of vacuum-assisted closure and moist wound dressing in the treatment of diabetic foot ulcers. *J Cutan Aesthet Surg* 2013; 6: 17-20.

[21] Sepulveda G, Espindola M, Maureira M, Sepulveda E, Ignacio FJ, Oliva C, Sanhueza A, Vial M and Manterola C. [Negative-pressure wound therapy versus standard wound dressing in the treatment of diabetic foot amputation. A randomised controlled trial]. *Cir Esp* 2009; 86: 171-177.

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- [22] Chen ZJ, Li GX and Huang ZZ. The closed negative pressure drainage technology of clinical effect for the treatment of diabetic foot ulcers. *Guangzhou Medical Journal* 2014; 24-26.
- [23] Guan XH, Li BJ, Guan TY, Yang CZ and Wu SB. Negative pressure wound therapy in a practical research for the treatment of diabetic foot gangrene patients. *Chinese Journal of Coal Industry Medicine* 2014; 1762-1764.
- [24] Han LY, Fu MX, Huang YL and Ju F. Ultrasonic debridement combined negative pressure wound therapy for treatment of diabetic foot. *Modern Preventive Medicine* 2012; 5713-5714, 5716.
- [25] He M, Zheng YL, Deng WQ, Deng F, Jiang YZ, Wu QN, Lu DB and Chen B. Negative pressure wound system combined ultrasonic debridement for treatment of diabetic foot ulcers. *Journal of Regional Anatomy and Operative Surgery* 2015; 1-3.
- [26] Hong YF, Liang CB, Deng BJ and Tan YY. Topical negative pressure drainage treatment of diabetic foot: 38 cases of clinical research. *Journal of Guangdong Medical College* 2013; 426-427.
- [27] Hu QX, Li YL, Wei HY and Wang WP. Effect of closed modified negative pressure drainage in the treatment of diabetic foot. *Today Nurse* 2013; 30-31.
- [28] Huang SC, Xiong XL, Li Y, Xiao RC and Yao XM. Continuous negative pressure drainage in the application of the infection of diabetic foot wound. *Today Nurse* 2014; 33-34.
- [29] Huang XL, Tan XY, Nong YC, Xu GL, Zhong M and Yan XD. Intelligent negative pressure wound therapy in the treatment of diabetic foot ulcers. *Journal of Nurses Training* 2013; 2040-2042.
- [30] Huang XL, Tan XY, Nong YC and Yan XD. Ultrasonic debridement combined negative pressure wound therapy for the treatment of diabetic foot ulcers. *Chinese Clinical Nursing* 2013; 285-287.
- [31] Li WP, Wu DQ, Zhang S and Guo X. Application of closed negative pressure wound therapy in the treatment of diabetic foot ulcer. *Modern Preventive Medicine* 2012; 4628-4629.
- [32] Li XT, Xu WC and Lin ML. Closed negative pressure wound therapy for treatment of diabetic foot ulcer. *Modern Journal of Integrated Chinese Traditional and Western Medicine* 2013; 282-283.
- [33] Liu SH. Negative pressure wound therapy for refractory diabetic foot ulcer. *Modern Diagnosis and Treatment* 2014; 2666-2667.
- [34] Lu QC, Lu SY, Wang MZ and Hou XC. Ultrasonic debridement in the treatment of diabetic foot ulcer. *China Medicine and Pharmacy* 2014; 7-9.
- [35] Wu HY, Chen QH and Lin SN. The application of negative pressure wound therapy for infectious diabetic foot. *Chinese Journal of Nosocomiology* 2014; 2735-2736.
- [36] Xin TF, Zhang C and Xin GY. Ultrasonic treatment for diabetic foot ulcer : 18 cases of clinical observation. *China Health Standard Management* 2014; 16-17.
- [37] Xu F. Application of closed negative pressure drainage technology in the treatment of diabetic foot care. *Journal of Luzhou Medical College* 2012; 323-325.
- [38] Yu H and Zhang D. The effect of negative pressure wound therapy for diabetic foot ulcers. *Nursing Research* 2013; 2919-2920.
- [39] Yu ZF and Fang ZH. Application of enclosed negative pressure drainage for diabetic foot. *Chinese Journal of Clinical Healthcare* 2013; 309-310.
- [40] Zhu J and Liu ZC. Clinical research on treatment of diabetic foot of closed negative pressure drainage. *Modern Medicine and Health* 2013; 1946-1947.
- [41] Zhu XH, Chai YM, Ye JZ, Han P, Wen G and Chen P. The comparison of closed negative pressure drainage and traditional wound therapy for healing diabetic foot. *Journal of Clinical Rehabilitative Tissue Engineering Research* 2014; 5548-5554.
- [42] Hinchliffe RJ, Valk GD, Apelqvist J, Armstrong DG, Bakker K, Game FL, Hartemann-Heurtier A, Löndahl M, Price PE, van Houtum WH and Jeffcoate WJ. A systematic review of the effectiveness of interventions to enhance the healing of chronic ulcers of the foot in diabetes. *Diabetes Metab Res Rev* 2008; 24 Suppl 1: S119-144.
- [43] Game FL, Hinchliffe RJ, Apelqvist J, Armstrong DG, Bakker K, Hartemann A, Löndahl M, Price PE and Jeffcoate WJ. A systematic review of interventions to enhance the healing of chronic ulcers of the foot in diabetes. *Diabetes Metab Res Rev* 2012; 28 Suppl 1: 119-141.
- [44] Ennis WJ, Valdes W, Gainer M and Meneses P. Evaluation of clinical effectiveness of MIST ultrasound therapy for the healing of chronic wounds. *Adv Skin Wound Care* 2006; 19: 437-446.