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Comparison between negative pressure and conventional wound dressing for diabetic foot ulcer: A systematic review

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ABSTRACT

Background: Diabetic foot ulcer (DFU) is a common complication of diabetes mellitus (DM), resulting in loss of limb or life. Negative pressure wound therapy (NPWT) is an emerging therapeutic option in the management of DFU. This study aims to compare the efficacy of NPWT to conventional moist wound dressing in the management of DFU.

Methods: Literature was searched from online public scientific databases, including PubMed, Google Scholar, ScienceDirect, and Portal Garuda. Our review included clinical trials and analytic studies comparing NPWT and conventional moist dressing to treat DFU published in 2017 or later. Outcome measures include the proportion of wound healing, healing time, ulcer size reduction, granulation time, amputation, infection, and bleeding.

Results: We include 11 articles, including eight randomized clinical trials (RCTs), two retrospective analytic studies, and one non-random clinical trial. There was methodological variation between studies on the application of NPWT, outcome measures reported, and length of follow up. Results mostly showed NPWT yielded a higher proportion of complete wound healing, shorter healing time, granulation time, and faster ulcer size reduction rate. However, NPWT was not associated with a reduction of amputation risks.

Conclusions: Our review found NPWT was superior in short-term treatment outcomes such as granulation time and wound closure; however, there was no difference in reducing amputation risk between NPWT and conventional moist dressing. Results are inconclusive due to variation in methodologies of included articles.

Keywords: Mean Platelet Volume, Independent Predictor, Varicocele, Late Adolescent

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INTRODUCTION

Diabetic foot ulcer (DFU) is a common complication of diabetes mellitus (DM). Defined as chronic ulceration on the lower extremity caused by diabetic neuropathy and microangiopathy, an estimated 6.3% of diabetic patients worldwide suffered from DFU.[1,2] This prevalence varied by regions and countries. North America was the region with the highest estimated prevalence of DFU, with an estimated 13% of diabetic patients, while Oceania has the lowest prevalence, with 3% of diabetic patients. By country, Belgium was estimated with 16.6% and Australia's highest prevalence the lowest with 1.5%.[2] Not only DFU was a common and prevalent complication of DM, but it also posed a risk toward patients' quality of life, and indeed, their life. Lower limb amputation is a big concern for DFU patients. Prospective studies estimated amputation to be necessary for 17% to 21% of DFU patients.[3,4] Further meta-analysis found the prevalence of amputation to be even higher, at an estimated around 30% of DFU patients.[5] Meanwhile, the risk of mortality is also high, with in-hospital mortality estimated at 12%.[3]

Currently, wound treatment for DFU includes conventional moist dressing. DFU wounds are to be debrided off necrotic tissues, rinsed in sterile normal saline, and maintained with a moist dressing.[6] While this treatment has proven sufficiently compelling, researchers continued to develop even better-wound treatment options for DFU patients. One emerging treatment was negative pressure wound treatment (NPWT). It involved the application of vacuum-assisted closure (VAC) device to control sub-atmospheric pressure, promote wound healing by removing fluid from open wounds, preparing the wound bed for closure, reducing edema, and promoting formation perfusion of granulation tissue.[7] Last review on the subject was published in 2017. More research has been conducted on the subject in the following years, especially comparing NPWT in conventional moist dressing for DFU treatment. Given these additional pieces of evidence, we find it appropriate to compile them into a systematic review. This review article aims to summarize the newest evidence on the effectiveness of NPWT to treat DFU compared to conventional moist dressing. We compare wound healing parameters, including size reduction and duration to heal, as well as complications between these two treatment options.

METHODS

Identification of Studies

We conducted literature searches on open access literature databases, including PubMed, ScienceDirect, Google Scholar, and Portal Garuda. Keywords used included 'negative pressure diabetic foot', 'negative pressure diabetic ulcer', and 'negative pressure diabetic foot ulcer'. We select for randomized clinical trial and a non-random clinical trial that compares NPWT and conventional moist wound dressing published in 2017 and later. We exclude descriptive studies and clinical trials with comparison other than NPWT and traditional moist dressing. We also include studies published prior to 2017. More specifically, included studies fulfilled the following PICO criteria:

- Population: diabetic foot ulcer patients.
- Intervention: negative pressure wound therapy (NPWT).
- Comparison: NPWT compared to conventional moist dressing.
- Outcomes: Wound healing, ulcer size reduction, granulation, time to heal, and cost-effectiveness.

Quality Appraisal

The quality of included studies was appraised using the CASP (Critical Appraisal Skills Program) Checklist for randomized-clinical trials. The checklist consists of questions on the study research questions, methodology, and data analyses to assess validity.

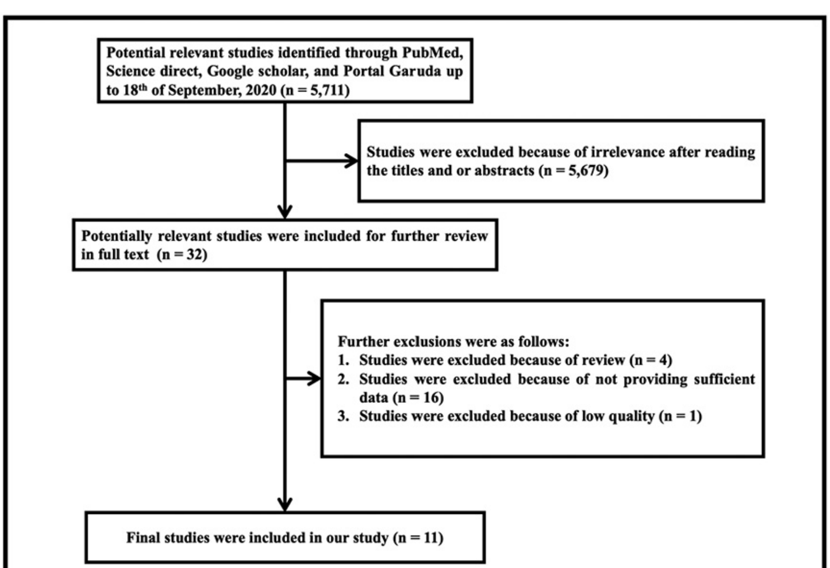

Figure 1. Selection of studies for inclusion in the systematic review

Data Extraction and Synthesis

Although we also put a PICO-based limitation on inclusion criteria, there are bound to be some variation between included studies. Application of negative pressure may differ between studies. Outcome measures may also vary. We would take into consideration these variations in interpreting the results and eventual synthesis.

RESULTS

Characteristics of Included Studies

Our initial literature search obtained around 900 hits. Screening through the titles yielded 33 articles relevant to our study objectives and underwent further PICO review and critical appraisal. From these 33 articles, 11 articles were found to fulfill PICO inclusion criteria and included for review. These 11 articles can be seen in Table 1.

Most included studies are randomized clinical trials or non-random clinical trials. Non-random clinical trials included are studies where subjects into NPWT or control groups are not randomized but are based on clinical indication.[10] Two studies utilized the retrospective analytic method with no mention of the subject placement method into study and control groups.[13,18] There is variation regarding NPWT application methods, both regarding VAC apparatus used, negative pressure used, and the interval between dressing changes. Some studies utilized a commercially available VAC apparatus.[10,11,13,14,16,18] Several articles described improvised VAC systems.[9,12,15,17] Variation on negative pressures used ranged from -80 mmHg to -150 mmHg, although standard, commercial-based VAC systems usually apply -125 mmHg of vacuum.[12,13,16,17] Meanwhile, the interval between dressing changes range from every two days to seven days.[9,15] Outcome measures used varied among the included studies. The proportion of complete wound healing, ulcer size reduction, and time to heal is the most used outcome measures. Several studies utilized granulation and granulation time as outcome measures. Fewer articles studied complications as outcome measures, including pain, infections, bleeding, and amputation.

Comparison of Wound Healing and Duration to Heal

Most studies found a significant difference in the proportion of complete healing and duration to heal between NPWT and conventional moist dressing. In all articles, NPWT was found with either a higher proportion of complete healing, shorter

Table 1. Characterization of studies included in the systematic review

Author	Title	Sample Size		Outcome Measures	Ref.
		NPWT	Control		
Al-Mallah et al., 2018	Negative Pressure Wound Therapy Versus Conventional Dressing in Treatment of Diabetic Foot Wound	25	25	Wound size, granulation, hospital stay, complication, and cost	(8)
Bahseer et al., 2019	Home-based negative pressure wound therapy and moist dressing in the treatment of diabetic foot ulcers	22	22	The proportion of wound healing and time to heal	(9)
Borys et al., 2018	Negative-pressure wound therapy for management of chronic neuropathic noninfected diabetic foot ulcerations – short-term efficacy and long-term outcomes	52	22	Wound size reduction, the proportion of wound healing	(10)
Chiang et al., 2017	Effects of topical negative pressure therapy on tissue oxygenation and wound healing in vascular foot wounds	12	10	The proportion of wound healing, tissue oxygenation	(11)
Gonzalez et al., 2017	Handcrafted Vacuum-Assisted Device for Skin Ulcers Treatment Versus Traditional Therapy, Randomized Controlled Trial	63	63	Systemic inflammatory response, pain, granulation	(12)
Hasaballah et al., 2017	Impact of negative pressure wound therapy in complete healing rates following surgical debridement in heel and ankle regions in diabetic foot infections	18	26	The proportion of wound healing	(13)
James et al., 2019	Comparison of vacuum-assisted closure therapy and conventional dressing on wound healing in patients with diabetic foot ulcer: A randomized controlled trial	27	27	Time to heal, complication	(14)
Kajagar et al., 2018	Efficacy of Vacuum-Assisted Closure Therapy versus Conventional Povidone Iodine Dressing in the Management of Diabetic Foot Ulcers: A Randomized Control Trial	30	30	Wound size reduction, complication	(15)
Seidel et al., 2020	Negative pressure wound therapy compared with standard moist wound care on diabetic foot ulcers in real-life clinical practice: results of the German DiaFu-RCT	44	110	The proportion of wound healing, duration to heal	(16)
Singh et al., 2018	Comparison of Negative Pressure Wound Therapy v/s Conventional Dressings in the Management of Chronic Diabetic Foot Ulcers in a Tertiary Care Hospital in North India	15	15	Time to heal, granulation	(17)
Sukur et al., 2018	Vacuum-assisted closure versus moist dressings in the treatment of diabetic wound ulcers after partial foot amputation: A retrospective analysis in 65 patients	31	34	Time to heal, granulation, complication	(18)

Table 2. Comparison of wound healing outcome measures between NPWT and conventional moist dressing from several studies

Author	Results		Notes	Ref
	NPWT	Control		
The proportion of complete wound healing				
Borys et al.	55.1%	73.7%	1 year follow up	(10)
Hasaballah et al.	72.3%	30.8%	120 days follow up	(13)
Seidel et al.	13.3%	14.6%	16 weeks follow up	(16)
Time to complete healing				
Singh et al.	41.2 days	58.9 days	Median	(17)
Ulcer area reduction				
Al-Mallah et al.	4.36 cm^2	0.89 cm^2	Mean, 3 weeks follow up	(8)
Borys et al.	1.1 cm^2	0.3 cm^2	Mean, 8 days follow up	(10)
	10.2%	18.0%		
Chiang et al.	7.0 cm^2	2.7 cm^2	Mean, 14 days follow up	(11)
	18.7%	7.9%		
Kajagar et al.	2.61 cm^2	0.91 cm^2	Mean, 14 days follow up	(15)
Granulation time				
James et al.	23.33 days	32.15 days	Mean, 75% granulation	(14)
Seidel et al.	22 days	49 days	Median, 95% granulation	(16)
Singh et al.	25.1 days	41.1 days	Mean, 100% granulation	(17)
Sukur et al.	7.8 weeks	11.1 weeks	Mean, 90% granulation	(18)

duration needed to achieve complete healing or both. The summary of the effectiveness of NPWT compared to conventional moist dressing can be seen in Table 2. Several studies reported complete wound healing as an outcome measure. Basheer et al. and Hasaballah et al. said NPWT to achieve a higher proportion of complete wound healing.[9,13] However, Seidel et al. reported different results with no statistically significant difference in complete healing rate between the two groups. In contrast, Borys et al. further reported ulcers' complete resolution to be lower in the NPWT group.[10,16]

There are differences in follow-up duration between these studies. Basheer et al., especially, did not report length of follow up although reported mean treatment time for the NPWT group to be around 2 months while the control group was treated for about 4 months.[9] The difference between NPWT and conventional dressing can also be seen in the comparison of size reduction, granulation time, and time to complete healing between NPWT and conventional moist dressing. James et al. and Kajagar et al. reported faster size reduction for the NPWT group.[14,15] Meanwhile, Al-Mallah et al. reported a higher rate of granulation achieved by the end of 3 weeks follow-up period.[8] Similarly, James et al., Seidel et al., Singh et al., and Sukur et al. reported faster achievement of granulation endpoint for NPWT group, although said endpoint varied from 75% granulation to 100% granulation.[14,16-18] Singh et al. also reported faster-wound closure in the NPWT group, which was achieved with a median of 41.2 days compared to the control group achieved in 58.9 days.[17] Survival analyses also showed faster wound healing in the NPWT group, as described by Hasaballah et al. and Seidel et al.[13,16]

Several included studies also showed no difference between NPWT and conventional dressing in wound healing parameters. Chiang et al. reported faster size reduction for NPWT, although the difference is not statistically significant.[11] Borys et al. further report faster relative size reduction in the control group, with 18% size reduction in 8 days, compared to 10% achieved in the NPWT group for the same period.[10] However, it has to be noted that Borys et al. did not employ randomization for subject placement. Instead, less severe cases of DFU (ulcer size < 1 cm^2) were used as an indication to treat the subject with a conventional moist dressing.

Comparison of Complications

Several included articles reported on complications as outcome measures of their researches. Complications included as outcome measures include amputation, infection, pain, and bleeding. In this regard, most included articles show no difference in risk of complication between NPWT and conventional moist dressing on all measures, despite variation in follow-up length. Four articles reported the incidence of amputation in the course of their studies. The incidence varied widely, from 0% and 4.55 % in Borys et al. to 49.1% and 30% in Chiang et al.[10,11] Length of follow up also varied from 6 months to unlimited follow up until endpoint is reached. However, it has to be noted that Sukur et al. reported the mean length of follow-up was 7.8 weeks for the NPWT group and 11.1 weeks for the control group.[18] The variation can be inferred to stem from the difference in inclusion criteria and length of follow up. Nevertheless, all reports on amputation incidence showed no statistically significant difference between NPWT

Table 3. Comparison of complication outcomes between NPWT and conventional moist dressing

Author	Results		Notes	Ref
	NPWT	Control		
Amputation				
Borys et al.	0%	4.55%	No significant difference. 1 year follow up	(10)
Chiang et al.	49.1%	30%	No significant difference. 1 year follow up	(11)
Seidel et al.	20.5%	20.7%	No significant difference. 6 months follow up	(16)
Sukur et al.	38.7%	41.2%	No significant difference. Follow up until the endpoint is reached, including amputation.	(18)
Infection				
James et al.	55.56%	59.26%	No significant difference. Follow up until the endpoint is reached, i.e., 100% granulation.	(14)
Kajagar et al.	6.7%	26.7%	Significant difference. Fourteen days follow up.	(15)
Bleeding				
James et al.	51.85%	59.26%	No significant difference.	(14)

and conventional moist dressing despite variation in the length of follow up.

Meanwhile, two studies reported an incidence of infection and bleeding. Infection was defined as bacterial growth on culture from wound specimen, while bleeding was defined as bleeding that necessitates dressing change due to soaking.[14,15] Kajagar et al. reported a significant difference in wound infection incidence where the NPWT group showed a lower infection incidence.[15] Although James et al. reported no significant difference in infection incidence, their result showed a difference in the differential distribution of bacterial growth. The NPWT was shown with lower polymicrobial growth and less likely to be found with Gram-negative bacterial growth.[14]

DISCUSSION

The use of NPWT has been established as one option to treat DFU, despite not yet recommended as a standard of care. Everett and Mathioudakis' review on treatments for DFU stated that RCTs that supported NPWT efficacy to treat DFU has risks of bias.[19] At the same time, there have been reviews and meta-analyses supporting the use of NPWT to treat DFU. The most recent of which, by Liu et al. in 2017, conducted a meta-analysis that involved 11 RCTs and 1,044 patients, which conclude NPWT as an efficacious, safe, and cost-effective option to treat DFU.[7] Similar and earlier review has also summarized NPWT's mechanism of actions against DFU, which include improvement of local blood flow, induction of angiogenesis and granulation, as well as reduction of edema and bacterial colonization.[20]

Our results seem to concur with conclusions of Everett and Matioudakis regarding the need to carefully interpret results of RCTs on the use of NPWT for DFU patients.[19] Our results showed a wide variation on methodologies employed in RCTs, including a variation on the application of NPWT, measures outcome, and length to follow up. As a result, we see the expected interpretation of results, which may or may not be associated with different methodologies employed in each study. There was also variation regarding subject recruitment and grouping methods. While most included articles employed RCT design, some employed non-random clinical trial, and some other used retrospective analytic design.

Non-random grouping seems to affect the outcome, as shown by Borys et al., which use clinical characteristics to treat the subject with NPWT or conventional moist dressing. As NPWT was employed to treat more severe DFU cases (> 1 cm^2 diameter), it showed NPWT as less effective in ulcer size reduction and healing time. This result may be associated with the grouping mechanism.[10] Hasaballah et al. and Sukur et al. employed retrospective design, both showed comparable baseline characteristics between groups and found NPWT as a more efficacious treatment option.[13,18] Regardless of the variation in methodologies, the outcome measure with the most uniform results was granulation time. Despite different outcome definitions employed by each study, ranging from 75% granulation to 100% granulation, NPWT consistently showed a shorter time to reach these outcomes.[14,16-18] All included RCTs that reported ulcer size reduction also showed a higher rate of size reduction for NPWT than conventional moist dressing.[8,11,15]

However, despite results that showed faster healing of DFU treated with NPWT, our results indicate no significant reduction of complication risk or long-term prognoses. James et al. reported no reduction in infection or bleeding risk associated with NPWT treatment.[14] Long term follow up, ranging from 6 months to 1 year, also reported no difference regarding the risk of amputation, one of the most severe complications of DFU.[10,11,16] Our review contributed to answering whether or not NPWT superior in treating DFU by summarizing the most recent results on the issue. However, it suffered from a lack of methodological uniformity of included studies, as such interpretation has been conducted carefully regarding specific methodologies employed by each article.

CONCLUSION

Our review yields no conclusive answer regarding NPWT efficacy compared to conventional moist dressing to treat DFU. Most results showed NPWT superior efficacy, as indicated by shorter granulation time and faster ulcer size reduction rate. However, NPWT was not found to reduce the risk of amputation, prevention of which was one of the main objectives in DFU treatment. Variation of methodologies employed by included articles also meant we could not exclude the possibility of bias regarding each.

CONFLICT OF INTEREST

We declare that there were no conflicts of interest in this study.

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AUTHOR CONTRIBUTION

All of the authors are equally contributed to the study.

REFERENCE

1. Netten JJ, Bus SA, Apelqvist J, Lipsky BA, Hinchliffe RJ, Game F, et al. Definitions and criteria for diabetic foot disease. Diabetes Metab Res Rev. 2020;14:36.
2. Zhang P, Lu J, Jing Y, Tang S, Zhu D, Bi Y. Global epidemiology of diabetic foot ulceration: a systematic review and meta-analysis. Annals of Medicine. 2017; 106–16.
3. Costa RHR, Cardoso NA, Procópio RJ, Navarro TP, Dardik A, de Loiola Cisneros L. Diabetic foot ulcer carries high amputation and mortality rates, particularly in the presence of advanced age, peripheral artery disease and anemia. Diabetes Metab Syndr Clin Res Rev. 2017;1(11):583–7.
4. Ndosi M, Wright-Hughes A, Brown S, Backhouse M, Lipsky BA, Bhogal M, et al. Prognosis of the infected diabetic foot ulcer: a 12-month prospective observational study. Diabet Med. 2018;35(1):78–88.
5. Sen P, Demirdal T, Emir B. Meta-analysis of risk factors for amputation in diabetic foot infections. Diabetes Metab Res Rev. 2019;35(7).
6. Lavery LA, Davis KE, Berriman SJ, Braun L, Nichols A, Kim PJ, et al. WHS guidelines update: Diabetic foot ulcer treatment guidelines. Wound Repair Regen. 2016;24(1):112–26.
7. Liu S, He C zhu, Cai Y ting, Xing Q ping, Guo Y zhen, Chen Z long, et al. Evaluation of negative-pressure wound therapy for patients with diabetic foot ulcers: Systematic review and meta-analysis. Therapeutics and Clinical Risk Management. 2017;533–44.
8. Abdullah Al-Mallah ABAA-S. Negative Pressure Wound Therapy Versus Conventional Dressing in Treatment of Diabetic Foot Wound. Egypt J Hosp Med. 2018;72(3):4054–9.
9. Basheer S, Kannanavil N, Rajendran S. Home based negative pressure wound therapy and moist dressing in the treatment of diabetic foot ulcers. Int Surg J. 2019;6(12):4303.
10. Borys S, Hohendorff J, Koblik T, Witek P, Ludwig-Slomczynska A, Frankfurter C, et al. Negative-pressure wound therapy for management of chronic neuropathic noninfected diabetic foot ulcerations – short-term efficacy and long-term outcomes. Endocrine. 2018;62(3):611–6.
11. Chiang N, Rodda OA, Sleigh J, Vasudevan T. Effects of topical negative pressure therapy on tissue oxygenation and wound healing in vascular foot wounds. J Vasc Surg. 2017;66(2):564–71.
12. Gonzalez IG, Angel MAL, Baez MVJ, Ruiz Flores B, de los Angeles Martinez Ferretiz M, Woolf SV, et al. Handcrafted Vacuum-Assisted Device for Skin Ulcers Treatment Versus Traditional Therapy, Randomized Controlled Trial. World J Surg. 2017;41(2):386–93.
13. Hasaballah A, Aboloyoun H, Elbadawy A, Ezeldeen M. Impact of negative pressure wound therapy in complete healing rates following surgical debridement in heel and ankle regions in diabetic foot infections. Egypt J Surg. 2019;38:165–9.
14. James S, Sureshkumar S, Elamurugan T, Debasis N, Vijayakumar C, Palanivel C. Comparison of vacuum-assisted closure therapy and conventional dressing on wound healing in patients with diabetic foot ulcer: A randomized controlled trial. Niger J Surg. 2019;25:14–20.
15. Kajagar BM, Joshi K. Efficacy of Vacuum-Assisted Closure Therapy versus Conventional Povidone Iodine Dressing in the Management of Diabetic Foot Ulcers: A Randomized Control Trial. Int J Heal Sci Res. 2017;7(5):47–51.
16. Seidel D, Storck M, Lawall H, Wozniak G, Mauckner P, Hochlenert D, et al. Negative pressure wound therapy compared with standard moist wound care on diabetic foot ulcers in real-life clinical practice: Results of the German DiaFu-RCT. BMJ Open. 2020;10(3):1–16.
17. Singh B, Sharma D. Comparison of Negative Pressure Wound Therapy v/s Conventional Dressings in the Management of Chronic Diabetic Foot Ulcers in a Tertiary Care Hospital in North India. Int J Sci Res. 2017;6(8):2319–7064.
18. Sukur E, Akar A, Uyar AÇ, Cicekli O, Kochai A, Turker M, et al. Vacuum-assisted closure versus moist dressings in the treatment of diabetic wound ulcers after partial foot amputation: A retrospective analysis in 65 patients. J Orthop Surg. 2018;26(3):1–5.
19. Everett E, Mathioudakis N. Update on management of diabetic foot ulcers. Annals of the New York Academy of Sciences. 2018; 153–65.
20. Hasan MY, Teo R, Nather A. Negative-pressure wound therapy for management of diabetic foot wounds: a review of the mechanism of action, clinical applications, and recent developments. Diabet Foot Ankle. 2015;6(1):27618.