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Review

Negative-pressure wound therapy in skin grafts: A systematic review and meta-analysis of randomized controlled trials

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ABSTRACT

Introduction: Although skin grafts are widely used in reconstruction of large skin defect and complex wounds, many factors lead to suboptimal graft take. Negative-pressure wound therapy (NPWT) reportedly increases the graft take rates when added to skin grafting, but a summary analysis of the data of randomized controlled trials has yet to be performed. We conducted this systematic review and meta-analysis of randomized controlled trials to compare the effectiveness and safety of NPWT and non-NPWT for patients with skin grafts.
Methods: We searched PubMed, Embase, Cochrane Library, and CNKI for relevant trials based on predetermined eligibility criteria from database establishment to February 2020. Two reviewers screened citations and extracted data independently. The quality of the included studies was evaluated according to the Cochrane Handbook, whereas statistical heterogeneity was assessed using chi-square tests and I2 statistics. Review Manager 5.3 was used for statistical analysis.
Results: Ten randomized controlled trials with 488 patients who underwent NPWT or non-NPWT were included. Compared with non-NPWT, NPWT yielded an improved the percentage of graft take, a reduction in days from grafting to discharge, with lower relative risk of re-operation, and no increased relative risk of adverse event. Further, the subgroup analysis showed an improved the percentage of graft take in negative pressure of 80 mmHg, and no improved the percentage of graft take in negative pressure of 125 mmHg.
Conclusion: NPWT is more effective than non-NPWT for the integration of skin grafts, and the negative pressure of 80 mmHg can be recommended. Data on adverse events and negative pressure are, however, limited. A better understanding of complications after NPWT and the ideal negative pressure for the integration of skin grafts is imperative.

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1. Introduction

Wounds undergoing reconstruction are usually large skin defect and complex wounds caused by diabetic foot ulcers, burns, degloving, pressure sores, etc. One of the principal tools of a the modern surgeon (such as burn surgeon, plastic surgeon) is skin grafting. The skin graft to survive consists of 3 phases: serum imbibition, revascularization, and maturation. The most critical phase is revascularization process, can be affected by many factors. Common culprits of skin graft loss are the result of the formation of seroma or of hematoma under the graft which interfere directly with serum imbibition and revascularisation, imprecise apposition of the graft to its bed, shear forces between the graft and the bed, and infection of the graft [1]. A method of wound coverage that prevents these events has always been sought. However, nowadays, no one method can close the skin defect and discharge the patient successfully in all the cases and conditions.

The technique of negative-pressure wound therapy (NPWT), is based on the use of a closed sealed system that places continuous or discontinuous sub-atmospheric pressure over a surface, initially used for better wound healing, described by Morykwas et al. [2] in the United States in 1997. Theoretical healing advantages of NPWT include increased local blood flow to the wound, promoting angiogenesis, stimulation and formation of healing granulation tissue [3]. NPWT covering and stabilizing the skin graft can be favorable to wound healing by enhancing adhesion of the skin graft through holding them firmly to the recipient site, reducing the formation of seroma or of hematoma beneath the graft and maceration under the dressing through exudate removal, and maintaining a moist environment.

In view of this compelling rationale, a series of clinical trials have assessed NPWT versus non-NPWT in the integration of skin grafts to the recipient site. Recognising that individual studies might not be able to provide sufficient data on their own to affect practice, and two previous meta-analyses have failed to demonstrate a relatively reliable conclusion, because of various limitations such as they have not included a relatively large number of randomised controlled trials (RCTs), a pooled analysis of days from grafting to discharge, in other words, this important clinical question remains unaddressed [4,5], In addition, three RCTs have been published recently [6–8]. We sought to objectively assess the potential role of this treatment versus conventional dressing methods in the management of skin grafts. Outcome parameters of interest for our search including: a subset of 9 studies reported the percentage of graft take when NPWT was used after grafting. In 3 studies the days from grafting to discharge was provided. In 5 studies the re-operation rate was provided and 6 studies reported adverse event. We therefore did a systematic review and meta-analysis of RCTs to establish the effectiveness and safety of NPWT versus non-NPWT on the key outcomes of the percentage of graft take, days from grafting to discharge, re-operation and adverse event in patients with skin grafts.

2. Methods

2.1. *Search strategy and selection criteria*

This systematic review and meta-analysis was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement [9], and was registered at International Prospective Register of Systematic Reviews (number CRD42020169538).

We selected relevant studies published from their earliest available dates through February 2020, by searching PubMed, Embase, Cochrane Library, and CNKI. We applied the restrictions of English-language text. Keywords according to Medical Subject Heading terms(MESH) with Boolean operators were impored. These search strategies retrived different records which were combined with the Boolean operator “AND” to obtain the first number of records. The bibliographies of related systematic reviews and clinical guidelines were searched, the reference section for each study was also searched. We also did a manual search, using the reference lists of key articles published in English. In addition, we manually searched the Chinese databases of journals, dissertations and magazines for related articles as well as the references to these articles.

2.2. Study selection and data extraction

We regarded studies as eligible for inclusion if they were randomised clinical trials done in patients with skin grafts, compared NPWT to non-NPWT, and reported changes in the percentage of graft take or days from grafting to discharge or re-operation or adverse event. Literature studies written in English have been included in this manuscript.

The outcomes assessed were as follows: the difference between two treatment modalities on the percentage of graft take, days from grafting to discharge, re-operation and adverse event were experienced by patients.

Two independent investigators (ZYJ, GHG) reviewed study titles and abstracts, and studies that satisfied the inclusion criteria were retrieved for full-text assessment. Trials selected for detailed analysis and data extraction were analysed by two investigators (XTY and XCL) with an agreement value (κ) of 96.5%; disagreements were resolved by a third investigator (MZL).

Data of the independent variables included: publication year, country of publication, sample size in each group, age of participants, proportion of men and women, thickness of skin grafts, mean size of the wound grafted, treatment interval, negative pressure in NPWT, covering time of dressings, follow up period and the values of the percentage of graft take and the days from grafting to discharge were summarized. Total numbers of participants with re-operation and adverse event were extracted from both modalities. Two independent reviewers (ZHF, DHM) assessed risk for bias according to the PRISMA recommendations.

2.3. Assessment of risk of bias in included studies

The risk of bias in included studies was assessed by two review authors independently according to the Cochrane Handbook for Systematic Reviews of Interventions, which included seven items: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias. Different opinions were resolved by discussing with a third author. Further more, in case of disagreements regarding the risk of bias judgement, discussion was conducted until a consensus was reached. All authors of this research had got the certification from Chinese Clinical Trial Registry Training Program. The quality of the systematic review and meta-analysis was assessed using the A MeaSurement Tool to Assess systematic Reviews (AMSTAR) 2 checklist [10].

2.4. Data analysis

We assessed the effectiveness and safety of NPWT versus non-NPWT on four outcomes: the percentage of graft take, days from grafting to discharge, re-operation and adverse event. We analysed the percentage of graft take, days from grafting to discharge at study end as continuous variables and calculated as mean difference (MD). For analyses of the proportion of participants needing for a 2nd coverage procedure and those having complications, calculated as an overall odds ratio(OR). We calculated the mean and variance from the reported median, range, and sample size if the standard deviation of continuous data was not reported in the published article [11].

We calculated pooled estimates of the mean differences and corresponding 95% confidence intervals (CI) in the percentage of graft take and days from grafting to discharge between two treatments, respectively by using a random-effects model and a fixed-effects model to adequately account for the additional uncertainty associated with inter-study variability in the effect of the two methods. For categorical outcomes, we also calculated pooled estimates of the odds ratio and 95% CI with a fixed-effects model. This comparison is the most important clinical question pertaining to the role of NPWT in the integration of skin grafts to the recipient site and also reduced the heterogeneity of the treatment-induced changes in outcomes in the comparator arm seen in the overall analysis.

Odds Ratios (OR) and mean difference (MD), 95% CI were calculated with Review Manager, version 5.3 (provided by the Cochrane collaboration network). The I^2 test for heterogeneity and fixed-effects model ($I^2 < 50\%$) and random-effects model ($I^2 \geq 50\%$) were applied and $P < 0.05$ was considered to indicate statistical significance.

3. Results

We identified 457 studies, including 168 from PubMed, 135 from EMBASE, 87 from Cochrane Library and 67 from CNKI; 208 duplicated studies and non-English language articles were deleted. At the stage of titles and abstracts screen, 238 studies, including 138 related with NPWT in traumatic wound, 67 related with NPWT in diabetic wound, and 33 related with NPWT in pressure ulcers, were excluded because they were not related with the efficacy and safety of NPWT versus non-NPWT in the integration of skin grafts to the recipient site, and the remaining 11 articles were retrieved for a full-text review. However, 1 study [12] did not provide sufficient data, so the study was excluded (Fig. 1A). Finally, the 10 trials were all published between 2004 and 2019 (Table 1), one of the included RCTs originated from USA, one of the included RCTs originated from China, one of the included RCTs originated from France, one of the included RCTs originated from New Zealand, one of the included RCTs originated from Canada, one of the included RCTs originated from England, one of the included RCTs originated from Chile, three of the included RCTs originated from India and compared NPWT versus non-NPWT for patients with skin grafts. The following variables were extracted from the included studies: publication year, country of publication, sample size in each group, age of participants, proportion of men and women, thickness of skin grafts, mean size of the wound grafted, treatment interval, negative pressure in NPWT, covering time of dressings, follow up period (Table 1).

3.1. Assessment of risk of bias of the included studies

Seven of the included studies [6,8,14–17,19] cited the method of random sequence generation. Five of the included studies [6,8,14–16] cited the procedure of allocation concealment. Only one of the included studies [14] cited blinding of participants

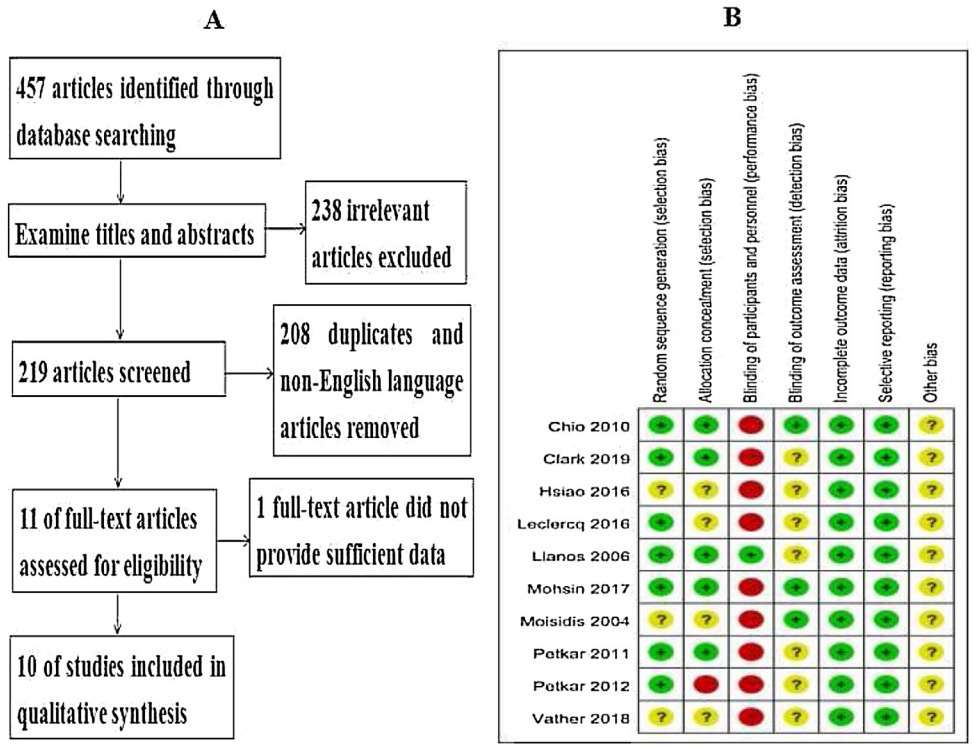

Fig. 1 – (A) Study selection process. (B) Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

and personnel. Three of the included studies [6,13,15] cited blinding of outcome assessment. Details of assessment of risk of bias of included studies were shown in Fig. 1B.

In the pooled analysis results regarding effectiveness after the treatment, nine randomised controlled studies [6,7,13–19] provided effectiveness data in terms of the percentage of graft take, which included 245 NPWT group cases and 239 control group cases. A heterogeneity test showed significant heterogeneity among the studies (I^2 = 64%, P = 0.004). A pooled analysis showed that the difference between the NPWT and control groups was significant (MD = 6.10, 95% CI [1.85 10.34], P = 0.005); hence, the NPWT group exhibited superior results compared with the control group (Fig. 2A). However, the study of Clark et al. [8] did not provide concrete data of the percentage of graft take and was excluded.

Further, assessment of four included studies [14,16,17,19] with regard to the percentage of graft take by subgroup analysis and showed no heterogeneity among the studies (I^2 = 0%, P = 0.77), and significant differences between the NPWT group and the control group in negative pressure of 80 mmHg (MD = 9.51, 95% CI [6.51 12.51], P < 0.00001), the NPWT group exhibited superior results compared with the control group. However, we assessed three other included studies [6,7,15] by subgroup analysis and showed significant heterogeneity among the studies (I^2 = 85%, P = 0.001), and no significant differences between the NPWT group and the control group in negative pressure of 125 mmHg (MD = 2.31, 95% CI [−8.61 13.23], P = 0.68) (Fig. 2B).

Three randomised controlled studies [14,16,17] provided useful data regarding significant decreases in days from grafting to discharge. These studies included 86 NPWT group cases and 85 control group cases. A heterogeneity test showed no heterogeneity among the studies (P = 0.78, I^2 = 0%). The pooled analysis showed that the difference between the NPWT group and the control group was significant (MD = −3.35, 95% CI [−4.21 −2.49], P < 0.00001). The NPWT group exhibited results that were superior to the control group (Fig. 3). However, six of the included studies [7,8,13,15,18,19] did not mention the days from grafting to discharge and the study of Mohsin et al. [6] did not provide concrete data of the variable, were excluded.

Five randomised controlled studies [6,8,13,14,17] provided effectiveness data in terms of re-operation following treatment. These studies included 147 NPWT group cases and 148 control group cases. A heterogeneity test showed no significant heterogeneity between the studies (P = 0.58, I^2 = 0%). The pooled analysis showed that the difference between the NPWT group and the control group was significant (OR = 0.25, 95% CI [0.10 0.61], P = 0.003). The total event percentage (7/147) of the NPWT group was less than that (23/148) of the control group, and similarly, the NPWT group performed better than the control group (Fig. 4). However, five of the included studies [7,15,16,18,19] did not provide concrete data of re-operation, were excluded.

Six randomised controlled studies [7,8,15,17–19] provided effectiveness data in terms of adverse event following

Table 1 – Characteristics of included studies.

Reference	Year	Funding	Sample size N/C	Age (years)N/C	Gender (M/F) N, C	Sort of wounds	Skin thickness	Grafted area (cm^2) N, C	Treatment N/C	Negative pressure (mmHg)	Type and company of NWPT	Covering Time (days)	Followed up
Moisidis et al. [13]	2004	–	20/20	64 (27–88)	12/8	Acute, subacute or chronic wounds	Split-thickness 11/1000 in., 1:1.5	128 (35–450)	Topical negative pressure dressing/standard bolster dressing	Continuous, −100	Kinetic concepts International, San Antonio, Texas	5	2 weeks
Llanos et al. [14]	2006	–	30/30	34 (20–52)/34.5 (19–58)	26/4, 24/6	Burns, exposed fractures, loxoscelism, degloving, other	Split-thickness 0.12 mm	33.8 (8.8–124.3), 31.2 (5.5–179.7)	Negative pressure closure dressing/similar dressing but without connection to negative pressure	Continuous, −80	The central aspiration system	4	–
Chioet al. [15]	2010	None	23/27	62.1/58.1	14/9, 16/11	The radial forearm free flap donor site	Split-thickness 0.012 in.	72.9 (27–160), 69.3 (28–165)	Negative pressure dressing/static pressure dressing	–, −125	V.A.C. device; KCI, San Antonio, TX	6	1 month
Petkar et al. [16]	2011	–	21/19	32 (7–68)/28.5 (7–60)	14/16	Acute and sub-acute burn wounds, chronic ulcers after burn (>3 months), contracture release and scar excisions, dermabrasion	Split-thickness	244 (16–1200), 183 (16–1000)	Negative pressure dressing/conventional dressing	–, −80	–	4	9 days
Petkar et al. [17]	2012	Fluid Grant, CMC Vellore	35/36	34.08 (2–69)/35.14 (16–77)	20/15, 22/14	Fresh surgical wound, acute wound, traumatic wound, burn wound, diabetic wound, inflammatory wound	Split-skin	239.77 ± 299.50, 269.06 ± 336.74	Vacuum closure/conventional dressing	Continuous, −80	–	4	3 weeks
Hsiao et al. [18]	2016	VGH-102-C-153 and 103-V-B-063	14/14	(24–76)	14/0, 13/1	Donor site for free flap, trauma wound	Split-thickness 0.15–0.20 mm 1:1.5	$11 \leq 120\ cm^2$ 3 > $120\ cm^2$, $9 \leq 120\ cm^2$ 5 > $120\ cm^2$	Occlusive drainage system/conventional indirect wet dressing	–, –	S56027 18FR, PAHSCO, Taiwan	7	3 months
Leclercq et al. [19]	2016	–	24/22	79.2 (63–89)/73.1 (38-100)	7/17, 6/16	Chronic leg ulcers	Thickness of 4 mm	22.8 (1.3–57), 19.8 (2.9–77)	VAC/hydrocolloid dressings	Continuous, −80	–	5	3 months
Mohsin et al. [6]	2017	None	50/50	39.5 ± 16.2/40.1 ± 17.4	36/14, 39/11	Trauma, diabetes, burn, after fasciotomy, infected and frostbite wonds	Split-thickness	93.78 ± 74.12, 135.68 ± 122.82	Negative-pressure wound therapy/convention-al dress	–, −125	–	4	–
Vather et al. [7]	2018	–	28/21	68.1/74.7	14/14, 12/9	Wounds in lower limb skin cancer	Split skin	–	Negative pressure device/softban and crepe dressing	Continuous, −125	–	5–7	12 weeks
Clark et al. [8]	2019	None	12/12	59.7 (12.6), 59.3 (11.8)	4/8, 10/2	The radial forearm free flap donor site	Split thickness	70.7 (24.9), 87.9 (44.3)	Negative pressure wound dressings/static pressure dressings	–, −80	PICO™ Smith & Nephew, Hull, UK	7	3 months

N, the NPWT group; C, the control group; –, not available.

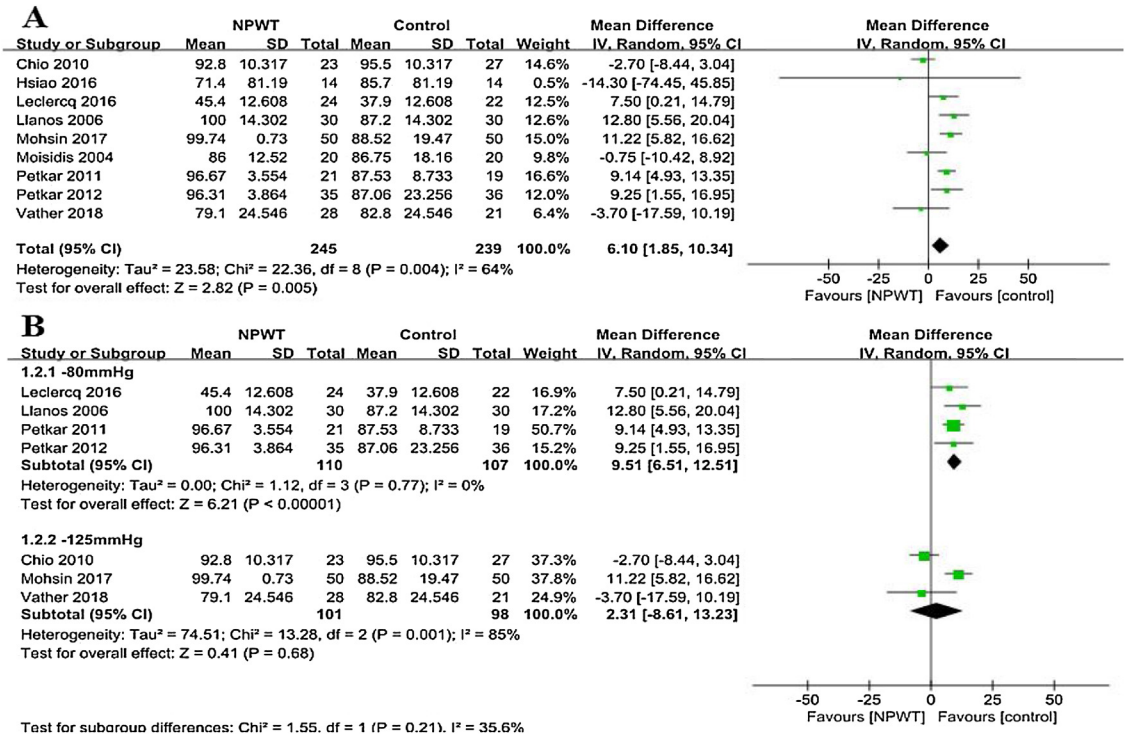

Fig. 2 – Meta-analyses of NPWT versus conventional dressing methods in the integration of skin grafts to the recipient site, comparing the percentage of graft take.

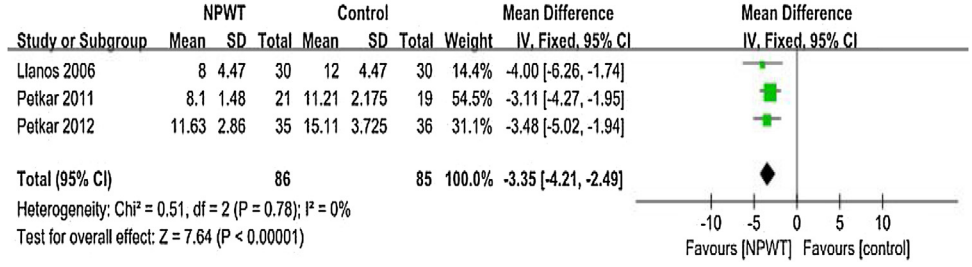

Fig. 3 – Meta-analyses of NPWT versus conventional dressing methods in the integration of skin grafts to the recipient site, comparing days from grafting to discharge.

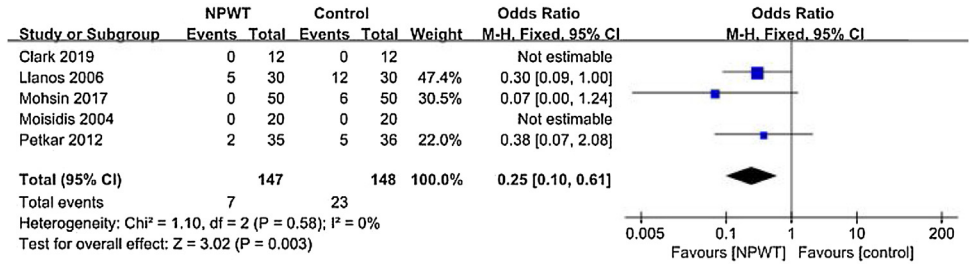

Fig. 4 – Meta-analyses of NPWT versus conventional dressing methods in the integration of skin grafts to the recipient site, comparing re-operation.

treatment. These studies included 136 NPWT group cases and 132 control group cases. A heterogeneity test showed no heterogeneity between the studies (P = 0.35, I^2 = 9%). The pooled analysis showed that no significant differences between the NPWT group and the control group (OR = 1.07, 95% CI [0.54 2.12], P = 0.85). The total event percentage (26/136) of the NPWT group was not significantly less than that (25/132) of the control group (Fig. 5). However, four of the included studies [6,13,14,16] did not provide concrete data of adverse event, were excluded.

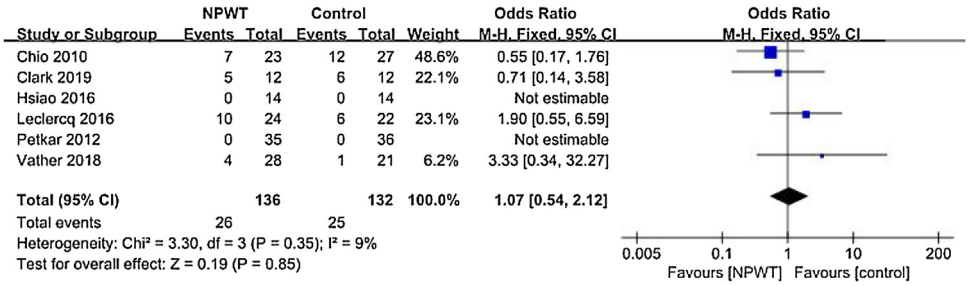

Fig. 5 – Meta-analyses of NPWT versus conventional dressing methods in the integration of skin grafts to the recipient site, comparing adverse event.

4. Discussion

Our results show that, compared with conventional dressing methods, NPWT was more effective in the integration of skin grafts to the recipient site, with more significant improvement in the percentage of graft take, a reduction in days from grafting to discharge, lower relative risk of re-operation, and no increased relative risk of adverse event. Further, the subgroup analysis demonstrates an improved percentage of graft take in −80 mmHg and no improvement of graft take in −125 mmHg groups. These data thus lend support to compared with conventional dressing methods, NPWT as a more effective therapeutic strategy that can improve the management of skin grafts, and −80 mmHg can be recommended.

In the management of skin grafts, numerous modalities have been described for covering and stabilizing the skin graft, ranging from conventional dressing to innovations attempted, such as non-adherent dressings along with cotton pads with or without a tie-over bolster dressing, petroleum gauze, immobilization with splints, hydrocolloid films and polyurethane films, fibrin glue, staplers and plastic syringe, rubber bands, etc. [20–22]. However, the optimal therapeutic strategy that yields universally accepted treatment resulting in the integration of skin grafts to the recipient site, has not been established. A ideal dressing material should not interfere with the process of wound healing, what is more, provide a good environment that prevents non-adherence of the graft, and protect the graft from infection. Last but not least, it should be comfortable and accessible for the patient [23].

The efficacy of NPWT for management of infected trauma and chronic and burn wounds has been well recognised. NPWT also known as vacuum-assisted closure, vacuum therapy and topical negative-pressure therapy in different parts of the world [24]. The device consists of a specialized pump system delivering an continuous or discontinuous sub-atmospheric pressure. The pump system is connected to a resilient, reticulated open-pore foam-surface dressing over a surface of soft tissues, covered with an adhesive drape to maintain a closed sealed system, and a canister to collect wound exudate [25]. Although NPWT has been demonstrated to improve wound healing in a number of settings, negative pressure is the critical factor affecting the therapeutic effect and should be tailored to each specific condition [26]. The ideal negative pressure of NPWT can increase local blood flow, stimulate granulation tissue formation, improve its irrigation and remove exudate, and decrease bacterial load within the wound, hence providing a favorable wound healing environment [27].

Subsequently, some case series and reports have proposed the use of NPWT as a modality for covering and stabilizing the skin graft,and some of the studies have shown encouraging results [28,29]. However, some studies showed that the NPWT does not appear to offer a significant improvement over conventional dressings in healing of skin graft [15,19].

Based on this, the study including 10 RCTs evaluating NPWT versus non-NPWT in the integration of skin grafts to the recipient site, has yielded robust and consistent findings that lend support to NPWT is more effective than conventional dressing in skin grafts. Moreover, compared with conventional dressing methods, NPWT yielded no increased relative risk of adverse event. Further, the subgroup analysis showed that for the percentage of graft take, NPWT was superior to non-NPWT in negative pressure of 80 mmHg, and NPWT was not superior to non-NPWT in negative pressure of 125 mmHg. In other words, the negative pressure of 80 mmHg can be recommended for the integration of skin grafts to the recipient site. This is consistent with the study led by Topaz [26]. Moreover, AMSTAR 2 is a critical appraisal tool for systematic reviews, the overall quality of our meta-review, rated via the AMSTAR-2 tool, found that this review had no potential critical problems. Indeed, this consistency is apparent despite the fact that these studies differ in several ways, including the baseline characteristics of wounds, covering time, and grafted area. Taken together, these studies are supportive of the generalisability across clinical settings of the observed more suitable of NPWT. In addition, it is reassuring that, for the percentage of graft take, the between-study heterogeneity that likely reflected the differences in the negative pressure, and four included studies [14,16,17,19] with regard to negative pressure of 80 mmHg by subgroup analysis and showed no heterogeneity among the studies.

However, based on a comprehensive analysis, several limitations were found pertaining to these studies. First, the ten articles included in this study primarily adopted random, controlled research and design methods; however, for three of the included studies the randomization method and allocation concealment are not described in detail, which may result in high risks of selection biases. Moreover, blinding was hard to

achieve due to the presence and application of the suction device over patient's wound. Second, the data on days from grafting to discharge, re-operation and adverse event are not collected as part of all the articles included. Third, the one included study with a self-made occlusive drainage system did not show the negative pressure. Fourth, the application time for the NPWT was not uniform, which may have hindered the synthesis of the results and analysis. Finally, it is difficult to cover the recipient site that has not enough healthy skin for draping in NPWT. For a large and irregular wound, maintaining sufficient negative pressure in the whole wound can also be a problem. Further study is needed in this case.

5. Conclusions

In conclusion, our study presents limited evidence from 10 individual trials that NPWT is more effective than non-NPWT in the integration of skin grafts to the recipient site, with more significant improvement in the percentage of graft take and reduction in days from grafting to discharge, as well as fewer re-operations and no increased relative risk of adverse events. The negative pressure of 80 mmHg can be recommended. Data on adverse event and negative pressure are, however, limited. A better understanding of complications after NPWT and the ideal negative pressure for the integration of skin grafts is imperative.

Conflict of interest

The authors declared that they have no conflicts of interest to this work.

Acknowledgments

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.burns.2021.02.012.

REFERENCES

[1] Scherer SS, Pietramaggiori G, Orgill DP. Skin graft. In: Neligan P, editor. Plastic surgery. London: Elsevier Saunders; 2013. p. 281–304.
[2] 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;38(6):553–62.
[3] Mouës CM, Heule F, Hovius SE. A review of topical negative pressure therapy in wound healing: sufficient evidence? Am J Surg 2011;201(4):544–56.
[4] Webster J, Scuffham P, Stankiewicz M, Chaboyer WP. Negative pressure wound therapy for skin grafts and surgical wounds healing by primary intention. Cochrane Database Syst Rev 2014;(10):CD009261.
[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;50:43–8.
[6] Mohsin M, Zargar HR, Wani AH, Zaroo MI, Baba PUF, Bashir SA, et al. Role of customised negative-pressure wound therapy in the integration of split-thickness skin grafts: a randomised control study. Indian J Plast Surg 2017;50(1):43–9.
[7] Vather R, Ker H, Rolfe G, Chen L, Hammodat H, Gale K, et al. Wound Outcomes in Negative Pressure Dressings (WOUND) study — a randomised trial in lower limb skin cancer grafts. J Plast Reconstr Aesthet Surg 2018;71(7):1100–2.
[8] Clark JM, Rychlik S, Harris J, Seikaly H, Biron VL, O'Connell DA. Donor site morbidity following radial forearm free flap reconstruction with split thickness skin grafts using negative pressure wound therapy. J Otolaryngol Head Neck Surg 2019;48(1):21.
[9] Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 2009;339:b2535.
[10] Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ 2017;358:j4008.
[11] Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol 2005;5:13.
[12] Halama D, Dreilich R, Lethaus B, Bartella A, Pausch NC. Donor-site morbidity after harvesting of radial forearm free flaps-comparison of vacuum-assisted closure with conventional wound care: a randomized controlled trial. J Craniomaxillofac Surg 2019;47(12):1980–5.
[13] Moisidis E, Heath T, Boorer C, Ho K, Deva AK. A prospective, blinded, randomized, controlled clinical trial of topical negative pressure use in skin grafting. Plast Reconstr Surg 2004;114(4):917–22.
[14] Llanos S, Danilla S, Barraza C, Armijo E, Piñeros JL, Quintas M, et al. Effectiveness of negative pressure closure in the integration of split thickness skin grafts: a randomized, double-masked, controlled trial. Ann Surg 2006;244(5):700–5.
[15] Chio EG, Agrawal A. A randomized, prospective, controlled study of forearm donor site healing when using a vacuum dressing. Otolaryngol Head Neck Surg 2010;142(2):174–8.
[16] Petkar KS, Dhanraj P, Kingsly PM, Sreekar H, Lakshmanarao A, Lamba S, et al. A prospective randomized controlled trial comparing negative pressure dressing and conventional dressing methods on split-thickness skin grafts in burned patients. Burns 2011;37(6):925–9.
[17] Petkar K, Dhanraj P, Sreekar H. Vacuum closure as a skin-graft dressing: a comparison against conventional dressing. Eur J Plast Surg 2012;35:579–84.
[18] Hsiao SF, Ma H, Wang YH, Wang TH. Occlusive drainage system for split-thickness skin graft: a prospective randomized controlled trial. Burns 2017;43(2):379–87.
[19] Leclercq A, Labeille B, Perrot JL, Vercherin P, Cambazard F. Skin graft secured by VAC (vacuum-assisted closure) therapy in chronic leg ulcers: a controlled randomized study. Ann Dermatol Venereol 2016;143(1):3–8.

[20] Alvarez OM, Mertz PM, Eaglstein WH. The effect of occlusive dressings on collagen synthesis and re-epithelialization in superficial wounds. J Surg Res 1983;35(2):142–8.
[21] Dainty LA, Bosco JJ, McBroom JW, Winter [97_TD$DIFF]3rd WE, Rose GS, Elkas JC. Novel techniques to improve split-thickness skin graft viability during vulvo-vaginal reconstruction. Gynecol Oncol 2005;97(3):949–52.
[22] Cheng LF, Lee JT, Chou TD, Chiu TF, Sun TB, Wang CH, et al. Experience with elastic rubber bands for the tie-over dressing in skin graft. Burns 2006;32(2):212–5.
[23] Wang TH, Ma H, Yeh FL, Lin JT, Shen BH. The use of "composite dressing" for covering split-thickness skin graft donor sites. Burns 2010;36(2):252–5.
[24] Fleischmann W, Strecker W, Bombelli M, Kinzl L. Vacuum sealing as treatment of soft tissue damage in open fractures. Unfallchirurg 1993;96(9):488–92.
[25] Fleischmann W, Russ M, Westhauser A, Stampehl M. Vacuum sealing as carrier system for controlled local drug administration in wound infection. Unfallchirurg 1998;101(8):649–54.
[26] Topaz M. Improved wound management by regulated negative pressure-assisted wound therapy and regulated, oxygen-enriched negative pressure-assisted wound therapy through basic science research and clinical assessment. Indian J Plast Surg 2012;45(2):291–301.
[27] Horch RE, Ludolph I, Müller-Seubert W, Zetzmann K, Hauck T, Arkudas A, et al. Topical negative-pressure wound therapy: emerging devices and techniques. Expert Rev Med Devices 2020;1–10.
[28] Blackburn [97_TD$DIFF][58_TD$DIFF]2nd JH, Boemi L, Hall WW, Jeffords K, Hauck RM, Banducci DR, et al. Negative-pressure dressings as a bolster for skin grafts. Ann Plast Surg 1998;40(5):453–7.
[29] Scherer LA, Shiver S, Chang M, Meredith JW, Owings JT. The vacuum assisted closure device: a method of securing skin grafts and improving graft survival. Arch Surg 2002;137(8):930–4.