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Negative-pressure wound therapy for donor-site closure in radial forearm free flap: A systematic review and meta-analysis

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Abstract

Negative-pressure wound therapy (NPWT) is often used for skin graft site dressing, and several studies have reported that its use improves skin graft failure in the forearm flap donor site. The present systematic review aimed to evaluate the efficacy of NPWT with skin graft for donor-site closure in radial forearm free flap (RFFF) reconstruction. A systematic search in PubMed, Web of Science, and Cochrane Library databases was conducted. The search terms used for PubMed were ([radial forearm]) AND ([donor]) AND ([negative pressure or vacuum]). This review was registered in the International Prospective Register of Systematic Reviews and performed in accordance with the preferred reporting items for systematic reviews and meta-analyses statement. Three prospective randomised controlled trials and three retrospective comparative studies were included. Compared with conventional bolster dressing, the use of NPWT dressing did not lead to significant improvements in partial skin graft loss, tendon exposure, and other complications. NPWT improved hand functionality earlier; nonetheless, the cost of the device and dressings was a disadvantage. The use of NPWT for skin graft fixation in the RFFF donor site is not generally recommended.

KEYWORDS

donor-site closure, dressing, negative-pressure wound therapy, radial forearm free flap, skin graft

Key Messages

- negative-pressure wound therapy (NPWT) is often used for skin graft site dressing, with a lower graft loss rate having been recently reported
- the efficacy of NPWT with skin graft for donor-site closure in radial forearm free flap reconstruction
- it is compared with conventional bolster dressing, the use of NPWT dressing does not lead to significant improvements in the rate of successful graft take

1 | INTRODUCTION

Negative-pressure wound therapy (NPWT) is commonly applied to chronic wounds, and its use has been recognised to be highly effective and reduces the length of hospital stay.[1,2] Molecular evidence suggests that NPWT dressing not only improves the blood flow and promotes granulation tissue production within the wound bed[3,4] but also accelerates tissue growth and wound reduction. In addition to chronic wounds, NPWT is also used for burns and acute wounds.[5-9] NPWT is often used for skin graft site dressing, with a lower graft loss rate having been recently reported.[5,10-12]

Yang et al first introduced the radial forearm free flap (RFFF) in 1981 for the resurfacing of burn contractures in the neck.[13] The use of forearm flaps in maxillofacial reconstruction is currently one of the most frequently performed microvascular tissue transfer methods worldwide[14,15] and offers several advantages, including the relative thinness of the flaps and their pliability when used in various areas, rare anatomic variation, and long vascular flaps. Nevertheless, the use of these flaps also has disadvantages, such as the typical inability to achieve primary closure of the donor area and the potential for skin graft failure in the forearm flap donor site, particularly over the forearm tendons, which often results in tendon exposure and partial skin graft necrosis.[16-18] When this occurs, the treatment period is extended and cosmetic problems arise.

NPWT dressing is useful in patients with head and neck cancer and has been shown to result in fewer graft-related complications than conventional bolster dressing.[19,20] Additionally, the use of NPWT has been reported to improve skin graft failure in the forearm flap donor site according to some case reports.[21,22]

The present systematic review aimed to evaluate the efficacy of NPWT with skin graft for donor-site closure in RFFF reconstruction and compare NPWT to conventional methods with respect to wound healing outcomes, including wound complications (e.g., skin graft failure, tendon exposure), hand function, and postoperative management.

2 | METHODS

This systematic review was conducted in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement. The protocol of this systematic review was submitted on 26 July 2020, and registered on 26 August 2020, in the International Prospective Register of Systematic Reviews (University of York, UK; CRD42020201020). Acquisition of formal institutional review board or ethics committee approval was not required for this systematic review.

2.1 | Eligibility criteria

Several eligibility criteria were applied in the present systematic review. The inclusion criteria were as follows: (a) English full-text articles that involved adults or children; (b) skin grafting performed on the donor site in RFFF reconstruction; (c) intervention with NPWT; (d) relevant clinical outcomes, effectiveness, safety, and healthcare cost; and (e) study designs including prospective randomised controlled trials and retrospective comparative studies. When a publication included relevant data from previous studies, the latest study was analysed. As for the exclusion criteria, non-English reports, ex vivo or in vitro animal studies, case series, narrative reviews, expert opinions, and letters were excluded from the analysis.

2.2 | Search strategy

A comprehensive electronic search of earliest records published until 31 July 2020 was conducted across three databases—namely, PubMed, Web of Science, and Cochrane Library. The search terms used for PubMed were ([radial forearm]) AND ([donor]) AND ([negative pressure or vacuum]).

2.3 | Study selection

Two reviewers read and selected potentially eligible studies and independently screened all abstracts of articles retrieved using the search strategy. Potentially eligible studies were selected according to the inclusion criteria, and the full text of these studies was subsequently retrieved and read. The following data were extracted from the studies: method, participant profile, type of intervention implemented for the study and control groups, and outcomes. Any disagreement between the reviewers concerning the eligibility of particular studies was resolved by a third reviewer, who decided on whether to include a certain study.

2.4 | Risk of bias in individual studies

The level of evidence was determined according to the method of the Oxford Centre for Evidence-Based Medicine.[23] Bias in prospective randomised controlled trials was examined using the Cochrane Collaboration's tool

for assessing risk of bias[24] and RevMan software version 5.4 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark),[25] whereas bias in retrospective comparative studies was evaluated using the Risk of Bias Assessment Tool for Non-randomised Studies.[26] Two of the authors independently assessed bias; in case of disagreement on bias between the authors, a third opinion was requested and a consensus was achieved.

2.5 | Statistical analysis

Meta-analysis was performed using RevMan software version 5.4 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark).[25] A random effect model for outcomes was used, and a P value of <.05 was considered to indicate statistical significance.

3 | RESULTS

3.1 | Included studies

Following the exclusion of duplicates, 28 studies were extracted from the three databases and 14 studies were identified after screening by evaluation of titles and abstracts. After full-text screening, a total of six studies (three prospective randomised controlled trials and three retrospective comparative studies) met the criteria for this review. The PRISMA flow diagram is illustrated in Figure 1. The study design and level of evidence of each study are summarised in Table 1, whereas the study outcomes are presented in Table 2.

3.2 | Graft take rate

Five studies reported wound area covered with skin graft.[27-30] Halama et al compared the mean size of the wound area covered with skin graft in the NPWT and control groups at 12 days, 3 weeks, and 8 weeks (t-test; $P = .68$, $P = .698$, and $P = .197$, respectively).[27] Ray et al reported a graft take rate of 97.5% for the NPWT group and 92.1% for the control group.[28] Chio et al reported a graft take rate of 69.5% for the NPWT group and 66.7% for the control group.[29] Koch et al reported a graft take rate of 49.4% for the NPWT group and 66.1% for the control group.[30] Vidrine et al reported a graft take rate of 85% for the NPWT group and 76% for the control group.[19] No significant difference was observed between the NPWT and control groups in the five studies.

3.3 | Partial skin graft loss

Four studies reported partial skin graft loss outcomes.[28-30] Chio et al reported skin graft failure in

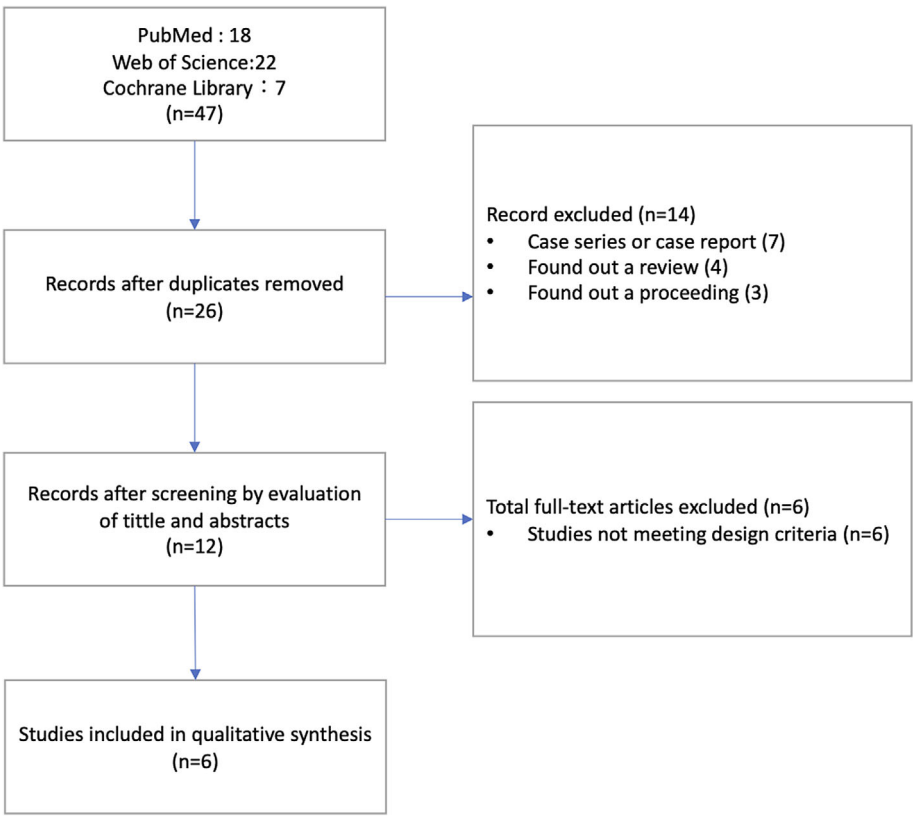

FIGURE 1 The PRISMA flow diagram adopted for the final selection of studies included in the review. PRISMA, preferred reporting items for systematic reviews and meta-analyses

TABLE 1 Study design and level of evidence

Study	Study design	Level of evidence[a]
Clark et al (2019)	Prospective randomised control study	1b
Halama et al (2019)	Prospective randomised control study	1b
Chio and Agrawal (2010)	Prospective randomised control study	1b
Ray et al (2018)	Retrospective comparative study	3b
Koch et al (2017)	Retrospective comparative study	3b
Vidrine et al (2005)	Retrospective comparative study	3b

[a]According to the levels of evidence of the Oxford Center for Evidence-Bases Medicine.

seven cases (30.4%) in the NPWT group and nine cases (33.3%) in the control group.[29] Koch et al reported partial graft necrosis in 15 cases (18.1%) in the NPWT group and 8 cases (14.3%) in the control group.[30] Ray et al reported skin graft loss in four cases (40%) in the NPWT group and five cases (50%) in the control group.[28] Vidrine et al reported skin graft loss in three cases (15%) in the NPWT group and six cases (24%) in the control group.[19] The forest plot results are presented in Figure 2; four was no significant difference between the two groups.

3.4 | Tendon exposure

Three studies evaluated the number of tendon exposure cases.[28-30] Chio et al reported four (17.3%) and seven (25.9%) tendon exposure cases at 2 weeks after surgery in the NPWT and control groups, respectively.[29] Koch et al identified tendon exposure in three cases (3.6%) in the NPWT group and four cases (7.1%) in the control group,[30] whereas Ray et al reported one (10%) case in the NPWT group and two cases (20%) in the control group.[28] The forest plot results are presented in Figure 3; no significant difference was observed between the two groups.

3.5 | Skin graft complications

Five studies reported skin graft complications, and no significant difference in these complications was identified in all studies.[28-31] Chio et al reported 7 (30.4%) and 12 (44.4%) cases of skin graft complications at 2 weeks after surgery in the NPWT and control groups, respectively.[29] Additionally, Chio et al reported donor-site complications during the first postoperative visit and at approximately 2 weeks after surgery in eight cases (34.8%) in the NPWT group and eight cases (44.4%) in the control group.[29] Clark et al reported five (45%) and six (50%) cases at 1 month after surgery in the NPWT and control groups, respectively.[31] Koch et al reported in 42 cases (50.6%) in the NPWT group and 18 cases (32.7%) in the control group.[30] Koch et al reported in 8 cases (40%) in the NPWT group and 12 cases (48%) in the control group.[19]

3.6 | Other wound complications

Koch et al reported the incidence rates of infection, seroma, dehiscence, and surgical revision. The infection incidence rate was 2.4% (two cases) in the NPWT group and 0% (zero case) in the control group. The seroma incidence rate was 9.6% (eight cases) in the NPWT group and 0% (zero case) in the control group. The dehiscence incidence rate was 7.2% (six cases) in the NPWT group and 7.1% (four cases) in the control group. The surgical revision rate was 9.6% (eight cases) for the NPWT group and 3.6% (two cases) for the control group.[30] Ray et al reported an infection incidence rate of 0% (zero case) for the NPWT group and 10% (one case) for the control group.[28] There was no significant difference in the two studies.

3.7 | Active wrist movement

Halama et al. identified differences in postoperative range of motion of the wrist at 12 days, 3 weeks, and 8 weeks (*t*-test; $P = .291$, $P = .441$, and $P = .608$, respectively) and postoperative wrist flexion movement at 12 days, 3 weeks, and 8 weeks ($P = .856$, $P = .844$, and $P = .857$, respectively) between the NPWT and control groups. No significant difference was noted between the two groups.[27]

3.8 | Hand grip strength

Halama et al compared the donor-site forearm and unaffected forearm using *t*-test.[27] In the control group, grip strength was significantly worse at 12 days ($P = .00003$), 3 weeks ($P < .0008$), and 8 weeks ($P = .037$). In the NPWT group, grip strength was significantly lower at 12 days ($P = .023$); however, this difference was no longer

TABLE 2 Outcome of studies

Study	NPWT device	PROCEDURE (NPWT/control)	% Graft take (NPWT/control)	%Tendon exposure (NPWT/control)	%Donor-site wound complications (NPWT/control)	Active wrist movement (extension/flexion)	Hand grip strength compared with the unaffected side (NPWT/control)	MHQ score (NPWT/control)	Cost for NPWT
Chio and Agrawal (2010)	VAC	23/27	69.6/66.7	17.4/25.9	68.8/80				$1000 USD
Clark et al (2019)	PICO	12/12			45/50			7 days: 43.3/70.8 $P = .021$ month: 64.5/69.2 $P = .523$ months: 70.5/83.8 $P = .06$	$135 CAD
Halama et al (2019)	VAC	25/25	FDGA areaT2: $P = .68$T3: $P = .698$T4: $P = .197$			T2 $P = .68$/0.856T3 $P = .441$/0.844T4 $P = .608$/0.857	T2 $P = .023$/0.00003 T3 $P = .089$/0.0008T4 $P = .354$/0.037		
Koch et al (2017)	VAC	83/55	49.4/66.1	3.6/7.1	50.6/32.7				(NPWT/control) €205/€38
Ray et al (2018)	PICO	10/10	97.5/92.1 $P = .14$	10 /20	40/50 $P = .33$				
Vidrine et al (2005)	VAC	20/25	85/76		40/48				$900 USD

Note: FDGA (forearm defect after graft attachment) area: the size of the covered wound area; T2: 12 days after surgery; T3: 3 weeks after surgery; T4: 8 weeks after surgery.
Abbreviations: €, Euro; CAD, Canadian dollar; NPWT, negative-pressure wound therapy; MHQ, Michigan Hand Outcomes Questionnaire; USD, US dollar; VAC, vacuum-assisted closure (KCI Medical Ltd., Witney, Oxfordshire, UK), PICO (Smith & Nephew, Hull, UK).

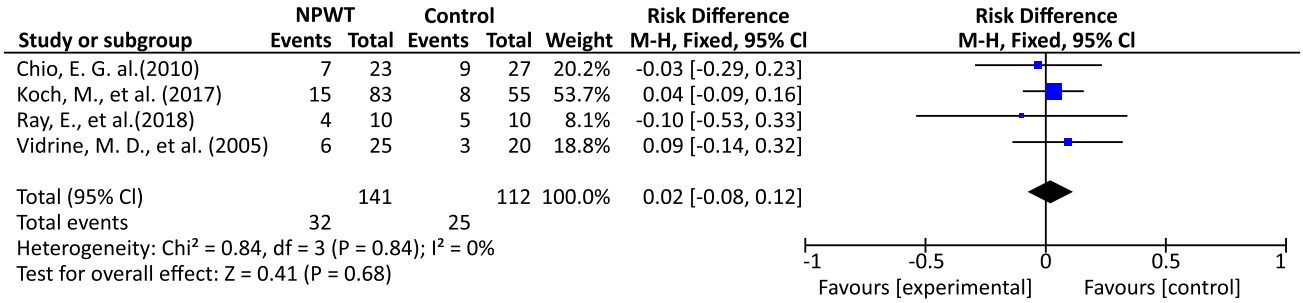

FIGURE 2 Meta-analysis of trials comparing the NPWT and control groups with respect to the incidence of partial skin graft loss. CI, confidence interval; M-H, Mantel-Haenszel; NPWT, negative-pressure wound therapy

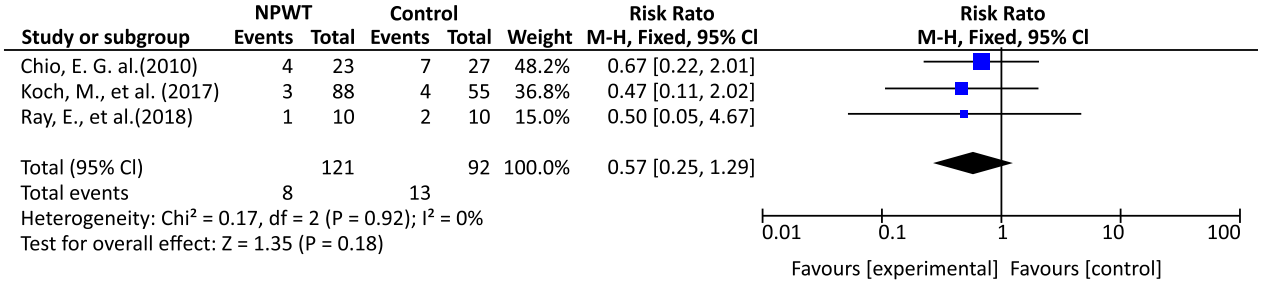

FIGURE 3 Meta-analysis of trials comparing the NPWT and control groups with respect to the incidence of tendon exposure. CI, confidence interval; M-H, Mantel-Haenszel; NPWT, negative-pressure wound therapy

detectable at 3 postoperative weeks (3 weeks: $P = .844$; 8 weeks: $P = .857$).

3.9 | Patient-reported hand and wrist function outcomes

Clark et al reported the hand and wrist function, as measured using the Michigan Hand Outcomes Questionnaire. Patients treated with NPWT had significantly better self-reported function for their operated hand at 7 postoperative days ($P = .02$).[31]

3.10 | Cost

Four studies reported cost.[29-31] According to Chio et al, the cost of a 6-day NPWT course ($1000 USD) was significantly higher than that of a foam bolster dressing ($10-15 USD).[29] Clark et al reported that the cost of PICO™ was $135 CAD, which is a very minor portion of a 1 to 2-week hospital stay, as is standard for a head and neck free flap reconstruction.[31] Koch et al reported that the cost was at least five times higher in the NPWT group than in the control group (€205 vs. €38).[30] Vidrine et al reported that the cost for 5 days of commercially available NPWT is approximately $900.[19]

3.11 | Risk of bias in studies

The risk of bias in the included studies is shown in Figure 4. Because there were only three prospective randomised controlled trials out of the six selected studies and much information was missing, the overall risk of bias was unclear. The major risks of bias included an unclear study protocol and poor description of the inclusion/exclusion criteria, which led to possible selection and detection biases.

4 | DISCUSSION

The use of a RFFF remains a reliable and versatile method for head and neck reconstruction. Several advantages of the RFFF include its pliability, relatively hairless skin, large vessel diameter, and long pedicle.[32] Nonetheless, this flap is limited by its inability to primarily close the donor site. Various techniques for donor-site closure have been reported; for instance, medium-sized defects may be managed with an ulnar flap,[33] Z-plasty,[34] bilobed flap,[35] or V-Y advancement flap.[36-38] However, these techniques may further distort the sensitivity and appearance of the forearm.

Most donor-site skin defects may be repaired with a full-thickness or split-thickness skin graft, and the donor

RCT study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blindness of outcome assessment	Incomplete outcome data	Selective outcome reporting
Clark et al (2019)	L	U	H	U	L	U
Halama et al (2019)	U	U	H	U	U	U
Chio and Agrawal (2010)	L	U	H	H	H	U
Retrospective Non-randomized studies	**Selection of participants**	**Confounding**	**Measurement of exposure**	**Blinding of outcome assessments**	**Incomplete outcome date**	**Selective outcome reporting**
Ray et al (2018)	H	H	U	H	L	U
Koch et al (2017)	U	H	U	H	L	U
Vidrine et al (2005)	H	H	U	H	L	U

FIGURE 4 Risk of bias in the included studies. H, high level of bias; L, low level of bias; RCT, randomised controlled trial; U, unclear level of bias

wound can be primarily closed with minimal morbidity.[39] Bardsley et al reviewed 100 radial artery free flap donor sites and 67 patients requiring skin grafting. They reported relatively pain-free donor sites with low pain scores in the subjective assessment, as well as an acceptable cosmetic outcome in men; however, the cosmetic outcome was less so in women.[16]

Several series have reported graft failure or tendon exposure rates as high as 30% to 50%.[40-43] The skin graft take rate varies depending on the layer of flap dissection. With subfascial dissection, the tendons are exposed, and wound healing is considerably delayed. A prospective randomised trial comparing morbidity at the suprafascial and subfascial donor sites reported that the overall incidence of exposed tendons was significantly lower at the suprafascial site (3%, 1 of 30) than at the subfascial site (21%, 6 of 28).[44]

The skin graft is easily displaced from the wound bed owing to its proximity to the wrist as well as the presence of tendons and muscles directly under the skin graft; hence, bolster fixation of the skin graft and wrist joint immobilisation with a splint are required.

The pressure of skin graft fixation is also important. Application of pressure to the skin graft aids in preventing hematoma formation under the skin graft and sticking to the wound bed. However, there exist various opinions on the pressure as well. Nakamura et al showed that multi-layered polyurethane foam dressing is effective for skin graft immobilisation and supplies a pressure of <30 mm Hg to the centre region of the skin graft, with a graft survival rate of 88.9%.[45] Sakurai et al determined that a pressure of 10 mm Hg on the skin graft is sufficient for good skin graft take.[46] Several reports have indicated that there is no problem for skin graft take even if the pressure of skin graft fixation is low. In addition to this, there is a concern that high pressure and overcompression can lead to skin graft necrosis.

Negative-pressure dressing closely adapts the skin graft to the recipient site, minimises movement, and eliminates dead space. Many studies have shown the advantages of NPWT dressing for the closure of RFFF donor-site defects with skin grafts. Zhang et al[22] described this procedure to be safe, simple, and effective in closing an RFFF donor-site defect with a full-thickness skin graft. Avery et al showed that this dressing could be rapidly and easily applied and there were no serious complications.[47] Nevertheless, these studies were case series; hence, there may be patient-selection bias or other biases.

In the studies included in the present systematic review, the NPWT dressing for the RFFF donor site did not show a statistically significant increased rate of graft take and decreased rate of donor-site complications such as tendon exposure. Chio and Agrawal concluded that negative-pressure dressing did not appear to offer considerable improvements when compared with static pressure dressing.[29] Halama et al reported that differences between the NPWT dressing group and static dressing group with respect to wound size (outcome variable) did

not reach statistical significance.[27] Furthermore, there was no significant difference in the skin graft take rate between the NPWT dressing group and conventional bolster group across randomised controlled trials included in our review. The lack of significant differences may be attributed to the sample size and patient population.

The following are our speculations as to why NPWT for the RFFF donor site was not effective. The reason for failure may be overcompression of the skin graft resulting from the compression pressure exerted by the NPWT dressing as well as the pressure imbalance created by the uneven shape and condition of the wound bed. To prevent air leaks, the pressure itself is higher with NPWT than with conventional methods. Pressures for NPWT have often been reported to be approximately 100 or 80 mm Hg when using the PICO system[28] and 125 mm Hg when using the vacuum-assisted closure system.[19] With NPWT, the graft and surrounding skin are suctioned up at a constant, flat, and unidirectional pressure. It is difficult to apply uniform pressure on the skin graft because of the irregularity caused by the tendons and underlying radial and ulnar bones. These considerations suggest that the advantage of NPWT for skin graft fixation at the distal forearm cannot be achieved. Nonetheless, improvements in early postoperative hand function were significantly better with NPWT dressing than with conventional bolster fixation because no hand joint immobilisation was required with NPWT dressing.

The impact of retained hand function could be even more profound and important to help patients manage their own care and recover more quickly.[31] It is important that hand function recovers early in RFFF reconstruction. Patients treated with NPWT had significantly better self-reported function for their operated hand on the Michigan Hand Outcomes Questionnaire at 7 postoperative days[31] and exhibited significantly faster grip strength recovery.[27] In these studies, the forearm was immobilised using an elastic bandage at 12 days and a volar splint at 7 days in the static dressing control group but was not immobilised in the NPWT dressing group. It is not necessary to extend the negative-pressure dressing over the hand, and the wrist may be immediately mobilised. [48] Hand function is preserved in the NPWT group because of no external fixation period.

Another potential disadvantage of NPWT dressing relates to its relatively higher cost, particularly when compared with that of conventional methods. From the reports of Chio and Agrawal, the cost of dressing materials for a 6-day NPWT course is approximately $1000 USD, which is significantly higher than the cost of a foam bolster dressing ($10-15 USD for supplies).[29] Furthermore, Koch et al reported that the production cost amounts to approximately €38 for conventional dressing and approximately €205 for NPWT dressing.[30] Vidrine et al reported that the cost for 5 days of commercially available NPWT is approximately $900 (with charges approaching $3000 including the device pump rental). Skin graft fixation using NPWT after skin graft is "off-label use" in some country like Japanese. The cost of the NPWT device and dressings is paid by the hospital in such country. In other countries, such as Europe and the United States, there are no restrictions on the use of NPWT after skin grafting. However, it should be used on a case-by-case basis because of cost issues, as described by Vidrine et al.[19]

The present systematic review has some limitations. The included studies were of poor quality and of relatively small size, and they had bias that cannot be ignored. Additionally, this review did not evaluate patient satisfaction with the NPWT dressing or patient-reported outcomes of NPWT dressing, as compared with those of conventional dressing. NPWT has been reported to be more comfortable for patients when used for skin graft fixation, especially when a single-use portable device is utilised.[31,47,49] Therefore, as far as patient satisfaction is concerned, NPWT may be more useful when there exists no considerable difference in skin graft failure.

In conclusion, compared with conventional bolster dressing, the use of NPWT dressing does not lead to significant improvements in the rate of successful graft take. Although NPWT improves hand functionality earlier, the cost for the device and dressings is a disadvantage. Therefore, the use of NPWT for skin graft fixation in the RFFF donor site is not generally recommended.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study

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