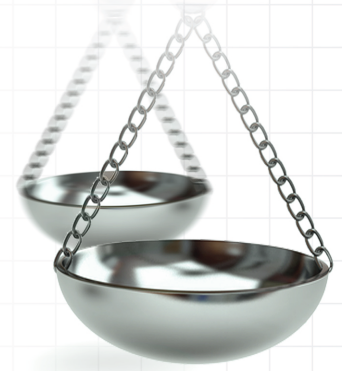




Negative pressure wound therapy in total hip and knee arthroplasty: a meta-analysis

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Journal of **Comparative
Effectiveness Research**

Aim: To assess the efficiency and safety of negative pressure wound therapy (NPWT) in the total hip and knee arthroplasty, we conducted a meta-analysis from randomized controlled trials. **Methods:** Potential academic articles were identified from the Cochrane Library, PubMed, Embase, Springer and ScienceDirect. Secondary sources were identified from the references of the included literature. RevMan 5.1 was used to analyze the pooled data. **Results:** Six randomized controlled trials met the inclusion criteria. Meta-analysis showed more superficial surgical site infection and blisters in patients with total knee arthroplasty. There were no significant differences between two groups in total infection and total complications. **Conclusion:** NPWT decreased the incidence of superficial surgical site infection. More blisters were noticed in patients with NPWT after total knee arthroplasty.

First draft submitted: 11 January 2019; Accepted for publication: 15 May 2019; Published online: 9 August 2019

Keywords: arthroplasty • hip • knee • negative pressure • wound

Total hip and knee arthroplasties (THA and TKA, respectively) are effective procedures to treat advanced stages of knee and hip osteoarthritis. Wound complications, especially the surgical site infection (SSI), are substantial problems. Although the rate of infection is relatively low (0.2–2.3%) [1], serious infection could require extra medical interventions and result in unsatisfactory outcomes [2]. Besides, extra money will cost for infections including surgical intervention, more tests and longer ward care. A recent retrospective study reported that infection significantly increased the cost of infection after total joint arthroplasty. Compared with the mean €7200 for a normal total joint arthroplasty, extra €12,800 were needed for debridement, antibiotics and implant retention treatment, and €44,600 for a two-stage revision [3]. Complex procedures also caused increased risk of heterotopic ossification after THA [4], high rate of joint dislocation [5].

Negative pressure wound therapy (NPWT) induces macro and micro deformation, improving wound healing. Besides that, NPWT decreases the accumulation of hematoma and seroma, producing a dryer wound, and with less chance of healing complication and infection. NPWT was reported to improve more formation of granulation and hasten wound closure by increasing blood flow, saturation of oxygen and stimulating angiogenesis [6]. NPWT has been proposed for closed wounds to provide a clean, dry wound environment in the immediate postoperative period [7]. Howell *et al.* performed a randomized clinical trial (RCT) to evaluate the effect of NPWT on intact postoperative wound after TKA. They found more blisters in the NPWT group than standard dressing group (63 vs 12%) [8]. Therefore, they stopped their study early on the behalf of safety and did not suggest its routine use in primary TKA. However, the device used in this study was an old version and modern devices were invented later. Promising effect of NPWT was showed in THA with significant reduction of seromas (44 vs 90%) in the closed wounds confirmed by ultrasound [9]. Recently, several studies demonstrated that NPWT was applied in total ankle arthroplasty [10], and TKA and THA [11–14]. The clinical effect of the application of NPWT in THA and TKA remains controversial.

Therefore, we conducted a large sample meta-analysis to evaluate the efficiency and safety of NPWT in THA and TKA from RCTs. Based on our clinical experience, we hypothesized that the NPWT can reduce SSI and perform differently for TKA and THA.

Materials & methods

Literature & search strategy

The meta-analysis was performed according to the prioritized reported items for systematic review and meta-analysis (PRISMA guidelines). The electronic databases, including PubMed, Cochrane CENTRAL, ScienceDirect and Embase were searched to identify the studies evaluating NPWT in THA or TKA from the inception of electronic databases to November 2018. Structured search strategies were used in combination, according to Boolean logic: 'negative pressure', 'arthroplasty or replacement', 'wound' and 'infection'. In addition, manual research of reference list was conducted for other potential included trials. The meta-analysis was based on acknowledged guidelines of the prioritized reported items for systematic review and meta-analysis.

Inclusion & exclusion criteria

Studies were considered eligible for inclusion if they satisfy the following criteria: population: patients treated with THA or TKA; intervention: NPWT, control: conventional dressing; outcome measures, one or more of the following outcomes were reported: SSI, reoperation, complications and other outcomes; and, study design: published RCTs.

We excluded articles that were studies without controlled groups; articles without available full-text versions; and no available outcomes data.

Data extraction & outcome measures

Two of the reviewers independently reviewed and extracted information from the identified studies including first author name, publication year, country, sample size, intervention characteristics and outcome measures. The major outcomes we concerned included SSI, wound complications (other than infection) and reoperation.

Quality assessment

The quality assessment of the randomized trial was conducted using the Cochrane Collaboration. The literature quality was evaluated separately by two reviewers. Consensus was reached through consultation for divergence.

Data analysis & statistical methods

The RevMan 5.1 (The Cochrane Collaboration, Oxford, UK) was used for analyzing the pooled data. Heterogeneity was estimated by the p-value and I^2 based on the standard χ^2 test. If there was significant heterogeneity ($I^2 > 50\%$, $p < 0.1$), a random-effects model was used for data analysis. When no significant heterogeneity was found ($I^2 < 50\%$, $p > 0.1$), a fixed-effects model was used for the data analysis. In cases of significant heterogeneity, a subgroup analysis was performed to investigate the sources. The mean differences and 95% CIs were determined for continuous outcomes. Dichotomous data were calculated by the odds ratio (OR) and 95% CIs.

Results

Search results

A total of 129 reports were identified as potentially relevant literature reports. By scanning title and abstract, 115 reports were excluded according to the eligibility criteria. Eight reports are eliminated after browsing the full text. Eventually, six RCTs were eligible for data extraction and meta-analysis. The searching process is shown in [Figure 1](#).

Study characteristics & risk of bias assessment

Demographic information of included studies was summarized in [Table 1](#) with statistically similar baseline between both groups. Two studies reported primary TKA [8,15], two studies reported primary THA [9,16] and one study reported primary TKA and THA [17]. Revisions of TKA and THA were performed in one study [12]. The data were pooled only from the randomized part in study by Manoharan *et al.* [15]. Sample size was from 9 to 107, including 320 cases in NPWT group and 339 patients in control group. Two major devices were applied with variable negative pressure of 80 or 125 mmHg. The duration of negative pressure ranged from 2 to 8 days. Details of the methodological quality of the included RCTs were illustrated in the [Figure 2](#).

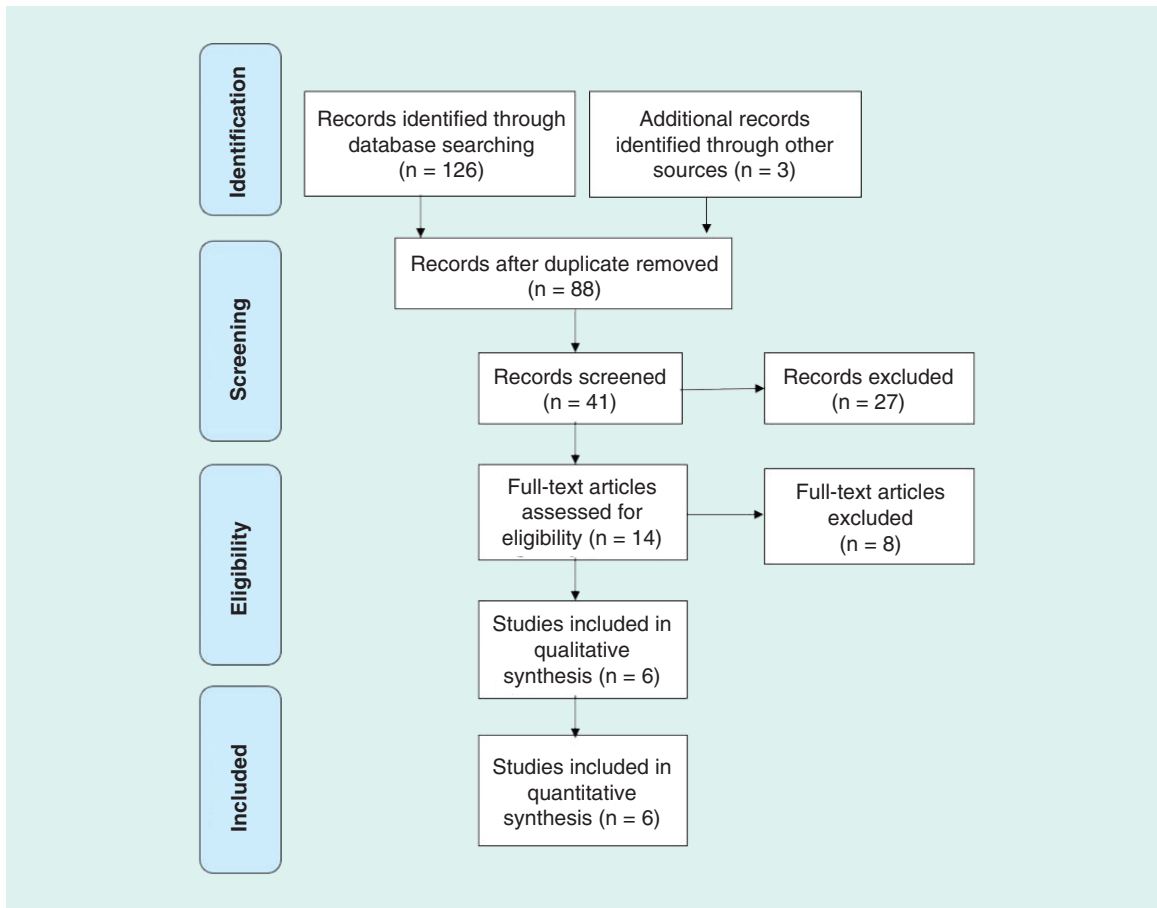


Figure 1. Flowchart of the study selection process.

Table 1. Characteristics of included studies.

Study	Year	Country	Type (primary or revision)	Device	Age (year)		Sample		Follow
					NPWT	Control	NPWT	Control	
Howell <i>et al.</i>	2011	USA	TKA (primary)	(KCI) 125 mmHg, 2 days	NA	NA	24	36	1 year
Pachowsky <i>et al.</i>	2012	Germany	THA (primary)	(KCI) 125 mmHg, 5 days	66.2 ± 17.8	70.0 ± 11.0	9	10	10 days
Gillespie <i>et al.</i>	2015	Australia	THA (primary)	(PICO) 80 mmHg, 5 days	63.8 ± 14.0	62.5 ± 12.4	35	35	6 weeks
Karlakki <i>et al.</i>	2016	UK	THA and TKA (primary)	(PICO) 80 mmHg, 7 days	69.0 ± 9.0	69.2 ± 9.0	102	107	6 weeks
Manoharan <i>et al.</i>	2016	Australia	TKA (primary)	(KCI) 125 mmHg, 8 days	NA	NA	21	21	NA
Newma <i>et al.</i>	2018	USA	THA and TKA (revision)	(KCI) 125 mmHg, 2 days	65 ± 11	65 ± 11	79	80	12 weeks
Giannini <i>et al.</i>	2018	UK	THA and TKA (revision)	(PICO) 80 mmHg, 7 days	66.8 ± 11.5	66.0 ± 8.9	50	50	7 days

KCI (Acelity company, TX, USA) and PICO (Smith & Nephew, Hull, UK, UK Prevena™ Incision Management System) were two kinds of negative pressure device.
NA: Not available; NPWT: Negative pressure wound therapy; THA: Total hip arthroplasty; TKA: Total knee arthroplasty.

Outcomes of meta-analysis

SSI was reported in three studies including deep incision infection in one study [8] and superficial infection in other two studies [16,17]. The organ or space infection was not counted in this study according to the function of NPWT on surgical incision. The incidence of total infection in NPWT group was 1.86% (3/161) while 6.18% (11/178) in control group. There was no significant difference between two groups in total infection (OR: 0.29; 95% CI: 0.08–1.05; $p = 0.06$) while less superficial infection in NPWT group (OR: 0.19; 95% CI: 0.04–0.90; $p = 0.04$). The deep incision infection was similar for NPWT group (1/24) and control group (1/36) in the only one study.

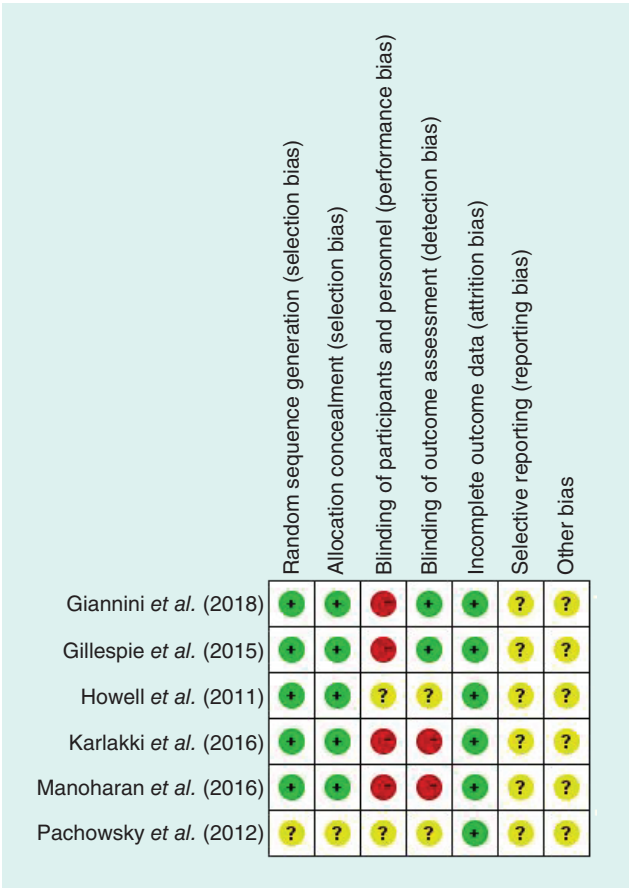


Figure 2. Risks of bias summaries for the randomized controlled trials.

Wound complications were reported in five studies. According to the number of patients who experienced wound complications, there were no significant difference between two groups (OR: 1.18; 95% CI: 0.21–6.60; $p = 0.85$). However, significant heterogeneity existed ($I^2 = 85\%$ and $p < 0.05$). First, sensitivity analysis was performed by excluding the study involving revision arthroplasty and no significant difference was found between two groups (OR: 1.76; 95% CI: 0.25–12.26; $p = 0.57$; $I^2 = 80\%$; $p < 0.05$). Further subgroup analysis according to primary TKA or THA did not confirmed no significant difference of wound complications between NPWT and control group with significant heterogeneity in THA subgroup (OR: 0.40; 95% CI: 0.03–5.85; $p = 0.50$; $I^2 = 80\%$; $p < 0.05$) or TKA subgroup (OR: 1.96; 95% CI: 0.12–32.45; $p = 0.64$; $I^2 = 85\%$; $p < 0.05$, Figure 3). Analysis based on number of total wound complications showed similar results in both groups. Because blister or seroma was a major or the only wound complication in some studies, meta-analysis showed more blisters in NPWT group following TKA (OR: 14.77; 95% CI: 4.45–48.97, $p < 0.05$; $I^2 = 0\%$; $p = 0.60$) while similar incidence for THA subgroup (OR: 0.85; 95% CI: 0.08–8.76; $p = 0.89$; $I^2 = 63\%$, $p = 0.07$; Figure 4). The trends of all these outcomes were not changed significantly after excluding the data from study by Howell *et al.*, in which an older device was used.

Re-operations were reported in two studies. Howell *et al.* showed one deep SSI in each group and both patients needed re-surgery for irrigation, debridement and polyethylene liner exchange [8]. One patient in control group in the study by Manoharan *et al.* was provided an extra negative therapy because of persistent wound drainage [15]. Limited by primary surgery or revision, we did not pool these data together.

Discussion

Due to the promising pain relief and improvement of function of hip or knee joints, THAs and TKAs continue to increase rapidly across the worldwide. Wound problems will cause huge economic cost and impact patient's quality of life. It is reported that more than 70% patients with wound complications were subsequently developed joint infections for THA or TKA [18]. The negative pressure therapy, which had perfect results in dealing open or

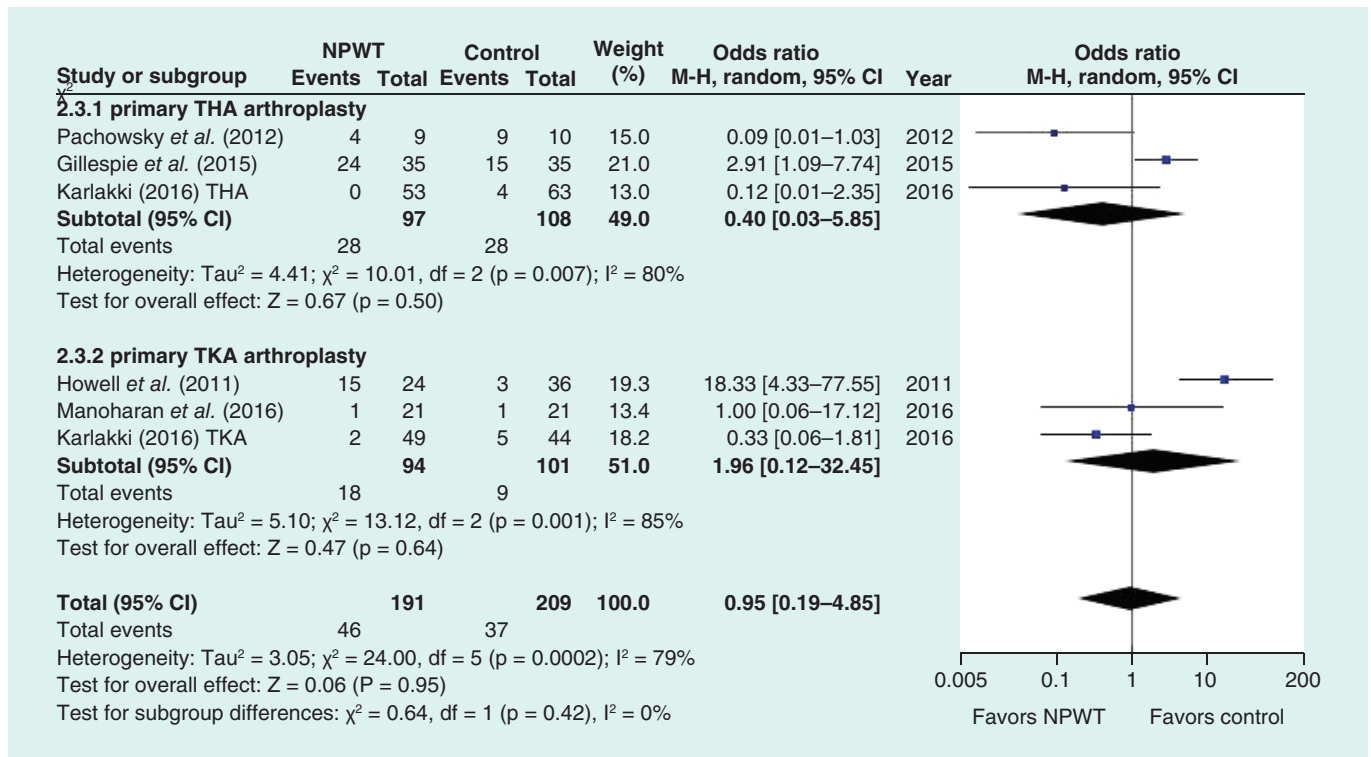


Figure 3. Forest plot showing total wound complications.

M-H: Mantel-Haenszel; NPWT: Negative pressure wound therapy; THA: Total hip arthroplasty; TKA: Total knee arthroplasty.

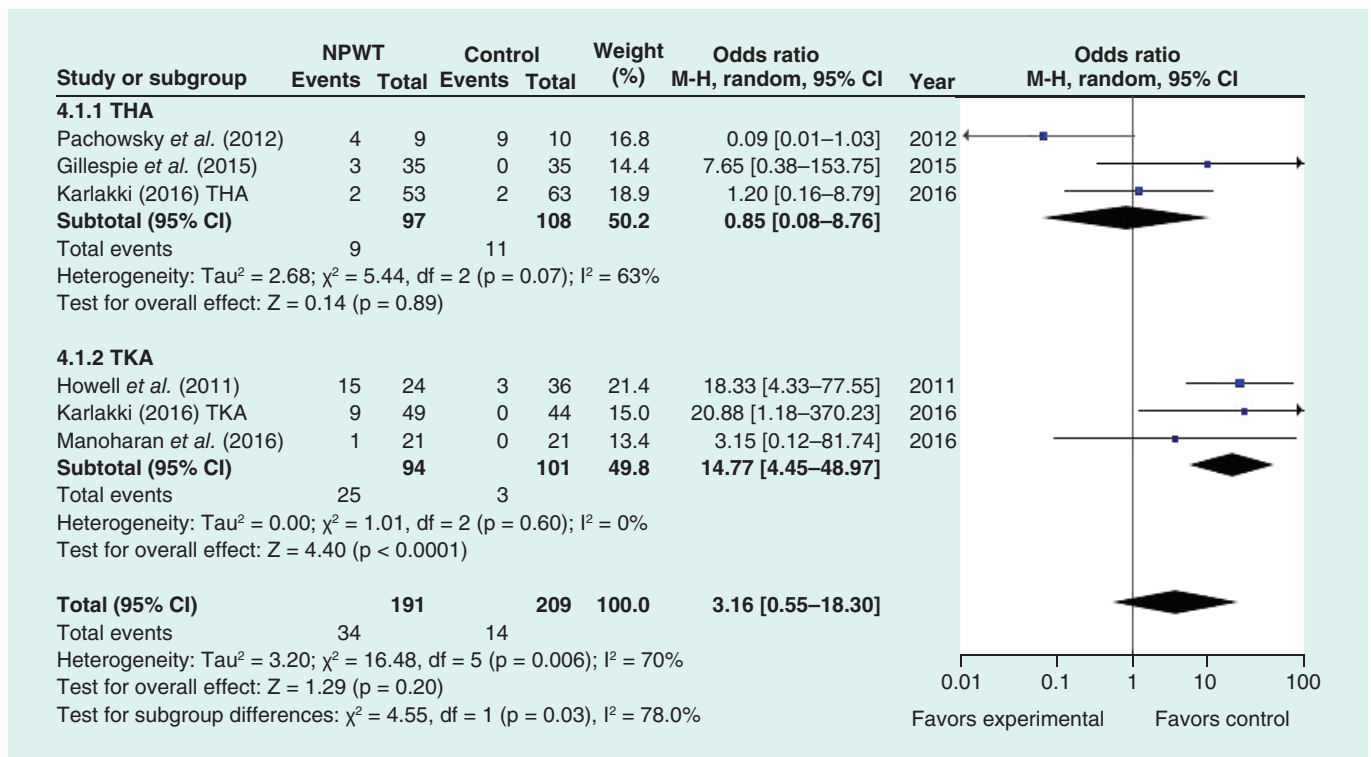


Figure 4. Forest plot showing wound blister.

M-H: Mantel-Haenszel; NPWT: Negative pressure wound therapy; THA: Total hip arthroplasty; TKA: Total knee arthroplasty.

chronic wound, was extended to arthroplasty [19]. The prophylactic use of NPWT after arthroplasty got support from several studies for patients who are at high risk for postoperative wound drainage [20].

Present meta-analysis pooled the results from RCTs and found that overall incidence of infection in NPWT group was 1.86% (3/161), which was less than that of 6.18% (11/178) in control group. Further analysis showed that NPWT only decreased the incidence of superficial SSI. Although the statistical p-value for deep infection was 0.06 while 0.04 for superficial site infection, we cannot draw a definitive conclusion because only three studies reported infection for TKA or THA, which weakened the confirming effect of NPWT on reducing infection. Besides, complexed comorbidities such as diabetes, obesity or smoking may influence the incidence of infection following THA or TKA [21,22]. Giannini *et al.* used the ASEPSIS score to quantitatively evaluate the severity of wound infection and found significantly higher ASEPSIS score of 10.5 in control group with more comorbidities than that of 5.4 in NPWT group [12]. Limited data of comorbidities could not be extracted for meta-analysis.

Except for definitive SSI, other wound complications were also reported in included studies. Present meta-analysis showed that NPWT do not decrease total complications in THA or TKA. Blisters were reported as the sole problems in some studies [8,9,12], and Howell did not suggest NPWT routine application in postoperative wound after primary TKA [8]. Friction of the negative dressing on intact skin was deemed as a reason for line blister formation. More comfortable devices have been designed and applied in knee arthroplasty after the one in study by Howell *et al.* Our results confirmed that more blisters were noticed in patients with NPWT following TKA while no difference following THA. Excluding the data from study by Howell did not change the situation. Relatively less soft tissue coverage of the knee than hip may lead to more blisters appeared following TKA. Besides, uncorrected procedure maybe another reason for more blisters [17].

Wound complications and related re-operations increase medical cost and length of hospitalization. Cooper *et al.* [23] and Newman *et al.* [11] showed lower re-operation rate in patients with NPWT. However, patients in their studies were following hip or knee revisions arthroplasty. And periprosthetic joint infection was one reason for revision in Newman's study. Two included studies reported the patients received subsequent re-operation. Howell *et al.* stated that irrigation, debridement and polyethylene liner exchange were reported for one patient in each group [8]. One patient in control group was provided an NPWT because of persistent wound drainage in the other study [15]. More studies are needed to further assess the effect of NPWT on re-operation.

Several potential limitations should be noted: only six RCTs were included, all of which had a relatively small sample size; methodological weaknesses exist in studies, the performance bias existed in four studies while detection bias in two studies; some outcome parameters were not fully described so that we failed to perform a meta-analysis; different duration of NPWT may bring some bias.

Conclusion

NPWT decreases the incidence of superficial SSI. More blisters were noticed on patients with NPWT after TKA. More high-quality RCTs are required due to the limited quality and data of the evidence currently available.

Summary points

- Total hip and knee arthroplasties (THA and TKA, respectively) are effective procedures to treat advanced stages of knee and hip osteoarthritis. Wound complications, especially the surgical site infection, are substantial problems.
- Negative pressure wound therapy (NPWT) induces macro and micro deformation, improving wound healing. Besides that, NPWT decreases the accumulation of hematoma and seroma, producing a dryer wound and with less chance of healing complication and infection.
- Recently, several published studies have reported on the oral application of NPWT in THA and TKA.
- A meta-analysis was conducted to evaluate the efficiency and safety of NPWT in THA and TKA from randomized controlled trials.
- PubMed, Cochrane CENTRAL, ScienceDirect and Embase searches (January 1966–November 2018) yielded 129 results; 6 studies were included for review.
- Meta-analyses were conducted using a fixed-effects or random model that reported odds ratio or mean differences and 95% credible intervals.
- More superficial surgical site infection and blisters were found in patients with TKA. There were no significant differences between two groups in total infection and total complications.
- NPWT decreased the incidence of superficial surgical site infection. More blisters were noticed in patients with NPWT after TKA.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

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