



Negative pressure wound therapy vs. conventional management in open tibia fractures: Systematic review and meta-analysis



Jun-Ho Kim, Dae-Hee Lee*

Department of Orthopaedic Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

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ABSTRACT

Background: Severe open tibia fractures are disastrous injuries associated with a high incidence of complications. Negative pressure wound therapy (NPWT) is a novel treatment for open tibia fractures; however, its efficacy remains unclear. This is a systematic review and meta-analysis performed to evaluate the effect of NPWT on decreasing the infection rate, amputation rate, nonunion rate, and flap-related complications in open tibia fractures.

Methods: The MEDLINE, EMBASE, and Cochrane Library databases were systematically searched. Complications were evaluated in terms of the rates of infection, amputation, nonunion, and flap-related complications.

Results: Twelve studies were included. In the meta-analysis, NPWT showed significantly lower soft-tissue infection rate (odds ratio [OR] 0.48, 95% confidence interval [CI] 0.34–0.68, $P < 0.0001$), nonunion rate (OR 0.61, 95% CI 0.39–0.95, $P = 0.03$), flap necrosis rate (OR 0.37, 95% CI 0.21–0.63, $P = 0.0003$), and flap revision rate (OR 0.44, 95% CI 0.22–0.89, $P = 0.02$) than conventional wound management. However, no significant difference was found in osteomyelitis rate (OR 0.54, 95% CI 0.09–3.28, $P = 0.50$) and amputation rate (OR 0.89, 95% CI 0.36–2.22, $P = 0.80$) between the 2 groups.

Conclusion: Lower rates of soft-tissue infection, nonunion, flap necrosis, and flap revision were observed in the NPWT group than in the conventional dressing group. However, additional high-quality studies are warranted to verify the efficacy of NPWT in the treatment of severe open tibia fractures. We could not make a definitive conclusion about the comparative efficacy of the 2 methods in terms of complications because of insufficient data.

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Introduction

High-energy open fractures are difficult-to-treat injuries that are frequently associated with complications. Open tibia fractures are particularly worse because they tend to show higher contamination, nonunion, and soft-tissue defects [1,2]. In the initial management, it is essential not only to temporarily fix the fracture but also to perform thorough debridement of the damaged soft tissue, which can lead to soft-tissue defects that often require flap coverage, especially in the treatment of Gustilo type III open tibia fractures [2–4]. As an open wound is relatively exposed to the nosocomial environment, wet-gauze sealing was traditionally applied to the wound until soft-tissue coverage was completed [2].

After negative pressure wound therapy (NPWT) was approved by the Food and Drug Administration in 1997, it has increasingly been used as an alternative form of dressing [2,5]. NPWT provides temporary soft-tissue coverage, reduces edema, and increases granulation tissue formation, which subsequently promotes wound healing [2,3,6]. Although several studies comparing between NPWT and conventional dressings have been conducted, the superiority of NPWT in reducing complications in open tibia fractures has not been conclusively established [3,5,7]. Further, few systematic reviews and meta-analysis have been performed to verify the effectiveness of NPWT, and those were only descriptive reviews, included very few studies, or included other types of wounds [2,8,9]. A recent systematic review and meta-analysis on the use of NPWT in the treatment of open fractures was reported; however, it did not focus on open tibia fractures [10].

Therefore, we performed a systematic review and meta-analysis to evaluate the effectiveness of NPWT in the treatment of open tibia fractures. We asked the following question: Does the use of NPWT in open tibia fractures decrease the rates of infection, am-

* Corresponding author at: Department of Orthopaedic Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 06351, Republic of Korea.

E-mail addresses: junojuno49@gmail.com (J.-H. Kim), eoak22@empal.com (D.-H. Lee).

putation, nonunion, and flap-related complications compared with conventional dressings?

Methods

Literature search

The study design was based on Cochrane review methods. This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [11]. According to the PRISMA guidelines, multiple comprehensive literature databases, including PubMed, EMBASE, Cochrane Library, Ovid MEDLINE, and SCOPUS, were searched for studies that evaluated the effectiveness of NPWT in the treatment of open tibia fractures. There were no restrictions on language or the year of publication. The search terms used in the title, abstract, Medical Subject Headings, and keyword fields included various combinations, as follows: (“negative pressure wound therapy” OR “sub-atmospheric pressure” OR “vacuum-assisted closure” OR “vacuum sealing”) AND (“tibia fractures” OR “diaphyseal tibia fractures” OR “tibia fractures” OR “tibia shaft fractures”) AND (“open fractures” OR “Guistilo III open fracture”).

Study selection

Two reviewers evaluated the titles and abstracts of the retrieved papers, and selected relevant studies for a full review. If

the abstract did not provide enough data, the full article was reviewed. Studies were included in the systematic review if they (1) included patients with open tibia fractures who underwent NPWT or application of conventional dressings for soft-tissue defects; (2) directly compared outcomes between NPWT and conventional dressings; and (3) completely reported the data, including means, standard deviations, sample numbers, and percentage of variables. Biomechanical and cadaveric studies, technical notes, letters to the editor, expert opinions, review articles, meta-analyses, scientific conference abstracts, and case reports were excluded. The exclusion criteria were as follows: (1) studies failing to provide a direct comparison between NPWT and conventional dressings; (2) studies in which the required data could not be obtained or calculated from the reported results; and (3) duplicate studies based on the same patients, which should have been counted as 1 study.

Data extraction

Two investigators independently extracted the following data from the included studies from both the NPWT group and the conventional dressing group (control group): patients’ age and sex, sample size, smoking status, follow-up period, initial injury severity including the Gustilo type, number of debridements before wound coverage, days until the wound was ready for closure, length of hospitalization, initial method of bony stabilization, definite method of soft tissue coverage, NPWT pressure level,

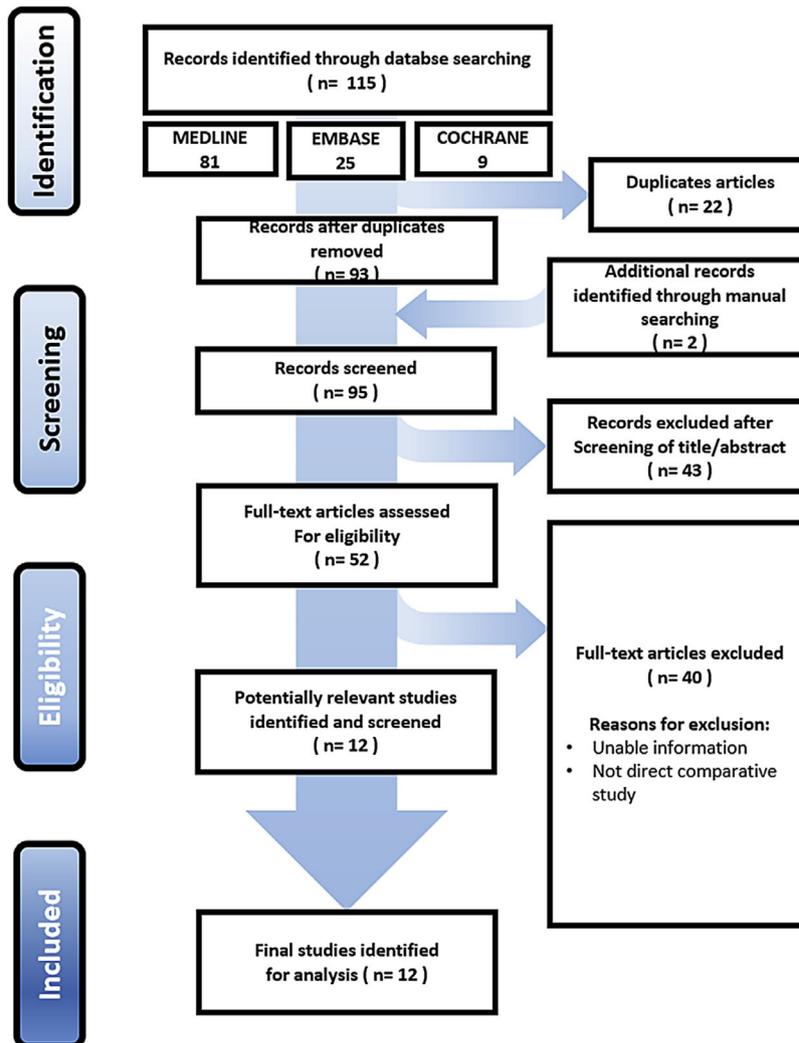


Fig. 1. This flow diagram shows the study search and selection process according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

soft-tissue infection, osteomyelitis, amputation, flap necrosis, and flap revision. Any disagreements unresolved by discussion were reviewed by a 3rd investigator, if needed.

Assessment of methodological quality

Two reviewers independently assessed the methodological quality of each study by using the Methodological Index for Non-randomized Studies (MINORS) checklist [12]. According to the MINORS checklist, the maximum scores are 16 for noncomparative studies and 24 for comparative studies. Furthermore, MINORS is a valid tool for assessing the qualities of randomized controlled trials (RCTs) as well as nonrandomized studies. Disagreements in scores were resolved by discussion and consensus between the 2 reviewers.

Statistical analysis

Data were analyzed using RevMan version 5.3 (Cochrane Collaboration) and STATA/MP 13.0. Dichotomous data were analyzed with the odds ratios (ORs), whereas standard mean differences with 95% confidence intervals (CIs) were calculated for continuous data. When the data were not mentioned in the articles, the study authors were contacted by email to request for the data. Heterogeneity was assessed using the I^2 statistic, in which 25% was considered low heterogeneity, 50% was considered moderate heterogeneity, and 75% was considered high heterogeneity. Forest plots were used to show the outcomes, pooled estimate of effects, and the overall summary effect of each study. Statistical significance was

set at $P < 0.05$. Data were pooled using a fixed-effect model if the I^2 value was within 50%. If the I^2 value was between 50% and 75%, a random-effect model was considered. If the I^2 value was $>75\%$ or definite heterogeneity existed, meta-analysis was abandoned and a descriptive review was adopted instead. Publication bias was also assessed using funnel plots and Egger's test.

Results

Identification of studies

Details of the study search and selection process are summarized in Fig. 1. Electronic search yielded 81 studies in PubMed (MEDLINE), 25 studies in EMBASE, and 9 studies in Cochrane Library. Two additional studies were identified through a hand search. After 22 duplicates were removed, 95 studies remained. After screening the titles and abstracts, and reading the full text, 83 studies were excluded. Thus, 12 studies were finally included. Of the 12 studies, 5 RCTs and 7 cohort studies were eligible for data extraction and meta-analysis.

Study characteristics and risk of bias assessment

A total of 1322 cases of tibia fractures were reported including 747 cases in the NPWT group and 575 cases in the control group. Details of study design, demographic data, follow-up period, percentage of smokers, and quality score (MINORS) of each included study are presented in Table 1. The median MINORS score of included studies was 15.5 of 24. In the NPWT group, a

Table 1
Details of study design, demographic data, quality scores, and summaries of results of the included studies.

| Study (year) | Study type | No. of tibias | | Mean age, years | | Percent male, % | | Mean follow-up, months (range) | | Percent smoking, % | | MINORS score |
|---|------------|---------------|---------|-----------------|---------|-----------------|---------|--------------------------------|-----------------|--------------------|---------|--------------|
| | | NPWT | Control | NPWT | Control | NPWT | Control | NPWT | Control | NPWT | Control | |
| Main findings | | | | | | | | | | | | |
| Arti et al. (2016) | RCT | 30 | 30 | 31.9 | | 24.4 | | 1.0 (NA) | | NA | | 19 |
| The NPWT group showed significantly better wound healing than the control group; however, there was no significant difference between the 2 groups in the incidence of infection. | | | | | | | | | | | | |
| Blum et al. (2012) | RCS | 166 | 63 | 40.3 | 36.8 | 76.1 | 78.7 | 13.7 (5.4-22) | 12.1 (4.8-56.9) | 25.6 | 29.5 | 20 |
| There was a lower rate of deep infection in the NPWT group than in the control group. | | | | | | | | | | | | |
| Costa et al. (2018) | RCT | 226 | 234 | 46.1 | 44.5 | 78.8 | 70.1 | Minimum 12 months | | 31.0 | 33.8 | 23 |
| The use of NPWT compared with conventional wound dressings did not improve self-related disability in the treatment of severe open tibia fractures at 12 months. | | | | | | | | | | | | |
| Jayakumar et al. (2013) | RCT | 20 | 20 | 32.0 | | NA | | 36.0 (NA) | | NA | | 15 |
| The infection rate in the NPWT group was much lower than that in the control group. Primary wound coverage can be done earlier in the NPWT group. The hospital stay was shorter and wound healing was faster in the NPWT group than in the control group. | | | | | | | | | | | | |
| Joethy et al. (2013) | RCS | 51 | 18 | 40.0 | 38.0 | NA | | NA | | NA | | 13 |
| The incidence of infection was statistically significantly lower in the NPWT group than in the control group. The incidence of flap failure was lower in the NPWT group; however, there was no significant difference between the 2 groups. | | | | | | | | | | | | |
| Labler et al. (2004) | RCS | 14 | 12 | 41.8 | 49.6 | 57.1 | 66.7 | Minimum 12 months | | NA | | 10 |
| The rate of infection in the NPWT group was substantially lower than that in the control group. The rates of amputation and nonunion were similar between the 2 groups. | | | | | | | | | | | | |
| Liu et al. (2012) | RCS | 78 | 25 | 42.3 | | 85.9 | 92.0 | Minimum 12 months | | 32.1 | 32.0 | 14 |
| NPWT provides effective temporary wound coverage but does not allow a delay in definitive free-flap reconstruction. | | | | | | | | | | | | |
| Parrett et al. (2006) | RCS | 53 | 35 | NA | | NA | | NA | | NA | | 7 |
| The results demonstrated a change in practice, with a trend of using fewer free flaps and increased delayed closure and use of skin grafts with the frequent application of NPWT. | | | | | | | | | | | | |
| Rezzadeh et al. (2015) | RCS | 12 | 20 | 37.4 | 37.8 | 91.7 | 90.0 | 31.0 (1-156) | | 16.7 | 40.0 | 15 |
| Compared with conventional open wound care, the use of NPWT reduced overall flap-related and non-flap-related complications associated with limb salvage surgery. | | | | | | | | | | | | |
| Rinker et al. (2008) | RCS | 17 | 38 | 40.0 | | NA | | 64.8 (16-186) | | NA | | 16 |
| The NPWT group had lower rates of overall complication, infectious complication, and flap-related complication than the control group. The time to union was significantly shorter with the NPWT dressings. | | | | | | | | | | | | |
| Stannard et al. (2009) | RCT | 37 | 25 | NA | | 74.3 | 56.5 | 28 (14-67) | | 51.4 | 30.4 | 23 |
| There was a significantly lower infection rate in the NPWT group than in the control group. The relative risk ratio was 0.199, suggesting that patients treated with NPWT were only one-fifth as likely to have an infection compared with the control group. | | | | | | | | | | | | |
| Virani et al. (2016) | RCT | 43 | 50 | 34.8 | 37.4 | 65.1 | 64.0 | 5.8 | | 25.6 | 28.0 | 21 |
| Patients in the control group had a significantly higher infection rate than those in the NPWT group. The relative risk was 5.5. All patients who developed osteomyelitis were from the control group. | | | | | | | | | | | | |

NPWT, negative pressure wound therapy; MINORS, Methodological Index for Nonrandomized Studies; NA, not applicable; RCT, randomized controlled trial; RCS, retrospective cohort study.

Table 2
Summary of fracture and treatment characteristics.

| Study (year) | Study indication of Gustilo and Anderson classification | No. of debridements before coverage | | Days until the wound was ready for closure | | Hospitalization days | | | Primary bony stabilization | | | | Definite soft-tissue coverage | | | | Details of wound management | | | |
|-------------------------|---|-------------------------------------|---------|--|---------|----------------------|---------|-------------------|----------------------------|-------------------|---------|----------------------------|-------------------------------|-------------------------|---------|-----------|-----------------------------|---------|---|---|
| | | NPWT | Control | NPWT | Control | NPWT | Control | Internal fixation | | External fixation | | Primary or delayed closure | | STSG or rotational flap | | Free flap | | | | |
| | | | | | | | | NPWT | Control | NPWT | Control | NPWT | Control | NPWT | Control | NPWT | | Control | | |
| Arti et al. (2016) | IIIB | NA | | NA | | 9.7 | | 11.2 | | NA | | | | | | | | | NPWT: Changed usually every 48 h and negative pressure continued for 10-14 days. Pressure was maintained at 125 mmHg continuously or intermittently (5 min on, 2 min off). Control Conventional dressings. | |
| Blum et al. (2012) | IIIA, IIIB, IIIC | 3.0 | 2.0 | 4.9 | 3.3 | 21.7 | | 19.1 | | NA | | | 55 | 28 | 55 | 26 | 56 | 9 | NPWT: VAC device was used. Control: Conventional dressings were variable including povidone-iodine-soaked gauze, saline-soaked wet-to-dry dressing, and paraffin gauze. NPWT: The exact details of the dressing and pressure level were left to the discretion of the treating health-care team. Control: Details of each dressing applied in the trial were recorded and classified according to British National Formulary classification. NPWT: VAC application Control: Sterile dressings | |
| Costa et al. (2018) | IIIA, IIIB, IIIC | NA | | NA | | NA | | | | 116 | 112 | 110 | 122 | | | | | | NPWT: 125 mmHg and continuous mode. Dressings were changed every 3-4 days. Control: Wounds were dressed with occlusive dressing. | |
| Jayakumar et al. (2013) | IIIA, IIIB | NA | | NA | | NA | | | | NA | | | | | | | | | NPWT: 125 mmHg and continuous mode. Dressings were changed every 3-4 days. Control: Wounds were dressed with occlusive dressing. | |
| Joethy et al. (2013) | IIIB | NA | | 10.8 | 16.8 | NA | | | | NA | | | 0 | 0 | 0 | 0 | 51 | 18 | NPWT: 125 mmHg and continuous mode. Dressings were changed every 3-4 days. Control: Wounds were dressed with occlusive dressing. | |
| Labler et al. (2004) | IIIA, IIIB | 4.3 | 2.2 | 12.3 | 4.1 | 53.3 | | 42.0 | | 1 | 4 | 13 | 8 | 1 | 3 | 4 | 2 | 9 | 7 | NPWT: Continuous negative pressure of 125 mmHg Control: Epigard system was used, which was covered with a sterile dressing. |
| Liu et al. (2012) | IIIA, IIIB, IIIC | 2.5 | 3.2 | NA | | NA | | | | NA | | | | 0 | 0 | 0 | 0 | 78 | 25 | NPWT or moist gauze dressings were applied before free-flap transfer; serial debridements were performed until the reconstructing surgeon was clinically satisfied with the wound vitality. |
| Parrett et al. (2006) | IIIA, IIIB, IIIC | NA | | NA | | NA | | | | NA | | | | | | | | | | Either NPWT or wet-to-wet dressing changes were performed. |

continued

| | | | | | | | | | | | | | | | | |
|------------------------|------------------|-----|-----|-----|------|------|----|----|----|----|---|---|----|----|----|--|
| Rezzadeh et al. (2015) | III B, IIIC | 6.3 | 8.0 | NA | 42.7 | 33.8 | NA | 0 | 0 | 0 | 0 | 0 | 12 | 20 | 20 | Either NPWT or wet-to-wet dressing changes were performed. |
| Rinker et al. (2008) | III B, IIIC | 3.2 | 3.2 | NA | 20.8 | 7.2 | NA | 0 | 0 | 0 | 0 | 0 | 17 | 38 | 38 | Either NPWT or wet-to-wet dressing changes were performed. |
| Stannard et al. (2009) | IIIA, IIIB, IIIC | 2.7 | 2.4 | 4 | 3.2 | 11.7 | NA | 21 | 18 | 14 | 6 | 0 | 0 | 1 | 1 | NPWT: VAC dressing with pressure of 125 mmHg over the open fracture. Control: Saline-soaked wet-to-moist dressings over the open fracture NPWT: 125 mmHg was applied intermittently. The wound was opened every 4th day for reapplication of dressing. Control: Daily cleaning, dressing, and debridement. |
| Virani et al. (2016) | IIIA, IIIB, IIIC | NA | 8.3 | 9.8 | NA | NA | 0 | 34 | 40 | 8 | 8 | 1 | 1 | 2 | 2 | NPWT: 125 mmHg was applied intermittently. The wound was opened every 4th day for reapplication of dressing. Control: Daily cleaning, dressing, and debridement. |

STSG, split-thickness skin graft; NPWT, negative pressure wound therapy; VAC, vacuum-assisted closure; NA, not applicable.

vacuum-assisted closure device (Kinetic Concepts Inc., San Antonio, TX) was applied. Details of wound management, Gustilo-Anderson classification, number of debridements before soft tissue coverage, days until the wound was ready for closure, days of hospitalization, percentage of external fixator for primary bony stabilization, and method of definite soft-tissue coverage are described in Table 2. Generally, publication bias need not be assessed if <10 studies were included. Thus, we only assessed the reported outcome with respect to soft-tissue infection. Funnel plots showed that the OR of soft-tissue infection was relatively symmetric, indicating absence of publication bias (Fig. 2). Egger's test also confirmed these trends in publication bias (P=0.451). Six parameters of clinical complication after treatment of open tibia fractures were compared between the 2 groups (Table 3).

Infection rates

Infection rate was divided into soft-tissue infection rate and osteomyelitis rate. Twelve studies compared the soft-tissue infection rate after treatment of open tibia fractures between the NPWT and control groups. The overall pooled soft-tissue infection rate was significantly lower in the NPWT group than in the control group (summary OR 0.48, 95% CI 0.34-0.68, P<0.0001) (Fig. 3A). However, in terms of osteomyelitis rate, the overall pooled result of 5 studies showed no difference between the NPWT and control groups (OR 0.54, 95% CI 0.09-3.28, P=0.50) (Fig. 3B).

Amputation rates

Six studies reported on the amputation rate in the lower extremity after treatment of open tibia fractures. The pooled analysis showed no difference between the NPWT and control groups (OR 0.89, 95% CI 0.36-2.22, P=0.80) (Fig. 4A).

Nonunion rates

Five studies compared the nonunion rates after treatment of open tibia fractures between the NPWT and control groups. The overall pooled analysis showed significantly lower nonunion rates in the NPWT group than in the control group (summary OR 0.61, 95% CI 0.39-0.95, P=0.03) (Fig. 4B).

Flap-related complication rates

Flap-related complication rate comprised flap necrosis rate and flap revision rate. The flap necrosis rates included the total flap necrosis rates and partial flap necrosis rates in the present study. Seven studies reported the flap necrosis rate. The pooled analysis showed significantly lower flap necrosis rates in the NPWT group than in the control group (summary OR 0.37, 95% CI 0.21-0.63, P=0.0003) (Fig. 5A). In terms of flap revision rates, the overall pooled result of 5 studies showed that the rate was lower in the NPWT group. The summary OR was 0.44, and significantly in favor of the use of NPWT (95% CI 0.22-0.89, P=0.02) (Fig. 5B).

Discussion

The principal finding of this study was that NPWT might reduce the risk of complications such as soft-tissue infection, nonunion, and flap-related complications compared with conventional dressings in severe open tibia fractures.

Open tibia fractures usually result from high-energy trauma and occur with severe soft-tissue injuries [13,14]. As the tibia is covered by thin soft-tissue, open tibia fractures are associated with more complications than other open fractures [15,16]. The main difficulty in the treatment of open tibia fractures is

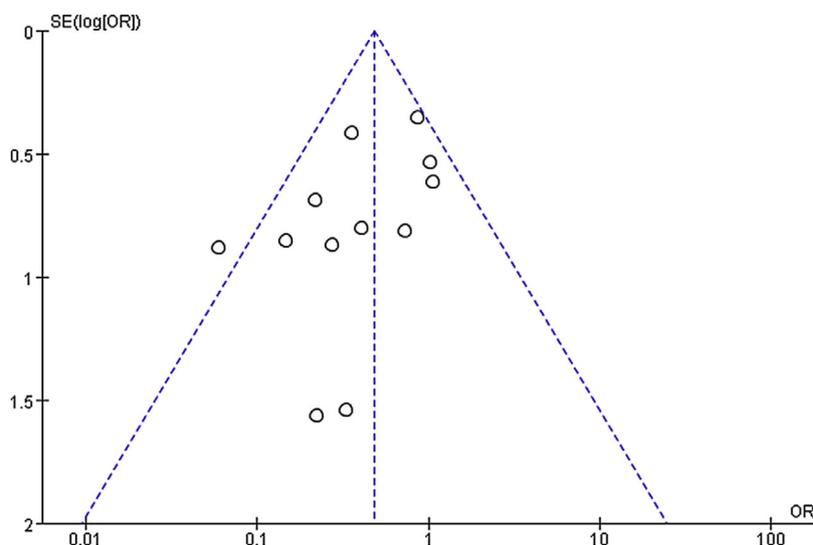


Fig. 2. This funnel plot shows the relatively symmetrical data of the incidence of soft-tissue infection comparing between the negative pressure wound therapy group and the control group. SE, standard error; OR, odds ratio.

Table 3

Overall clinical complication in the included studies.

| Study (year) | No. of tibias | | Soft-tissue infection (%) | | Osteomyelitis (%) | | Amputation (%) | | Nonunion (%) | | Flap necrosis (partial or total) (%) | | Flap revision (%) | |
|-------------------------|---------------|---------|---------------------------|---------|-------------------|---------|----------------|---------|--------------|---------|--------------------------------------|---------|-------------------|---------|
| | NPWT | Control | NPWT | Control | NPWT | Control | NPWT | Control | NPWT | Control | NPWT | Control | NPWT | Control |
| Arti et al. (2016) | 30 | 30 | 10.0 | 13.3 | NA | | NA | | NA | | 20.0 | 35.6 | 3.3 | 3.3 |
| Blum et al. (2012) | 166 | 63 | 8.4 | 20.6 | NA | | NA | | 28.9 | 34.9 | 2.7 | 5.6 | NA | |
| Costa et al. (2018) | 226 | 234 | 7.1 | 8.1 | NA | | 1.8 | 2.6 | 4.4 | 7.7 | NA | | NA | |
| Jayakumar et al. (2013) | 20 | 20 | 35.0 | 90.0 | NA | | NA | | NA | | NA | | NA | |
| Joethy et al. (2013) | 51 | 18 | 9.8 | 33.3 | NA | | NA | | NA | | 5.9 | 11.1 | NA | |
| Labler et al. (2004) | 14 | 12 | 21.4 | 50.0 | 0.0 | 0.0 | 7.1 | 8.3 | 14.3 | 25.0 | 0.0 | 16.7 | 28.6 | 28.6 |
| Liu et al. (2012) | 78 | 25 | 24.4 | 24.0 | 16.7 | 0.0 | NA | | NA | NA | 41.0 | 52.0 | 24.4 | 44.0 |
| Parrett et al. (2006) | 53 | 35 | 15.1 | 14.3 | NA | | NA | | NA | | NA | | NA | |
| Rezzadeh et al. (2015) | 12 | 20 | 25.0 | 45.0 | 0.0 | 30.0 | 0.0 | 0.0 | 8.3 | 40.0 | 0.0 | 15.0 | 33.3 | 35.0 |
| Rinker et al. (2008) | 17 | 38 | 0.0 | 7.0 | 5.9 | 9.3 | 5.9 | 4.7 | 5.9 | 7.0 | 17.6 | 39.5 | 11.8 | 18.6 |
| Stannard et al. (2009) | 37 | 25 | 5.4 | 28.0 | NA | | 5.4 | 0.0 | NA | | NA | | NA | |
| Virani et al. (2016) | 43 | 50 | 0.0 | 4.0 | 4.7 | 18.0 | 0.0 | 2.0 | NA | | NA | | NA | |

NPWT, negative pressure wound therapy; NA, not applicable.

wound management [17]. NPWT is commonly used to manage open tibia fractures, and it has shown many advantages in promoting wound healing [2]. However, there are some concerns about cost-effectiveness, skin maceration, and blister formation [18–20]. Although many previous studies have compared the 2 dressing methods with respect to complications after open tibia fractures, these comparative studies have not consistently demonstrated either method to be superior [1,3,7]. To our knowledge, this is the first systematic review and meta-analysis to evaluate NPWT and conventional dressings focusing on open tibia fractures.

This study suggests that NPWT results in lower soft-tissue infection rates than conventional dressings in the treatment of open tibia fractures. Our findings are in concordance with the results of previous systematic reviews, although they included either few studies or fractures involving whole bones [2,10]. As the incidence of infection remains high (up to 66%), the present results might provide evidence supporting the treatment of open tibia fractures with NPWT [7,21,22]. According to our meta-analysis, the OR was 0.48, which indicated that NPWT could reduce the infection rate by half. This may be a consequence of the effect of NPWT on bacterial clearance and resultant inflammatory cells, as reported in prior experimental studies [5,23,24]. Further, im-

proved local tissue perfusion and accelerated wound-healing process might have contributed to the lower infection rates in the NPWT group [10,25]. Although soft-tissue infection commonly extends to the bone, resulting in osteomyelitis, the current systematic review failed to demonstrate a significant difference between the 2 groups.

Our study showed no differences between the 2 groups in amputation rates. This might be because of preoperative intergroup incomparability or inadequate sample size. The reason for amputation after open tibia fractures is multifactorial. Moreover, patients who underwent primary or secondary amputation were ambiguously combined in the pooled studies, because primary amputation might be the result of injury severity, not of the lack of efficacy of dressing methods [1,17,25].

The current study showed that the nonunion rate was lower with NPWT than with conventional dressings. A recent systematic review failed to find any advantage or disadvantage of NPWT in terms of nonunion rate, although the study did not focus on open tibia fractures [10]. However, our systematic review and meta-analysis showed an overall OR of 0.61 (95% CI 0.39–0.95, $P=0.03$), indicating that NPWT would facilitate healing of open tibia fractures. Fracture healing in severe open tibia fractures is always

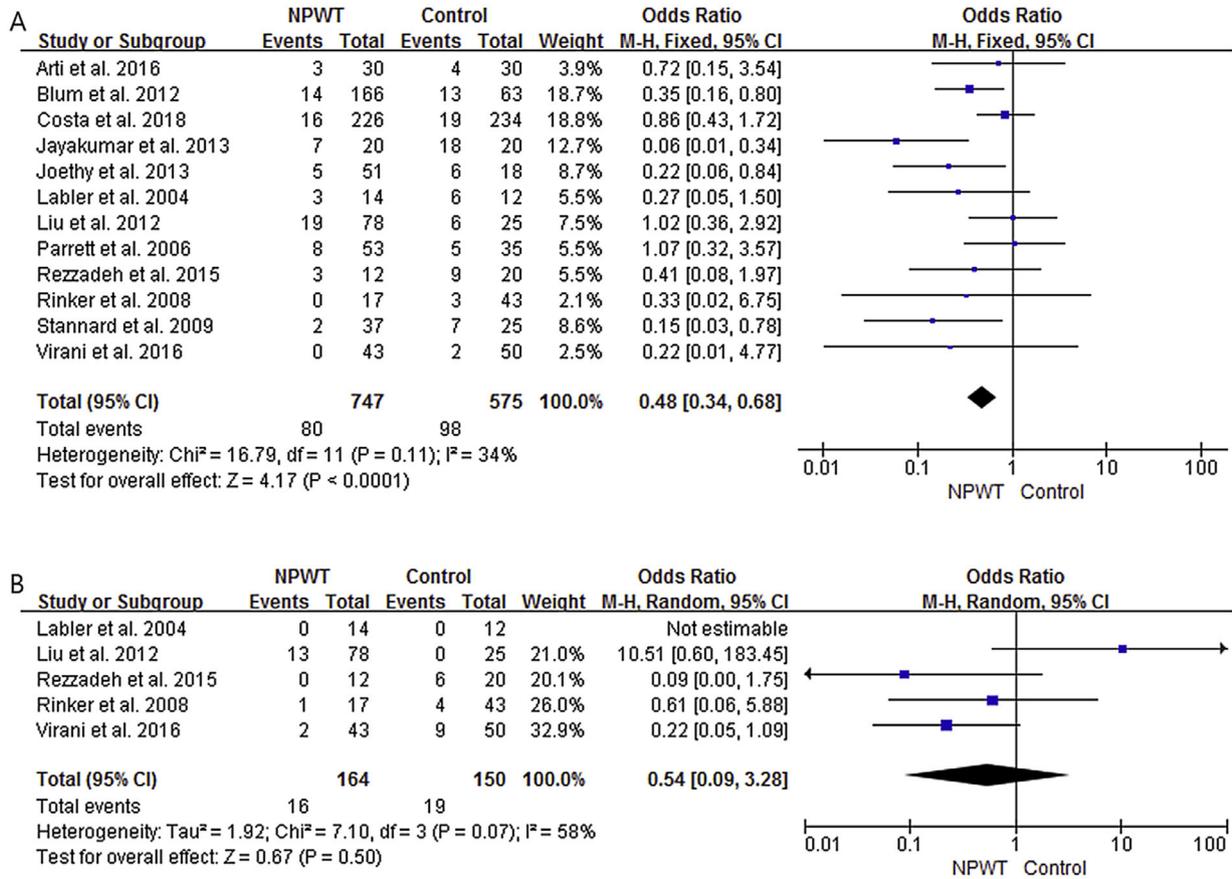


Fig. 3. A–F. These forest plots show the overall results of pooled studies reporting the soft-tissue infection rate (A), osteomyelitis rate (B), amputation rate (C), nonunion rate (D), flap necrosis rate (E), and flap revision rate (F). NPWT, negative pressure wound therapy; CI, confidence interval.

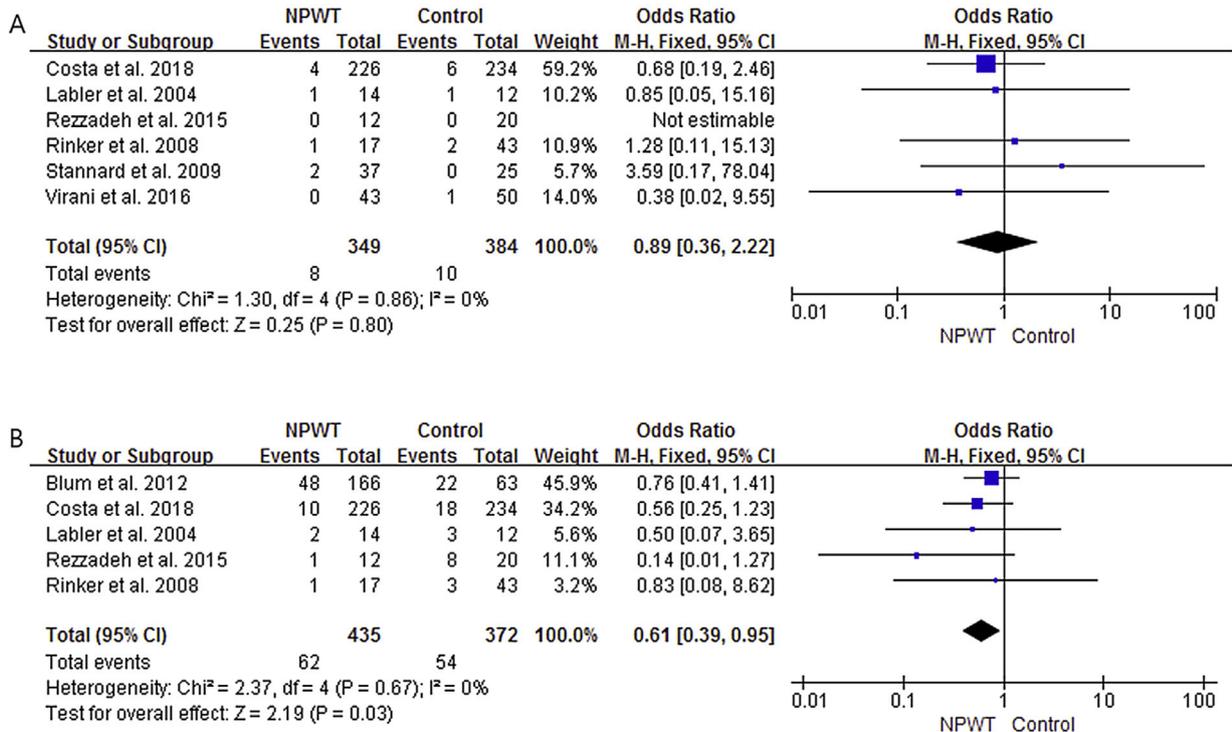


Fig. 4. A,B. These forest plots show the overall results of pooled studies reporting the amputation rate (A) and nonunion rate (B). NPWT, negative pressure wound therapy; CI, confidence interval.

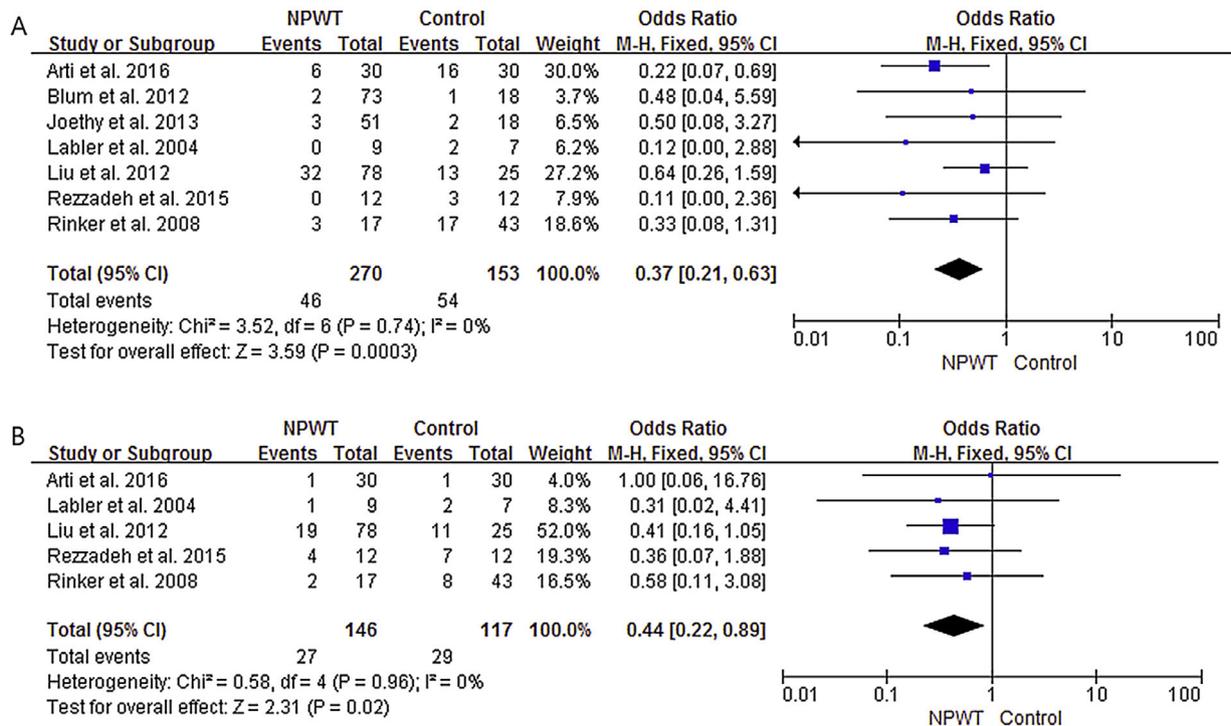


Fig. 5. A,B. These forest plots show the overall results of pooled studies reporting the flap necrosis rate (A) and flap revision rate (B). NPWT, negative pressure wound therapy; CI, confidence interval.

challenging, which often leads to considerable problems requiring additional surgery such as bone grafting or bone transfer.

Castillo et al. [26] reported that 58% of open tibia fractures required repeated operations to stimulate bone union. Previous studies demonstrated that nonunion is correlated with increased infection rates [15,27,28]. Our study showed that NPWT might reduce the infection rate, which would consequently decrease the nonunion rate of open tibia fractures. Although NPWT seemed to have significantly reduced the complications associated with failure of bony union in the current study, the success of fracture healing could be mainly influenced by the fixation method used in open tibia fractures. However, the pooled studies reported limited details about fixation.

In Gustilo-Anderson type IIIB/C open tibia fractures, soft-tissue coverage including flap procedures is necessary because primary closure is difficult [2,15]. Flap failure is a constant concern of surgeons. This systematic review analyzed the efficacy of NPWT against flap-related complications comprising flap necrosis (partial or total) and flap revision. Our literature search revealed that NPWT could reduce both flap necrosis and flap revision. The effect of NPWT on flap necrosis has been controversial. A high negative pressure level (>100 mmHg) might be a risk factor for flap necrosis, because degeneration and necrosis of bones, tendons, and nerves are inevitable with irreparable circulatory damage [10,29]. However, in the present study, a significant difference was observed in favor of NPWT in terms of flap necrosis, although the pressure level in the pooled data was mostly 125 mmHg. This indicates that NPWT may be safe in terms of flap necrosis. Revision of flap surgery is a devastating problem because of its surgical difficulty, financial demand, and effect on the patient's life quality [21,30]. The higher flap revision rate may be due to nosocomial wound infection, tissue fibrosis, and flap necrosis [2]. Pooled analysis showed that NPWT reduced the incidence of flap revision, compared with conventional dressings. One possible advantage of NPWT in flap surgery is that it simplifies complex wounds by promoting tissue granulation, which makes flap procedures easier to

perform [21]. Further, the beneficial effects of NPWT on the wound bed (preventing a chronic wound environment, including edema, hypoxia, necrosis, and fibrosis) may have contributed to the lower flap revision rate [21,25]. However, the reasons for flap failure can be multifactorial. Therefore, the application of NPWT before flap surgery should be done with caution, until its precise effect on flaps is fully elucidated.

This study has several limitations. First, the included studies were mostly cohort studies, although systematic reviews and meta-analyses provide the strongest evidence when pooling data from high-quality RCTs. Second, the injury severity and treatment protocol varied, and not all studies reported the details. Moreover, limited and nonspecific information about either bony stabilization or soft-tissue coverage was reported. This heterogeneity could be a potential confounder. Third, because the number of studies per variable was small except for the soft-tissue infection rate, drawing conclusion about the efficacy of NPWT should be done with caution.

Conclusion

We believe that the present results, which are based on the best available evidence, lend some support for the stronger consideration of wound management with NPWT when treating patients with severe open tibia fractures. This meta-analysis demonstrates lower rates of soft-tissue infection, nonunion, flap necrosis, and flap revision in the NPWT group than in the conventional dressing group. However, additional high-quality studies should be performed to verify the efficacy of NPWT in the treatment of severe open tibia fractures.

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