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Negative Pressure Wound Therapy versus Conventional Dressing in Lower Limb Fractures: Systematic Review and Meta-analysis

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Summary: Gustilo 3 lower limb fractures represent a significant challenge because of high complication risk. Two management strategies are commonly used for wound coverage until final closure: negative pressure wound therapy (NPWT) and conventional wound dressing (CWD), also described as standard wound coverage without subatmospheric pressure. Understanding their relative effectiveness is essential to improve patient outcomes. The aim of this systematic review and meta-analysis was to compare the efficacy of NPWT and CWD in Gustilo 3 lower limb fracture management, with a focus on overall rates, superficial infection, and deep infection rates. A systematic review of medical research databases was conducted in accordance with PRISMA guidelines. Studies comparing NPWT with CWD for Gustilo 3 fractures were included. Data extraction and quality assessment were performed. Treatment with CWD was associated with significantly higher rates of overall infection [pooled risk ratio (RR): 0.33; 95% confidence interval (CI): 0.14–0.51] and pooled risk difference (RD: 0.27; 95% CI: 0.15–0.38), superficial infection (pooled RR: 0.35; 95% CI: 0.04–0.66), and deep infection (pooled RR: 0.20; 95% CI: 0.02–0.38) compared with NPWT treatment. Overall infection rate remained significantly higher in the CWD group after analyzing only open tibia fractures (pooled RR: 0.35; 95% CI: 0.21–0.48). Nonunion rate was significant higher in the CWD group (pooled RR: 0.30; 95% CI: 0.00–0.59). Flap failure rate was similar in both groups (pooled RR: 0.09; 95% CI: −0.05 to 0.23). NPWT appears to be a reasonable option for wound management in Gustilo 3 lower limb fractures in terms of infection rates. *(Plast Reconstr Surg Glob Open 2024; 12:e5806; doi: 10.1097/GOX.0000000000005806; Published online 15 May 2024.)*

INTRODUCTION

Gustilo 3 fractures, defined as extensive soft-tissue damage with open wounds, represent an important challenge in trauma care.[1] In the lower limb, these fractures are notorious for their high rate of complications, including infection, the need for additional procedures, and high flap failure rate when reconstruction involves tissue transfers.[2,3] Compared with Gustilo fractures type 1 and 2, treatment of Gustilo 3 fractures is associated with higher healthcare costs and prolonged hospital stays.[4] Gustilo 3B fractures represent a significant subset of open fractures, oftentimes affecting the lower limbs, and are known for their challenging medical management. These fractures are distinguished by severe bone injuries, extensive soft-tissue damage, and the imperative for intricate reconstructive surgery.[5]

The complexity of these injuries complicates wound care and increases susceptibility to infections.[6] Severe open bone fractures that are frequently comminuted or substantially displaced add a layer of difficulty in managing soft-tissue damage and can hinder realignment and healing.[7]

Moreover, Gustilo 3B fractures necessitate free flap surgical coverage.[8] This becomes imperative to address exposed bones or hardware and restore essential blood flow.

In 1986, Godina[9] introduced a fundamental concept in lower limb injury treatment, advocating free flap reconstruction within the first 72 hours after injury. This approach has been demonstrated to significantly reduce

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free flap failure, infections, and need for subsequent surgical interventions.[10] However, early reconstruction in hospitals without specialized trauma center or in war settings is difficult to achieve.[11,12] Additionally, performing early reconstruction in all cases of Gustilo 3 fractures can be impractical, particularly when patients have associated injuries and underlying medical conditions that may delay the final reconstruction.[13]

In most centers, management of Gustilo type 3 fractures follows a multistage approach, typically using a systematic algorithm, to handle open fractures and improve patient outcomes while minimizing complications.[14] Initial measures to address infection risks include tetanus prophylaxis, wound irrigation, debridement, and broad-spectrum antibiotic administration. Temporary fracture stabilization follows, to restore anatomical alignment, especially in Gustilo 3 fractures or severe cases with soft-tissue contamination, where external fixation acts as a bridge. Soft-tissue management aims to optimize final wound closure and replace compromised tissues. Depending on wound extent, either delayed closure, skin graft, or flap reconstruction can be performed.

In the absence of early reconstruction, provisional wound coverage is crucial.[2] Two main approaches have emerged to address this critical problem: negative pressure wound therapy (NPWT) and conventional wound dressing (CWD).[15,16] Both CWD and NPWT are used to treat Gustilo 3 lower limb fractures. NPWT produces a negative pressure environment that enhances blood flow, reduces edema, and may lessen bacterial colonization while promoting wound healing.[17–20] Conversely, CWD, which includes bandages and gauze among other topical dressings, is easier to apply, seals the wound, and absorbs exudate.[21] NPWT is more expensive and needs specific tools and training but has advantages in wound care, especially for complicated fractures.[22,23] CWD is inexpensive, adaptable, and simple to use but may be less effective for deep wounds and needs more frequent changes.[24,25] Although NPWT has evolved considerably and has become widely adopted in a variety of clinical settings, with promising results in terms of wound healing, reduced infection, and shorter hospital stays,[26–29] its specific application in Gustilo 3 fractures continues to be an area of investigation with limited literature.[6,30] The purpose of this study was to conduct a systematic review and meta-analysis to comprehensively assess outcomes of NPWT versus CWD in Gustilo 3 lower limb fractures.

METHODS

Study Design and Registration

A systematic review and meta-analysis were conducted to assess the effectiveness of NPWT compared with CWD in the management of Gustilo 3 lower limb fractures. The study was conducted in accordance with PRISMA guidelines.[31] The protocol for this study was prospectively registered on the Prospective International Register of Systematic Review (registration ID: CRD42023466050).

> **Takeaways**
>
> **Question:** Does negative pressure wound therapy (NPWT) provide better outcomes compared with conventional wound dressing (CWD) in the management of Gustilo 3 fractures of the lower limb?
>
> **Findings:** Treatment with NPWT was associated with significantly lower overall, superficial, deep infection, and nonunion rates compared with CWD in the management of Gustilo 3 lower limb fractures. The overall flap failure rate was similar with both treatment modalities.
>
> **Meaning:** NPWT is an efficient wound coverage option in lower limb open fractures until definitive reconstruction.

Search Strategy

A systematic literature review of PubMed/MEDLINE, Web of Science, and the Cochrane Library was conducted on June 30, 2023. Search terms including a combination of Medical Subject Headings (MeSH) and keywords related to Gustilo 3 lower limb fractures, NPWT and conventional dressings, linked with Boolean operators (AND, OR), were used to construct the search queries: (((((((negative pressure wound therapy) OR (negative-pressure wound therapy)) OR (NPWT)) OR (sub-atmospheric pressure dressing)) OR (VAC)) OR (vacuum-assisted closure)) OR (vacuum assisted closure)) AND (open fracture).

Inclusion and Exclusion Criteria

Studies comparing the use of NPWT and CWD for the management of Gustilo 3 fractures were included if the design was randomized controlled trials (RCTs), non-RCTs, cohort studies, and case-control studies. Studies published in English were included, with no restriction on publication year. Studies were excluded if they did not meet the inclusion criteria or if they were conference abstracts, reviews, case reports, or animal studies. Only studies comparing NPWT and CWD reporting outcomes specifically referring to Gustilo type 3 fractures in the lower limbs were included. Noncomparative studies, studies on Gustilo types 1 and 2 fractures, and studies on fractures in regions other than the lower limbs were excluded. Primary outcomes of interest included overall, superficial and deep infection rates. Superficial infection was clinically defined as a soft-tissue infection located above the deep fascia with purulent discharge at the wound site. Deep infection was defined as contamination occurring below the deep fascia or osteomyelitis. The overall infection outcome involved consolidating all reported infections from each study, including cases with both superficial and deep infections, and cases of only superficial or only deep infections. Secondary outcomes included flap failure and nonunion.

Data Extraction and Management

The resulting articles were processed using Rayyan (https://www.rayyan.ai/; accessed on July 3, 2023), the blind initial screening of titles and abstracts for deduplication and to identify potentially eligible studies was then carried out by three authors (A. S. A., J. M., and M. S.). Disagreements were solved after consultation with the senior author (C. M.O). Selected articles were then retrieved and fully read for further evaluation. Data extraction was performed using a standardized data extraction form, which included information on study characteristics (author, year of publication, study design), participant characteristics (sample size, age, gender), intervention details (NPWT, CWD), and relevant outcome measures.

Quality Assessment

The methodological quality of studies was assessed independently by two reviewers (A. S. A. and J. M.) using the Cochrane risk-of-bias tool for RCTs and the risk of bias in nonrandomized studies of interventions tool for nonrandomized studies.[32–35] Studies were classified as having low, moderate, high, or unknown risk of bias.

Summary and Analysis of Data

A meta-analysis was performed for outcomes where data from several studies were available and sufficiently homogeneous. Heterogeneity was quantified using the I^2 value. Levels of heterogeneity were defined as low and high at values of I^2 less than 25% and I^2 greater than or equal to 25%, respectively.[36] Pooled effects estimates were calculated using fixed-effects Mantel–Haenszel models in the case of low heterogeneity and a random-effect DerSimonian-Laird model in the case of high heterogeneity.[37,38] Publication bias was assessed using funnel plots and the nonparametric trim-and-fill analysis. Finally, the Egger test was used to assess the effect of small studies.[39] Statistical analysis was performed using STATA (StataCorp, 2023, Stata Statistical Software: Release 18; StataCorp LLC, College Station, Tex.).

Subgroup and Sensitivity Analyses

Subgroup analyses were planned according to study design, fracture subtype (3a, 3b, 3c), and localization (tibia). Sensitivity analyses were performed to explore the robustness of the results.

RESULTS

Study Selection and Eligibility

We initially identified 456 articles (Fig. 1). After elimination of duplicates and screening of titles and abstracts, 27 articles were fully read, with six studies meeting inclusion criteria. In addition, three relevant articles were identified by reviewing the references of the included studies, yielding to the final inclusion of nine studies.[40–48]

Study Characteristics

The selected studies, published between 2004 and 2022, reported 535 lower limb fractures classified as Gustilo 3 (Table 1), with 323 managed with NPWT and 212 treated with CWD. The studies were conducted in various regions, including three in India,[43,47,48] two in the United States,[41,42] one in Iran,[45] one in Australia,[44] one in Switzerland,[40] and one in Singapore.[46] Five studies were RCTs and four were retrospective studies. Three studies reported all Gustilo 3 types (3a, 3b, 3c), three reported types 3a and 3b, one reported types 3b and 3c, and two focused exclusively on type 3b fractures. Of the total 535 Gustilo 3 open fractures, 71 were categorized as 3a, 276 as 3b, and 5 as 3c, and 183 Gustilo 3 fractures were not specifically categorized. When reported, the mean wound size ranged from 63 to 192 cm^2.[42,43,46] Eight studies explicitly mentioned the use of vacuum-assisted closure with −125 mm Hg continuous pressure as a specific NPWT modality and three of them specifically mentioned using V. A. C. (Kinetic Concepts, Inc, San Antonio, Tex.). Conventional dressing was defined differently across studies, encompassing wet-to-dry dressing, wet-to-wet dressing, sterile dressing, Epigard (Biovision GmbH, Ilmenau, Germany), or standard dressing.

Quality Assessment

According to the Cochrane risk-of-bias tool for RCTs, all included studies had unclear risk of bias (Fig. 2). Using the risk of bias in nonrandomized studies of interventions tool for non-RCTs, the quality of two studies was unclear; one displayed moderate quality; and there was one serious issue due to bias regarding confounding, selection of participants, and outcome measurement.

Meta-analysis Results

Compared with the NPWT group, patients treated with CWD had significantly higher overall infection rate [pooled relative risk (RR) ratio: 0.33; 95% confidence interval (CI): 0.14–0.51; I^2: 0.00%; $P = 0.0006$ and pooled risk difference (RD): 0.27; 95% CI: 0.15–0.38; I^2: 57.09%; $P = 0.0000$], superficial infection rate (pooled RR: 0.35; 95% CI: 0.04–0.66; I^2: 64.42%; $P = 0.03$ and pooled RD: 0.27; 95% CI: 0.07–0.46; I^2: 72.23%; $P = 0.01$), and deep infection rate (pooled RR: 0.20; 95% CI: 0.02–0.38; I^2: 71.21%; $P = 0.03$ and pooled RD: 0.18; 95% CI: 0.03–0.32; I^2: 76.23%; $P = 0.01$; Figs. 3 and 4). Moreover, a significant reduction of nonunion rate was observed in the NPWT group (pooled RR: 0.30; 95% CI: 0.00–0.59; I^2: 0.00%; $P = 0.0489$ and pooled RD: 0.23; 95% CI: 0.02–0.44; I^2: 0.00%, $P = 0.04$). However, no significant difference was observed in the flap failure rate between both treatment techniques (pooled RR: 0.09; 95% CI: −0.05 to 0.23; I^2: 0.00%; $P = 0.21$ and pooled RD: 0.09; 95% CI: −0.03 to 0.20; I^2: 0.00%; $P = 0.14$).

Assessment of Heterogeneity and Subgroup Analysis

Heterogeneity between the included studies was assessed using subgroup analysis to ensure the validity of the meta-analysis results (Table 2). A pooled analysis was performed using only studies reporting at least 50 fractures. The overall infection rate was still significantly different across groups (pooled RR: 0.18; 95% CI: 0.04–0.32; I^2: 41.83%; $P = 0.01$). When pooling only studies reporting specifically on tibial fractures, NPWT was still associated with a significantly reduced overall infection rate (pooled RR: 0.35; 95% CI: 0.21–0.48; I^2: 16.90%; $P = 0.0000$ and

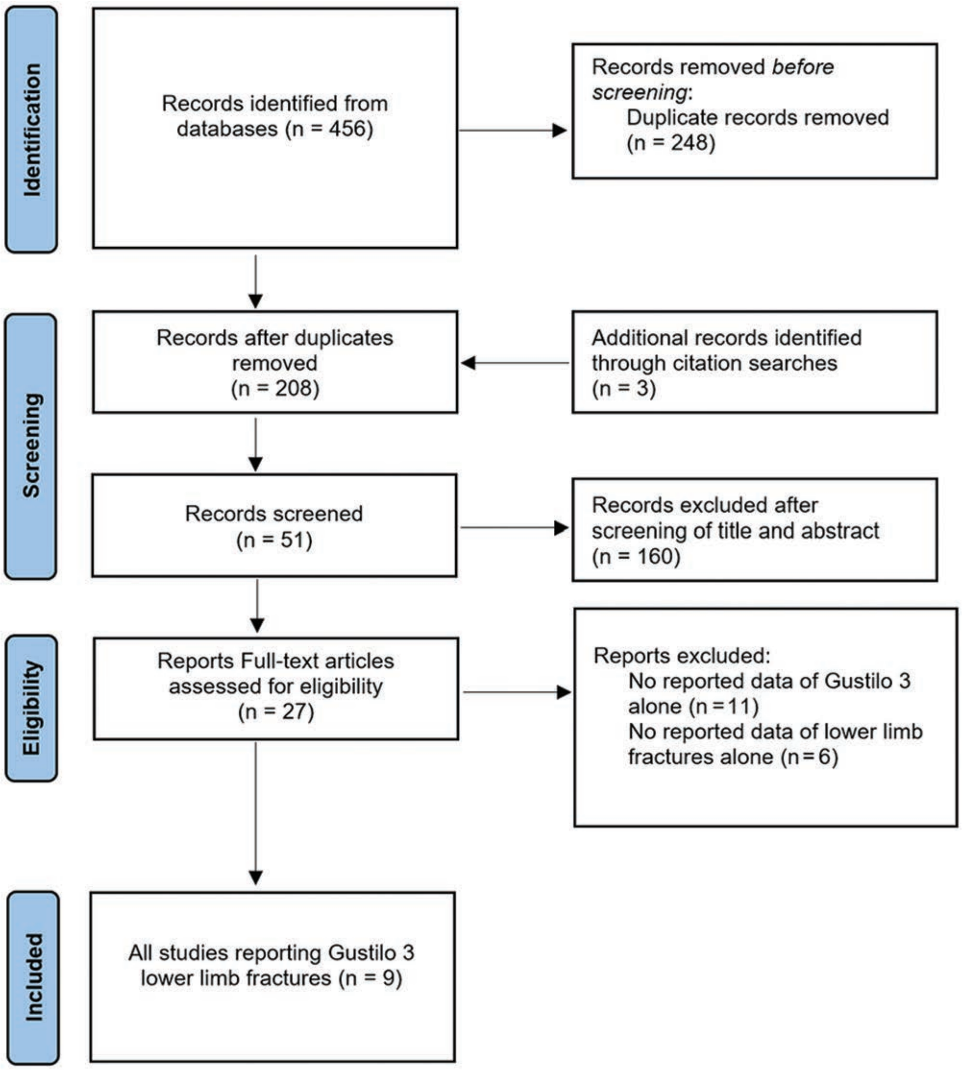

Fig. 1. Flowchart of the study selection.

pooled RD: 0.26; 95% CI: 0.17–0.35; I^2: 0.00%; $P = 0.0000$). The deep infection rate was also significantly lower in this tibial fracture NPWT subgroup (pooled RR: 0.29; 95% CI: 0.15–0.43; I^2: 0.00%; $P = 0.0001$ and pooled RD: 0.18; 95% CI: 0.04–0.32; I^2: 41.83%; $P = 0.01$). Finally, specific subgroup analysis was performed on studies including all Gustilo 3 types (3a, 3b, and 3c). The overall and deep infection rates remained significantly lower in patient treated with NPWT (pooled RR: 0.28; 95% CI: 0.13–0.43; I^2: 0.00%; $P = 0.0004$ and pooled RD: 0.22; 95% CI: 0.11–0.33; I^2: 0.00%; $P = 0.0001$).

Publication Bias

Visual analysis of funnel plot displayed asymmetrical funnel shape, with most studies clustering at the top (Fig. 5). Considering potential small-study effects, the Egger regression-based test was conducted to assess funnel plot asymmetry and quantify its impact. The analysis revealed a slope (b1) of 2.38 with a standard error of 0.595, resulting in a test statistic (z) of 3.99 and a *P* value of 0.0001, indicating significant evidence of funnel plot asymmetry. A subsequent analysis, incorporating sample size as a moderator, exhibited a slope (b1) of 2.63, a standard error of 0.642, a z-statistic of 4.10, and a *P* value of 0.0000, further supporting the presence of publication bias. This bias may be attributed not only to small-study effects but also to factors such as time-lag bias, language and citation biases, funding influences, methodological variability, and geographic disparities. A nonparametric trim-and-fill analysis of publication bias was conducted, revealing four potentially missing studies. The impact of this bias on the beneficial effect of NPWT in reducing overall infection was noteworthy, causing the estimated risk ratio to decrease from RR = 0.33 (95% CI: 0.14–0.51) to RR = 0.21 (95% CI: 0.02–0.41).

DISCUSSION

The results of the present study provide compelling evidence for the protective role of NPWT against overall infection, superficial infection, deep infection, and

Table 1. Characteristics of the Selected Studies

Author	Year	Country	Design	Gustilo	Limb	Fractures (n)	NPWT (n)	CWD (n)	Definition NPWT	Definition CWD	Reconstruction Method	Definition Superficial Infection	Definition Deep Infection	Soft-tissue Recon-struction NPWT, Mean Days	Soft-tissue Reconstruc-tion CWD, Mean Days
Labler	2004	Switzerland	RS	IIIa, IIIb	Femur, knee, tibia, foot	23	12	11	VAC (KCI) (125)	Epigard	Delayed closure, skin graft, flap	Soft-tissue infection		12.3 (2–35)	4.1 (2–8)
Rezzadeh	2015	The United States	RS	IIIb, IIIc	Tibia	32	12	20	NPWT	WDD	Flap	Surgical site infection	Osteomyelitis		
Stannard	2009	The United States	RCT	IIIa, IIIb, IIIc	Tibia	22	12	10	VAC (KCI) (125)	WMD	Delayed closure, skin graft, flap		Osteomyelitis		
Virani	2016	India	RCT	IIIa, IIIb, IIIc	Tibia	80	38	42	VAC (125)	WD 1×/24 h	Delayed closure, skin graft, flap	Wound infection	Osteomyelitis	8.3*	9.8*
Blum	2012	Australia	RS	IIIa, IIIb, IIIc	Tibia	159	123	36	VAC (KCI) (125)	WDD	Delayed closure, skin graft, flap	Above deep fascia	Below deep fascia	4.9 (3–7)*	3.3 (2–5)*
Arti	2016	Iran	RCT	IIIb	Tibia, fibula, femur	80	40	40	VAC (125)	WD 2×/24 h	Skin graft, flap	Clinical or positive culture of the wound		9.7 (7–12)*	11.2 (8–14)*
Joethy	2013	Singapore	RS	IIIb	Tibia	69	51	18	VAC (125)	WD 1×/72–96 h	Flap	Clinical		10.8	16.8
Jayakumar	2013	India	RCT	IIIa, IIIb	Leg	40	20	20	VAC (125)	WD 1×/48–72h		Clinical			
Sibin	2017	India	RCT	IIIa, IIIb	Tibia	30	15	15	VAC (125)	WD		Clinical			

*Reported data including not exclusively Gustilo 3 types and fractures on the lower limb.
KCI, Kinetic Concepts, Inc; PS, prospective study; RS, retrospective study; VAC, vacuum-assisted closure; WD, wet dressing; WDD, wet-to-dry dressing; WMD, wet-to-moist dressing.

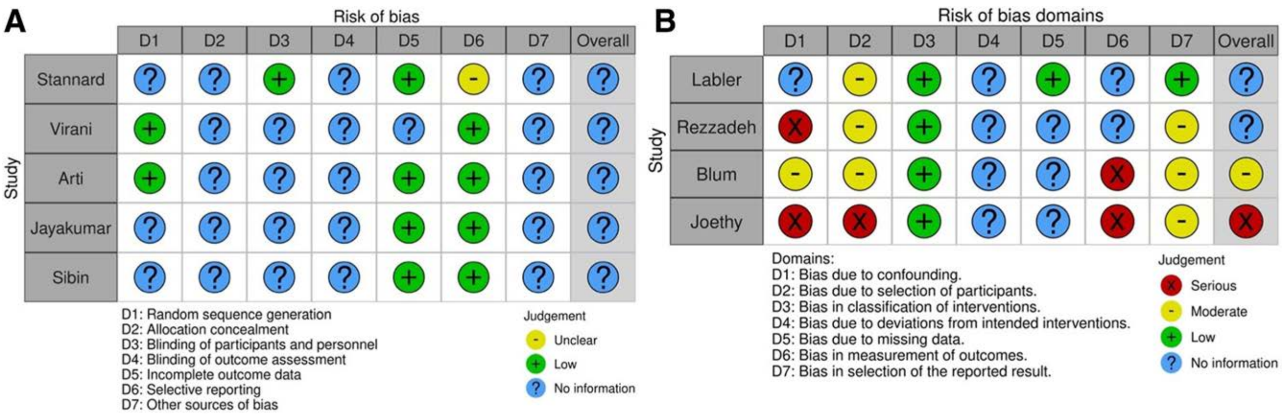

Fig. 2. Risk of bias assessment. A, RCT studies according to the criteria of the Cochrane collaboration risk of bias tool. B, Non-RCT studies assessed with risk of bias in nonrandomized studies of interventions tool.

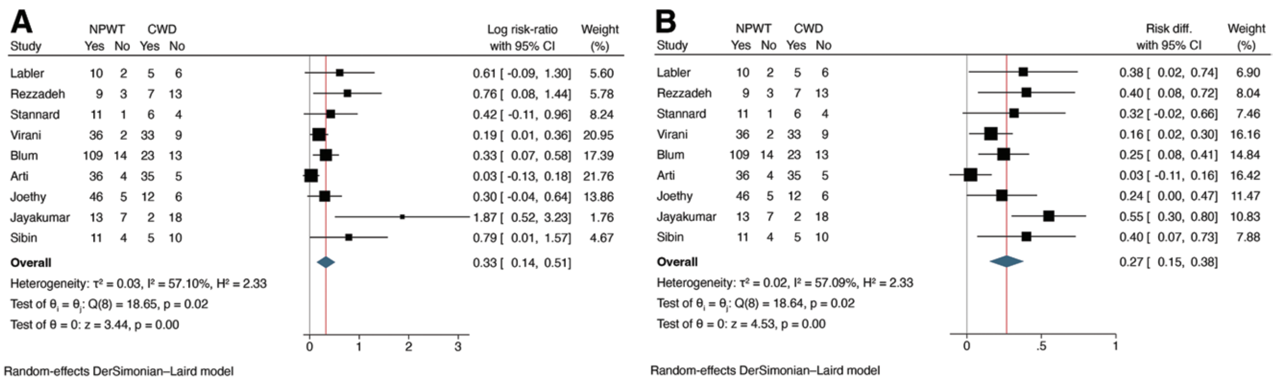

Fig. 3. Forest plots comparing the overall infection rate between NPWT and CWD. A, RR. B, RD.

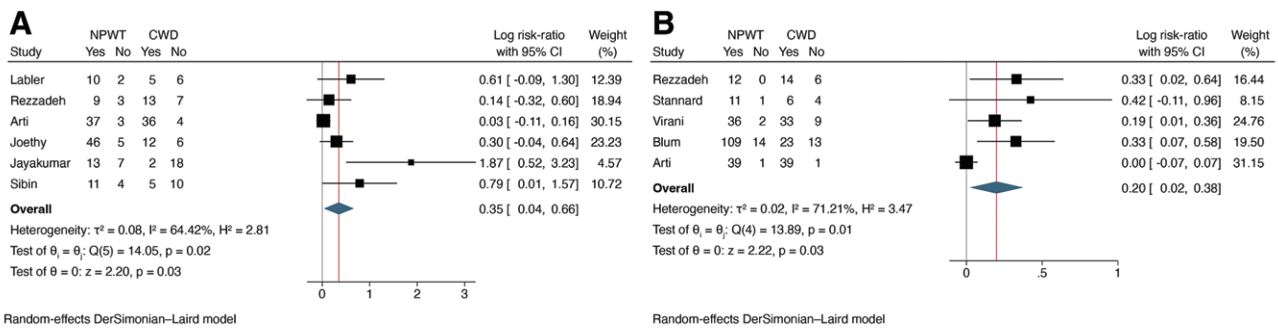

Fig. 4. Forest plots of relative risk (RR) of infection between NPWT and CWD. A, Superficial infections. B, Deep infections.

Table 2. Pooled Effect for Overall Infections Using Subgroup Analyses

Subgroup Analyses	Studies (n)	RR (95% CI)	I^2 (%)	*P*	RD (95% CI)	I^2 (%)	*P*
RCT	5	0.29 (0.01–0.56)	67.45	0.04	0.26 (0.07–0.73)	74.77	0.01
>50 fractures	4	0.18 (0.04–0.32)	41.83	0.01	0.15 (0.05–0.26)	39.61	0.0046
3a, 3b, 3c	3	0.28 (0.13–0.43)	0.00	0.0004	0.22 (0.11–0.33)	0.00	0.0001
Tibia	6	0.35 (0.21–0.48)	16.90	0.0000	0.26 (0.17–0.35)	0.00	0.0000
Studies published before 2014	5	0.41 (0.17–0.65)	26.83	0.0008	0.31 (0.20–0.42)	14.89	0.0000
Studies published after 2014	4	0.23 (−0.02 to 0.48)	62.99	0.0661	0.19 (0.03–0.36)	60.90	0.0218

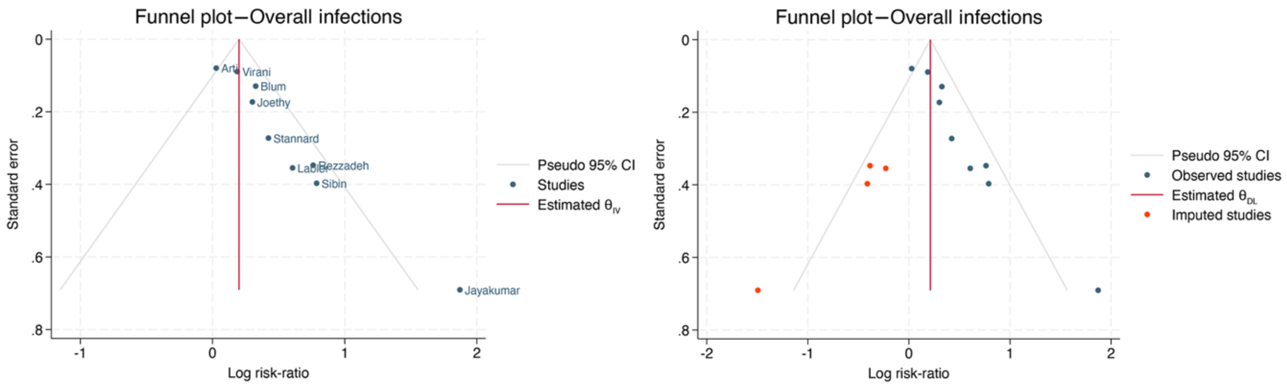

Fig. 5. Evaluation of meta-analysis robustness and data agreement.

nonunion in the management of Gustilo 3 lower limb fractures. It highlights the efficacy of NPWT as a viable solution for wound coverage until definitive closure. Regarding treatment protocols, small variations subsisted among studies, but most studies reported application of NPWT or CWD right after initial debridement until definitive closure. Regarding NPWT, dressing change frequency ranged from 2 to 4 days.[40,42–46,48]

Our meta-analysis demonstrates a significant reduction in the overall infection in patients treated with NPWT compared with patients treated with CWD. This is consistent with the existing literature, demonstrating that NPWT effectively reduces infection rates in a variety of surgical settings.[49–51] The vacuum-assisted closure system creates a closed, controlled environment that minimizes bacterial contamination, promotes tissue perfusion, and accelerates granulation tissue formation.[52] By reducing the risk of infection, NPWT treatment helps to improve patient outcomes and shorten hospital stays.[53] Open fractures, particularly those affecting the tibia, often resulting from high-energy trauma, present various challenges due to the limited soft-tissue coverage in this specific area.[54–56] Despite existing evidence leaning towards the efficacy of NPWT, studies comparing CWD and NPWT in this anatomical region have produced disparate and inconclusive results regarding superiority.[45,46] This variability could be attributed to the pooled analysis of all Gustilo types, introducing confounding biases associated with differing severity levels, different fracture locations, and prognostic factors.

Similarly, our study shows a substantial reduction in superficial and deep infection rates in patients treated with NPWT. This result aligns with the expected benefits of NPWT because it improves tissue oxygenation by promoting angiogenesis, eliminates excess exudate, and modulates cytokine in the wound environment.[57] These factors collectively limit the growth of pathogenic bacteria and reduce the likelihood of infection spreading to deeper structures.[58–60]

Flap reconstruction stands as a pivotal component of the final stage of wound coverage, especially in 3b and 3c Gustilo fractures.[11,61] Delayed closure, frequently involving temporary wound coverage, continues to be the predominant approach.[10,43] Recent studies suggest that early wound closure may be advantageous for most open fractures, provided that complete debridement is successful, infection is controlled, and there is effective fracture stabilization.[62,63] In our pooled analysis, an exclusive focus on patients undergoing flap reconstruction was reported in two studies. The overall infection rate was significantly increased in the CWD group compared with NPWT (RR = 0.43, $P = 0.04$). However, the failure rate across groups was not significantly different despite trending towards an increased risk in the CWD group (RR = 0.09, $P = 0.21$).

We found evidence that NPWT might reduce the bone nonunion. Previous studies evidenced that bones which are not completely surrounded by muscle like the tibia heal slowly.[64] Gustilo 3 fractures present a higher risk of nonunion due to the frequent comminution fractures, high rate of contamination, extensive soft-tissue damage, and compromised blood supply.[65] Dressing choice, while influential, may not be the sole determinant of nonunion in these complex cases. Other factors, including fracture stabilization type and overall treatment approach, are likely to play a crucial role in nonunion rates.[66]

Several limitations must be acknowledged. First, there is a paucity of high-quality RCTs specifically addressing Gustilo 3 lower limb fractures. Second, treatment protocols varied across studies, and most did not provide full details of their wound care protocol. Additionally, details of bone fixation and soft-tissue coverage were often limited and lacked specificity. Final reported outcomes were mainly based on subjective and nonquantifiable measures. These variations in study design and reporting standards highlight the complexity and heterogeneity of Gustilo 3 fractures. Furthermore, the present meta-analysis may not capture all the relevant clinical nuances and patient-specific factors influencing treatment decisions.

Unfortunately, only one of the included selected studies[45] compared the amputation rate between NPWT and CWD, not allowing for analysis of this outcome. This remains an important endpoint when considering open fracture treatment because it is associated with important morbidity and significantly impacts patient's quality of life. This study is subject to several limitations that require attention when interpreting the results. Strong variability among populations, wound care protocols, and management algorithms was observed during the data extraction, which might explain the high heterogeneity observed in the meta-analysis. Despite these limitations, we noticed a trend toward a reduction in infection risk with the use of NPWT, which remains the most feared complication in Gustilo 3 patients, because it can lead to dramatic consequences such as lower limb amputation or patient death. Furthermore, subgroup analysis between Gustilo 3a, 3b, and 3c was not possible, as selected articles did not report outcomes separately among subgroups. Finally, variability in the timeframes for reporting infection between articles is a major limitation.[41,45–48] Although Stannard et al[42] and Virani et al[43] distinguished early from delayed infection, other studies lacked adequate information on infection timelines, hindering the possibility of a subgroup analysis.

CONCLUSIONS

This meta-analysis provides comprehensive results and important information on the efficacy of NPWT compared with CWD in the management of Gustilo 3 lower limb fractures. The statistically significant reductions in overall infection, superficial infection, deep infection, and nonunion rates associated with NPWT treatment highlight its potential as a valuable intervention for wound care in these complex injuries.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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