Research Question: What is the role of continuous irrigation with negative pressure dressings designed for instillation therapy?

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Section 1: Background:

Negative pressure wound therapy (NPWT) is well described adjunct treatment after debridement in open musculoskeletal injuries. It promotes wound healing through several complementary mechanisms. These include approximation of wound edges, removal of exudate, reduction of tissue oedema, enhancement of local blood flow, and induction of microdeformation at the wound surface, which stimulates cellular proliferation and tissue repair. One of its most notable clinical effects is progressive wound contraction accompanied by the development of healthy granulation tissue. Despite these benefits, certain contaminated and infected wounds may respond inadequately to conventional NPWT.

To address these challenges, negative pressure wound therapy with instillation (NPWTi) was developed. The principles of this advanced system involves controlled instillation of normal saline or topical antibiotic/antiseptic solution into the wound, allowing it to dwell and irrigate the tissues for a predetermined period. This is followed by the application of negative pressure, which removes the instilled fluid along with wound exudate while maintaining the dressing in place.

In open fractures NPWTi is most commonly performed using normal saline instillation with a dwell time of approximately 10 minutes followed by continuous negative pressure of −125 mmHg for 2–3 hours between cycles. Dressing changes are typically performed every 48–72 hours.

Despite increasing clinical use, the evidence regarding the effectiveness of NPWTi in preventing infection and improving overall treatment outcomes remains heterogeneous. Furthermore, there is no consensus regarding the optimal instillation solution, dwell time, cycle frequency, or duration of therapy. Consequently, NPWTi is generally regarded as an adjunct to, rather than a replacement for, meticulous surgical debridement, timely soft-tissue management, and appropriate systemic antimicrobial therapy.

Section 2: Data extraction table

S.No	Author/Year/ Country	Study Design	Population	Intervention	Key Outcomes	Results	Follow-up
1	Petrou et al., 2019, United Kingdom[1]	Economic evaluation conducted alongside a multicenter, randomized controlled trial (the WOLLF trial)	460 adults with severe open lower-limb fractures, grade II and III	NPWT (n=226) vs standard dressing (n=234) after debridement	**Clinical**: DRI score at 12 months; **Economic**: Incremental cost per QALY gained from NHS/PSS perspective; Costs in £ (2014–15 prices); EQ-5D-3L utilities; Resource use	12 months FU, NPWT was **not cost-effective**;	12 months

					(inpatient, outpatient, community, medications, PSS, aids/adaptations)		
2	Brinkert et al., 2013, France[2]	Prospective case series (Non-randomised)	131 complex/infected wounds (Open fracture, n =46; 35%)	NPWT with **saline instillation**	Wound closure rate; Granulation tissue formation; Duration of therapy; Transition to conventional NPWT; Need for surgical closure	128/131 wounds closed; mean NPWTi duration 12.19 days; 98% positive healing progression.	Not specified
3	Kim & Lee, 2019, South Korea[3]	Systematic review/meta-analysis	12 studies, open GA grade III tibia fractures (1322 open tibia fractures, 747 cases in the NPWT group and 575 cases in the control group.)	NPWT vs conventional dressing	Soft-tissue infection, Osteomyelitis, Amputation, Nonunion, Flap necrosis, Flap revision	**Significant benefit for NPWT:** - Soft-tissue infection (OR 0.48) - Nonunion (OR 0.61) - Flap necrosis (OR 0.37) - Flap revision (OR 0.44) **No significant difference:** - Osteomyelitis (OR 0.54) - Amputation (OR 0.89)	12 months to a mean of 31.0 months in some studies
4	Suzuki et al., 2014, Japan[4]	Retrospective case series	14 open fractures (GA II and IIIA),	NPWT directly over surgically	Wound condition, complications (maceration,	Mean NPWT 9.1 days; no flap necrosis or infection; all fractures	Not specified

			lower leg/foot-ankle/knee	closed wounds	blisters, necrosis, infection), fracture union.	united; minor maceration/blisters.	
5,	Costa et al., 2018, United Kingdom[5]	Multicenter RCT, WOLLF trial	460 adults with open GA II and III lower-limb fractures	NPWT (226) vs standard dressing (234)	**Primary:** Disability Rating Index (DRI) score at 12 months (0-100, higher = worse disability; MCID=8 points). **Secondary:** Deep surgical site infection (SSI) at 30 days; Health-related quality of life (EQ-5D-3L and SF-12).	No significant improvement in 12-month disability, deep infection, or quality of life; findings did not support routine NPWT for high grade open fractures. No differences in the patients' Disability Rating Index score at 12 months (mean score,45.5 in the NPWT group vs 42.4 in the standard dressing group, P = .13), in deep surgical site infections (7.1% in NPWT vs 8.1% in standard dressing, P = .64), or quality of life between groups (difference in EuroQol 5-questionnaire, 0.02, Short Form–12 Physical Component Score, 0.5 and Mental Health Component Score, −0.4).	12 months

6	Arti et al., 2016, Iran[6]	Prospective randomized clinical trial	90 GA IIIb open fractures	NPWT (45) vs conventional dressing (45)	Wound healing rate (wound surface reduction), Incidence of infection, Duration of hospital stay	1. Significant difference in wound surface reduction in favor of NPWT (P=0.011). 2. No significant difference in infection rate (P=0.6). 3. Significant reduction in hospital stay for NPWT group (P=0.01).	1 month
7	Virani et al., 2016, India[7]	Prospective randomized trial	93 open GA II/ III diaphyseal tibial fractures	NPWT (43) vs periodic irrigation, cleaning, debridement (50)	1. Incidence of deep infections/osteomyelitis. 2. Incidence of positive bacterial cultures. 3. Time required for wound to be ready for delayed primary closure or skin grafting.	Infection: 4.6% NPWT vs 22% control; positive cultures 6.9% vs 34%; osteomyelitis only in control group.	23 ± 6 weeks
8	Back et al., 2013,, Germany [8]	Review/recommendation article	Contaminated/infected acute and chronic wounds	NPWTi with saline/antiseptic solutions	To summarize evidence and provide clinical recommendations on when, where, and how to use NPWTi with antimicrobial solutions	Recommended NPWTi as promising adjunct; suggested 20-min soak, 4–8 cycles/day; emphasized need for RCTs.	Not Applicable

9	Choi et al., 2025, Korea[9]	Retrospective comparative study	20 patients with open GA II/ III pelvic fractures and pelvic-perineal soft tissue infection (NPWTi=10, NPWT=10)	Instillation NPWT (NPWTi) vs Conventional NPWT	- NPWT duration - Time to definitive wound coverage - Hospital length of stay (LOS) - Medical costs	NPWTi resulted in significantly shorter NPWT duration (24 vs 46 days, p=0.023), shorter time to definitive wound coverage (30 vs 49 days, p=0.026), reduced hospital LOS (56 vs 158 days, p=0.001), and lower treatment costs (USD 67,800 vs 144,200, p=0.009). Mortality and complication rates were similar..	Not specified

Gustilo Anderson (GA), Negative pressure wound therapy (NPTW)

Section 3: Results summary

A total of seven studies evaluating negative pressure wound therapy (NPWT) and negative pressure wound therapy with instillation (NPWTi) in open fractures and complex orthopaedic wounds were included. These consisted of two randomized controlled trials, one prospective randomized study, three observational studies, and one cost-effectiveness analysis, representing 808 patients.

The largest study was the multicentre WOLLF randomized controlled trial involving 460 adults with severe open lower-limb fractures. Patients were randomized to NPWT (n=226) or standard wound dressings (n=234). At 12 months, no significant differences were observed in disability scores, deep surgical site infection rates (7.1% vs 8.1%), or quality-of-life outcomes. A subsequent economic analysis demonstrated that NPWT was not cost-effective, with an incremental cost-effectiveness ratio of £267910 per quality-adjusted life year gained.

In contrast, smaller trauma-focused studies demonstrated potential benefits of NPWT. Virani et al. prospectively randomized 93 patients with open diaphyseal tibial fractures and reported significantly lower infection rates with NPWT compared with conventional wound management (4.6% vs 22%; $p<0.05$). Positive wound cultures occurred less frequently in the NPWT group (6.9% vs 34%), and all five cases of osteomyelitis occurred in the conventional dressing group.

Similarly, Arti et al. randomized 90 patients with open fracture wounds and demonstrated significantly faster wound healing with NPWT than conventional wound dressings, although infection rates were comparable between groups.

Evidence specific to instillation therapy was provided by Brinkert et al., who evaluated 131 complex wounds, including 46 open fractures. NPWTi achieved successful wound closure in 128 patients (98%), with a mean treatment duration of 12.2 days and progressive wound improvement in almost all cases. The most recent comparative study by Choi et al. evaluated 20 patients with open pelvic fractures and pelvic-perineal soft-tissue infections treated with either conventional NPWT (n=10) or NPWTi (n=10). NPWTi significantly reduced the duration of therapy (24 vs 46 days, p=0.023), number of surgical debridements (10 vs 20, p=0.005), time to definitive wound coverage (30 vs 49 days, p=0.026), hospital length of stay (56 vs 158 days, p=0.001), and overall medical costs (USD 67800 vs USD 144200, p=0.009). Patients treated with NPWTi also demonstrated a higher rate of primary wound closure without flap or graft procedures (60% vs 10%).

Collectively, the available evidence demonstrates mixed results regarding the use of NPTW in open fractures. Most small randomized and observational studies reported improved wound management outcomes with NPWT compared with conventional dressings, including reduced infection rates, enhanced wound healing, and improved wound bed preparation. Emerging evidence also suggests that NPWT with instillation (NPWTi) may further facilitate wound bed optimization by reducing the number of surgical debridements, accelerating definitive wound closure, shortening hospital stay, and lowering overall treatment costs. However, the largest and highest-quality multicentre randomized controlled trial (WOLLF trial) failed to demonstrate any significant benefit of NPWT over standard wound dressings with respect to functional outcomes, infection rates, or quality of life. Therefore, while NPWT and NPWTi may offer advantages in selected complex wounds, the overall evidence remains inconclusive. It can be concluded that NPWT/NPWTi cannot be considered superior to the conventional wound dressing in open fracture management.

Section 4: Discussion

Open fractures continue to pose a major challenge in orthopaedic trauma because successful outcomes depend on both fracture stabilization and effective soft-tissue management. NPWT has been widely adopted because of its ability to remove exudate, reduce tissue oedema, improve local perfusion, and promote granulation tissue formation. NPWT with instillation (NPWTi) was subsequently developed to enhance these effects through periodic irrigation and mechanical cleansing of the wound bed.

The available evidence regarding the effectiveness of NPWT in open fractures remains mixed. Several smaller randomized and observational studies have reported improved wound healing and reduced infection rates compared with conventional wound management. Virani et al. demonstrated a nearly fivefold reduction in infection rates (4.6% vs. 22%) and complete elimination of osteomyelitis in patients treated with NPWT. Similarly, Arti et al. reported faster wound healing with NPWT compared with conventional dressings. These findings support the biological rationale that negative pressure therapy may improve wound bed conditions during the interval between debridement and definitive closure.

The strongest synthesis of evidence is provided by the systematic review and meta-analysis by Kim and Lee, which evaluated 12 comparative studies involving open tibial fractures. The review included both randomized and non-randomized comparative studies and demonstrated significantly lower rates of soft-tissue infection (OR 0.48, 95% CI 0.34–0.68), nonunion (OR 0.61, 95% CI 0.39–0.95), flap necrosis (OR 0.37, 95% CI 0.21–0.63), and flap revision (OR 0.44, 95% CI 0.22–0.89) in patients treated with NPWT compared with conventional dressings. No significant differences were observed for osteomyelitis or amputation rates. These findings suggest that NPWT may improve several clinically relevant outcomes in severe open fractures.

However, interpretation of these pooled findings requires caution. The included studies were heterogeneous with respect to fracture severity, timing of soft-tissue coverage, wound management protocols, and outcome definitions. In addition, several studies were retrospective and therefore susceptible to selection bias and confounding. Importantly, although the WOLLF trial was included within the available evidence base, its findings differed from many of the smaller studies. The WOLLF trial, a multicentre randomized controlled trial involving 460 patients with severe open lower-limb fractures, demonstrated no significant differences in disability scores, deep infection rates, quality-of-life measures, or reoperation rates between NPWT and standard wound dressings. Furthermore, the accompanying economic evaluation found NPWT unlikely to be cost-effective. Consequently, the positive findings observed in pooled analyses should be interpreted in the context of substantial clinical and methodological heterogeneity and the neutral results of the largest randomized trial.

Evidence specifically evaluating NPWTi remains considerably more limited than that for conventional NPWT. Nevertheless, NPWTi may offer additional advantages through repeated irrigation, dilution of bacterial contamination and removal of inflammatory exudate,. Brinkert et al. reported successful wound closure in 98% of complex wounds, including a substantial proportion of orthopaedic trauma wounds. More recently, Choi et al. evaluated patients with open pelvic fractures complicated by pelvic-perineal soft-tissue infection and demonstrated significant reductions in the number of surgical debridements (10 vs. 20), NPWT duration (24 vs. 46 days), time to definitive wound coverage (30 vs. 49 days), hospital length of stay (56 vs. 158 days), and overall treatment costs (USD 67800 vs. USD 144200) with NPWTi compared with conventional NPWT. Additionally, primary wound closure without flap or graft was achieved in 60% of NPWTi-treated patients compared with only 10% in the conventional NPWT group. These findings suggest that NPWTi may facilitate wound bed optimization and earlier reconstruction in highly contaminated orthopaedic trauma wounds.

In summary, the current evidence does not support the routine use of NPWT for all open fractures. While some studies and pooled analyses suggest reductions in wound-related complications and improved soft-tissue management, the highest-quality randomized evidence has not demonstrated a clear advantage of NPWT over standard wound dressings with respect to infection prevention, functional outcomes, or quality of life. Therefore, routine application of NPWT in all open fractures cannot be recommended. NPWT may be considered in selected severely contaminated wounds with substantial soft-tissue loss, or delayed reconstruction based on individual clinical circumstances.

The evidence supporting NPWT with instillation (NPWTi) in open fractures is currently limited and consists predominantly of observational studies with small sample sizes. Although preliminary data suggest potential benefits in wound bed preparation, reduction in repeated debridement procedures, facilitation of definitive wound closure, and reduction in hospital stay, the available evidence is insufficient to make a recommendation either for or against its routine use. Further high-quality, adequately powered randomized controlled trials are required to define the role of NPWTi in the management of open fractures and fracture-related infections.

Section 5: Risk of bias of included studies

Study	Design	Assessment Tool	Risk of Bias
Costa et al. (WOLLF), 2018	Multicentre RCT	RoB 2	Low
Virani et al.	Prospective randomized study	RoB 2	Some concerns (Moderate)
Arti et al.	Randomized study	RoB 2	Some concerns (Moderate)
Choi et al., 2025	Retrospective comparative study	ROBINS-I	Serious (High)
Brinkert et al., 2013	Prospective case series	MINORS	Moderate
Omar et al., 2016	Comparative cohort study	ROBINS-I	Serious (High)
Suzuki et al., 2014	Retrospective case series	MINORS	Moderate

Overall risk of bias: MODERATE

Section 5: Response/Recommendation

Current evidence does not demonstrate clear superiority of NPWT over standard wound dressings for routine management of open fractures with respect to infection prevention or clinical outcomes. Evidence specifically supporting NPWT with instillation/irrigation remains limited; therefore, no recommendation for or against its routine use in open fracture care can currently be made.

Section 6: Level/ strength of Evidence:

Level of Evidence: MODERATE

Justification:

Study Design: The available evidence comprises one large multicentre randomized controlled trial (Costa et al., WOLLF trial), two additional prospective randomized studies (Arti et al., Virani et al.), one retrospective comparative study evaluating NPWTi (Choi et al.), and two observational case series (Brinkert et al., Suzuki et al.). Supporting evidence is available from a systematic review and meta-analysis of 12 comparative studies involving open tibial fractures. However, evidence specifically evaluating NPWT with instillation (NPWTi) remains limited and is derived predominantly from observational studies.

Risk of Bias: The overall risk of bias was judged to be moderate. The highest-quality evidence was provided by the WOLLF multicentre randomized controlled trial, which demonstrated a low risk of bias. Two additional randomized studies were assessed as having some concerns due to limitations in reporting of allocation concealment and blinding. The observational studies were generally at moderate to high risk of bias because of retrospective design, small sample sizes, lack of control groups, and potential selection bias. The only comparative study evaluating NPWTi (Choi et al.) was assessed as having a serious risk of bias due to confounding and non-randomized treatment allocation.

Sample Size: The evidence base consists of 808 patients across seven clinical studies. The largest contribution comes from the WOLLF trial (460 patients), which accounts for more than half of the total study population. In contrast, evidence specific to NPWTi is limited to relatively small cohorts, including the 131-patient case series by Brinkert et al. and the 20-patient comparative study by Choi et al.

Outcome Measures: Substantial heterogeneity existed in outcome definitions, fracture severity, wound characteristics, and follow-up duration, limiting direct comparison between studies.

Conclusion on Strength of Evidence: The available evidence provides conflicting results regarding the role of NPWT in open fracture management. While several smaller randomized and observational studies reported reductions in infection rates and improvements in wound healing, the highest-quality randomized evidence did not demonstrate superiority of NPWT over standard wound dressings with respect to functional outcomes, infection prevention, or quality of life. Evidence supporting NPWTi is currently limited but suggests potential benefits. Given the predominance of observational data, small NPWTi-specific sample sizes, and moderate overall risk of bias, the strength of evidence is considered **MODERATE**, and further high-quality open fracture-specific randomized controlled trials are required before stronger recommendations can be made.

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