Effect of Negative Pressure Wound Therapy vs Standard Wound Management on 12-month Disability Among Adults with Severe Open Fracture of the Lower Limb: The WOLLF Randomized Clinical Trial

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Matthew L Costa PhD, [1,2,3], Juul Achten PhD[2], Julie Bruce PhD[1], Elizabeth Tutton PhD[1,2], Stavros Petrou PhD [1], Sarah E Lamb PhD[1,2], Nick R Parsons PhD[4] for the UK WOLLF collaboration.

1. *Warwick Clinical Trials Unit, Warwick Medical School, The University of Warwick, Gibbet Hill Campus, Coventry CV4 7AL*
2. *Oxford Trauma, Nuffield Department of Orthopaedics, Rheumatology & Musculoskeletal Sciences, University of Oxford, Oxford, OX3 9DU, UK*
3. *University Hospitals Coventry and Warwickshire NHS Trust, Clifford Bridge Road, Coventry, CV2 2DX, UK*
4. *Statistics and Epidemiology Unit, Warwick Medical School, The University of Warwick, Gibbet Hill Campus, Coventry, CV4 7AL, UK*

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Corresponding Author:

Professor Matthew Costa

Oxford Trauma, Nuffield Department of Orthopaedics, Rheumatology & Musculoskeletal Sciences, University of Oxford, Oxford, OX3 9DU, UK

Matthew.costa@ndorms.ox.ac.uk

Key points

Question: Does either negative pressure wound therapy or standard wound dressing result in less disability 12 months after sustaining an open fracture of the lower limb.

Findings: In this randomized clinical trial that included 460 adults, there was no statistically significant difference in self-rated disability between negative pressure wound therapy or standard wound dressing at 12 months (45.5 vs 42.4 points out of a possible 100).

Meaning: Negative pressure wound therapy did not improve 12-month disability for patients with severe open fracture of the lower limb compared with standard wound dressing

ABSTRACT

Importance

Open fractures of the lower limb occur when a broken bone penetrates the skin. These are life-changing injuries where wound healing complications are common.

Objectives

To assess the disability, rate of deep infection and quality of life in patients with severe open fracture of the lower limb treated with negative pressure wound therapy (NPWT) versus standard wound management after the first surgical debridement of the wound.

Design, Setting and Participants

Multi-center, randomized trial, embedded in the UK Major Trauma Network, recruiting 460 patients ≥16 years with a severe open fracture of the lower limb from July 2012 through December 2015. Final outcome collected November 2016. Exclusions: presentation > 72 hours after injury; inability to complete questionnaires.

Interventions

NPWT (n=226) where an open cell solid foam or gauze was placed over the surface of the wound and connected to a suction pump which created a partial vacuum over the dressing vs standard dressings not involving negative pressure (n=234).

Main outcomes and Measures

Disability Rating Index (DRI); score 0 [no disability] to 100 [completely disabled] at 12 months was the primary outcome measure, with a minimal clinically important difference (MCID) of 8 points. Secondary outcomes were complications including deep infection, and quality of life (QOL; score ranged from 1 (best possible) to -0.59 (worst possible), MCID 0.08) collected at 3, 6, 9 and 12 months.

Results

Among 460 patients who were randomized (mean age, 45.3 years; 74% men), 88% (374/427) of available study participants completed the trial. There was no statistically significant difference in the patients' DRI at 12 months (mean score 45.5 (sd=28.0) in the NPWT group vs 42.4 (24.2) in the standard dressing group; mean difference of -3.9 (95%CI; -8.9 to 1.2; p=0.13). There was no statistically significant difference in the number of deep surgical site infections (16 (7.1%) in the NPWT group vs 19 (8.1%) in the standard dressing group; difference 1.0% (95% CI; -4.2% to 6.3%; p=0.64). There was no statistically significant difference in QOL between groups; difference in EQ-5D 0.02 (95% CI; -0.05 to 0.08), SF-12 PCS 0.5 (95% CI; -3.1 to 4.1) and SF-12 MCS -0.4 (95% CI; -2.2 to 1.4).

Conclusions and relevance

Among patients with severe open fracture of the lower limb, use of negative pressure wound therapy compared with standard wound dressing did not improve self-rated disability at 12 months. The findings do not support this treatment for severe open fractures.

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Background

Fractures of the lower limb are common injuries in civilian and military populations.[1,2] Most fractures are 'closed'; the skin overlying the fracture is intact. However, if the fracture is 'open', the broken bone is exposed to contamination and the risk of healing complications is greatly increased.[3] In severe, open fractures of the lower limb, infection rates up to 27% are reported, even in specialist trauma centres.[4] The costs of treating wound complications is extremely high for both patients and healthcare systems.[5]

The initial management of open fractures involves surgical debridement with excision of damaged tissue and contamination, and the administration of antibiotics. [6,7] The fracture is usually immobilized with fixation of the bone and a dressing is applied to the surface of the wound. Traditionally, a sealed, non-adhesive layer is applied to protect the open fracture from further contamination. Reassessment and further debridement of the wound typically performed 48-72 hours later.

Negative-pressure wound therapy (NPWT) is an alternative form of dressing. This device creates a vacuum using suction which removes blood and fluid that may collect in the wound. The vacuum may also encourage the formation of granulation (healing) tissue.[4,8] However, NPWT dressings and the vacuum machines are considerably more expensive than traditional wound dressings.

Before this study, there was only one randomized clinical trial comparing standard wound dressing with NPWT for patients with open fractures of the lower limb.[11] That trial suggested improved outcomes in patients treated with NPWT but included only 59 patients at a single trauma center. Despite the lack of strong evidence, clinical guidelines around the world incorporated the use of NPWT for open fracture wounds. [6,7,12]

The aim of this pragmatic, multicenter RCT was to compare standard wound dressings with negative pressure wound therapy for adults with an open fracture of the lower limb.

Methods

Study design and eligibility criteria

The National Research Ethics Service approved the study, the approved protocol and statistical analysis plan are available as an online supplement. The trial was overseen by independent steering and data and safety monitoring committees.

The trial took place in 24 major trauma hospitals representing the UK Major Trauma Network; in the UK, patients with serious injuries such as open fractures are transported directly to a specialist trauma center with joint orthopedic and plastic surgery facilities. Eligible patients were aged 16 years or older and had a severe open fracture of the lower limb graded as Gustilo and Anderson II or III; type II is an open fracture with a laceration more than one centimeter long without extensive soft-tissue damage, flaps, or avulsions and type III either an open segmental fracture or an open fracture with extensive soft-tissue damage.[14] Since surface NPWT can only be applied to wounds which are left open, the surgeons could only include the most severe injuries i.e. where is was not possible to safely suture the wound edges the end of the first surgical debridement. Patients had to present to the trial hospital within 72 hours of their injury, including those who were transferred from other hospitals. Patients were excluded if they had known contra-indications to anesthesia or were deemed unable to adhere to trial procedures or complete questionnaires, for example those with a pre-existing diagnosis of dementia. For patients with acute confusional states or temporary impairment of consciousness, we approached a Consultee to provide agreement on behalf of the patient, as per the UK Mental Capacity Act 2005. All participants randomized under this provision, were subsequently approached for consent once capacity was restored, with the option to continue or discontinue involvement in the trial. For this reason, we anticipated higher levels of post-randomization withdrawal than might be expected in most clinical trials.

RANDOMISATION AND MASKING

A computer-generated randomization algorithm was created by the trial statistician and delivered by an accredited Clinical Trials Unit to ensure that the allocation sequence was concealed. The individual patient was allocated treatment on a 1:1 basis, stratified by trial center and Gustilo and Anderson grade; the Gustilo and Anderson grade. When a patient entered the trial, non-identifiable details were logged on the secure, encrypted, web-based system.

Participants were assigned to their treatment allocation intraoperatively at the end of initial surgery, but before any wound dressing was applied.

It was not possible to blind trial participants to treatment allocation as wound dressings were clearly visible. In addition, the treating surgeons could not be blind to the intervention, but the surgical and healthcare team were not involved in any trial assessments. Wound photographs taken at six weeks and standard radiographs were used to look for signs of delayed wound healing and non-union of the bone respectively. These were reviewed by independent clinicians who were blind to the treatment allocation.

INTERVENTIONS

At presentation, all patients were listed for the next available trauma operating list. In the operating theatre, all patients received a general or regional anesthetic. The wound associated with the fracture was surgically debrided and the fracture immobilized with either internal (under the skin) or external fixation. At the end of the initial operation, if the wound could not be closed primarily i.e. direct suture of the wound edges was not possible, the patient was randomized to either standard dressings or NPWT. All other elements of postoperative care remained the same for all patients.

Standard Dressing Group. All hospitals used a sterile dressing sealed from external contamination. However, the details of the materials used were left to the discretion of the treating healthcare team as per routine care at their center. Details of each dressing applied in the trial were recorded and classified according to British National Formulary (BNF) classification.

NPWT group. The NPWT dressing used an 'open-cell' solid foam or gauze laid onto the wound followed by an adherent, sealed dressing. A sealed tube was connected from the dressing to a suction pump which created a partial vacuum over the wound. The basic features of the NPWT are universal, but the exact details of the dressing and pressure (mmHg) were left to the discretion of the treating healthcare team. Details of the NPWT were recorded in trial documentation.

Patients with an open fracture of the lower limb that could not be closed primarily, had a second operation at 48-72 hours, where a further wound assessment and debridement was performed and the wound closed either primarily with sutures or by soft-tissue reconstruction as necessary.

DATA COLLECTION AND OUTCOME MEASURES

The primary outcome was the patient-reported Disability Rating Index (DRI) at 12 months after randomisation.[15] The DRI provides a 100-point score, where zero represents normal function and 100 complete disability, with a minimum clinically important difference of 8 points.

Secondary outcomes were health-related quality of life using EuroQol (EQ-5D-3L) [16,17] and Short form 12 (SF-12) [18,19] deep surgical site infection (SSI) at 30 days as per CDC definition[20] and other complications. EQ-5D-3L responses were converted into an overall utility score [17], that ranged from 1 (best possible) to -0.59 (worst possible), where zero represents the quality of life associated with death; the minimum clinically important difference is 0.08 points. Physical and mental health Composite Scores (PCS and MCS) were computed from SF-12 responses [21]; these scores range from 0 to 100, where a 0 score indicates the lowest level of health. Infection outcomes and complications were extracted from the patients' medical records by independent research staff in each trial center. Wound photographs and radiographs were reviewed independently and blind to treatment allocation.

Deep infection following an open fracture is a key driver of subsequent disability. However, a deep infection which is treated early and definitively may resolve completely with no disability. Similarly, wounds which are not infected may still heal with excess scar-tissue or require extensive tissue

grafts which can lead to reduced mobility and chronic pain. Therefore, the DRI was considered to be more important as a primary outcome measure than the rate of deep infection or size of the wound per se. Patient-reported outcomes (DRI, EQ-5D-3L, SF-12) and self-reported complications were collected by questionnaire. Pre-injury baseline scores were collected retrospectively at the time of consent and again by postal questionnaire at three, six, nine, and twelve months.

STATISTICAL ANALYSIS

A minimum clinically important difference for the Disability Rating Index of 8 points was selected to power the study;[13] for an individual patient, at the lower level this represents the ability to climb stairs or run, with 'some difficulty' versus, at the higher level with 'great difficulty' and at a population level, eight points represents the difference between a 'healthy patient' (score=1 points)and a 'patient with a minor disability'(score=9 points). The standard deviation (SD) of the DRI used in the sample size calculation was 25 points. Allowing a margin of 10% loss during follow-up, including the small number of patients who die in the first year following their injury, gave a total sample size of 460 patients. Therefore, 230 patients consented to each intervention group would provide 90% power to detect a difference of eight points in DRI at 12 months at the 5% significance level.

When calculating summary statistics for assessing treatment efficacy, NPWT data were subtracted from control group data; such that a positive difference indicated that a score or outcome measure was larger in the control group. We investigated differences in the primary outcome measure, the DRI score at one year after injury, between the two treatment groups on an intention-to-treat basis. Early and mid-term disability was assessed and reported at three, six and nine months. A secondary per-treatment analysis was also performed. Mixed-effects regression analysis, with recruiting center as a random effect, and fixed terms to adjust for age group, sex, baseline pre-injury score and Gustilo and Anderson grade was used to test for treatment group differences using complete case

214 data. Secondary endpoints were not adjusted for multiple comparisons, and should be interpreted
215 as exploratory. In a post hoc sensitivity analysis for the primary outcome, missing data were imputed
216 using the chained equation methodology [22] and models fitted to give a pooled estimate of the
217 treatment effect.

218 All tests were two-sided and significance was assessed at the 5% level. Analyses of primary and
219 secondary outcomes used complete-case data and all analyses were implemented in R version 3.3.0
220 [23], using packages base, graphics, mice, lme4 and nlme (see https://cran.r-project.org/).

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Results

A total of 625 patients were randomized between July 2012 and December 2015. Some patients who did not have mental capacity before surgery, were unable or not willing to provide informed consent after randomization. The majority of the 165 patients who did not provide consent were found to be ineligible after randomization; for example, due to primary closure of the wound or permanent cognitive impairment which could not be predicted before surgery/randomization. Only 29 potentially eligible patients declined to participate in the trial; 14 in the NPWT group and 15 in the standard dressing group (Figure 1).

A total of 460 patients consented to take part in the WOLLF trial: 85% were grade III injuries and 82% involved the tibia. The characteristics of the two groups were well balanced after randomization (Table 1).

Figure 1

Table 1

On an intention-to-treat basis, there was no significant difference in the DRI at 12 months between those patients treated with NPWT versus those treated with standard wound dressings (Figure 2). The mean DRI in the NPWT group was 45.5 versus 42.4 in the standard dressing group, giving a difference of -3.9 (95%CI; -8.9 to 1.2) in favor of standard dressings, p-value=0.13; from adjusted mixed-effect regression analysis (Table 2). Therefore, the results of this trial are consistent with a -8.9 worse disability rating attributable to the use of NPWT which, based on the minimal clinically important difference, would be clinically important but also ranging to a non-clinically important benefit of these dressings of 1.2 points on the DRI scale. Similarly, there was no significant difference in disability rating at three months, six months or nine months (Figure 2).

The secondary per-protocol (per treatment) analysis of the DRI did not significantly differ from the primary intention-to-treat analysis; the difference between groups being -4.0 (95% CI; -9.1 to 1.0) in favour of the standard dressings (p-value 0.12).

Table 2

Secondary exploratory analysis showed that there was no significant difference in the health-related quality of life scores between the treatment groups at any point in the 12 months following the injury. The mean SF-12 Physical Component Score at 12 months in the NPWT group was 32.2 (17.4) versus 32.7 (15.5) in the standard dressing group, giving an adjusted difference of 0.4 (-3.0 to 3.8) in favor of standard dressings (p-value=0.82; from adjusted mixed-effect regression analysis). The mean EQ-5D score in the NPWT group was 0.55 (0.33) versus 0.56 (0.32) in the standard dressing group, giving a difference of 0.01 (-0.06 to 0.07) in favor of standard dressing (p-value=0.82).

There was no significant difference in the number of deep surgical site infections between the treatment groups (Table 3). In total 35 of the 460 participants (7.6%) had a deep SSI at 30 days; 16 (7.1%) in the NPWT treatment group and 19 (8.1%) in the standard dressing group, giving an estimated odds ratio 0.85 (95% CI; 0.42 to 1.70) and percentage difference in rates 1.0% (95% CI; -4.2% to 6.3%) in favor of NPWT (p-value=0.64 from adjusted mixed-effect logistic regression analysis). There was no significant difference in the proportion of wounds found to be fully healed on the six-week photographs; 52.0% (91/175) in the NPWT group and 51.7% (93/180) in the standard dressing group, giving an odds ratio of 1.0 (95%CI; 0.6 to 1.6, p-value=0.99) and difference in rates -0.3% (95% CI; -11.1% to 10.4%). There was no significant difference in the proportion of patients with complete bone union on the radiographs at 12-months; 69.6% (112/161) in the NPWT group and 71.9% (110/153) in the standard dressing group, giving an odds ratio of 1.1 (95%CI;0.7 to 1.9, p-value=0.68) and difference in rates 2.3% (95% CI; -8.4% to 13.0%).

The primary outcome data were 88% complete (374 of 427 available study participants provided final outcome data) and there was no evidence for non-random patterns of missingness. Imputing

missing data gave pooled estimates of the treatment effect for DRI at 12 months as - 4.5 (95% CI; -9.3 to 0.4), with the percentage of the variability attributable to the uncertainty caused by the missing data estimated at 12.8%.

Table 3

Discussion

This multi-center trial of patients with severe open fractures of the lower limb, found no significant difference in the Disability Rating Index between those patients treated with NPWT versus those treated with standard wound dressings at 12 months post-injury. There was no significant difference in the rate of deep surgical site infection, or other healing complications. Nor was there a significant difference in health-related quality of life at any point in the first 12 months after the injury.

Before this trial,a review of the literature [24] showed only one RCT comparing standard wound dressing with NPWT for the initial management of patients with severe open fractures of the lower limb. Stannard et al [11] demonstrated a difference in health-related quality of life and a reduction in the rate of deep wound infection in patients treated with NPWT compared with control (5.4% versus 20%; RR 0.199, 95% CI 0.05, 0.87). However, this was a small trial (59 patients, 63 fractures), and there were only 7 deep infections in the control group and 2 in the NPWT group. It is possible that this difference in the rate of deep infection was due to systematic differences in the patients and/or treatment pathway in a single center in the US, compared with the WOLLF trial which took place in the much broader setting of 24 major trauma centers. However, given the relatively small number of cases in the Stannard et al trial, it is possible that the result represents a lack of precision in the estimate of the incidence of deep infection. A trial published in 2016 also comparing NPWT with standard dressings in the context of open fractures. This study took place in Pakistan and used negative pressure dressings over a prolonged period of time (weeks) to reduce the size of the wound.[25] This is a very different use of NPWT than advocated by current guidance for the management of open fractures, where early definitive wound closure - within 72 hours - is

recommended.[6,7] Therefore, it is not clear whether the results of that trial are pertinent to other healthcare systems.

Limitations

This study has several limitations. Firstly, patients with an open fracture of the lower limb have usually experienced severe trauma and present to hospital with variable states of consciousness and cognition. For emergency interventions, it was anticipated that some patients who were randomized would subsequently found not to be eligible or not able to provide informed consent; for example patients who had significant head injury or who died of their injuries in the early post-operative period. Some patients were also found to be ineligible after randomization due to the surgeon deciding that the wound could be closed by direct suturing, which may reflect the difficulties of classifying these injuries at the time of the initial debridement of the wound; only patients where the surgeon felt that the wound had to be left open were included in the trial [26]. However, 460 of the 485 (95%) patients who were randomized and eligible for the trial agreed to participate, suggesting that participants were representative of the overall population with severe open fractures of the lower limb. Second, after randomization some patients crossed over from one treatment group to another. However, 95% percent of patients received the treatment to which they were allocated. Third, there was loss to follow-up, with study completion by only 88% of the original participants. However, multiple imputation analysis resulted in consistent findings. Finally, although patients were only eligible to enter the study if they presented to the treating hospital within 72 hours of their injury, we were not able to adjust for the exact time of the open fracture which is a possible confounder in the analysis.

Conclusion

Among patients with severe open fracture of the lower limb, use of negative pressure wound therapy compared with standard wound dressing did not improve self-rated disability at 12 months.

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Author contributions

MC, NP, JB, SL, LT, SP and JA were responsible for the trial design. MC and JA were responsible for acquisition of data. NP was responsible for the statistical analysis.

All authors were responsible for the interpretation of the data and for drafting and approving the final submitted manuscript.

UK WOLLF Collaborators

Keith Willett, Damian Griffin, Steven Jeffery, Jill Arrowsmith, Gorav Datta, Mick Dennison, Mark Farrar, Peter Giannoudis, Andrew Gray, Philip Henman, Peter Hull, Umraz Khan, Charlotte Lewis, David Loveday, Jitendra Mangwani, Andrew McAndrew, Damian McClelland, Mike McNicholas, David Noyes, Ben Ollivere, Ian Pallister, Keith Porter, Manoj Ramachandran, Rory Rickard, Benedict Rogers, Hemant Sharma, Adel Tavakkolizadeh, Jonathan Young.

Conflicts of interest

M Costa is a member of the UK NIHR HTA General Board; S Lamb is a member of the UK NIHR HTA Additional Capacity Funding Board, HTA end of life care and add-on studies, HTA Prioritisation Group and HTA Trauma Board.

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funded the excess treatment costs of the NPWT dressings but had no part in the design, conduct or reporting of the trial.

Prof Matthew Costa and Dr Nick Parsons have full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis

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Figure 2

Temporal trends in main study outcomes. Disability Rating Index (DRI), the primary outcome (Panel A), EQ-5D quality of life (Panel B) and SF-12 physical component score (PCS) and mental component score (MCS) (Panel C). Shown are means, with 95% confidence intervals, at each study follow-up time point (3, 6, 9 and 12 months) and at baseline (Base). Pre-injury assessments were made retrospectively by all study participants and immediately post-injury for EQ-5D. Minimum clinically important differences (MCID) are shown for DRI and EQ-5D.

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Table 1. Characteristics of the Study Participants

Characteristic		NPWT (n = 226)	Standard (n = 234)
Age (years);	mean (sd)	46.1 (19.9)	44.5 (19.0)
	median (IQR)	42 (29 – 61)	44 (26 – 57)
Height (meters); mean (sd)		1.74 (0.12)	1.72 (0.16)
Weight (kg); mean (sd)		80.9 (16.8)	80.9 (19.4)
Male sex; n (%)		178 (78.8)	164 (70.1)
Diabetes; n (%)		14 (6.2)	13 (5.6)
Smoker; n (%)		70 (31.0)	79 (33.8)
no. per day; mean (sd)		15.4 (10.9)	15.3 (10.4)
years; mean (sd)		17.6 (12.4)	17.4 (12.0)
Employment; n (%)			
Employed		147 (65.0)	160 (68.4)
Retired or Inactive		44 (19.5)	44 (18.8)
Unemployed		28 (12.4)	25 (10.7)
Unknown		7 (3.1)	5 (2.1)
Mechanism of injury; n (%)			
Road traffic accident		125 (55.3)	139 (59.4)
Low energy fall		34 (15.0)	39 (16.7)
High energy fall		34 (15.0)	25 (10.7)
Crush injury		17 (7.5)	19 (8.1)
Other		13 (5.8)	9 (3.8)
Contact sports injury		3 (1.3)	1 (0.4)
Unknown		0 (0.0)	2 (0.9)
Injuries associated with the open fracture† ; n (%)		58 (25.7)	76 (32.5)
Upper limb		17 (7.5)	32 (13.7)
Chest		24 (10.6)	22 (9.4)
Spine		21 (9.3)	22 (9.4)

Head	14 (6.2)	11 (4.7)
Pelvis	8 (3.5)	15 (6.4)
Ipsilateral lower limb	6 (2.7)	16 (6.8)
Contralateral lower limb	4 (1.8)	14 (6.0)
Abdomen	3 (1.3)	12 (5.1)
Gustilo & Anderson grade; n (%)		
Grade 2	34 (15.0)	30 (12.8)
Grade 3	171 (75.7)	180 (76.9)
Grade 3 + VI	21 (9.3)	24 (10.3)
Fracture fixation; n (%)		
External fixator-half-pin	107 (47.3)	111 (47.4)
Nail	49 (21.7)	56 (23.9)
Plate and screws	38 (16.8)	32 (13.7)
Other	21 (9.3)	21 (9.0)
External fixator-fine-wire	3 (1.3)	11 (4.7)
Wires/tension band wires	7 (3.1)	3 (1.3)
Unknown	1 (0.4)	0 (0.0)

IQR = interquartile range; sd = standard deviation;
† Some study participants had multiple injuries associated with the open fracture

Table 2. Primary and secondary outcomes

	NPWT		Standard		Difference (95% CI)		P value for adjusted analysis
	Mean (sd)	n	Mean (sd)	n	Raw†	Adjusted‡	
Primary outcome							
DRI (12 m)	45.5 (28.0)	179	42.4 (24.2)	195	-3.1 (-8.5 - 2.2)	-3.9 (-8.9 - 1.2)	0.13
Secondary outcomes							
Disability scores over time							
DRI (3 m)	64.3 (22.3)	166	65.6 (20.1)	188	1.3 (-3.1 - 5.8)	0.7 (-3.7 - 5.0)	0.76
DRI (6 m)	53.2 (23.8)	154	50.3 (24.1)	175	-2.8 (-8.0 - 2.4)	-3.5 (-8.4 - 1.5)	0.17
DRI (9 m)	49.2 (25.9)	153	45.4 (25.2)	161	-3.8 (-9.5 - 1.9)	-4.4 (-10.0 - 1.3)	0.13
Quality of life							
EQ-5D (12 m)	0.55 (0.33)	172	0.56 (0.32)	192	0.02 (-0.05 - 0.08)	0.01 (-0.06 - 0.07)	0.82
SF-12 PCS (12 m)	32.2 (17.4)	154	32.7 (15.5)	175	0.5 (-3.1 - 4.1)	0.4 (-3.0 - 3.8)	0.82
SF-12 MCS (12 m)	44.7 (8.4)	154	44.3 (8.2)	175	-0.4 (-2.2 - 1.4)	-0.2 (-2.1 - 1.6)	0.80

† Mean of Standard group minus mean of NPWT (Negative Pressure Wound Therapy) group; for DRI a negative value is in favor of the Standard treatment, as a lower score indicates less disability
‡ Mixed effects regression based on a complete case analysis with, treatment group, age group, gender, baseline pre-injury score and wound grade as covariates (fixed effects) and recruiting center as a random effect; p-values are from analysis of variance (ANOVA) F-test
sd = standard deviation
Disability Rating Index (DRI) is assessed on a 100-point score scale, where zero represents normal function and 100 complete disability, with a minimum clinically important difference of 8 points

EuroQol EQ-5D-3L (EQ-5D) is a measure of health-related quality of life, in the range -0.59 (worst possible state) to 1 (perfect health), anchored at 0 (death), with a minimum clinically important difference 0.08 points
SF-12 Physical and Mental health Composite Scores (PCS and MCS) are computed from the short form health survey and range from 0 to 100, where a 0 score indicates the lowest level of health

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Table 3: Post-operative complications reported as secondary outcomes during 12 months follow-up

Complication	NPWT (n = 226)	Standard (n = 234)	Difference (%)	Odds ratio‡	P value‡
Wound complications at 30 days					
Red and inflamed; n (%)	13 (5.8)	19 (8.1)	2.4 (-2.7 - 7.4)	0.64 (0.28 - 1.42)	0.27
Swollen; n (%)	38 (16.8)	49 (20.9)	4.1 (-3.4 - 11.7)	0.70 (0.42 - 1.16)	0.15
Painful/tender; n (%)	35 (15.5)	33 (14.1)	-1.4 (-8.3 - 5.5)	1.01 (0.58 - 1.77)	0.99
Fluid leaking; n (%)	28 (12.4)	27 (11.5)	-0.9 (-7.2 - 5.5)	1.01 (0.55 - 1.86)	0.99
Fluid (pus) cloudy; n (%)	11 (4.9)	10 (4.3)	-0.6 (-4.8 - 3.7)	1.21 (0.43 - 3.46)	0.81
Gaping open; n (%)	6 (2.7)	4 (1.7)	-0.9 (-4.1 - 2.2)	1.48 (0.34 - 7.22)	0.75
Surgeon opened; n (%)	2 (0.9)	0 (0.0)	-	-	-
Fever > 38°C; n (%)	0 (0.0)	0 (0.0)	-	-	-
Abscess/infection; n (%)	3 (1.3)	5 (2.1)	0.8 (-2.0 - 3.6)	0.57 (0.09 - 2.95)	0.49
Deep surgical site infection at 30 days					
Deep SSI†; n (%)	16 (7.1)	19 (8.1)	1.0 (-4.2 – 6.3)	0.85 (0.42 -1.70)	0.64
Other postoperative complications related to the index wound / injury reported during follow-up					
Soft Tissue^; n (%)	20 (8.8)	17 (7.3)	-1.6 (-7.0 - 3.8)	1.24 (0.60 - 2.59)	0.61
Neurovascular; n (%)	5 (2.2)	8 (3.4)	1.2 (-2.2 - 4.7)	0.64 (0.16 - 2.26)	0.58
Persistent pain; n (%)	8 (3.5)	11 (4.7)	1.2 (-2.9 - 5.2)	0.74 (0.25 - 2.08)	0.64
DVT/PE^^; n (%)	6 (2.7)	4 (1.7)	-0.9 (-4.1 - 2.2)	1.57 (0.37 - 7.65)	0.54
Further surgery related to the open fracture reported during follow-up					
Revision fixation; n (%)	18 (8.0)	15 (6.4)	-1.6 (-6.7 - 3.6)	1.26 (0.58 - 2.77)	0.59
Wound management; n (%)	19 (8.4)	21 (9.0)	0.6 (-5.0 - 6.1)	0.93 (0.46 - 1.88)	0.87
Bone graft; n (%)	10 (4.4)	18 (7.7)	3.3 (-1.5 – 8.0)	0.56 (0.22 - 1.31)	0.17
Amputation; n (%)	4 (1.8)	6 (2.6)	0.8 (-2.3 - 3.9)	0.69 (0.14 - 2.93)	0.75

‡ Unless stated otherwise, odds ratio, 95% confidence interval and p-value from Fisher's exact test; a value > 1 indicates a greater risk in the NPWT group; where testing was not possible or sensible, then these are marked as '-'

† Deep SSI was recorded according to CDC criteria: involvement of deep tissues with purulent drainage from the incision, or spontaneous dehiscence or incision deliberately opened by a surgeon and there was fever or localized pain or tenderness, or confirmation of abscess, or deep SSI diagnosed by a surgeon/attending physician.

^ Complications that are not related to the bone and not included under wound infection, for example problems causes by scar tissue or tendon irritation.

^^ Deep vein thrombosis/Pulmonary Embolism