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Surgical site infection following incisional negative pressure wound therapy in lower limb amputation closure: A randomized controlled trial

Satya Prakash Meena, Spoorthi D. Shetty, Mayank Badkur, Mahendra Lodha, Mahaveer Singh Rodha, Ramkaran Chaudhary, Naveen Sharma

Abstract:

BACKGROUND: Major amputations are a standard procedure being done for various etiologies of the lower limb. Surgical site infections often complicate the postoperative outcome of patients. Negative pressure wound therapy has evolved to have a preventive role in SSI. According to the best of our knowledge, this is the first study that compared the wound and overall outcomes of incisional application of NPWT against standard dressing in patients undergoing stump closure following major lower limb amputations. The primary goal was to compare the rate of surgical site infections. The secondary objectives were to compare the postoperative hospital stay, reinterventions, readmission, and mortality.

MATERIALS AND METHODS: A randomized controlled trial was conducted in a healthcare institute and included 62 patients who underwent closure of major lower limb amputation stumps. After stump closure, patients were randomized into iNPWT and standard groups for the dressing over the suture line. Surgical site infection and other outcomes were assessed.

RESULTS: A statistically significant difference was found in the rate of surgical site infection (16% vs 51%, $P = 0.003$). Also, it appreciated a significant reduction in the number of patients needing reinterventions (26% vs 52%, $P = 0.037$) and the duration of postoperative hospital stay (5.8 days vs 8.2 days, $P = 0.043$) in the iNPWT group.

CONCLUSION: Incisional application of NPWT following lower limb amputations is an effective tool to reduce surgical site infections, the need of multiple reinterventions, the cost of treatment, and hospital stay. We should use this special dressing as a standard protocol for the high-risk patients undergoing stump closure following major amputations; therefore, it can reduce the morbidity of patients.

Keywords:

Amputation, incisional NPWT, lower limb, surgical site infection

Introduction

Surgical site infection (SSI) is the most common local complication following lower limb amputation. The incidence of which ranges from 5.5 to 11%, followed by local hematoma.[1-4] A complication-free postoperative period allows early prosthesis fitting, mobilization, and return to routine activity.[5] Wound infections following amputations may require interventions ranging from a course of antibiotics, opening up of sutures, and debridement to revision of the stump, all of which prolong the duration of hospital stay and add to the financial and psychological burden.[6]

The study aimed to compare the wound and overall outcomes of incisional application of NPWT (iNPWT) against standard dressing

Department of General Surgery, All India Institute of Medical Sciences Jodhpur, Rajasthan, India

Address for correspondence:
Dr. Satya Prakash Meena, Department of General Surgery, All India Institute of Medical Sciences Jodhpur, Rajasthan, India.
E-mail: drsatyaprakash04@gmail.com

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in patients undergoing stump closure for major lower limb amputations.

Hypothesis

Incisional application of the NPWT technique has a better outcome than standard dressing following major lower limb amputations.

Material and Method

Study design and setting

A randomized controlled trial study was conducted in the Department of General Surgery of healthcare institute of North India, between July 2021 and December 2022.

Study participants and sampling

A total of 62 patients and 31 patients in each group were included [Figure 1 CONSORT Diagram]. The study included all patients, undergoing skin closure following major lower limb amputation. The study excluded all patients who have allergy or hypersensitivity to the materials used in iNPWT and have a skin disease with lesions at the site of the iNPWT application. The patients or family members, who were not willing to participate in the study, were also excluded.

Sample size calculation

Vikas Kotha *et al*.,[7] in their systematic review, have found the rate of SSI to reduce from 48 to 7 % on using NPWT. Considering this for calculation, we estimated a sample size of 31 patients per group at 95% CI, 90% power, and 10% contingency.

Novelty and rational of study

Many randomized trials prove the superiority of iNPWT over standard dressings in managing high-risk wounds in other surgeries like cesarean sections, and vascular and cardiothoracic surgeries. Many retrospective studies, case series, systematic reviews, and meta-analyses are available regarding its use over amputations. However, no good prospective, randomized trial has been done to date.

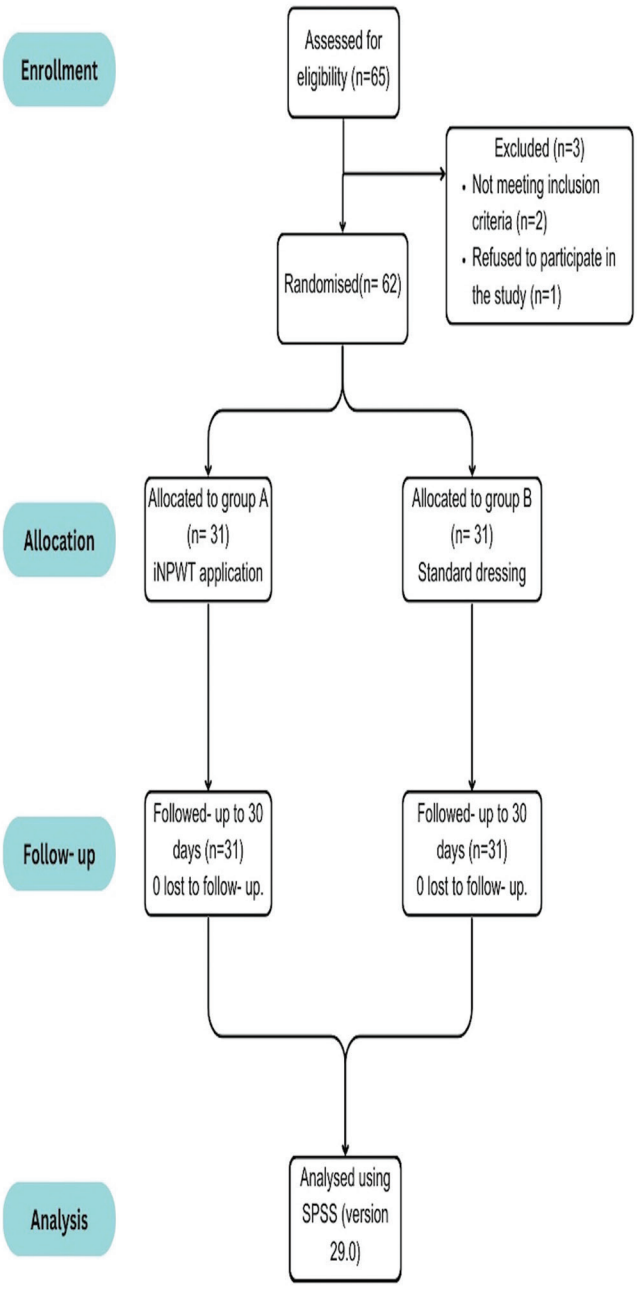

Figure 1: CONSORT flow diagram

Definition of surgical site infection (According to CDC)[8,9]

It is an infection that occurs in any part of body where the surgery took place within 30 days or 90 days in high-risk patients. Usually, it is superficial and involves the skin only, but sometimes may involve deep soft tissues, deep organ space, and underlying implants in high-risk patients.

Study procedures

In the Department of General Surgery, this randomized controlled trial was carried out with the approval of the institutional research committee and institutional ethics committee. Patients underwent a basic preoperative clinical evaluation, regular laboratory tests, and screening for any exclusion criteria. After determining that the patient (or relative) was fit to be included in the study, informed consent was obtained after thoroughly explaining the study's design to them using the patient information sheet. Patients were transferred to the operating room, and following skin closure of above or below knee amputation, if done, patients were randomized into incisional NPWT application group and standard dressing group. This randomization–block randomization using random permuted blocks was done based on the sequence

generated by the website www.randomization.com and was an open-label study, with no blinding. The allotment concealment was done by sequentially numbered opaque sealed envelopes.

All lower limb amputation stumps were closed in layers and the skin was closed with nonabsorbable sutures with a negative suction drain, which was removed on the postoperative day (POD-2). All patients had antibiotic cover in the form of amoxicillin–clavulanate drug half an hour before surgery followed by 8 hours after surgery for 3 days.

In the first group, following skin closure, a thin strip of VAC foam was applied in a sterile manner, as a postoperative dressing. An adhesive transparent film was applied on top of it, and a negative pressure of 80 mmHg (±20 mmHg) was applied using the VAC machine. [Figure 2] The dressing was opened on POD-4 and the wound was assessed. The iNPWT in this study made use of the same VAC foam and apparatus that is used for open wounds—the CCNPWT dressing kit by Triage Meditech and applied the foam strip over a strip of paraffin gauze placed on the incision line, followed by the adhesive dressing.

In the second group, following skin closure, the standard sterile postoperative dressing was applied and removed on POD-2. They had daily dressings until the incision site appeared dry and the wound was assessed on POD-4. The presence of SSIs was recorded, based on the CDC criteria for SSI.[9] [Figure 3] In the absence of SSI, the patient was discharged and followed up weekly on an outpatient basis or telephonically for a total duration of 4 weeks (30 days). If SSI was present, it was managed accordingly, and the total duration of hospital stay was recorded. During the follow-up period, the reinterventions required, readmissions for stump complications, and mortality were recorded.

Statistical analysis

Data was entered and analyzed using the Statistical Package for Social Sciences (SPSS) version (29.0). Descriptive data was reported for each variable. Descriptive statistics such as mean, standard deviation for continuous variables, and frequency along with percentages of categorical variables were calculated. Summarised data was presented using graphs and tables. Student *t* test was used for comparison of quantitative data with normal distribution. Mann–Whitney *U* test was used to compare numerical data without normal distribution. The Chi-square test or Fisher exact test was used for categorical data. A P value of < 0.05 was taken as significant.

Ethical consideration

Consent was obtained or waived by all participants in this study. Institutional Ethics Committee, All India Institute of Medical Sciences, Jodhpur, issued research approval (AIIMS/IEC/2021/3611). Also, the study is registered in the Clinical Trial Registry of India with the registration number CTRI/2021/09/036945.

Results

The mean age of patients enrolled in the study was 57.17 years (SD-14.1). More than 75% of the study population were male. In the study population, diabetes mellitus was the most common comorbidity followed by hypertension. Out of all, 52% of patients enrolled in the study were habitual smokers or had a history of tobacco chewing. [Table 1] Fifty percent of all patients had wet gangreene followed by dry gangreene due to chronic vascular insufficiency. Most of the patients underwent below-knee amputation and had primary closure of stump or skin [Table 2].

Five amputation stumps (16%) of the iNPWT group and 16 amputation stumps (51%) of the standard dressing

Figure 2: Application of iNPWT over a below-knee amputation stump

Figure 3: Surgical site infection

group had SSI and were found to be statistically significant (P = 0.003). Seven percent patients in the iNPWT group had superficial SSI compared to the standard dressing group (51%) which was significant (P = 0.02). Ten percent of patients in iNPWT group had deep SSI compared to the standard dressing group (23%) and was not significant (P = 0.17) [Table 3].

The risk ratio (RR) of a patient with standard dressing developing an SSI, compared to iNPWT, was 3.2 (95% CI, 1.33–7.65). This means that a patient undergoing standard dressing after amputation is thrice as likely to develop an SSI than a patient who underwent the iNPWT application. Among the amputation stumps that underwent primary closure, the SSIs were significantly reduced in the iNPWT group (17.8%) compared to the standard dressing group (52.2%) (P value of 0.0096) calculated using the Chi-square test. [Table 4] The most common organism isolated from the infected stumps was Klebsiella pneumoniae (28.5%), followed by *Escherichia coli* (19%) and Pseudomonas aeruginosa (14.3%).

A total of 12 additional procedures were performed on the amputation stump in the iNPWT group and 17 in

Table 1: Baseline characteristics and comparison between iNPWT and standard dressing groups

Variable		iNPWT group (*n*=31)	Standard group (*n*=31)	Total (*n*=62)
Mean age in years (SD)		59.2 (11.3)	55.2 (16.4)	57.17 (14.1)
Gender, *n* (%)	Male	24 (77%)	25 (81%)	49 (79%)
	Female	7 (23%)	6 (19%)	13 (21%)
Comorbidities	Diabetes mellitus	10 (32%)	15 (48%)	25 (40%)
	Hypertension	10 (32%)	14 (45%)	24 (39%)
	Obstructive airway disease	3 (10%)	2 (6%)	5 (8%)
	Coronary artery disease	4 (13%)	3 (10%)	7 (11%)
Substance abuse	Tobacco chewing	5 (16%)	8 (26%)	13 (21%)
	Smoking	16 (52%)	13 (42%)	29 (47%)
	Alcohol	1 (3%)	4 (13%)	5 (8%)

Table 2: Indications, level of amputation, and timing of stump closure

Variable		iNPWT group (*n*=31)	Standard group (*n*=31)	Total (*n*=62)
Wet gangrene	A) Infected lower limb with diabetes	5 (16%)	12 (39%)	17 (27%)
	B) Vascular insufficiency	10 (32%)	4 (13%)	14 (23%)
	Total	15 (48%)	16 (52%)	31 (50%)
Chronic vascular insufficiency with dry gangrene		15 (48%)	9 (29%)	24 (39%)
Trauma		1 (4%)	6 (19%)	7 (11%)
Level of amputation	Above knee amputation	12 (39%)	17 (55%)	29 (46%)
	Below knee amputation	19 (61%)	14 (45%)	33 (54%)
Timing of stump closure	Primary	28 (90%)	23 (74%)	51 (82%)
	Delayed	3 (10%)	8 (26%)	11 (18%)

Table 3: Postoperative outcomes inluding morbidity, mortality of study patients during 6-month follow-up

Variable		iNPWT group (*n*=31)	Standard group (*n*=31)	Total (*n*=62)	*P**
Surgical site infection (SSI)	Total	5 (16%)	16 (51%)	21 (34%)	0.003
	Superficial	2 (7%)	9 (29%)	11 (18%)	0.02
	Deep	3 (10%)	7 (23%)	10 (16%)	0.17
Patients who needed a reintervention, *n* (%)		8 (26%)	16 (52%)	24 (39%)	0.037
Duration of postoperative hospital stay in days, mean (SD)		5.8 (2.5)	8.2 (5.9)	7.0 (4.7)	0.043
Number of patients who had readmission *n* (%)		4 (13%)	6 (19%)	10 (16%)	0.490
Mortality, *n* (%)		4 (13%)	4 (13%)	8 (13%)	1.000
Patients who used prosthetic limb, *n* (%)		22 (70.9%)	19 (61.2%)	41 (66.1%)	0.421
Return to work, *n* (%)		20 (64.5%)	18 (58%)	38 (61.2%)	0.602

Table 4: Surgical site infection based on timing of stump closure (*n*=62)

Variable	Primary closure (*n*=51)		*P*	Delayed closure (*n*=11)		*P*
	iNPWT group (*n*=28)	Standard group (*n*=23)		iNPWT group (*n*=3)	Standard group (*n*=8)	
Total SSI	5 (17.85%)	12 (52.17%)	0.0096	0 (0%)	4 (50%)	0.2364
A) Superficial SSI	2 (7.14%)	6 (26.08%)		0 (0%)	3 (37.5%)	
B) Deep SSI	3 (10.71%)	6 (26.08%)		0 (0%)	1 (12.5%)	

the standard group, ranging from partial suture removal to stump revision. A total of four amputation stumps progressed from a below-knee level to an above-knee amputation due to stump complications. This comprised two (10%) out of 19 BKA in the iNPWT group and two (14%) out of 14 BKA in the standard group. Eight patients (26%) belonging to the iNPWT group and 16 (52%) of the standard dressing group needed some form of reintervention to manage the stump complications and the result was statistically significant ($P = 0.037$).

The mean duration of postoperative hospital stay differed between the two groups and was 5.8 days (SD-2.5) for iNPWT, while it was 8.2 days (SD-5.9) for the standard group. The difference in hospital stay between groups was statistically significant ($P = 0.043$). The iNPWT group had a mortality rate of 6% (two patients), while in a standard group, it was 3% (one patient) in 30 days ($P = 0.554$) and four patients in each group died in 6 months ($P = 1.000$). Hence, no significant difference was found in mortality between groups.

By the 6-month follow-up, the number of patients needing readmission after surgery was 4 (13%) in iNPWT and 6 (19%) in the standard group ($P = 0.490$). Of the 54 patients, 41 (75.9%) had a prosthetic limb fitted and had resumed return to work ($P = 0.602$). There was no significant difference in the use of prosthesis between both groups ($P = 0.421$). The patients had no features of deep vein thromosis, pulmonary embolism, strock, and gastrointestinal bleed during the postoperative period in both groups.

Discussion

This randomized control trial suggests that the SSIs following major lower limb amputations are significantly reduced by applying iNPWT over the suture line compared to standard dressing. Based on the wound assessment done on POD-4, there was a reduction in the rate of both superficial and deep SSIs with the iNPWT application. The patients receiving standard dressing had a threefold higher risk for developing SSI than those receiving iNPWT dressings.

Chang *et al*.[10] did a retrospective comparative cohort study to evaluate the use of closed incision negative pressure wound therapy in reducing wound complications after major lower limb amputations, including SSIs. They demonstrated that applying iNPWT on lower limb amputation stump incisions significantly reduced the SSIs. The wound assessment was done twice, first on the removal of the dressing (5–7 days for the NPWT group and 3–5 days for the control group) and the second after 30 days. This contrasts with the present study, where wound assessment was done only on POD-4, and patients were followed up for other outcomes. That study was nonrandomized, retrospective, and based on a prospectively maintained database.

Multiple meta-analyses also showed results in favor of iNPWT about SSIs. Semsarzadeh *et al*.[11] performed a meta-analysis to assess the effectiveness of iNPWT in reducing SSIs as compared to standard dressings. They evaluated incisions in different specialities and areas of the body. The results were in favor of iNPWT, and they concluded that iNPWT is potentially effective in reducing SSIs.

Another meta-analysis by Frodl *et al*.[12] on the iNPWT application over amputation stumps concluded that the use of iNPWT as postoperative dressing reduces the postoperative wound complications, but has no significant effect on the 30-day mortality. All included studies were retrospective and had no randomized controlled studies.

Masden *et al*.[13] conducted a randomised controlled study on the application of iNPWT on high-risk wounds. They included various incisions, most of which belonged to the lower limb. This study showed no significant reduction in the SSIs in patients who underwent the iNPWT application.

In the present study, the requirement of reintervention for stump complications was also significantly lesser in the iNPWT group. Patients who underwent standard dressing over the amputation stump were twice as likely to need a reintervention for stump complications. In the studies of the iNPWT application on amputation stumps performed by Chang *et al*., Gantz *et al*., Stenqvist *et al*., and the meta-analysis by Frodl *et al*., there was no reduction in the reinterventions for amputation stumps managed postoperatively with iNPWT compared to standard dressing.[10-15]

Some studies on the iNPWT application in vascular surgery like the ones conducted by Kwon *et al*.[16] and Pleger *et al*.[17] showed reduced reoperation rates with iNPWT use.

In this study, the postoperative hospital stay was significantly shorter in the iNPWT group. Patients of both groups were observed on an in-patient basis for four days postoperatively and discharged based on wound assessment on POD-4. Any further prolongation of hospital stay in the index admission was due to early stump complications, which were higher in the standard dressing group or for managing systemic medical illnesses. The prolonged postoperative hospital stay in the standard dressing group can be attributed to the higher wound infections and reinterventions needed to manage them.

Stenqvist *et al*. and Chang *et al*. reported no reduction in the duration of hospital stay, while Gantz *et al*. reported a longer hospital stay after the iNPWT application on amputation stumps even with a reduction in SSIs in this group.[10,14,15] Other studies where iNPWT was applied over other incisions like arthroplasty by Newman *et al*.[18] and cardiac surgery, by Lee *et al*.,[19] found a reduced length of hospital stay in the iNPWT group. In the current published literature on iNPWT use over amputation stumps, no other studies have reported a reduction in the length of hospital stay.

All the deaths within 30 days of surgery happened due to other associated causes like one patient had a sequela of cerebral toxoplasmosis, the second had massive pulmonary thromboembolism, and the third had myocardial infarction following stump infection.

Gantz *et al*.,[14] in their retrospective study, demonstrated a five-fold reduction in the SSIs in the iNPWT group compared to the standard dressing group, and also clinically, but not statistically significant decrease in the 30-day readmissions by 25% and mortality by 50%. Chang *et al*.[10] concluded that the iNPWT application, although reduced SSIs, did not affect the rates of readmission and mortality.

In this study, regular follow-up was done for all patients—in the outpatient clinic when feasible or telephonically. Exceptions were for the patients who deceased before the 30-day follow-up period.

The patients were allocated to groups based on a computer-generated random sequence into either group. Consequently, risk factors for SSI were also randomly distributed between both groups. On assessing these risk factors within both groups, it was found that few risk factors were more in the iNPWT group—higher mean age, smoking, and indication for amputation being chronic vascular insufficiency. On the other hand, the standard group—which had more wound infections, had more patients with diabetes, hypertension, tobacco chewing, and alcohol consumption. Although the infective indications for amputations were similar in both groups, more amputations were done for traumatic indications in the standard group than in the iNPWT group.

This study included stumps closed at the time of initial surgery (primary closure), as well as stumps closed in a staged manner after an initial guillotine amputation (delayed closure). In the latter, serial dressings and debridements were done following the initial guillotine amputation. The decision for stump closure was taken by the treating surgeon, based on clinical assessment of the stump.

Between both groups, more amputation stumps were primarily closed in the iNPWT group compared to the standard dressing group. Some studies, like the one conducted by Ali *et al*.,[20] have reported lesser wound complications in amputation stumps that underwent delayed closure than primary closure, while others, done by Katiyar *et al*.[21] on traumatic amputations, found no significant difference.

With these differences in both groups, the application of incisional NPWT reduced the incidence of SSIs in lower limb amputation stumps significantly.

In addition to patient outcomes, some studies performed by Kwon *et al*.[16] on vascular surgeries and Ruhstaller *et al*.[22] on Caesarean sections have evaluated the cost-effectiveness of iNPWT. While the VAC material is expensive, its application has been shown in this study to reduce SSIs, reinterventions, and duration of hospital stay, which makes up for the cost of materials. In the present study, cost-effectiveness was not an outcome that was studied, and being conducted in a government setup, the application of iNPWT was not chargeable for the patient and was provided by the institute.

In this study, the total number of patients who needed reintervention was greater than the total number of patients with SSI. This can be explained by wound dehiscence in the absence of infection, progression of limb ischemia, and late presentations of wound infections.

The positive results shown by this study can evoke a change in the current practices for the management of amputation stumps—advocating the use of the incisional application of NPWT over closed amputation stumps and more so in patients with multiple risk factors for SSIs.

More economical alternatives for iNPWT can be explored in future research. Furthermore, cost-effectiveness analyses and other outcomes like quality of life, time to prosthesis fitting, and recommencement of routine activities can also be compared between iNPWT and standard dressings.

Conclusion

Incisional negative pressure wound therapy as a postoperative dressing is an effective tool for managing amputation stumps. Its use over the surgical site leads to a reduction in the SSIs, the number of reoperations, and hospital stay. The application of iNPWT should be considered as a special postoperative dressing over the suture line of the amputated stump. Therefore, it may reduce the morbidity caused by wound infection in amputees.

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Abbreviation
CDC—Centers for Disease Control and Prevention, NPWT—Negative pressure wound therapy, iNPWT—Incisional application of negative pressure wound therapy, SSI—Surgical site infection, POD—Postoperative day, BKA—Below-knee amputation.

Ethical consideration
Consent was obtained or waived by all participants in this study. Institutional Ethics Committee, All India Institute of Medical Sciences, Jodhpur, issued research approval (AIIMS/IEC/2021/3611).

Authors' contributions and approval
This manuscript is read by all authors and has been approved for submission in your journal.

All authors have made contributions to the manuscript's concept, design, definition of intellectual content, literature search, clinical studies, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing, and manuscript review.

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Conflicts of interest
There are no conflicts of interest.

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