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Original Research Article

Incisional Negative Pressure Wound Therapy for Wounds in Patients with Lower Intestinal Perforations

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Abstract
Objectives: Laparotomy for lower intestinal perforation is associated with a high incidence of surgical site infections. This study aimed to assess whether incisional negative pressure wound therapy (iNPWT) could reduce the incidence of these infections and wound dehiscence in patients with lower intestinal perforation.
Methods: This single-center prospective study was conducted between September 2019 and July 2022. In the therapy group, wounds were closed with subcuticular sutures, and iNPWT was applied at -120 mmHg for 5 days. A total of 10 days of iNPWT was employed. These patients were compared with a historical control group. The iNPWT group (Group A) comprised 22 patients.The historical control group (Group B) had 65 patients. Table 1 outlines patient characteristics and compares the two study groups.
Results: Patient characteristics were demographically similar. The incidence of surgical site infections was lower in the therapy group than in the control group (9.1% vs. 52.3%, $p < 0.001$). Wound dehiscence was not observed in the therapy group but was noted in three patients (4.6%) in the control group. In univariate and multivariate analysis, an application of the therapy device was associated with reduced incidence of surgical site infections ($p < 0.001$ and $p = 0.002$, respectively).
Conclusions: The application of iNPWT in patients with lower intestinal perforation was associated with reduced surgical site infections.

Keywords
perforation, surgical site infections, negative pressure wound therapy

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Introduction

Lower intestinal perforation is a serious condition requiring emergency surgery, leading to multiple postoperative complications, among which surgical site infections (SSIs) are the most common (32%-63%)[1,2]. SSIs require frequent wound irrigation and dressing changes and markedly reduce patient satisfaction because of prolonged hospital stays, increased medical costs, negative impact on the quality of life, and a high risk of incisional hernias[3-5]. Therefore, developing effective preventive measures for SSIs is essential.

Incisional negative pressure wound therapy (iNPWT) is a relatively new technique that has been applied in multiple fields of surgery to prevent SSIs[6-8]. However, to the best of our knowledge, no previous studies have assessed iNPWT in lower intestinal perforations. This study aimed to evaluate whether iNPWT is associated with a lower incidence of SSIs and wound dehiscence than standard postoperative dressings in patients with lower intestinal perforations.

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Table 1. Patient Characteristics.

Factor		Group A (n=22)	Group B (n=65)	*P*-Value
Age (range), years		75 (48-96)	73 (18-95)	0.574
Male gender		12 (54.5)	32 (49.2)	0.806
Body mass index (range), kg/m^2		20.8 (14.5-32.3)	20.7 (14.0-30.7)	0.857
Diabetes mellitus		4 (18.2)	10 (15.4)	0.745
Steroid use		2 (9.1)	3 (4.6)	0.597
Site of perforation				
Large bowel	Perforated colorectal cancer	3 (13.6)	6 (9.2)	0.538
	Diverticular perforation	9 (40.9)	26 (40.0)	
	Anastomotic leakage	5 (22.7)	15 (23.1)	
	Others	0 (0.0)	7 (10.8)	
Small bowel	Iatrogenic	3 (13.6)	1 (1.5)	
	Foreign body	0 (0.0)	2 (3.1)	
	Reason unknown	2 (9.1)	7 (10.8)	
	Others	0 (0.0)	1 (1.5)	

Data are reported as a percentage or as a range.

Methods

Study design

This single-center prospective study was conducted from September 2019 to July 2022 at the Jikei University Daisan Hospital, Japan. This study included patients who underwent emergency open surgery for lower intestinal perforations. Patients were managed using an iNPWT device and compared with a historical control group with lower intestinal perforations (from January 2015 to August 2019), who were managed using standard postoperative dressings. Cases of additional surgery and death within 30 days of surgery were excluded owing to challenges in the assessment of SSIs. We evaluated the differences in the incidence of SSIs and wound dehiscence between the two groups. Data for the historical control group were obtained from a prospectively collected SSI surveillance database and electronic medical records. The study protocol was approved by the Ethics Committee of the Jikei University School of Medicine (registration no. 32-340 [10427]). Informed consent was obtained from all patients who participated prospectively in the study, while study participants whose data were collected retrospectively could opt out.

Definition of SSIs

Incisional SSI was defined as an infection at the incision site within 30 days of surgery, according to the standardized criteria outlined by the Centers for Disease Control and Prevention[9]. SSIs are characterized by at least one of the following features: purulent drainage from the incision; isolation of an organism in a culture of fluid from the incision; incisional pain, tenderness, localized swelling, redness, or heat upon opening the incision; or diagnosis by the surgeon or attending physician. Superficial incisional SSIs involve only the skin or subcutaneous tissue at the incision site. Deep incisional SSIs affect soft tissues at the incision site.

Wound management

In the historical group, the method of wound closure depended on the surgeon, and wound management was performed using only regular dressings. In the iNPWT group, the abdomen was closed with absorbable sutures, and the wound was closed with subcuticular sutures using 4-0 absorbable monofilament sutures. iNPWT (RENASYS-AB Abdominal Dressing and RENASYS EZ pump (Smith & Nephew, Hull, United Kingdom)) was applied at -120 mmHg for 5 days beginning immediately or on the day after surgery (Figure 1). If NPWT could not be maintained for 5 days for any reason, the wound was checked constantly, and NPWT was re-applied when judged possible. The duration of NPWT was 10 days in all cases. NPWT was replaced 1-3 times.

Statistical analysis

All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (R Foundation for Statistical Computing, Vienna, Austria[10]).

Demographic data, clinical variables, and operative measures were collected for all the patients. Medians/ranges and means/standard deviations were reported for all continuous data depending on the data distribution. Counts and percentages were calculated for categorical data. Univariate analyses were performed using Pearson's chi-square or Fisher's exact tests for categorical variables and the Mann-Whitney U test for continuous variables, as appropriate. Univariate and multivariate analyses were performed using logistic regression analysis. The 95% confidence intervals were calculated using the Clopper-Pearson method. All p values were two-sided. Statistical significance was set at $p < 0.05$.

Results

This study included 103 patients who underwent emergency open surgery for lower intestinal perforations between January 2015 and July 2022 (Figure 2). The iNPWT group (Group A) comprised 22 patients, excluding two with reoperations and four deaths within 30 days of surgery. The historical control group (Group B) had 65 patients, excluding five with early reoperations and five with premature deaths.

Table 1 outlines patient characteristics and compares the two study groups. The groups were demographically similar in age, sex, body mass index, diabetes mellitus, and steroid use. The site of perforation was similar between the groups.

Figure 1. Application of incisional negative pressure therapy device. The wound was roughly closed using subcuticular sutures with absorbable monofilament sutures. The extension foam was covered with tape, and the suction track was placed over it. Suction was applied at 120 mmHg.

A comparison of the operative and postoperative findings between the two groups is shown in Table 2. The NPWT device was scheduled to be worn for 5 consecutive days, replaced only once, and continued for 10 days. However, in stoma cases, the iNPWT device was sometimes removed at the same time the stoma was replaced. The NPWT device replacement frequency averaged 1.68 times over the entire study period. No significant differences were observed in blood perfusion, operative time, stoma creation, respiratory or cardiovascular complications, or median length of intensive care unit stay between the groups. Two out of 22 patients (9.1%) in Group A and 34 out of 65 (52.3%) in Group B had SSIs. SSIs and postoperative complications were significantly less frequent in Group A ($p < 0.001$) than in Group B. Wound dehiscence was not observed in Group A but in three patients (4.6%) in Group B. The median length of hospital stay was slightly shorter in Group A than in Group B (30 days vs. 24 days), but the difference was not statistically significant.

Table 3 shows the risk factors for SSIs. Applying the iNPWT device was associated with a reduced incidence of SSIs in univariate and multivariate analyses ($p < 0.001$ and $p = 0.002$). No significant differences were found in the other factors.

Discussion

This is the first study to evaluate using an iNPWT device in patients who underwent open emergency surgery for lower intestinal perforation. The results of this study suggest that the application of the iNPWT device in patients with lower intestinal perforation is associated with a reduced incidence of SSIs (iNPWT vs. standard postoperative dressing, 52.3% vs. 9.1% [$p < 0.001$]). Wound dehiscence was not observed in the iNPWT group.

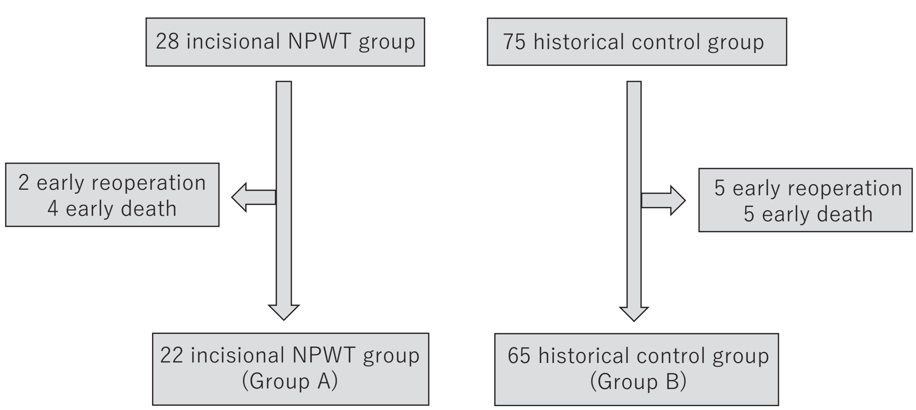

Figure 2. Flowchart of the patient selection.
NPWT: negative pressure wound therapy

Table 2. Operative and Postoperative Findings.

Factor	Group A (n=22)	Group B (n=65)	*P*-Value
Operative findings			
Blood perfusion	7 (31.8)	22 (33.8)	1
Operative time (range), min	166 (73-280)	145 (74-283)	0.632
Stoma creation	17 (77.3)	58 (89.2)	0.17
Postoperative findings			
Overall postoperative complications	13 (59.1)	47 (72.3)	**<0.001**
Surgical site infections	2 (9.1)	34 (52.3)	**<0.001**
Superficial	1 (4.5)	12 (18.5)	0.109
Deep	0 (0.0)	12 (18.5)	0.033
Organ/Space	1 (4.5)	10 (15.4)	0.568
Wound dehiscence	0 (0.0)	3 (4.6)	0.568
Respiratory complications	3 (13.6)	4 (6.2)	0.362
Cardiovascular complications	2 (9.1)	9 (13.8)	0.687
Median length of ICU stay (range), day	3 (0-17)	3 (0-80)	0.781
Median length of hospital stay (range), day	24 (12-150)	30 (8-180)	0.423

Data are reported as a percentage or as a range.
ICU: intensive care unit

Table 3. Univariate and Multivariate Analyses of Risk Factors for Surgical Site Infections.

Factor	Univariate Analysis				Multivariate Analysis		
Category	Event Rate %	OR	95% CI	*P*-Value	OR	95% CI	*P*-Value
Male sex	17 (47.2)	0.797	0.310-2.036	0.661			
Age≥ 80 years	11 (30.6)	0.963	0.341-2.657	1.000			
Body mass index≥ 25 kg/m^2	6 (16.7)	1.254	0.314-4.851	0.765			
Transfusion	16 (44.4)	2.314	0.854-6.423	0.105	2.400	0.861-6.710	0.094
Diabetes mellitus	5 (13.9)	0.755	0.180-2.810	0.771			
Steroid use	1 (2.8)	0.339	0.007-3.628	0.399			
Stoma creation	34 (94.4)	4.088	0.792-40.90	0.112	2.910	0.530-16.00	0.219
Operative time≥ 100 min	34 (94.4)	2.677	0.469-28.02	0.296			
Large bowel	31 (86.1)	1.694	0.480-6.895	0.413			
Application of iNPWT device	2 (5.6)	0.093	0.010-0.435	**<0.001**	0.087	0.018-0.422	**0.002**

iNPWT: incisional negative pressure wound therapy

SSIs pose significant physical, psychological, and economic burdens; therefore, emphasis should be placed on lowering healthcare costs and enhancing the quality of care. SSIs are associated with a near-doubling length of hospital stay and cost of admission[3,11] and an increased risk of incisional hernias[4]. Delayed primary closure (DPC) is a valuable technique to reduce SSIs in contaminated wounds[12]. However, patients experience discomfort until the open wound is closed, and long-term wound management is required until healing is complete.

Management of severely contaminated wounds has improved over the past few decades with the development of NPWT. NPWT was first introduced in 1997, leading to increased blood flow and granulation tissue formation with decreased bacterial growth[13]. NPWT has been clinically proven to accelerate wound healing and is commonly used to treat open contaminated wounds. Ota et al. conducted a prospective multicenter cohort study of patients with lower intestinal perforation who underwent open NPWT followed by DPC, resulting in low SSIs, and concluded that this approach is promising as an alternative to traditional DPC alone[14]. Healing time and inconvenience to patients have decreased using NPWT. However, this technique requires wound closure under local anesthesia, and the dressing must be changed two to three times a week, complicating the procedure.

NPWT has been used in closed surgical incisions as iNPWT since 2006[15]. Mechanisms of the effect of NPWT in closed incisions are thought to be partially different from those in open wounds: (i) protection of the incision from external contamination, (ii) decreased lateral tension and dead space, (iii) decreased edema due to increased skin perfusion and lymphatic flow, and (iv) applied pressure causing micro-deformation and the release of local growth factors, which accelerate healing of the surgical incisions[16,17]. These mechanisms result in a decrease in SSIs. In surgeries for lower intestinal perforation, the wound is potentially exposed to digestive juices and feces, and wound healing may be impaired due to inadequate circulation. Therefore, iNPWT is expected to reduce the number of bacteria, remove exudates, and increase blood and lymphatic flow at the wound site. Frazee et al. defined complete healing as epithelialization of the wound and removal of staples/dressings and compared open NPWT and iNPWT for contaminated and dirty surgical wounds. The dressing was changed three times per week in the open NPWT group, while the dressing placed at the time of closure remained in place for 7 days and then removed in the iNPWT group[6]. Wound healing occurred at a median of 48 days (range, 6-126 days) in the open NPWT group and 7 days (range, 6-12 days) in the iNPWT group. Therefore, iNPWT is likely an effective method for preventing SSIs.

The effect of iNPWT on incisional hernias could not be accurately evaluated in this study because of the short follow-up period in Group A. However, incisional hernias occurred in one out of 22 patients in Group A (4.5%, median follow-up: 19 months) and 18 out of 65 patients in Group B (27.7%, median follow-up: 66 months) (p = 0.034). iNPWT is expected to help decrease the incidence of incisional hernias, although long-term follow-up is needed.

Our study had some limitations. First, this was a single-center study with a relatively small sample size and was not a randomized controlled trial. However, there were no significant differences between the two groups. Second, chronological differences were observed between the two groups. Group A received iNPWT from September 2019 to July 2022, while the historical group received standard post-operative dressing from September 2015 to August 2019. The quality of medical care and the proficiency of surgeons have improved during this time. Therefore, the iNPWT group has benefited from improved perioperative management, which may accentuate the low SSI rate. Third, the choice of NPWT device type, optimal negative pressure, and duration were not determined. These parameters differed depending on the study. The PICO® (Smith & Nephew, Hull, United Kingdom) device is easier to use, but its maximum negative pressure is 80 mmHg. Negative pressure of 120 mmHg was considered more suitable for patients with thick subcutaneous fat, and RENASYS® was preferred. The duration of application of 4-7 days was used across studies. Although no evidence suggests the superiority of a longer duration of NPWT therapy regarding wound outcomes, our standard period was 10 days, with one exchange after 5 days, because we believed that SSIs could be reduced by application for a more extended period than that in previous studies.

In conclusion, our results suggest that applying iNPWT in patients with lower intestinal perforation is associated with a reduced incidence of SSIs and wound dehiscence. Further studies are needed to determine the appropriate guidelines for NPWT management.

Conflicts of Interest
There are no conflicts of interest.

Author Contributions
Yuhei Tsukazaki and Hiroya Enomoto contributed equally to this study. Yuhei Tsukazaki and Hiroya Enomoto collected and interpreted the data and wrote the manuscript. Nana Takeuchi, Takuro Ushigome, Katsuhito Suwa, Tomoyoshi Okamoto, and Ken Eto made substantial contributions to the conception and design of the study and were involved in drafting the manuscript and revising it critically for important intellectual content. All authors declare that they have contributed to this article and have approved the final submitted version. Authors have full control of all primary data and agree to allow the journal to review the data if requested.

Approval by Institutional Review Board (IRB)
The study protocol was approved by the Ethics Committee of the Jikei University School of Medicine (registration no. 32-340 [10427]).

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