

New Advances in Negative Pressure Wound Therapy (NPWT) for Surgical Wounds of Patients Affected with Crohn's Disease

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ABSTRACT

Surgical site complications (SSC) negatively affect costs of care and prolong length of stay. Crohn's disease (CD) is a risk factor for SSC. CD patients often need surgery, sometimes requiring stoma. Our primary aim was to compare the effects on SSC of a portable device for NPWT (PICO, Smith & Nephew, London, UK) with gauze dressings after elective surgery for CD. Secondary aims were manageability and safety of PICO and its feasibility as home therapy. Between 2010 and 2012, 50 patients were assigned to treatment with either PICO (n = 25) or conventional dressings (n = 25). Each patient completed 12-month follow-up.

Parameters of interests for primary aim were SSC, surgical complications, and readmission rates. Data on difficulties in managing PICO and device-related complications were also collected.

Patients receiving PICO had less SSC, resulting in shorter hospital stay. At last follow-up, readmission rates were lower with PICO. No differences were observed in surgical complications between groups. No patients reported difficulties in managing the device. Among patients discharged with PICO, none needed to come back to the hospital for device malfunctioning or inability to manage it.

PICO reduces SSC and length of stay in selected CD patients compared with conventional dressings. The device is safe and user friendly.

INTRODUCTION

Surgical site complications (SSC) are known to cause morbidity in surgical patients.^{1,2} SSC negatively affects costs of hospital care, with more than \$1.5 billion in excess cost in the United States.³ The length of stay can be prolonged by SSC.^{1,2} Colorectal surgery^{4,5} and Crohn's disease (CD) are independent risk factors for SSC.⁶⁻⁹ Also, patients affected with CD may need surgery more than once,^{6,7} making it crucial to achieve optimal results in terms of length of hospital stay and wound complications.

Although many measures have been suggested to reduce SSC, controversy exists as to their actual effectiveness.¹⁰ Negative pressure wound therapy (NPWT) has been reported to be a viable option to reduce the incidence of SSC in patients at risk,^{9,11-16} with similar cosmetic results.⁹

The aim of our study was to evaluate the potential for a new NPWT device in

reducing SSC in patients undergoing abdominal surgery for CD and its effect on length of stay and patients' compliance with the device.

METHODS

This prospective, open-label, controlled study enrolled 50 consecutive patients suffering from stricturing CD scheduled for bowel resection or strictureplasty between January 2010 and December 2012 in our unit.

Our primary aim was to investigate whether SSC, surgical complications, and readmission rates could be modified by application of NPWT; secondary aims were to assess patients' compliance with the device and difficulty in managing it. The study was approved by our Ethical Committee.

Inclusion criteria were: ≥ 18 -year-old patients; established CD; symptomatic CD not amenable for medical treatment; laparotomy, converted-laparoscopy, or hand-assisted laparoscopy (HAL) with bowel resection/s or strictureplasty/ies; primary wound closure; adherence to periodical follow-up; signed informed consent. Exclusion criteria were: unconverted laparoscopy; explorative laparotomy/ laparoscopy without bowel opening; massive bowel resections (less than 30% of anatomical length preserved).^{9,17,18} Diagnosis of CD was made following the clinical, endoscopic, imaging, and pathological criteria of the updated Guidelines of the European Crohn's and Colitis Organization (ECCO).¹⁹

Twenty-five patients were assigned to NPWT treatment (Group A); twenty-five patients were treated with conventional dressings (Group B).

Intervention

At the end of each procedure the wound edges were approximated by means of running sub-cuticular suture with non-absorbable stitches (3/0, polypropylene/polyethylene). In Group A patients special gauzes were placed over the entire length of the incision and connected to a portable NPWT device (PICO, Smith & Nephew, London, UK, Figs. 1-4) set at -80 mmHg. In patients with stomas, the dressings were placed before stoma maturation to avoid enteric contamination. Gauzes were changed when too wet or after 3 days for the follow-up; the device was always removed on the postoperative day 7. An additional PICO cycle was administered in selected patients, who were evaluated for removal after 4 days. All patients gave written, informed consent to device application and were preoperatively informed about its effects.

In Group B patients, basic wound contact absorbent dressings were used, removed sterilely for control after 48



Figure 1. Placement of PICO on a wide laparotomy. The black arrow shows the tube connecting the device (white arrow) to the special absorbent gauzes applied to the surgical wound.

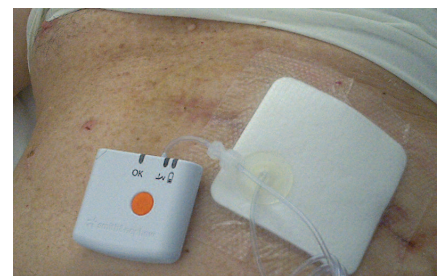


Figure 2. Placement of PICO in a patient receiving corticosteroids who underwent a laparoscopic large bowel resection for a single stenosis of the transverse colon. Intraoperative pathology of the resected specimen ruled out the development of a cancer. A laparotomy was performed on a previous left subcostal surgical incision to allow specimen extraction, small bowel tactile exploration, and extracorporeal anastomosis.

Table I
Global ASEPSIS score⁹

<i>Pt id</i> _____ <i>Medication n</i> _____ <i>Date</i> _____						
<i>Criterion</i>	<i>Proportion of wound involved (%)</i>					
	0	<20	20-39	40-59	60-79	>80
Serous discharge	0	1	2	3	4	5
Erythema	0	1	2	3	4	5
Purulent exudate	0	1	2	3	4	5
Separation of deep tissues	0	1	2	3	4	5
Sample for culture?	<input type="radio"/> Yes <input type="radio"/> No					
$\frac{\text{1st medication score} + \text{2nd medication score}}{\text{number of medications}} \times 5 = \text{ASEPSIS Score}$						
<i>Additional Criteria (30-day follow-up)</i>	<i>Additional Points</i>					
Antibiotics for wound infection	10					
Drainage of pus under local anesthesia	5					
Isolation of bacteria in wound	5					
Debridement of wound under general anesthesia	10					
Length of stay prolonged over 14 days for wound infection	5					
ASEPSIS score + Additional points = Global ASEPSIS score						
<i>Infection Categories according to Global ASEPSIS score</i>						
0 – 10: satisfying healing						
11 – 20: healing disturbance						
21 – 30: minor wound infection						
31 – 40: moderate wound infection						
> 40 : severe wound infection						



Figure 3. Same patient as in Fig. 2. Appearance of the gauze after 5 days. PICO was still working due to residual absorbent capability of the gauze.



Figure 4. Same patient as in Fig. 2. Appearance of the wound at 30 days follow-up.



Figure 5. Placement of PICO in a patient with ileostomy.

hours, and NPWT was not applied. On postoperative day 3, gauzes were removed sterily and wounds left exposed if no complications occurred.

All patients received intraoperative cefotaxime 1 g iv and metronidazole 500 mg iv and continued on postoperatively as needed.

Data of Interest and Follow-up Protocol

Demographics, ASA score, Body Mass Index (BMI), comorbidities, disease activity, concomitant medical treatment, disease localization, surgical procedure performed, length of incision, length of surgical procedure, in-

hospital stay, and perioperative complications were collected.

Disease severity was assessed by means of the Crohn's Disease Activity Index (CDAI), hemoglobin and serum albumin levels, ESR, and CRP preoperatively. SSC were evaluated on postoperative days 3, 7, and 30. Noninfectious

Table II
Patient characteristics and surgical data. Data are means ± SD and n (%)

Patient Variable	Group A (n=25)	Group B (n=25)	p
Age, years	36±11	32±15	0.7
Male gender	14 (56)	10 (40)	0.4
BMI, kg/m ²	24±6	22±5	0.5
Diabetes	4 (16)	4 (16)	>0.99
Tobacco smoking habit	14 (56)	12 (48)	0.8
CDAI	290±100	280±110	0.7
ESR, mm/hr (nv 0-10)	32±25	30±25	0.9
CRP, mg/dL (nv 0-0.5)	7±10	5±15	0.6
Hb, g/dL (nv 13-16)	10±3	10±7	0.7
Albumin, g/dL (nv 3.5-4.5)	3±1	3±0.5	>0.99
Previous treatment with anti-TNF-α	6 (46)	9 (53)	>0.99
On AZA or MTX at surgery	8 (32)	11 (44)	0.5
On steroids at surgery*	13 (52)	12 (48)	>0.99
ASA III	3 (12)	3 (12)	>0.99
Colonic or ileocolonic disease	11 (44)	12 (48)	>0.99
Previous surgery	7 (28)	8 (32)	>0.99
Surgical Variables			
Operative time, min	169±81	190±75	0.7
Stoma	7 (28)	6 (24)	>0.99
Wound length, cm	12±7	12±8	>0.99
Length of stay, days	7±2	12±2	0.0001
<i>SD: standard deviation BMI: Body Mass Index CDAI: Crohn's Disease Activity Index n.v.: normal value ESR: Erythrocyte Sedimentation Rate CRP: C-Reactive Protein Hb: Hemoglobin AZA: azathioprine MTX: methotrexate ASA: American Society of Anesthesiology min: minutes *patients taking ≥ 20 mg of corticosteroid</i>			

and septic wound complications were classified according to Centers for Disease Control and Prevention (CDC) criteria²⁰ and Global ASEPSIS score (Table I),^{21,22} respectively. All patients were included in a multivariate analysis to identify independent predictors of SSC in this series. Significant variables were used for sub-group analyses.

After discharge, standard follow-up intervals for this study were at 7, 15,

and 30 days, then subsequently every two weeks for 3 months. Twelve patients of Group A were sent home with PICO and were given a mobile number to call in case of difficulty in managing the device or if complications occurred. Early readmissions, defined as need for repeated hospitalization within 6 months from discharge for wound-related complications, were recorded.



Figure 6. Same patient as in Fig. 5. Appearance of the wound at 30-day follow-up.

Statistical Analysis

Results are expressed as mean±SD, unless otherwise indicated. Categorical data were compared using 2-tailed Fisher's exact test or Chi-squared test; continuous variables were compared using Mann-Whitney test. P < .05 was considered statistically significant.

RESULTS

Baseline disease characteristics and demographics were homogeneous between groups (Table II). Operative time was 169±81 and 190±75 minutes in Group A and Group B, respectively (p = 0.7). No significant differences were observed in type of surgery, stoma formation, minor and major complications between Group A and Group B patients. Length of stay was significantly longer in patients with conventional dressings (7±2 versus 12±2, p = 0.0001) (Table II).

Antibiotic treatment was discontinued after 3±2 days. PICO was removed after a 7±4 days. In patients of Group A

sent home with PICO, this was removed after 4±2 days.

Patients receiving PICO experienced significantly less postoperative SSC compared with those who received conventional dressings (Table III). Wound seroma was less frequent with PICO. Infectious wound complications were significantly higher in Group B patients (2 vs 12, p = 0.04) (Table III).

A multivariate analysis including all demographical, clinical, and surgical data of all 50 patients found that incisional NPWT was significantly protective against SSC (OR 0.21, 95% CI 0.15–0.5, p = 0.001), while concomitant corticosteroid treatment at surgery (OR 1.95, 95% CI 1.12–4.33, p = 0.02) was an independent risk factor for SSC. A sub-group analysis of patients receiving steroids at surgery showed a significant reduction of infectious SSC with PICO compared with conventional medications (1/13 vs 9/12 p = 0.001) (Table III).

Early readmission rate was higher in Group B patients, with all PICO patients discharged uneventfully (0 vs 24%, p = 0.02).

Concerning management of the device, no complications were observed during the recovery. Two patients contacted us with unscheduled calls after discharge (8%): one because the medication was not perfectly sealed (4%); another one because he detached the device from the connecting tube (4%). Problems were self-addressed by the patients placing an additional strip of patch and PICO and reconnecting the device to the suction tube, allowing NPWT to restart normally. No patients experienced difficulties with PICO requiring unplanned outpatient visits.

Figures 1–6 depict some patients included in the present trial.

DISCUSSION

Our study found that NPWT with PICO in patients with CD reduces SSC, allowing shorter length of stay and reducing the risk of readmissions for wound-related complications. Concomitant corticosteroid treatment is an independent risk factor for SSC. The benefits of PICO are more apparent in these patients. The device is safe and easily managed by patients.

SSC are a common problem in gen-

Surgical complications	Group A (n=25)	Group B (n=25)	p
Death	0 (0)	0 (0)	>0.99
Major complications	6 in 5* patients	9 in 7† patients	0.5
Patients requiring reoperation	2 (8)	5 (20)	0.4
Wound outcome			
Seroma	2 (8)	11 (44)	0.008
Infectious SSC according to CDC criteria ²⁰			0.004
Superficial incisional	2 (8)	6 (25)	
Deep incisional	0 (0)	4 (16)	
Organ/space	0 (0)	2 (8)	
Global ASEPSIS score(9,21,22)	14±7	28±5	0.001
Patients receiving corticosteroids‡			
	Group A (n=13)	Group B (n=12)	p
Infectious SSC according to CDC criteria ²⁰			0.001
Superficial incisional	1(8)	6(50)	
Deep incisional	0(0)	2(17)	
Organ/space	0(0)	1(8)	
<i>CDC: Centers for Disease Control and Prevention SSI: Surgical Site Infections</i> <i>* 1 anastomotic leak, 2 postoperative hemorrhage, 1 intra-abdominal abscess, 2 stoma complication</i> <i>† 2 anastomotic leak, 3 postoperative hemorrhage, 3 intra-abdominal abscess, 1 stoma complication</i> <i>‡ ≥20 mg</i>			

eral surgery. Infectious SSC account for approximately 10% of hospital-acquired infections and have a detrimental effect on costs of hospital care and length of stay.^{1,2} This is much more relevant when considering CD patients. Approximately three out of four CD patients will need surgery during their lives.⁶ A relevant portion of surgical CD patients will also need repeated surgery within 20 years.^{6,7}

Inflammatory bowel diseases are considered an independent risk factor for infectious complications and SSC, which can impair quality of life.^{5,6,23–26} CD patients are usually managed medically, and surgery is advocated when conservative treatments fail. Although it can achieve good results in perianal CD — particularly when combined with biological drugs²⁷ — and in localized

CD of the terminal ileum, surgery is regarded as the last resort for abdominal disease. Patients often need surgery in emergency and/or during concomitant treatment with immunosuppressives.²⁸ These drugs further impair the local host defenses and regenerative capability.²⁸ Corticosteroids are often needed to obtain remission during acute flares of CD, but these agents are known predictors of SSC, almost doubling the risk of infectious complications in inflammatory bowel disease.^{24,28,29} We recently found that CD patients taking steroids at surgery receiving PICO over closed surgical incisions showed a trend toward lower rates of SSC.⁹ In the present series we found that a concomitant treatment with corticosteroids at surgery was an independent predictor of SSC, doubling the risk of this compli-

cation (OR 1.95). We were able to demonstrate a significant difference in SSC between patients receiving steroids treated with PICO and conventional dressing (Table III). These patients must be considered at higher risk and are ideal candidates for NPWT with PICO.

No differences were observed between the pattern of CD as classified by the Montreal revision of the Vienna classification (stricturing, penetrating, non-stricturing, non-penetrating),³⁰ suggesting that NPWT can be applied in CD with good results irrespective of disease behavior. Even if patients with penetrating disease showed higher rates of re-hospitalization, this happened after a mean of 14±4 months, and was mainly due to CD relapse rather than SSC. A penetrating pattern is known to be an independent risk factor for CD recurrence.³¹

The cost-effectiveness of NPWT in the home-care setting of patients needing advanced medications is well described.^{9,16} PICO is a portable NPWT device that is easily transportable and does not need maintenance. PICO generates continuous vacuum pressure (-80 mmHg) by means of two AA lithium batteries without a canister, as it is directly connected with special gauzes directly covering the surgical incision.⁹ PICO adsorbs the exudate but keeps a moist environment, which is crucial for good wound healing. It reduces tissue edema and causes a mechanical stimulus for the wound bed. Healing is also favored by the stimulation of angiogenesis and granulation tissue formation¹² in a "sealed" wound. NPWT reduces SSC,⁹ even in the eventuality of high-risk wounds.¹³ In our patients PICO exerted a protective effect against SSC, and had no influence on postoperative complications requiring further surgery (Table III).

Authors suggested that NPWT can cause significant morbidity in abdominal surgery by reducing the blood flow of the small bowel.^{32,33} Conversely, these negative effects are limited to bowel loops directly exposed to NPWT and are strictly correlated with the values of negative pressure applied.³³ We showed the safety of PICO over surgical incisions of patients undergoing major surgery for CD. PICO did not increase the risk of postoperative complications when compared with conventional dressings. The benefits of NPWT are

not affected by the presence of a stoma, as previously described.⁹

Patients' compliance with medical devices is to be taken into account when considering their potentials and shortcomings. Hoeller et al. showed good adherence to treatment with NPWT in pediatric patients.³⁴ The user-friendliness and manageability of PICO makes it easier to achieve patients' compliance. None of our patients receiving PICO complained of disturbances or required removal of the device.

CONCLUSION

The present study on two homogeneous groups of CD patients undergoing surgery showed that PICO is safe and effective, achieving better results in terms of SSC and length of stay compared with conventional medications. Patient satisfaction is high and the device can be easily self-managed. The routine application of PICO in CD patients receiving concomitant steroid treatment seems reasonable. **STI**

AUTHORS' DISCLOSURES

The authors have no financial relationships to disclose.

REFERENCES

1. Emmerson AM, Enstone JE, Griffin M, et al. The Second National Prevalence Survey of infection in hospitals—overview of the results. *J Hosp Infect* 1996;32:175–90.
2. Reilly J, Twaddle S, McIntosh J, et al. An economic analysis of surgical wound infection. *J Hosp Infect* 2001;49:245–9.
3. de Lissovoy G, Fraeman K, Hutchins V, et al. Surgical site infection: incidence and impact on hospital utilization and treatment costs. *Am J Infect Control* 2009;37:387–97.
4. Wick EC, Vogel JD, Church JM, et al. Surgical site infections in a "high outlier" institution: are colorectal surgeons to blame? *Dis Colon Rectum* 2009;52(3):374–9.
5. Anthony T, Murray BW, Sum-Ping JT, et al. Evaluating an evidence-based bundle for preventing surgical site infection: a randomized trial. *Arch Surg* 2011;146(3):263–9.
6. Uchino M, Ikeuchi H, Tsuchida T, et al. Surgical site infection following surgery for inflammatory bowel disease in patients with clean-contaminated wounds. *World J Surg* 2009;33:1042–8.
7. Terdiman JP. Prevention of postoperative

- recurrence in Crohn's disease. *Clin Gastroenterol Hepatol* 2008;6:616–20.
8. Peyrin-Biroulet L, Loftus EV Jr, Colombel JF, et al. The natural history of adult Crohn's disease in population-based cohorts. *Am J Gastroenterol* 2010;105:289–97.
9. Pellino G, Sciaudone G, Candilio G, et al. Effects of a new pocket device for negative pressure wound therapy on surgical wounds of patients affected with Crohn's Disease: A Pilot Trial. *Surg Innov* 2013 Jul 24. [Epub ahead of print].
10. Stulberg JJ, Delaney CP, Neuhauser DV, et al. Adherence to surgical care improvement project measures and the association with postoperative infections. *JAMA* 2010;303(24):2479–85.
11. Canonico S, Campitiello F, Della Corte A, et al. Treatment of leg chronic wounds with dermal substitutes and thin skin grafts. In: *Skin Grafts*, Gore M (Ed.), 2013 InTech publications Rijeka, Croatia ISBN: 978-953-51-0973-0, DOI: 10.5772/51852. Available from: <http://www.intechopen.com/books/skin-grafts/treatment-of-leg-chronic-wounds-with-dermal-substitutes-and-thin-skin-grafts>.
12. Malmström M, Borgquist O. NPWT settings and dressing choices made easy. *Wounds International* 2010;1:1–6.
13. DeCarbo WT, Hyer CF. Negative-pressure wound therapy applied to high-risk surgical incisions. *J Foot Ankle Surg* 2010;49:299–300.
14. Baharestani MM, Gabriel A. Use of negative pressure wound therapy in the management of infected abdominal wounds containing mesh: an analysis of outcomes. *Int Wound J* 2011;8:118–25.
15. Stannard JP, Atkins BZ, O'Malley D, et al. Use of negative pressure therapy on closed surgical incisions: a case series. *Ostomy Wound Manage* 2009;55:58–66.
16. Philbeck TE Jr, Whittington KT, Millsap MH, et al. The clinical and cost effectiveness of externally applied negative pressure wound therapy in the treatment of wounds in home healthcare Medicare patients. *Ostomy Wound Manage* 1999;45:41–50.
17. Fleming CR, Remington M. Intestinal failure. In: Hill GL, ed. *Nutrition in the surgical patient*. Edinburgh: Churchill Livingstone; pp 219–35, 1981.
18. Bakker H, Bozzetti F, Staun M, et al. Home parenteral nutrition in adults: a European multicentre survey in 1997. ESPEN-Home Artificial Nutrition Working Group. *Clin Nutr* 1999;18:135–40. doi: 10.1016/S0261-5614(99)80002-8.
19. Van Assche G, Dignass A, Panes J, et al. The second European evidence-based Consensus on the diagnosis and management of Crohn's disease: definitions and diagnosis. *J Crohn's Colitis* 2010;4:7–27. doi: 10.1016/j.crohns.2009.12.003.
20. Mangram AJ, Horan TC, Pearson ML, et al. Guideline for prevention of surgical site infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. *Am J Infect Control* 1999;27:97–132.
21. Wilson AP, Treasure T, Sturridge MF, et al. A scoring method (ASEPSIS) for postoper-

- ative wound infections for use in clinical trials of antibiotic prophylaxis. *Lancet* 1986;1: 311–3.
22. Wilson AP, Gibbons C, Reeves BC, et al. Surgical wound infection as a performance indicator: agreement of common definitions of wound infection in 4773 patients. *BMJ* 2004;329:720.
23. Pellino G, Sciaudone G, Candilio G, et al. Complications and functional outcomes of restorative proctocolectomy for ulcerative colitis in the elderly. *BMC Surg* 2013;13 Suppl 2:S9. doi: 10.1186/1471-2482-13-S2-S9. Epub 2013 Oct 8.
24. Pellino G, Sciaudone G, Canonico S, et al. Role of ileostomy in restorative proctocolectomy. *World J Gastroenterol* 2012;18(15): 1703–7.
25. Sciaudone G, Pellino G, Guadagni I, et al. Disseminated *Cryptococcus neoformans* infection and Crohn's disease in an immunocompetent patient. *J Crohn's Colitis* 2011;5(1):60–3.
26. Selvaggi F, Sciaudone G, Limongelli P, et al. The effect of pelvic septic complications on function and quality of life after ileal pouch-anal anastomosis: a single center experience. *Am Surg* 2010;76(4):428–35.
27. Sciaudone G, Di Stazio C, Limongelli P, et al. Treatment of complex perianal fistulas in Crohn's disease: infliximab, surgery or combined approach. *Can J Surg* 2010;53(5): 299–304.
28. Busti AJ, Hooper JS, Amaya CJ, et al. Effects of perioperative anti-inflammatory and immunomodulating therapy on surgical wound healing. *Pharmacotherapy* 2005;25: 1566–91.
29. Ismael H, Horst M, Farooq M, et al. Adverse effects of preoperative steroid use on surgical outcomes. *Am J Surg* 2011;201: 305–9.
30. Satsangi J, Silverberg MS, Vermeire S, et al. The Montreal classification of inflammatory bowel disease: controversies, consensus, and implications. *Gut* 2006;55:749–53.
31. Wolters FL, Russel MG, Sijbrandij J, et al. Phenotype at diagnosis predicts recurrence rates in Crohn's disease. *Gut* 2006; 55: 1124–30. doi:10.1136/gut. 2005. 084061.
32. Lindstedt S, Malmsjö M, Hansson J, et al. Microvascular blood flow changes in the small intestinal wall during conventional negative pressure wound therapy and negative pressure wound therapy using a protective disc over the intestines in laparostomy. *Ann Surg* 2012;255:171–5.
33. Hlebowicz J, Hansson J, Lindstedt S. Microvascular blood flow response in the intestinal wall and the omentum during negative wound pressure therapy of the open abdomen. *Int J Colorectal Dis* 2012;27: 397–403.
34. Hoeller M, Schintler MV, Pfurtscheller K, et al. Trop M. A retrospective analysis of securing autologous split-thickness skin grafts with negative pressure wound therapy in paediatric burn patients. *Burns* 2014;pii: S0305-4179(13)00414-2. doi: 10.1016/j.burns.2013.12.007. [Epub ahead of print].