Original Article

Surgical Outcome of Stoma Closure in IBD Surgery

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Key Words
Inflammatory bowel disease;
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Stoma

Purpose. A stomais often performed in IBD surgery. However, complications after stoma creation, stoma closure and permanent stoma can be challenging for both IBD patients and surgeons. We evaluated the surgical outcome of stoma closure in IBD surgery to aid the doctors better understanding of making the stoma to improve the benefits of surgery treatment.
Methods. We enrolled IBD patients who underwent surgery between December 2001 and October 2019 at our department. Preoperative evaluation, surgical indications, surgical type, and stoma-related complications, timing of stoma closure, causes for delayed stoma closure and permanent stoma were analyzed.
Results. Crohn's disease patients had significantly lower BMI ($p = 0.02$), higher chance of body weight loss > 5% ($p = 0.046$), higher nutritional risk before surgery ($p < 0.001$), previous bowel surgery history ($p = 0.01$), and biological agent use ($p = 0.011$). A significant difference was also noted in primary stoma creation between UC and CD (79.2% vs. 25%, $p = 0.002$). The stoma closure rate was 57.8% for UC and 42.8% for CD ($p = 0.495$). Stoma-related Grade III complications were observed in 26.3% of UC cases and 57.1% of CD cases ($p = 0.143$). Complication of stoma closure was significant lower in UC when compared to CD (0% vs. 33%, $p = 0.047$). End ileostomy status with disease poor control were the most common etiology for delayed stoma closure or permanent stoma.
Conclusion. In order to achieve inflammation control, a stoma is often being created in IBD surgery. However, there's a certain portion of patient suffered from stoma related morbidity, especially in CD. And the incidence of permanent stoma is still high in IBD patients.
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Inflammatory bowel disease (IBD) is a complex, gastrointestinal tract disease with chronic inflammation. Crohn's disease (CD) and ulcerative colitis (UC) are the two most common types. The incidence of IBD has gradually increased in Asia[1] including in Taiwan,[2] but is still relatively rare. Medical therapy is the major treatment for IBD, and the rate of IBD surgery has decreased with the development of biological therapies.[3,4]

Nevertheless, surgical intervention still plays an essential role in IBD patients, especially for those with severe inflammation and therapy-refractory disease.[5]

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In IBD surgery, stoma creation is common in the emergent setting to reduce the impact of intra-abdominal infection, especially in life-threatening conditions such as sepsis, bowel perforation, massive bleeding, poor nutrition, and severe bowel inflammation status. Instead, in elective surgery, a protective stoma is sometimes being made to prevent infection caused by suspected anastomosis leakage. Besides, a diverting stoma could benefit some patient who suffered from anorectal disease, such as refractory fistula, incontinence. However, complications after stoma creation, stoma closure and permanent stoma can be challenging for both IBD patients and surgeons. Many factors should be taken into consideration, such as surgery type, disease pattern, inflammation index, steroid or biological drug use, and nutritional status.

In this study, we evaluated the surgical outcome of stoma closure in IBD surgery to aid the doctors better understanding of making the stoma to improve the benefits of surgery treatment.

Materials and Methods

Between December 2001 and October 2019, data pertaining to IBD patients who underwent surgical intervention for disease control were collected retrospectively from the database of the colorectal surgery department, Linkou Chang Gung Memorial Hospital. This study was approved by the Chang Gung Medical Foundation Institutional Review Board (IRB No. 2021 00587B0).

The diagnosis of UC or CD was based on the clinical examination, colonoscopy, radiological, and pathological findings. The patients' characteristics (sex, age, smoking habits, preoperative body mass index [BMI], previous bowel surgery, and disease extension) and preoperative evaluation data (nutrition risk, laboratory findings, and steroid and anti-TNF drug use) were reviewed.

According to the disease extension, IBD is classified into different types, as follows: proctitis, left colitis, and pancolitis for UC,[6] while ileal, colonic, and ileocolonic disease for CD.[7] Preoperative nutritional status was evaluated using a mini nutritional assessment (MNA). Nutrition risk was defined as a MNA score < 11 or total parental nutrition (TPN) use. Preoperative corticosteroid and anti-tumor necrosis factor (TNF) use were defined as the use of medication up to three months before surgery. Preoperative laboratory data including white blood cell (WBC) counts, hemoglobin, C-reactive protein (CRP), and albumin levels were also collected for analysis. Surgical information, including type of surgery, type of stoma, purpose of stoma, stoma-related Grade III[8] complications, timing of stoma closure, causes for delayed stoma closure and permanent stoma were documented.

All analyses were performed using IBM SPSS Statistics Data Editor 24.0 (SAS institute Inc, Cary, NC, USA). Quantitative variables are presented as the mean (range), and qualitative variables are presented as number (percentage). Quantitative variables with normal distribution were compared using the Student's t-test. For qualitative variables, a Pearson chi-square test was used, as appropriate. The threshold for statistical significance was set at p value less than 0.05.

Results

The clinical characteristics of the study population at the time of the intestinal resection are summarized in Table 1. A total of 36 patients (24 UC and 12 CD) were enrolled, including 25 men (69%). The mean age at surgery was 43 ± 13 years (range, 20-67 years); CD patients were much younger than UC patients. Pancolitis was observed in 62% of UC patients, and ileocolonic lesions were observed in 75% of CD patients.

CD patients had significantly lower BMI values ($p = 0.02$), a higher chance of body weight loss > 5% ($p = 0.046$), a higher nutritional risk before surgery ($p < 0.001$), a history of previous bowel surgery ($p = 0.01$) and current use of biological agent ($p = 0.011$). There were four other CD patients who underwent appendectomies before major operations. No differences were noted in the perioperative laboratory data including inflammation markers and serum albumin levels. The mean follow-up periods for UC and CD were 129 and 71 months, respectively.

Table 1. Clinical characteristics in patients with ulcerative colitis and Crohn's disease

Item	UC (n = 24)	CD (n = 12)	*p*-value
Male	17 (70.8%)	8 (66.7%)	0.798
Age at surgery (yrs)	48.1 ± 11.1	33.6 ± 11.5	0.001
Smoking	6 (25%)	5 (41.7%)	0.306
Disease extension	Proctitis: 1	Ileal: 2	
	Left colitits: 7	Colonic: 1	
	Pancolitis: 15	Ileocolonic: 9	
BMI (kg/m^2)	22.6 ± 3.9	19.3 ± 2.9	0.020
Overweight, BMI > 25	8 (33.3%)	0 (0%)	0.021
Weight loss > 5%	4 (16.7%)	8 (66.7%)	0.003
Pre-op nutrition risk	5 (20.8%)	10 (83.3%)	< 0.001
Previous bowel surgery	1 (0.04%)	5 (41.7%)	0.010
ASA score [≥ 3]	6 (25%)	8 (66.7%)	0.016
Steroids > 20 mg	10 (41.7%)	5 (41.7%)	1.000
Anti-TNF > 3 months	0 (0%)	3 (25%)	0.011
Pre-operative laboratory			
Hgb g/dL	12.12 ± 1.99	1.61 ± 3.18	0.560
WBC 10^3/uL	10.01 ± 4.64	10.49 ± 4.99	0.777
Segment %	69 ± 16.16	76.55 ± 9.2	0.150
CRP mg/dL	168 ± 158	104 ± 100	0.260
Albumin g/dL	3.51 ± 0.82	3.12 ± 0.66	0.180

A total of ten (27%) patients underwent emergent surgery (Table 2). Intra-abdominal abscesses were detected intraoperatively in significantly more CD patients than in UC patients (58.3% vs. 20.8%, p = 0.024). Among UC patients, 54.2% underwent colectomy, and 41% received proctocolectomy with ileal pouch-anal anastomosis (IPAA). In CD patients, 58% underwent ileocolectomy. Exploratory laparotomies

Table 2. Surgical information of IBD patients

Surgical information	UC (n = 24)	CD (n = 12)	*p*-value
Emergent surgery	6 (25%)	4 (33.3%)	0.599
Abscess at surgery	5 (20.8)	7 (58.3%)	0.024
Type of surgery			
T-colostomy	1 (4.2%)	0	
Large bowel resection	14 (58.4%)	2 (16.7%)	
Large bowel resection and IPAA	9 (37.5%)	0	
Small bowel resection	0	1 (8.3%)	
Small and large bowel resection	0	7 (58.3%)	
Bowel repair	0	2 (16.7%)	
Exploratory laparotomy	19 (79.2%)	8 (66.7%)	0.414
Laparoscopic	5 (20.8%)	4 (33.3%)	
Primary stoma	19 (79.2%)	3 (25%)	0.002
End ileostomy	7	2	
Loop ileostomy	10	0	
Loop transverse colostomy	2	1	
Secondary stoma after leakage	0 (0%)	4* (33.3%)	0.008
End ileostomy	NA	2	
Loop ileostomy	NA	2	

IPAA, ileal pouch anal anastomosis; Ana., anastomosis.

* One patient had primary transverse-loop stoma, but converted to end-ileostomy after leakage.

were performed in 27 (75%) surgeries. A significant difference was noted in primary stoma creation between the UC and CD groups (79.2% vs. 25%, p = 0.002). In most cases, loop ileostomy was performed, followed by end-ileostomy. In addition, secondary diverting stoma creation after a leakage event was higher in CD than in UC (33.3% vs. 0%, p = 0.008).

In UC group, all 19 stomas were made primarily. For CD patients, three stomas were created primarily during major surgery, and four were made secondarily after anastomosis leakage events. Overall, stoma-related Grade III complications[8] were observed in 26.3% of UC patients and 57.1% of CD patients (Table 3). Stoma ulcerations with mucocutaneous dehiscence were the most common complications that required surgical management in our study. One CD patient suffered from perastomal pyoderma gangrenosum that surgical intervention (Fig. 1).

Generally, the stoma closure rate was 57.8% for UC and 42.8% for CD. The timing of stoma closure ranged widely from 94 to 2193 days postoperatively in UC, and from 139 to 663 days in CD. Almost half (5/11, 45%) of the UC patients accomplished stoma closure within 180 days, while only one of CD patient could do so. Stoma closure complication was significant lower in UC when compared to CD (0% vs. 33%, p = 0.047). There were no grade III complications in a total of 11 UC stoma closures. On the other hand, one enterocutaneous fistula was noted in a CD stoma closure, in which small bowel resection and another diverting ileostomy construction were necessary.

The causes of delayed stoma closure or permanent stoma were listed in Table 4. End ileostomy status with disease poor control and anastomotic stenosis were the most common etiology for delayed closure. Besides, each one of UC and CD patient experienced fistula formation that stoma closure was postponed till the fistula healed.

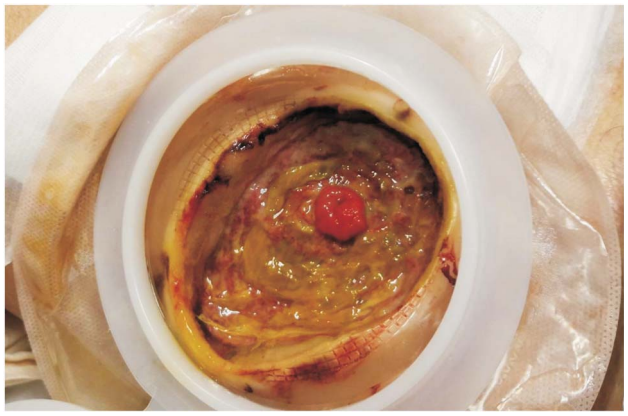

Fig. 1. Perastomal pyoderma gangrenosum in a Crohn's disease patient.

Table 4. Information of delayed stoma closure and permanent stoma

The cause of delayed closure and permanent stoma	UC	CD
Delayed closure	6	3
End ileostomy status with disease poor control	2	2
Anastomosis stenosis	2	0
Fistula formation	1	1
Wound infection and ileus	1	0
Permanent stoma	8	3
End ileostomy status with disease poor control	1	3
Transverse loop colostomy with disease poor control	1	0
Anastomosis stenosis	1	0
Mental retardation	1	0
Colorectal cancer with distant metastasis	2	0
Mortality due to underling disease	2	0

Table 3. Stoma complications, stoma closure rate, timing and closure complications

Stoma related grade III complications	UC	CD	p-value
Total complications/stoma number (%)	5/19 (26.3%)	4/7 (57.1%)	0.143
Stoma ulceration	2	2	
Stoma stenosis	1	1	
Stoma fistula	1	0	
Stoma prolapse	1	0	
Perastomal pyoderma gangrenosum	0	1	
Stoma closure rate (%)	11/19 (57.8%)	3/7 (42.8%)	0.495
Closure time after major surgery (days)	94-2193 days	139-663 days	
Delayed closure (over 180 days)	6/11 (54.5%)	2/3 (66.6%)	
Stoma closure complications (%)	0/11 (0%)	1*/3 (33%)	0.047

* Enterocutanous fistula, which need bowel resection and re-do ileostomy.

Two of UC patients with permanent were due to malignancy with terminal stage and two had mortality from their underlying disease. Disease poor control were noted in two UC patients that the stoma cannot be reversal. All CD patients suffered from permanent stoma because of their end ileostomy status with active disease even under biological therapy. One of them also had to use long term total parenteral nutrition support.

Discussion

The primary stoma rate was significant higher in UC patients than that of CD in our study (79% vs. 25%, $p = 0.002$). These differences may be related to surgical type. For Crohn's disease, ileocolonic resection with ileocolonic anastomosis is the most commonly performed surgery, depending on the type of CD behavior.[9] However, since restorative proctocolectomy with IPAA is the standard procedure for UC,[10] a diverting stoma is often performed for two or three staged surgery. However, patient with CD has many factors for anastomotic leakage than UC patients, such as malnutrition, previous bowel surgery and biological agent use at present study. Therefore, a protective stoma should always be considered in these patient with high leakage risk. Because half of the secondary stoma in our study were end ileostomy, which would have higher risk of delayed stoma closure or being a permanent stoma in the end.[11]

Although there's no significantly difference in stoma complications between both group, patient with CD had higher percentage of stoma related mortality that surgical intervention was needed. Takahashi et al. had reported that the incidence of stoma complications was higher in patients with CD than in those with UC[12] which is compatible with our study. Mechanical and ischemia factors are believed to be the most common reasons for postoperative complications associated with stoma, while body habitus and an underlying IBD status can also contribute to stoma problems.[13] In our study, parastomal ulcerations were noted in both UC and CD patients. Stoma ulcerations can occur soon after surgery, and may result from infected hematomas or hidden fistulas.[14] Special attention should be paid that fistula-related parastomal ulcers, especially those refractory to topical treatment, may be a demonstration of active IBD.[15] The other complications at present study included stoma stenosis, stoma fistula, stoma prolapse and perastomal pyoderma gangrenosum (PPG). Stoma stenosis and fistula could happen at different level from the skin, the entry of stoma to the abdominal fascia due to ischemic etiology after surgery. However, caution should be taken if the stenosis occurred at the new intestine beyond the level of abdominal fascia, it may be related to the underlying IBD.[13] Stoma prolapse happened more easily in obesity patient with a large opening in the abdominal wall at stoma surgery while the loop transverse colostomy has the highest risk for prolapse (7-25%).[16] One UC patient with transverse colostomy had stoma prolapse and necrosis. Therefore, colostomy revision was performed. Perastomal pyoderma gangrenosum is a serious complication in IBD patients. It is a form of neutrophilic dermatosis which is clinically characterized by chronic, recurrent, and painful cutaneous ulcerations.[17] PPG occurred more frequently in IBD patients with stoma construction, with an incidence up to 4%.[18,19] The etiology and pathogenesis of PPG are not entirely understood. This condition can develop weeks to years after stoma surgery.[14,20] Systemic steroids constitute first-line therapy, while biological agent could provide concomitant control of active inflammatory bowel disease. Surgical approaches such as stoma closure and resection of active inflammatory bowel disease have an effective role in PPG management.[21] We had one CD patient suffered from this complication (Image 1) and stoma revision was required after multiple medical treatment failure.

Studies had showed that a stoma status could cause depression,[22] anxiety[23] and decreased social satisfaction[24] in IBD patient. Therefore, stoma closure and it's timing are always concerned by patient. The duration between stoma construction and closure in colorectal cancer patients ranged widely from six weeks[25,26] to nearly six months.[27,28]

Many factors such as end-ileostomy, intra-abdominal abscess, and old age, affect delayed or non-rever-

sal events in non-IBD patients.[11] However, closure rate and time of an IBD stoma may be more varied due to disease complexity, post-operative medical therapy, inflammatory status, and surgical methods.

The overall stoma closure rate is only 57.8% for UC and 42.8% for CD at present study. Furthermore, stoma reversal within six months was performed in only five UC patients and one CD patients, in a mean of 117 ± 18 days post major surgery. For UC, there's total nine patients underwent IPAA surgery with eight stoma creation in our study. The stoma reversal rate was 87.5%. But for non-IPAA patient, the stoma reversal rate was only 36.3%. The reasons of non-closure in this group included mortality (4 cases), anastomosis stenosis (1 case), mental retardation (1 case) and poor disease control (1 case). Their mortality was resulted from pneumonia, liver cirrhosis and cancer progression with distant metastasis. Usually, the failure of stoma closure is little caused by poor disease control in UC patients with non-IPAA operation. Muller et al. published a study[29] of 686 UC patients who underwent two- or three-staged IPAA surgery with ileostomy revealed a 98.5% stoma reversal rate. The stoma closure was performed approximately three months after the major surgery as scheduled. Another study showed that the time until closure of the loop ileostomy ranged from nine to 470 days, with a median of 92 days in 70 UC patients with a 98% closure rate.[30] But on the other hand, the reported rate of stoma closure following major surgery for Crohn' s disease ranged widely from 19% to 76%.[31,32] and it was much lower in the complicated, refractory perianal type of CD (10% to 51%).[11,33-35] Bitner et al. reported that ileostomy reversal was uncommon (20%) in Crohn's colitis patients who underwent subtotal colectomy; the mean time in which the patients underwent ileostomy reversal was 8.4 months.[36] This indicated the difference of disease character and the importance of inflammation control in IBD treatment. Because surgery such as IPAA to remove the whole inflammatory bowel can cure UC, but there's no operation alone can treat CD well. A population time-trend study by Ma et al.[37] revealed the overall emergent stoma rate and temporary stoma rate are declined yearly in CD patient, but the permanent stoma rate remains stable (around 10%). Several studies also showed that the permanent stoma rate was still high for patient with Crohn's colitis[38] or perianal disease[39] even under strong biological therapy. To lower the permanent stoma rate, more research with new medication is needed to aid inflammation control in patient with refractory disease.

Taking down a stoma is routinely performed by colorectal surgeons. The complications related to stoma closure were low in the present data that only one enterocutaneous fistula were noted in a CD patient. Although all UC patient had no morbidity related to stoma reversal after their disease well controlled. Park et al. had showed that overall complication after ileostomy closure in 70 UC patients was 29%, with 9% required a reoperation.[30] A larger systemic review[40] of 2146 patients revealed that the morbidity of ileostomy closure after restorative proctocolectomy for UC may up to 16.5% with a redo surgery for complications in 3% of the patients.

Several factors resulted in higher post-ileostomy closure complication. First, the steroid and biological agent medication might cause higher wound infection rate. Second, the ileostomy site usually was located more proximal in the ileum without ileocecal valve, furthermore, the lack of ileocecal valve and of residual colon in the IPAA surgery could make a difference particularly for postoperative bowel obstruction. Third, patient might suffer from pouch related complications, especially those patients supposed to have ulcerative colitis will later be diagnosed as having Crohn's disease. Therefore, surgeon should always keep in mind that no matter stoma creation or closure could cause certain complications in IBD patient. We may solve one problem (leakage) but create another (complication of stoma creation, stoma closure and permanent stoma).

These complications also have led surgeons to revisit the issue that whether stoma omitting is possible. Study had showed that a one-stage procedure without protective ileostomy is available in certain situations for UC patients who undergo IPAA surgery.[29,41,42] Generally, the patients are less obese, without anemia and malnutrition, and did not receive immunosuppressive medications preoperatively.[43] To lower the stoma creation rate in UC, surgeons can also choose to

perform an ileorectal anastomosis. Andersson et al.[44] reported that the stoma rate was very low (4%) in the IRA group when compared to the IPAA group (96%), with a similar leakage rate. But patient should be well informed that the cumulative cancer risk after follow-up 25 years was 8.7% for IRA and 1.8% for IPAA even though there's no significant difference. (p = 0.59). In the present study, five UC patients underwent ileorectal anastomosis without diverting stoma, and no leakage events were noted. IRA has the advantages of easier operation, lower infertility rate, lower risk of urinary and sexual dysfunction, and better continence. However, the shortcomings of IRA include the need for maintenance therapy, the potential risk of recurrent or persistent disease, and a higher risk of neoplastic degeneration.[45] Therefore, we suggest close monitoring for rectal conditions as well as an aggressive dietary and medical control of inflammation.

Conclusion

The purpose of IBD surgery is to help in disease control and to improve patient's quality of life. In order to achieve inflammation control, a stoma is often being created in staged surgery. However, stoma could affect patient's quality of life, especially for those with stoma morbidity. Besides, the incidence of permanent stoma is still high in IBD patients. As the superior medication developed, advanced surgical techniques, precise monitoring method and multidisciplinary team management in the future, we are looking forward to lowering the stoma rate in IBD surgery.

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原　著

發炎性腸道疾病手術中腸造口關閉之預後

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目的　為了疾病控制，在發炎性腸道疾病的手術中時常會伴隨腸造口，然而做腸造口時，關閉造口後與永久腸造口等併發症對於患者跟外科醫師皆是一個挑戰。我們分析發炎性腸道疾病病患造口關閉之預後，以幫助外科醫師了解腸造口手術對於發炎性腸道疾病的影響。

方法　挑選本院 2001 年至 2019 年發炎性腸道疾病的患者，分析術前因子，手術適應症，手術方式，術後併發症。另外也深入探討永久性腸造口的比例與原因。

結果　克隆氏症病患，術前有較低的 BMI ($p = 0.02$)，體重減輕大於 5% 的比例較高 ($p = 0.046$)，較高的營養風險 ($p < 0.001$)，較多的腸道手術史 ($p = 0.01$) 以及較多的生物製劑使用 ($p = 0.011$)。而且克隆氏症病患在主要手術時一併做腸造口的比例較低 ($p = 0.002$)。26.3% 的發炎性大腸炎患者與 57.1% 的克隆氏症病患有發生嚴重腸造口併發症需要開刀處理。57.8% 發炎性大腸炎患者與 42.8% 克隆氏症之病患能接受腸造口關閉。腸造口關閉手術後，只有一位克隆氏症病患因皮腸廔管需在需再次重做腸造口分流。終端迴腸造口伴隨的疾病控制不佳是造口延遲或是無法關閉的最大因素。

結論　發炎性腸道疾病的患者，因腸造口產生的併發症不少，特別是克隆氏症克隆氏症病患。而雖然關閉造口時的併發症很少，但是無法關閉的永久性腸造口還是佔有一半左右的比例。

關鍵詞　發炎性腸道疾病、發炎性大腸炎、克隆氏症、腸造口。