Frequency and risk factors of surgical recurrence of Crohn's disease after primary bowel resection

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ABSTRACT

Background/Aims: *The purpose of this study was to evaluate the frequency and risk factors associated with Crohn's disease (CD) reoperation after primary bowel resection.*

Materials and Methods: *We identified 166 patients suffering from CD with primary bowel resection and primary anastomosis from the clinical database of a university hospital. The cumulative recurrence rate and median recurrence-free survival (RFS) were calculated using the Kaplan-Meier analysis. Categorical variables were compared using a log-rank test. A Cox proportional hazard model was used for multivariate analysis.*

Results: *The median age of reoperation was 30 years, and the median RFS was 30 months. The reoperation intervention rate was 16.9%. It was shown that smoking (p=0.015) and jejunoileal anastomosis (p=0.002) were significantly closely correlated to an increased risk of surgical recurrence, whereas laparoscopy (p=0.039), side-to-side anastomosis (p=0.018), and anastomotic stoma wider than 3 cm (p=0.024) were significantly closely correlated to a reduced risk of surgical recurrence.*

Conclusion: *This study provided a robust result that smoking and small intestinal lesions were the risk factors of surgical recurrence for patients with CD upon the initial gut resection. Laparoscopy, side-to-side anastomosis, and wide anastomotic stoma were found to be protective factors against surgical recurrence.*

Keywords: *Crohn's disease, recurrence, CD*

INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory bowel disease (IBD) that can affect any part of the gastrointestinal tract but is usually located in the terminal ileum. CD is usually treated with a drug regimen, but 70% to 90% of patients with CD needs surgical intervention for the rest of their lives (1). Indications for surgery include failure of medical treatment, intestinal obstruction, hemorrhage, penetrating lesions, and tumor formation. Unfortunately, CD cannot be cured with surgery. After initial surgery, 33% to 82% of patients require a second operation, and 22% to 33% of patients need a third surgical treatment (2). In one study, Michelassi et al. (3) observed a 20% reoperation rate at 5 years and 34% at 10 years after initial surgery. The Cleveland Clinic Center study found that 146 patients with CD had a 50% reoperation rate at 14 years after their first operation (4). Postoperative recurrence of CD includes endoscopic recurrence, clinical recurrence, and surgical recurrence (5). Surgical recurrence refers to further resection for CD after a first operation.

A large body of literature suggests that factors affecting CD clinical recurrence include smoking, type of anastomosis, duration of disease, penetrating diseases (6), perianal lesions (7), and upper gastrointestinal lesions (8). Although still controversial, factors including sex (9), family history (10), age at diagnosis (9,10), and bowel resection over 100 cm (11) are also risk factors for subsequent CD surgery. Although host genetic and environmental factors are considered to be the principal factors in the pathogenesis of CD, the mechanism by which CD recurs after surgery is unclear. CD is a heterogeneous disease with multiple phenotypes. Epidemiology and genetic susceptibility (12) are noticeably different in Asian populations than in people of European descent.

The purpose of this study is to investigate the surgical recurrence of Chinese populations suffering from CD with primary bowel resection and one-stage anastomosis in a specialist IBD medical center at the Nanjing General Hospital in Nanjing, in eastern China, and to identify risk factors for surgical recurrence of CD.

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MATERIALS AND METHODS

Patients

All patients and their relatives provided the informed consent, and the clinical study was approved by the ethics committee of hospital. This clinical study was performed in accordance with relevant guidelines and regulations. We identified 166 patients with CD with primary bowel resection and anastomosis from the clinical database of a university hospital, which included 980 hospitalized patients with CD in the hospital from January 2001 to October 2016. We retrospectively analyzed the outpatient and hospital records of all patients through letters, scheduled medical exam, and telephone interviews. We excluded patients with CD with a prior bowel resection or those who had undergone enterostomy at other institutions. Patients with CD who were dead, undiagnosed, who had not undergone surgery, who had been lost to follow-up, and whose medical records were incomplete were excluded. We also excluded patients with CD who had undergone strictureplasty or enterostomy in our department but still had residual disease after the operation. All patients included in the study met the criteria issued by the ECCO consensus recommendation for diagnosis and treatment (13,14). The strategies used on selected patients are shown in Figure 1.

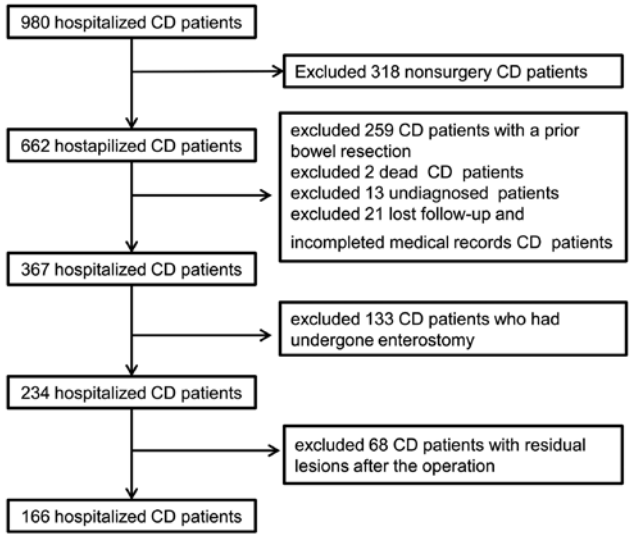

Figure 1. Images show the strategies used on selected patients

Protocol

All medical records, including demographic and detailed clinical characteristics, were prospectively recorded for every patient by two independent individuals. General data obtained included gender, smoking history, duration of disease (time from diagnosis to first resection), family history of IBD, preoperative appendectomy, preoperative abdominal abscess drainage, surgical approach, age at diagnosis, disease location and behavior, type of anastomosis, location of anastomosis, width of anastomosis, number of anastomosis procedures, length of bowel resection, other abdominal operations, postoperative complications, and surgical relapse were evaluated.

Perioperative Medication

Preoperative internal medicine medication

Of 166 patients who underwent surgery, 5 cases received no medication, whereas 30 cases were treated with mesalazine administered orally; 8 cases required parenteral nutrition treatment, 6 cases required combined nutrition treatment, and 117 patients were treated with nasogastric enteral nutrition, including 20 cases of single full-dose enteral nutrition, 25 cases combined with glucocorticoid therapy, 23 cases combined with tripterygium glycosides treatment, 11 cases combined with azathioprine maintenance treatment, 36 cases combined with the anti-TNF-a treatment, 1 case combined with CellCept maintenance treatment, and 1 case undergoing fecal microbiota transplantation.

Postoperative internal medicine medication

All patients were treated with enteral nutrition in the early period after surgery and then with azathioprine administered orally (1.5mg/kg per day) at 2 weeks after surgery. Patients that could not tolerate azathioprine were treated with CellCept, continued full-dose enteral nutrition, or other therapy.

Definitions

The diagnosis of CD was made according to clinical manifestations and radiological, endoscopic, and pathological diagnosis of surgical specimens. *Surgical recurrence* was defined as the presence of symptoms such as increased bowel diarrhea frequency and abdominal pain, which were severe enough to need a reoperative procedure in which the bowel was resected for active CD. In our study, the starting point was time of primary bowel resection, and the endpoint was time of surgical recurrence or time of last follow-up. All patients were followed up until surgical relapse or October 1, 2016, whichever came first. "Smoking history" was divided into two categories. Current and former smokers were classified as one group and lifelong non-smokers as another. Duration of disease was

defined as the time from diagnosis to the first resection. We used the Montreal classification to describe the age at diagnosis, disease location, and behavior. According to the patient age at diagnosis, the patients were divided into three groups: A1 (≤16 years), A2 (17-40 years), and A3 (>40 years). According to the disease location, the patients were divided into four groups: L1 (ileum), L2 (colonic), L3 (ileocolonic), and L4 (upper gastrointestinal tract). According to the disease behavior, the patients were divided into four groups: B1 (non-structuring and non-penetrating), B2 (structuring), B3 (penetrating), and P (perianal lesions). Patients were classified based on the presence of preoperative appendectomy, preoperative abdominal abscess drainage, parenteral manifestations, preoperative nutritional support, other intraoperative abdominal manipulations, and postoperative complications. Other intraoperative abdominal manipulations included intraoperative simultaneous enterolysis, cholecystectomy, gastrostomy, intravesical fistula repair, and small intestine repair. Postoperative complications included incision infection, hemorrhage, and intestinal obstruction. Surgeries were classified as emergency or elective, and laparoscopic or open abdominal. Anastomoses were divided into two groups: side-to-side in one and end-to-end and end-to-side in another. Anastomotic sites were jejuno-ileum, ileocolon, or colorectum. An anastomotic stoma 30 mm in width served as the threshold for grouping. In addition, patients were sub-divided into two groups based on the number of intraoperative anastomotic stomas. A 100-cm-long excised gut served as the threshold for grouping. When multiple segments of gut were excised, the total length of excised gut was calculated.

Statistical analysis

Data analysis was accomplished using the Statistical Package for Social Sciences (SPSS) version 21.0 (IBM Corp.; Armonk, NY, USA) software package. The cumulative recurrence rate and median recurrence-free survival (RFS) were calculated using the Kaplan-Meier analysis, and then the survival curve was plotted. Categorical variables were compared using a log-rank test. The method of screening variable is forward selection. The Cox proportional hazard model was used for multivariate analysis. The hazard ratio (HR) and 95% confidence interval (CI) were calculated, and the risk factors of postoperative recurrence were then screened out. Graphpad 5.0 (GraphPad Software Inc.; La Jolla, CA, USA) was used to plot the survival curve. Among all the analyses, a $p<0.05$ was considered as significant difference.

RESULTS

Patient clinical characteristics

The clinical data of all the patients in this study are presented in Table 1. Of all the included patients, 63% were male and 37% were female. A total of 15 patients (9%) had a history of smoking, whereas 151 patients (91%) did not. Only 1 patient had a family history of IBD, which was significantly lower than in reports from Western countries. Twenty-seven patients (16%) had a disease that lasted no longer than 6 months, whereas 139 patients (84%) had a disease that lasted longer than 6 months. Forty-two patients (25%) had a previous history of preoperative appendectomy. Here, 32 patients (19%) had a history of preoperative abdominal abscess incision and drainage, and 14 (8%) developed parenteral manifestations. Here, 114 patients (69%) had preoperative nutritional support. Another 97 patients (58%) chose open abdominal operations, whereas 69 patients (42%) chose laparoscopy. Only 1 patient had emergency primary anastomosis. According to the Montreal classification, the majority of patients, approximately 121 (73%), were between 17 and 40 years old when diagnosed, 13 patients (9%) were younger than 17 years, and 32 patients (19%) were older than 40 when diagnosed. A total of 53 patients (32%) had lesions of the terminal ileum, 15 patients (9%) had lesions of the colon, 98 patients (59%) had lesions of the ileocecal junction, and 13 patients (8%) had lesions of the upper gastrointestinal (GI) tract. There were 16 type B1 patients (10%), 90 type B2 patients (54%), 60 type B3 patients (36%), and 39 type P patients (23%). The most common anastomotic site was the ileocolon. A total of 100 patients (60%) had side-to-side anastomoses. Here, 97 patients (58%) had an anastomotic stoma larger than 30 mm. There were 17 patients (10.2%) with an excised gut longer than 100 cm, and 149 patients (89.8%) with an excised gut shorter than 100 cm. Other intraoperative abdominal manipulations were conducted in only 11 patients (7%). Postoperative complications were detected in 15 patients (9%). Two patients died of multiple organ failure after enterectomy (1.2%).

Univariate analysis of patient clinical characteristics

The median age of surgical recurrence was 30 years, and the RFS was 30 months. The overall recurrence rate of operation was 16.9%. The results of cumulative surgical recurrence rate calculation using the Kaplan-Meier analysis were presented in Figure 2. The results of the univariate analysis of all the categorical variables were presented in Table 2. This result showed that smoking, a history of preoperative appendectomy, the mode of operation,

Table 1. Patient clinical variables (n=166)

Clinical Variable	No. of Patients	Percentage (%)
Gender		
male	105	63
female	61	37
Smoking history		
never	151	91
former and current	15	9
Duration of disease		
≤6 months	27	16
>6 months	139	84
Preoperative appendectomy		
no	124	75
yes	42	25
Preoperative abdominal abscess drainage		
no	134	81
yes	32	19
Parenteral manifestations		
no	152	92
yes	14	8
Preoperative nutritional support		
no	52	31
yes	114	69
Surgical approach		
open	97	58
laparoscopic	69	42
Age of diagnosis		
A1	13	8
A2	121	73
A3	32	19
Location of disease		
L1	53	32
L2	15	9
L3	98	59
L4		
no	153	92
yes	13	8
Behavior of disease		
B1	16	10
B2	90	54
B3	60	36
P		
no	127	77
yes	39	23
Type of anastomosis		
SSA	100	60
EEA and ESA	66	40
Location of anastomosis		
ileojejuno	50	30
ileocolic	109	66
colocolic	7	4
Width of anastomosis		
≤30mm	69	42
>30mm	97	58
Number of anastomosis		
1	155	93
2	11	7
Length of bowel resection		
<100cm	149	90
≥100cm	17	10
Postoperative complications		
no	151	91
yes	15	9
Other abdominal operation		
no	155	93
yes	11	7

A1: ≤16 years; A2: 17-40 years; A3: >40 years; L1: ileum; L2: colonic; L3: ileocolonic; L4: upper gastrointestinal tract; B1: non-structuring and non-penetrating lesions; B2: structuring lesions; B3: penetrating; P: perianal lesions; SSA: side-to-side anastomoses; EEA: end-to-end anastomoses; ESA: end-to-side anastomoses

anastomotic site, anastomotic type, width of anastomotic stoma, and number of anastomotic stomas influenced surgical recurrence after operations.

Cox proportional hazard model for surgical recurrence after resection

Factors such as smoking history, preoperative appendectomy, surgical mode, anastomotic site, anastomotic type, width of anastomotic stoma, and number of anastomotic stomas were included into the multivariate Cox proportional hazards model to analyze the risk factors of postoperative recurrence. It was shown that smoking (p=0.015) and jejunoileal anastomosis (p=0.002) were significantly closely correlated to increased risks of re-

Table 2. Univariate analysis of categorical clinical variables

Clinical Variable	Model Coefficient	HR (95%CI)	p
Gender			
male	0.263	1.301 (0.599-2.824)	0.506
female	0	1	
Smoking history			
never	-1.136	0.321 (0.121-0.853)	0.023
former and current	0	1	
Duration of disease			
≤6 months	-0.061	0.940 (0.357-2.479)	0.901
>6 months	0	1	
Preoperative appendectomy			
no	-0.743	0.476(0.223-1.017)	0.049
yes	0	1	
Preoperative abdominal abscess drainage			
no	0.609	1.838 (0.554-6.100)	0.320
yes	0	1	
Parenteral manifestations			
no	0.537	1.710 (0.403-7.251)	0.467
yes	0	1	
Preoperative nutritional support			
no	-0.041	0.96 (0.442-2.083)	0.917
yes	0	1	
Surgical approach			
open	1.850	6.357 (1.490-27.117)	0.012
laparoscopic	0	1	
Age of diagnosis			
A1	0.269	1.308 (0.331-5.165)	0.701
A2	-0.331	0.718 (0.299-1.721)	0.458
A3	0	1	
Location of disease			
L1	0.717	2.047 (0.947-4.428)	0.069
L2	-0.249	0.780 (0.175-3.468)	0.744
L3	0	1	
L4			
no	-0.234	0.791 (0.239-2.622)	0.701
yes	0	1	
Behavior of disease			
B1	-0.054	0.947 (0.259-3.466)	0.934
B2	0.033	1.034 (0.463-2.306)	0.936
B3	0	1	
P			
no	0.065	1.067 (0.431-2.640)	0.888
yes	0	1	
Location of anastomosis			
ileojejuno	0.169	1.184 (0.269-5.217)	0.823
ileocolic	-1.089	0.337 (0.074-1.53)	0.159
colocolic	0	1	
Type of anastomosis			
SSA	-0.962	0.382 (0.166-0.882)	0.024
EEA and ESA	0	1	
Width of anastomosis			
≤30mm	1.215	3.369 (1.339-8.479)	0.010
>30mm	0	1	
Number of anastomosis			
1	-1.182	0.307 (0.116-0.812)	0.017
2	0	1	
Length of bowel resection			
<100cm	0.059	1.061 (0.319-3.532)	0.923
≥100cm	0	1	
Other abdominal operation			
no	-0.639	0.528 (0.158-1.764)	0.299
yes	0	1	
Postoperative complications			
no	-0.312	0.732 (0.254-2.114)	0.565
yes	0	1	

A1: ≤16 years; A2: 17-40 years; A3: >40 years; L1: ileum; L2: colonic; L3: ileocolonic; L4: upper gastrointestinal tract; B1: non-structuring and non-penetrating lesions; B2: structuring lesions; B3: penetrating; P: perianal lesions; SSA: side-to-side anastomoses; EEA: end-to-end anastomoses; ESA: end-to-side anastomoses

currence, whereas laparoscopy (p=0.039), side-to-side anastomosis (p=0.018), and anastomotic stoma wider than 3 cm (p=0.024) were significantly closely correlated to reduced risks of recurrence. The results of the multivariate Cox proportional hazards model analysis for surgical recurrence are presented in Table 3.

DISCUSSION

This study retrospectively analyzed the postoperative recurrence rate and the influencing factors of patients with CD who initially underwent bowel resection and primary anastomosis in our hospital. The Institute of General Surgery in our hospital established an IBD diagnosis and

Table 3. Significant risk factors at the multivariate Cox proportional hazards model analysis for surgical recurrence

Variable	Model Coefficient	HR (95%CI)	p
Smoking history			
former and current	1.279	3.594 (1.277-10.117)	0.015
never	0	1	
Preoperative appendectomy			
yes	0.414	1.513 (0.656-3.493)	0.332
no	0	1	
Surgical approach			
laparoscopic	-1.45	0.235 (0.104-0.531)	0.039
open	0	1	
Location of anastomosis			
ileocolic	-1.45	0.235 (0.104-0.531)	0.002
colocolic	-0.044	0.956 (0.172-5.308)	0.959
ileojejuno	0	1	
Type of anastomosis			
EEA and ESA	1.103	3.012 (1.212-7.486)	0.018
SSA	0	1	
Width of anastomosis			
>30mm	-0.962	0.382 (0.166-0.882)	0.024
≤30mm	0	1	
Number of anastomosis			
2	1.052	2.864 (0.93-8.818)	0.067
1	0	1	

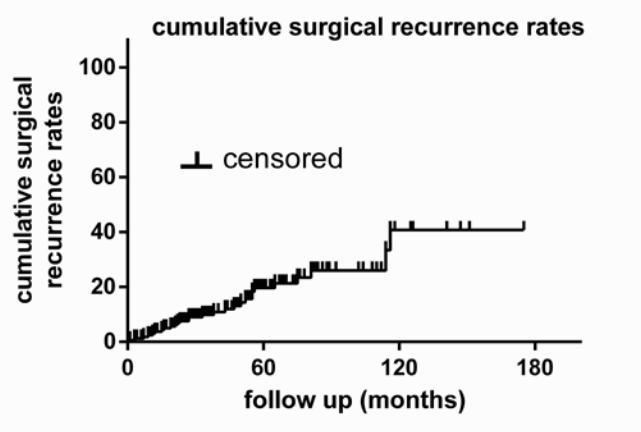

Figure 2. Follow-up (months), cumulative surgical recurrence rates. The axial (follow-up) and coronal (cumulative surgical recurrence rates) image shows the results of cumulative surgical recurrence rate calculation using the Kaplan-Meier analysis

treatment center in 2000 and began to receive patients with CD from all over China. The number of patients has grown each year. This study aimed to identify the influencing factors of postoperative recurrence, to optimize the treatment protocols of CD, and to improve the quality of life of patients with CD.

The mortality of patients with CD after enterectomy is 1.2%, which is low and may be related to the long-term enteral nutrition support given preoperatively for improving malnutrition and the carrying out of surgical treatment during the remission period of CD.

Gender was not found to be a factor associated with postoperative recurrence for CD, which was consistent with current literature reports (9). In this study, only 1 out of 166 patients had a family history of IBD, which was significantly lower than in Europe or the United States. There are two possible explanations: First, specific diagnosis and treatment centers of IBD were established in China only relatively recently and thus only a few patients were admitted. Second, CD is heterogeneous with multiple manifestations. The hereditary susceptibility of Asian populations is different from that of Western populations (12). Previous studies (10,15) have suggested that there hadn't been agreed conclusions on the effect of the IBD family history on postoperative recurrence. Only 1 out of 166 patients underwent emergency surgery. The others underwent elective surgeries. This might be due to patients' choices in this study. In our center, patients with emergency surgery seldom underwent primary anastomosis. Because the positive events of surgical opportunity and IBD family history were not enough, these two factors were not included into survival analysis. Yang et al. (16) found that emergency surgery would increase the risk of a second gut resection.

This study did not find any effect of age at diagnosis, location of lesion, and illness behavior in the Montreal classification on postoperative recurrence. Monteiro et al. (17) found that a shorter duration of disease was a significant risk factors of endoscopic recurrence after ileocolic resection with patients suffering from CD. In this study, penetrating lesions did not affect the recurrence rate, which was to the contrary of many studies (18). Sachar et al. proved penetrating lesions increased the risks of both clinical and postoperative recurrence. These contrary results might be related to the treatment protocols. Some patients with penetrating lesions were considered to have stenotic lesions during surgical exploration. In our IBD center, patients with penetrating lesions who did not

show diffuse peritonitis were regularly given an indwelling double-lumen catheter in the abdominal cavity for continuous washing and drainage. Nutritional supportive treatment was also added. Surgery was indicated if the local fistula healed and became a stenotic lesion.

In our study, perianal lesions were not the risk factor of recurrence of CD, which is not consistent with the ECCO guidelines (19). This may be related to ethnic differences between Chinese and Western countries. The existing literature (20) shows that pathological factors are closely related to postoperative recurrence of CD. However, this study was a large sample sized retrospective study and spanned a long period of time; moreover, partial pathological data were lacking, and partial histological results were not detected. Therefore, we did not take this factor into account.

Complications, such as postoperative incision infection, did not increase the risk of recurrence, which was consistent with the study published by Yamamoto et al. (21). The length of resected gut during the operation does not affect the risk of recurrence. However, the effect of the length of resected gut on postoperative recurrence is still under debate (11). Onailet al. (22) held the view that preoperative appendectomy was a risk factor for the recurrence of CD. In the present study, however, we hold the opinion that preoperative appendectomy and preoperative abdominal drainage with indwelling catheters are not risk factors for recurrence. The present study demonstrated that the preoperative disease course was not a risk factor for recurrence. Currently, there is little agreement regarding the effect of preoperative disease course on postoperative recurrence, which might be a result of different subtyping of disease course in each study (23,24).

The present study showed that smoking was an independent risk factor for recurrence. The recurrence risk of smokers was 3.6 times as that of non-smokers, which was consistent with many literature reports (24,25). Smoking was found to lead to higher chances of second operations among patients with CD, whereas smoking cessation was found to reduce the activity of CD and reduce the risk of postoperative recurrence. Currently, possible mechanisms explaining how smoking aggravates CD and increases the risk of recurrence are as follows: 1. Nicotine leads to excessive bacterial production inside the gut by inhibiting the immune function of intestinal mucosa (26); 2. Smoking leads to the formation of local intravascular thrombus at the intestinal mucosa and thus disturbs the local blood circulation of intestinal mucosa (27); 3. Smoking might alter the components of gut mucus and so exacerbate local neutrophil infiltration and free radical production (28). We strongly suggest immediate smoking cessation to all patients with CD, particularly those who are about to undergo surgeries.

In this study, patients with laparoscopic operations had significantly lower recurrence rates and superior median RFS than patients with open abdominal operations. This might be due to patient selection bias, as patients with laparoscopic operations tended to have milder conditions. Furthermore, one meta-analysis (29) showed that patients with CD who underwent laparoscopic operations had low recurrence rates. Patients with laparoscopic operations had faster recovery of intestinal functions, fewer complications, and shorter postoperative hospital stays. We here suggest laparoscopy to patients with CD upon initial surgical treatment. As for patients with CD selecting laparoscopic surgery, we mostly chose those with lesions located in the ileocecus or colorectal lesions, only a history of appendectomy before surgery, and expected mild abdominal adhesions.

In the present study, patients with CD and with side-to-side anastomoses and those with wide anastomotic stomas showed more significant benefits after operations than those with other anastomoses. This was consistent with the studies published by of Scarpa et al. (30). Recurrence was most common around the anastomotic stoma. Bacteria in the feces have been identified as one of the reasons for recurrence around the anastomotic stoma. Side-to-side anastomosis maintains the patency of gut and is less likely to lead to remaining feces and stenosis of anastomotic stoma. Side-to-side anastomosis with wide anastomotic stoma should be strongly recommended as the first choice. According to our experience, side-to-side anastomosis was mostly carried out using a disposable linear cutting closer (specifications: 75 mm, 80 mm, 100 mm, etc.; after anastomosis, the aperture of the anastomotic stoma was generally greater than 60 mm). Then, 4-0 absorbable sutures were used to strengthen the suture of the seromuscular layer of the anastomotic stoma; meanwhile, 4-0 absorbable sutures were used to close the stump, for further strengthening the suture of the seromuscular layer of the stump.

Postoperative medical therapies, including antibiotics, mesalazine, azathioprine/purinetho, anti-TNF agents, and enteral nutrition, have all been proven effective. Patients with CD who underwent surgery were given enteral nutrition through nasogastric feeding early and then with

oral administration of azathioprine (1.5mg/kg per day) for 2 weeks after surgery. Azathioprine was given incrementally. Starting at a low dosage, azathioprine was increased gradually every 4 weeks until the peripheral blood leukocyte count dropped to a critical value or the dosage recommended by the guidelines was met. Re-examination by colonoscopy took place regularly after the operations. The time period of the study was 15 years, so the medical management that improved substantially during those years may have an impact on the outcomes.

Overall, this study demonstrated that the risk factors of postoperative recurrence for patients with CD upon the initial gut resection included smoking and small intestinal lesions. Laparoscopy, side-to-side anastomosis, and wide anastomotic stoma were found to be protective factors against postoperative recurrence. However, there were a few limitations to this study. First, this study was a retrospective analysis on the medical records, so there may be bias with respect to the terms used to express the research data. Second, because our IBD center is the only diagnosis and treatment center in China geared to CD that emphasizes surgical intervention, patients transferred to our center usually showed more severe symptoms and more complicated conditions. Consequently, the postoperative recurrence rate might be higher than at other centers. Third, because this study excluded the patients who did not undergo gut resection upon initial operations in our center, the sample size was small. Finally, the effect of drug intervention on postoperative recurrence was not evaluated. Our institute is the only IBD diagnosis and treatment center in China capable of collecting this many patients with CD who had undergone surgery. Hopefully, the results of this study will help optimize the treatment protocols and improve the postoperative life quality for patients with CD. A prospective study will be carried out to verify these results.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Nanjing Medical University.

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - W.Z.; Design - W.Z.; Supervision - W.Z.; Resources - W.Z.; Materials - J.Z., Y.L., J.G.; Data Collection and/or Processing - J.Z., Y.L., J.G.; Analysis and/or Interpretation - J.Z., Y.L., J.G.; Literature Review - J.Z., Y.L., Y.G.; Writing Manuscript - J.Z.; Critical Review - J.Z., Y.L., J.G.

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