



Risk factors for proctectomy in consecutive Crohn's colitis surgical patients in a reference colorectal centre

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Abstract

Purpose Crohn's colitis carries a risk for permanent stoma with extirpation of the rectum. We aimed to estimate the proctectomy rate and identify risk factors for proctectomy in patients with Crohn's colitis.

Methods For this study, we retrospectively reviewed data from consecutive patients with Crohn's disease (CD) affecting the colon or anorectal region undergoing bowel resection in a reference colorectal centre between 2006 and 2016. The cumulative risk for proctectomy was calculated using the Kaplan-Meier curve. We used univariate and multivariate logistic regression analyses to determine independent risk factors for proctectomy. Outcomes after proctectomy concerning reoperation frequency and perineal wound healing are also described.

Results In total, this study included 125 patients. Proctectomy was performed in 36 patients (28.8%), of whom 14 patients (38.9%) experienced perineal wound healing problems. The rates of proctectomy were 5.6% and 32.0% 10 and 20 years after CD diagnosis, respectively. Female gender (odds ratio (OR) 3.375, 95% confidence interval (CI) 1.304–8.733, $P=0.012$), disease duration (OR 1.067, 95% CI 1.011–1.126, $P=0.018$) and history of perianal disease (OR 3.160, 95% CI 1.215–8.219, $P=0.018$) were independent risk factors for a proctectomy procedure, whereas thiopurine medication (OR 0.170, 95% CI 0.060–0.486, $P=0.001$) was an independent protective factor for proctectomy.

Conclusions The duration of Crohn's disease, female gender and a history of perianal disease were significant risk factors for a proctectomy procedure. Future research should examine whether immunosuppressive and biological medications reduce the risk for proctectomy.

Keywords Crohn's colitis · Crohn's disease · Definitive stoma · Proctectomy · Risk factors

Introduction

According to population-based studies, the incidence of Crohn's colitis has increased in recent decades [1, 2]. It is estimated that more than 60% of Crohn's disease (CD) patients have colonic involvement. Isolated Crohn's colitis is found in 20% of patients suffering from CD, but ileocolonic involvement is more common [3]. CD of the colon or anorectal region is associated with a risk for definitive stoma requiring extirpation of the rectum. Many patients affected by this type of CD fear permanent stoma. Temporary stoma

formation may be used to control disease while allowing for the recovery of the bowel distal to the covering stoma. However, a recent meta-analysis has shown that only 34% of CD patients with temporary stoma will ever have their stoma closed and only 16% of these patients will improve without undergoing a new stoma construction [4]. Furthermore, previous studies reported proctectomy rates of 20% in Crohn's colitis patients [5, 6].

One randomized controlled trial described a diminished need for perianal disease surgery in patients treated with thiopurine medication [7]. In addition, biological medications appear to improve perianal disease [8–10]. However, previous studies did not specifically evaluate the effect of CD medications in preventing proctectomy and further investigations are needed.

Construction of end colostomy with preservation of part of the large bowel increased postoperative CD recurrence in Crohn's colitis patients according to previous studies [11, 12].

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Concomitant terminal ileum disease was also described as a risk factor for postoperative CD recurrence in Crohn's colitis patients [13, 14].

Our study aimed to determine the proctectomy rate and identify the risk factors for proctectomy in surgical Crohn's colitis patients. Furthermore, we evaluated the frequency of reoperations and delayed perineal wound healing after proctectomy.

Material and methods

Clinical records from all patients with colonic or anorectal CD undergoing bowel resection in a reference colorectal centre between 2006 and 2016 were retrospectively reviewed for this study. We excluded patients with disease limited to the small bowel or terminal ileum without involvement of the colon or anorectal region. We collected data on patient age, gender, date of CD diagnosis, history of perianal disease and terminal ileum disease, as well as the use of corticosteroids, thiopurine and biological medications. As preoperative medication, we considered the medication in use for the last 6 months before surgery. The index operation was either proctectomy or other bowel resection in patients not referred for proctectomy during the study period. Proctectomy date, indication, approach and the frequency of perineal complications and reoperations during follow-up were also recorded. Reoperation was defined as the need for a new bowel resection due to recurrent disease. CD duration was

calculated from the date of diagnosis until the date of the index operation.

The Kaplan-Meier curve was used to calculate the cumulative risk for proctectomy from CD diagnosis until the end of follow-up. Risk factors for proctectomy were identified using univariate and multivariate logistic regression analyses. Univariate variables with $P < 0.05$, which we considered statistically significant, were included in the multivariate analyses. The Fisher's exact test was used to compare subgroups in patients undergoing reoperation after proctectomy.

Results

All patients

A total of 125 patients with colonic or anorectal CD underwent bowel resection between 2006 and 2016, all of whom we included in our study. Table 1 shows the patient characteristics, while the types of index operations appear in Table 2.

At least one previous CD operation was performed on 61 patients (48.8%); 32 patients (25.6%) underwent two or more previous CD operations. Previous CD operations consisted of the following: 15 ileocaecal resections, 12 small bowel resections, 30 segmental colon resections, 7 colectomies with ileorectal anastomosis, 4 colectomies with ileostomy and multiple operations for perianal abscesses and fistulas.

Table 1 Patient descriptive data

Patient characteristics	All cases	Proctectomy	
		No	Yes
Number of patients	125 (100%)	89 (71.2%)	36 (28.8%)
Median age at index operation	39.0 (14.8–74.1)	34.0 (14.8–74.1)	40.5 (22.9–69.4)
Median age at diagnosis	21.8 (3.1–69.9)	22.2 (5.2–69.9)	20.5 (3.1–53.3)
Gender			
Male	66 (52.8%)	54 (60.7%)	12 (33.3%)
Female	59 (47.2%)	35 (39.3%)	24 (66.7%)
Median duration of CD	12.0 (0–36.8)	9.1 (0–36.8)	16.9 (5.0–32.3)
Median time from index surgery	4.4 (0–10.7)	4.4 (0.3–10.7)	4.6 (0–10.5)
Median time from diagnosis	16.7 (0.5–39.8)	14.8 (0.5–39.8)	19.0 (5.5–38.0)
Preoperative biological medication	43 (34.4%)	34 (38.2%)	9 (25.0%)
Preoperative corticosteroid medication	43 (34.4%)	35 (39.3%)	8 (22.2%)
Preoperative thiopurine medication	98 (78.4%)	77 (86.5%)	21 (58.3%)
History of perianal CD	63 (50.4%)	37 (41.6%)	26 (72.2%)
History of terminal ileum CD	89 (71.2%)	72 (80.9%)	17 (47.2%)

CD Crohn's disease; values are in years (range) for continuous variables and frequencies (proportion) for categorical variables

Table 2 Types of index operations

Operation	Total (<i>n</i> = 125)
Small bowel resection	5 (4.0%)
Right colon resection	59 (47.2%)
Left colon resection	15 (12.0%)
Segmental or subtotal colon resection	7 (5.6%)
Colectomy	3 (2.4%)
Proctocolectomy	5 (4.0%)
Proctectomy	31 (24.8%)

The cumulative rates of proctectomy were 5.6% and 32.0% 10 and 20 years from CD diagnosis, respectively (Fig. 1).

Table 3 shows the risk factors for proctectomy. In the multivariate analysis, CD duration, female gender and perianal CD were independent risk factors for proctectomy. The use of thiopurines was an independent protective factor for proctectomy.

Proctectomy patients

A proctectomy was performed on 36 patients (28.8%) at a median of 16.9 years (5.0–32.2 years) from CD diagnosis. The indications for proctectomy are listed in Table 4. Proctectomy was performed by the perineal approach in 3 patients (8.3%), the abdominal approach in 5 patients (13.9%) and the combined abdominoperineal approach in 28 patients (77.8%).

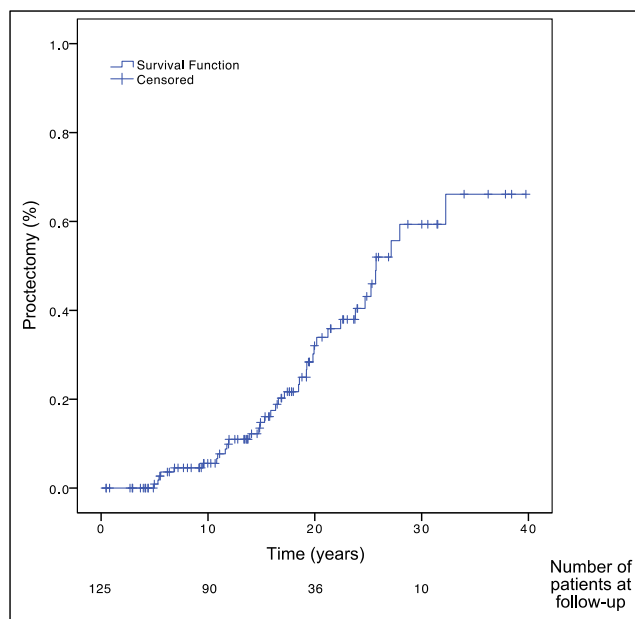


Fig. 1 Cumulative probability of proctectomy in surgical Crohn's colitis patients

Altogether, 14 patients (38.9%) experienced problems with perineal wound healing. Furthermore, two patients (5.6%) who underwent proctectomy through the abdominal approach only, subsequently required reoperation for the removal of the anus.

After proctectomy, 8 patients (22.2%) required at least 1 reoperation due to recurrent CD. Reoperations consisted of 7 ileal resections performed on 5 patients and 6 colon resections performed on 5 patients.

The reoperation frequency in patients with a history of terminal ileum disease was 29.4% (5 of 17 patients); the frequency in patients without terminal ileum disease was 15.8% (3 of 19 patients, $P = 0.28$). The reoperation frequency involving only ileal resections was 23.5% (4 of 17 patients) in patients with a history of terminal ileum disease and 5.3% (1 of 19 patients) in patients with no such history ($P = 0.14$).

The reoperation frequency in patients who underwent proctectomy with end colostomy was 31.6% (6 of 19 patients) and 11.8% (2 of 17 patients) in patients who underwent proctectomy with end ileostomy ($P = 0.15$).

In the proctectomy group, 20 patients (55.6%) had an end ileostomy, 9 patients (25.0%) had an end transversostomy and 7 patients (19.4%) had an end sigmoideostomy at the end of the follow-up.

Discussion

In our cohort of Crohn's colitis patients who underwent bowel resection, 28.8% had a proctectomy performed during follow-up. This is comparable with previous studies that described a 19.2 to 25.4% proctectomy rate after colectomy [5, 6, 15]. Our group of patients is more heterogeneous and included patients referred for different bowel resections, but all patients had colonic or anorectal CD.

The proctectomy rate in our study group calculated with the Kaplan-Meier curve was only 5.6% 10 years from CD diagnosis. This low rate can be explained by the fact that some of our patients may not have had colonic involvement at the beginning of disease. Proctectomy risk increases over time, with rates as high as 32% 20 years after CD diagnosis. By contrast, this high rate must be interpreted with caution, since our study included only Crohn's colitis patients who underwent bowel resection. That is, this patient group may be at higher risk for proctectomy. Previous population-based studies have estimated the rate of definitive stoma as around 14% 20 years after CD diagnosis [16, 17].

We found that the presence of perianal disease is a risk factor for proctectomy, a result also observed by others [16, 18, 19]. In comparison, O'Riordan et al. [6] did not find perianal disease to be a risk factor for proctectomy in their study that included patients who underwent colectomy with ileorectal anastomosis. According to their

Table 3 Logistic regression analyses of risk factors for proctectomy in surgical Crohn's colitis patients

	Univariate analysis		Multivariate analysis	
	Unadjusted	<i>P</i> value	Adjusted	<i>P</i> value
	OR (95% CI)		OR (95% CI)	
Age at diagnosis	0.984 (0.954–1.015)	0.312	–	–
Female gender	3.086 (1.369–6.958)	0.007	3.375 (1.304–8.733)	0.012
Duration of CD	1.084 (1.034–1.136)	0.001	1.067 (1.011–1.126)	0.018
History of perianal CD	3.654 (1.574–8.484)	0.003	3.160 (1.215–8.219)	0.018
Biological medication	0.539 (0.227–1.283)	0.163	–	–
Corticosteroid medication	0.441 (0.180–1.077)	0.072	–	–
Thiopurine medication	0.218 (0.089–0.536)	0.001	0.170 (0.060–0.486)	0.001

OR odds ratio; CI confidence interval; CD Crohn's disease; *n* = 125

study, smoking was the only independent risk factor for proctectomy. We could not analyse the influence of smoking in our study, since smoking data at the time of proctectomy was not available.

The risk of perianal disease development in CD patients has been estimated to be as high as 42.7% 20 years after diagnosis [20]. According to that population-based study, perianal disease not only can manifest many years before CD is diagnosed, but can also occur three decades after CD diagnosis. Furthermore, perianal disease is known to be more common in patients with Crohn's colitis [11, 21, 22].

In our study, female gender was an independent risk factor for proctectomy, a finding consistent with one previous study that concluded that female gender is a risk factor for reoperation following segmental colonic resection for CD [19]. The reason for this remains unclear, but might be due to different attitudes to perianal disease and to permanent stoma between genders.

In addition, the use of thiopurines was an independent protective factor for proctectomy in our study. However, this result should be interpreted with caution since this was a retrospective study. It is possible that patients receiving thiopurines had less aggressive CD and, therefore, did not require proctectomy during follow-up. A meta-analysis of 5 randomized controlled trials showed a 54% improvement of perianal disease in CD patients after thiopurine treatment in contrast to a 21% improvement

in the control group [23]. More recently, one randomized controlled trial showed that thiopurines reduced the need for surgery in perianal disease patients [7].

Biological medications are effective in the treatment of perianal disease [8–10]. Combined anti-tumour necrosis factor- α and thiopurine therapy represents the treatment of choice in refractory perianal disease [24]. These studies detected an improvement in perianal disease, but did not specifically evaluate the effect of biological medications in preventing proctectomy.

Coscia et al. [15] compared the risk for permanent stoma surgery before and after the biological medication era. They concluded that the risk for permanent stoma surgery was significantly reduced after the introduction of biological medications. By contrast, a meta-analysis of 556 patients on the requirement for stoma surgery in CD patients concluded that biological medications did not decrease proctectomy rates and only the absence of rectal involvement was significant in the maintenance of bowel continuity [4].

Previous studies have detected a high recurrence rate in Crohn's colitis in patients with a history of concomitant terminal ileal disease [13, 14]. In our study, these patients also had more reoperations. However, the difference was not significant perhaps due to the small number of patients in the subgroups. Previous studies have also described an increased recurrence rate after end colostomy compared with end ileostomy in Crohn's colitis patients [11, 12]. The same tendency was observed in our study, although our subgroup analysis did not achieve statistical significance. From a clinical point of view, we would expect disease recurrence in the remaining colon after colostomy. However, it is usually beneficial for the patient to retain some colon as long as possible, even if further operations are needed.

Perineal wound healing problems after proctectomy in CD have been previously described [25, 26]. Yamamoto et al. [25] detected persistent perineal sinuses in 23% of

Table 4 Indications for proctectomy

	Total (<i>n</i> = 36)
Severe perianal disease	17 (47.2%)
Intensive proctitis	10 (27.7%)
Incontinence	5 (13.9%)
Rectal cancer	2 (5.6%)
Rectal dysplasia	2 (5.6%)

patients who had proctocolectomy. In our study, 38.9% of the patients who underwent proctectomy experienced delayed perineal wound healing. Furthermore, previous perianal CD has been described as a risk factor for perineal wound healing difficulties after proctectomy [26].

Our study has some limitations due to its retrospective design, possibly causing selection bias. We emphasize that our results may not reflect Crohn's colitis population as a whole, since we only included patients undergoing bowel resection in this study. Patients who did not have proctectomy had a shorter follow-up time from diagnosis than patients with proctectomy. As previously mentioned, patients treated with thiopurines may have had less aggressive CD than those treated with biological medications.

In conclusion, CD duration, female gender and the presence of perianal CD are significant independent risk factors for proctectomy in Crohn's colitis patients undergoing bowel resection. Further research is necessary to determine if immunosuppressive and biological medications can reduce proctectomy rates in CD patients.

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Compliance with ethical standards

All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and comparable ethical standards. For this type of study, formal consent was not required.

Conflict of interest The authors declare that they have no conflicts of interest.

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