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Leading Off

The Severity of Rectal Inflammation and Pouch Surgery Outcome in Patients with Ulcerative Colitis: A Retrospective Cohort Study

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Abstract

Background: Pouch failure after ulcerative colitis (UC) necessitates either pouch excision or establishment of a permanent diverting stoma. The aim of this study was to explore if rectal inflammation prior to pouch creation affected the risk of developing pouch failure.

Methods: Patients 18 years and older with ulcerative colitis undergoing J-pouch surgery at Odense University Hospital between 1983 and 2020 were included. Pouch failure was defined as either the presence of ileostomy more than 1 year after ileo pouch-anal anastomosis (IPAA) or pouch removal. Rectal inflammation was defined by 3 measures: using the Nancy index on pathology examination of the resected rectum, endoscopically using latest Mayo score from the year preceding the IPAA, and as active anti-inflammatory treatment four weeks prior to IPAA.

Results: A total of 434 patients met the inclusion criteria, with 66 patients (15%) experiencing pouch failure with mean time of 5.63 years. Acute inflammation (Nancy grade 2-4) was observed in 70% of the patients. Active anti-inflammatory treatment was observed in 37% of patients, and 67% had undergone endoscopy within 1 year prior to IPAA. No significant association was found between the Nancy Index Grade and pouch failure, time to pouch failure, postoperative complications, or long-term pouch complications. Furthermore, neither the Mayo score grade nor active medical UC therapy predicted the risk of pouch failure.

Conclusion: Rectal inflammation prior to IPAA does not increase risk of pouch failure, postoperative complications, or long term pouch dysfunction.

Lay Summary

Rectal inflammation at time of ileo pouch-anal anastomosis does not impact postoperative complications or long term pouch function among adult ulcerative colitis patients.

Key Messages

What is already known?

Several risk factors for pouch failure are known such as anastomotic leakage, underlying Crohn's disease, fistulation, and low hospital expertise.

What is new here?

Presence of rectal inflammation at time of pouch surgery does not impact risk of complications or long-term dysfunction.

How can this study help patient care?

These results can assist clinicians in making informed decisions when planning pouch surgery.

Introduction

Ulcerative colitis (UC) refractory to medical treatment often results in surgery. Proctocolectomy and reconstruction with an ileo-pouch anal anastomosis (IPAA) eliminates the disease and preserves defecation continuity. Complications to pouch surgery may result in pouch failure, resulting in pouch removal and/or permanent stoma. Identification of risk factors for pouch failure is important in improving pouch function and reducing risk of pouch failure.[1–5]

Anastomotic leakage, abscess, stenosis, chronic pouchitis, fistulation, underlying diagnosis as Crohn's disease, and low hospital expertise are among the most acknowledged associations to pouch failure.[1,3,6–9] The risk of leakage and pelvic sepsis is approximately10% in highly specialized centers.[6] Choice of

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open vs laparoscopic surgery, handsewn vs stapled anastomosis, 2 vs 3-staged IPAA, and formation of a diverting ileostomy do not seem to impact long-term complications, such as pouch failure.[6,10,11] After introduction of IPAA in 1978, studies have shown increasing cumulative risk of pouch failure over time,[7,9,12] with one study finding a 20-year risk of 18.2%.[9]

Only a few studies have investigated the influence of rectal inflammation on postoperative complications after establishing IPAA.[4,13–17] One study found that significant mucosal edema and inflammation in muscularis propria was associated with pouch-related complications.[4] Other studies found the degree of inflammation to be a predictor of pouchitis and earlier pouch failure,[13,14] whereas others found no association with pouchitis or postoperative anastomotic leakage.[15,16]

The primary aim of this study was to examine the impact of preoperative rectal inflammation on pouch failure rate in adult patients with ulcerative colitis. We studied whether the degree of preoperative rectal inflammation on pathology examination influenced (1) the incidence of pouch failure; (2) the time to pouch failure after pouch surgery, and (3) the impact on short- and long-term complications.

Secondly, we wanted to study whether preoperative use of UC targeted medicine and endoscopic findings pre-IPAA increased the risk of pouch failure.

Methods

Study design

Data for this retrospective study covered a tertiary university hospital between1983 and 2020 and were retrieved from patients' medical files. The study was reported using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for retrospective cohort studies.[18]

Patients and data collection

We included adult patients (≥18 years) with a preoperative diagnosis of ulcerative colitis, who underwent J-pouch surgery at Odense University Hospital (OUH). Patients with a diagnosis of Crohn's disease, familial adenomatous polyposis, other non-UC diagnosis, or rectal dysplasia were excluded. Data were collected from the patients' electronic medical records using pouch surgery procedure codes (supplementary data). An existing database at the Department of Surgery, OUH[19] was the base model and was then expanded to fit our study.

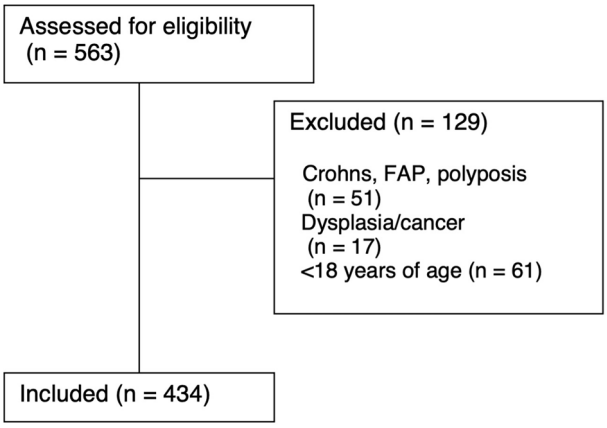

Figure 1. Inclusion flowchart.

Baseline was the time of IPAA. Follow-up continued until the last contact with a surgeon or gastroenterologist, time of death, or the end of data collection on August 31, 2020, whichever came first.

Study data were collected and managed using REDCap electronic data capture tools,[20,21] hosted at OPEN (see Acknowledgements).

End points

The primary end point was pouch failure, defined as the presence of a permanent stoma more than 1 year after IPAA with or without pouch removal. Secondary end points included time from IPAA to pouch failure, re-admission(s), postoperative complications within 90 days of IPAA according to the Clavien Dindo classification (CDC), especially anastomotic leakage and intraabdominal abscess, antibiotic treatment after surgery, and long-term complications, such as pouchitis, fistula, and pouch stenosis. Pouchitis was defined as the medical treatment of pouchitis due to clinical findings with or without endoscopy or pathology confirmation.

Inflammation and endoscopy

Rectal inflammation was defined as the following 3 variables since they are all part of clinical evaluation, with the main focus on histopathologic inflammation in our analyses: the histopathologic examination of the resected rectal specimen, macroscopic findings at endoscopy within 1 year prior to pouch surgery, or the use of anti-inflammatory medical treatment up to 4 weeks prior to pouch surgery. The histopathologic inflammation was graded using the Nancy Index.[22] Information on rectal inflammation was collected from the Danish National Pathology Registry. Pathology descriptions not including a Nancy grading were scored by a reviewer, based on the pathology report using the guide by Marchal-Bressenot et al.[23]

Anti-inflammatory treatment 4 weeks prior to IPAA included the use of local suppositories, systemic steroids, immunologic modulators, and biologic agents and was analyzed as a dichotomous variable for each type of medication (yes/no). Data on anti-inflammatory treatment were found in preoperative admission reports of patients.

Macroscopic inflammation in the rectum and colon was reported using the Mayo Score within 12 months leading up to the IPAA.[24] Missing reporting of the Mayo score on endoscopy was scored by interpretation of the findings by the reviewer.

Surgery and complications

Stages of pouch surgery were defined as either: stage 1 (proctocolectomy and IPAA in the same procedure without ileostomy), modified stage 2 (colectomy with ileostomy, completion proctectomy and IPAA without diverting ileostomy), stage 2 (proctocolectomy and IPAA with diverting ileostomy, ileostomy closure), or stage 3 (colectomy with ileostomy, completion proctectomy and IPAA with diverting ileostomy, ileostomy closure). Other variables included demography, comorbidities, open vs laparoscopic surgery, CDC[25] of postoperative complications, and use of antibiotics related to postoperative complications. Postoperative use of intravenous fluids and total parenteral nutrition (TPN) was not reported as complications on the CDC. Only anastomotic leakage and intra-abdominal abscess requiring surgery or radiologic intervention were included in the analyses (CDC >2). The Comprehensive

Complication Index (CCI) was used in the analysis to assess the weighted severity of complications reported in the CDC, ranging from 0 (no complication) to 100 (death).[26]

Statistics

Wilcoxon rank sum test or *t* test was used for continuous variables dependent on normality of data as evaluated by quantile-quantile plots.

As this is a retrospective study based on existing registry data, no prior power calculation was performed. The sample size was determined by the available data within the specified inclusion criteria. A post hoc power calculation was performed: Based on the observed prevalences of inflammation and pouch failures, we would have 80% power to detect a relative risk of at least 1.9 between these 2 factors.

Association between the grade of inflammation, medication status, endoscopic findings, and pouch failure was explored using the Fisher exact test or Pearson χ^2 test. A Nancy Index grade of 0 was used as reference point when testing for association of higher Nancy Index grades (1-4). Odds ratios (ORs) were estimated using logistic regression, adjusting for age, sex, body mass index (BMI), operative staging, operation type, and comorbidities. In adjusted analyses, BMI was categorized as underweight <19, normal weight 19-25, overweight 25-30 and obese >30, while age was categorized as young adults 18-30 years, adults 31-45 years, middle age adults 46-60 years, and elderly as over 60 years old. Association between rectal inflammation and secondary end points were also tested. Impact of rectal inflammation on CCI was tested using linear regression. Association between rectal inflammation and time of pouch failure, and time to first pouch complication were tested using Cox regression. A *P* value <.05 was considered statistically significant.

Stata software 14.1 (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, Texas) was used for statistical analyses.

Results

Patient characteristics

Between 1983 and 2020, 563 patients underwent pouch surgery at OUH, with 61 patients being younger than 18 years old. Other diagnoses than UC (Crohn's disease, familial adenomatous polyposis, or other) and dysplasia/cancer in the rectal specimen were found in 51 and 17 patients, respectively. Ultimately, 434 patients were included in the analysis (Figure 1), with a median follow-up time of 3133 days (IQR, 560-5052). The cohort patients were 49.8% female, and 80% were between 18 and 45 years old, with 3.3% being older than 60 years at time of IPAA. Nancy index grading could not be given to 6 patients due to insufficient pathologic description, and 3 pathologic examinations were missing. Data of possible pouch failure were missing in 7 patients. Pre-IPAA BMI was not registered in 55 patients, history of active UC therapy was not reported in 5 patients, pre-IPAA endoscopy status was unknown in 47 patients, and Mayo Score could not be evaluated in 155 patients.

Acute inflammation on pathology examination (Nancy grade 2-4) was documented in 69.8% of patients. Anti-inflammatory medication administered preoperatively was reported in 37% of patients. Almost two-thirds of the patients (62.67%) had open pouch surgery, either primarily or converted. A shift towards laparoscopic IPAA was seen around the turn of the millennium, however, as this became the preferred surgical technique. Furthermore, a shift towards modified 2-stage operation, and thereby omitting ileostomy, was seen after 2018. In total, 74.2% of patients had a diverting ileostomy. Patient demographics are displayed in Table 1.

Pouch failure

Pouch failure was documented in 15.2% ($n=66$) of patients. Mean time to pouch failure was 5.63 years (SD 7.07 years), with 12 pouch failures missing date of failure. Histopathologic inflammation in the rectal specimen showed no association with pouch failure, regardless of Nancy Index score, neither on univariate nor on multivariate analysis, when adjusting for age group, sex, BMI, comorbidities, operation type, or operation stages. Anti-inflammatory therapy pre-IPAA was not associated with pouch failure regardless of medication type. Edema on endoscopy was associated with pouch failure in univariate analysis (OR, 2.01; 95% CI, 1.21-3.49; $P=.008$) but not in multivariate analysis ($P=.059$). No other endoscopic finding was associated with pouch failure, and neither was the number of endoscopies. There were too few observations of Mayo score 0 to make a qualified analysis. These results are shown in Table 2.

Postoperative complications and long-term complications

Readmissions occurred for 42.63% ($n=185$) of patients within 90 days of IPAA and were not associated with rectal inflammation degree on the Nancy Index. Nancy Index grades 1 and 2 were not associated with postoperative complications measured by CCI on univariate analysis but were significantly associated in multivariate analysis with respective observed coefficients of 10.76 (3.11-18.32, $P=.006$) and 8.30 (1.63-14.97, $P=.015$). Anastomotic leakage and intra-abdominal abscess requiring surgery (CDC ≥3) occurred in 4.2% ($n=18$) of patients and 6.5% ($n=28$) of patients, respectively. Neither of these was associated with a Nancy Index grade. Need for nonprophylaxic antibiotic treatment was seen in 20.28% ($n=88$) of patients after IPAA. Use of postoperative antibiotics was significantly higher among patients with Nancy Index grade 1 (moderate to severe chronic inflammation) on both univariate analysis, with an OR of 2.94 (1.10-7.86, $P=.031$), and multivariate analysis, with an OR of 4.63 (1.33-16.04, $P=.016$).

Pouch complications occurred among 47.5% ($n=206$) of patients experiencing at least 1 pouch complication, and the mean time to any pouch complication was 3.1 years (1115 days, 14-9307). Pouchitis was the most frequent complication experienced by 41.5% ($n=180$) of patients. Development of pouch-related fistula was seen in 8.76% ($n=38$) of patients, and 14.98% ($n=65$) developed anal stenosis at any point postoperatively. Data regarding treatment of fistulas and stenosis was not collected. No association was found between Nancy grade and any type of complication. These results are displayed in Table 3.

Table 1. Patient characteristics at baseline (time of IPAA).

Baseline	n (%) N=434
Sex	
– female	49.8% (216)
– male	50.2% (218)
Age groups	
– 18-30	38.7% (168)
– 31-45	41.2% (179)
– 46-60	16.8% (73)
– >60	3.2% (14)
BMI	
– <18,5	4.6% (20)
– 18,5-25	42.6% (185)
– 25-30	30.9% (134)
– >30	9.2% (40)
Surgery	
– Open	62.7% (272)
– Laparascopic	34.8% (151)
– Converted	2.5% (11)
Stages of surgery	
– 3 stage	47.2% (205)
– 2 stage	27.0% (117)
– Modified 2 stage	19.1% (83)
– 1 stage	6.7% (29)
Diverting stoma	74.2% (322)
UC medication at baseline medicine	
– None	62.9% (273)
– Suppositories*	7.4% (32)
– Systemic steroids	19.1% (83)
– Immunomodulatory agents**	25.4% (110)
– Biologic treatment	2.1% (9)
Coloscopy/sigmoidoscopy/rectoscopy 1 year prior to IPAA	
– Yes	67.4% (291)
– No	22.2% (96)
Nancy index grading	
– Grade 0	12.0% (52)
– Grade 1	18.2% (79)
– Grade 2	20.7% (90)
– Grade 3	16.1 (70)
– Grade 4	30.9% (134)
Comorbidity* **	20.1% (87)
Mayo Score	
– Grade 0	1.4% (6)
– Grade 1	8.5% (37)
– Grade 2	20.3% (88)
– Grade 3	34.1% (148)
– Missing	35.7% (155)
Pouch failures	15.2% (66)
Mean follow-up	3133 days (SD 3039)

*5-ASA suppositories and budesonid.
**5-ASA 83.0%, 5-ASA derivates 6.7%, ciclosporin 1.2% and azathioprine 1.2%.
***Comorbidities: cardiac, pulmonary, liver, kidney, diabetes or other.

Discussion

Among ulcerative colitis patients 15–25% will require surgical treatment,[11] and 1.2% of UC patients have a pouch created each year.[27] Good pouch function is essential, as dysfunction is associated with lower quality of life.[28] The etiologies of pouch failure and pouchitis are multifaceted and complex; continuous exploration of risk factors is required in order to provide the best counselling and treatment.

This study found no association between rectal inflammation, prior to and at time of IPAA, and short-term and long-term complications or pouch dysfunction. In contrast, Frese et al[13] demonstrated lower pouch survival if any grade of proctitis was present compared to no proctitis. Furthermore, they found severe proctitis to have increased risk of pouch failure and pouchitis compared to no or mild-medium proctitis. Explanations for our different results may be that we lacked pathologist revision, and they did not use a validated histopathologic

Table 2. Nancy grade of rectal inflammation, UC medication, endoscopic findings, and the risk of pouch failure.

Pouch failure	Univariate analysis		Multivariate analysis*	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Nancy grade 0	1 (Reference)		1 (Reference)	
Nancy grade 1	2.24 (0.76-6.59)	0.144	3.24 (0.92-11.35)	0.067
Nancy grade 2	1.75 (0.59-5.19)	0.309	1.61 (0.46-5.64)	0.456
Nancy grade 3	1.46 (0.46-4.65)	0.523	1.35 (0.34-5.34)	0.665
Nancy grade 4	1.88 (0.18-19.45)	0.229	1.69 (0.50-5.77)	0.400
No pre-OP medicine	0.76 (0.45-1.30)	0.322	0.47 (0.21-1.05)	0.065
Steroids	1.29 (0.68-2.43)	0.430	2.24 (0.96-5.24)	0.062
Immunologic modulators	1.24 (0.69-2.22)	0.478	2.21 (0.87-5.58)	0.094
Biologic agents	0.78 (0.09-6.43)	0.816	0.74 (0.08-7.03)	0.790
Suppositories	1.94 (0.83-4.52)	0.126	2.15 (0.76-6.09)	0.152
Number of endoscopies	1.00 (0.99-1.00)	0.603	1.00 (0.99-1.00)	0.532
Normal endoscopy	1 (Reference)		1 (Reference)	
Edema	2.01 (1.21-3.49)	**0.008**	1.80 (0.98-3.32)	0.059
Granularity	1.31 (0.74-2.33)	0.360	1.40 (0.71-2.77)	0.332
Light friability	0.91 (0.30-2.70)	0.859	1.42 (0.38-5.36)	0.606
Severe friability	0.89 (0.50-1.58)	0.685	0.97 (0.51-1.84)	0.915
Decreased vascular pattern	2.10 (0.54-8.14)	0.282	2.55 (0.60-10.76)	0.204
Loss of vascular pattern	0.76 (0.33-1.75)	0.513	0.76 (0.27-2.12)	0.594
Mild hyperemia	1.47 (0.61-3.52)	0.391	1.16 (0.40-3.36)	0.786
Severe hyperemia	1.23 (0.69-2.20)	0.472	1.27 (0.64-2.51)	0.489
Mucous exudates	1.41 (0.73-2.70)	0.306	0.89 (0.39-2.05)	0.785
Erosions	1.58 (0.69-3.62)	0.281	2.30 (0.93-5.69)	0.072
Ulcerations	1.29 (0.74-2.24)	0.373	0.94 (0.48-1.85)	0.866
Spontaneous bleeding	1.10 (0.58-2.10)	0.773	1.26 (0.60-2.68)	0.539
Other	0.69 (0.23-2.01)	0.494	0.54 (0.15-1.97)	0.353
Mayo Score 0	Too few observations			
Mayo Score 1	0.78 (0.75-8.15)	0.837	1.60 (0.13-19.77)	0.712
Mayo Score 2	1.23 (0.13-11.25)	0.853	2.10 (0.20-21.53)	0.533
Mayo Score 3	0.98 (0.11-8.73)	0.982	1.14 (0.11-11.55)	0.911

*Adjusted for age group, sex, BMI, comorbidities, operation type and operations stages. Abbreviations: OP, operative; OR, odds ratio.
P<0.05 was significant.

scoring system, were more selective in patient inclusion, and excluded procedures omitting stomas.

Likewise, Wassmann et al[14] observed active inflammation in the resected rectal margin to be associated with pouchitis. The rectal margin was revised by a pathologist and given a validated Geboes score. Overall, postoperative complications were not associated with inflammation. However, active inflammation incidence was 81.9%, resulting in a small control group of only 37 patients. In addition, patients with stage 1 or stage 2 IPAA were excluded, which limits their results to modified stage 2 and stage 3 IPAA.

Tan et al found an association between rectal inflammation and pouch complications as well in patients with either UC (93%) or indeterminate colitis. No standardized histopathologic scoring system was used, but inflammation in the muscularis propria and subucosal odema was associated with pouch failure and pouchitis. However, pouch failure rate was low (2.81%), and not all patients had a pathology report.[4]

Similar to Wasmann et al but contrary to Tan et al, we found no association between rectal inflammation and anastomic leakage, re-admissions, or abscesses. Nor did a matched case-control study find association with anastomotic leakage, although the study period was limited to 30 days.[16] We only included complications with a CDC score of ≥3 in our analyses to distinguish severe from minor clinical complications. Despite this cutoff, our rate of anastomotic leakage and pelvic abscesses was similar to other studies.[3,11,16,29]

Comparing the results in these studies is complicated due to heterogeneous study groups, different end points and different histopatholigic registration and coring systems available in different time periods.[30]

In a review, Schieffer et al[31] concluded that roughly 50% of patients will suffer from pouchitis, which is similar to the 41.5% documented in our study. Anatomical extension and disease severity on colonic specimens were found to be risk factors, while anal transition zone inflammation was not, despite the risk factors varying between studies.[15,17,31] Our results oppose this notion.

During the study period, we performed an average of 15 IPAAs per year, meeting European Crohn's and Colitis Organisation (ECCO) guidelines.[6] The pouch failure rate of 15.21% was similar to some and higher than other purely ulcerative colitis studies.[3,9,13] A possible explanation is the long follow-up period as risk cumulates over time, with the highest incidence the first year after pouch creation according to previous studies.[9,12] Data on reason for pouch failure were not collected in this study.

We found no association of medical treatment for UC preoperatively and subsequent pouch failure. Studies of this association are sparse: Karjalainen et al found low dose steroids (<20 mg/day) to increase the risk of pouch failure, while high

Table 3. The impact of rectal inflammation on postoperative and long-term complications.

	Univariate analysis		Multivariate analysis*	
CCI	**Coef (95% CI)**	***P* value**	**Coef (95% CI)**	***P* value**
Nancy grade 0	0 (Reference)		0 (Reference)	
Nancy grade 1	5.77 (-0.47-12.00)	0.070	10.76 (3.11-18.42)	**0.006**
Nancy grade 2	5.55 (-0.20-11.30)	0.059	8.30 (1.63-14.97)	**0.015**
Nancy grade 3	0.99 (-5.14-7.14)	0.750	2.50 (–4.76 to 9.77)	0.499
Nancy grade 4	–1.18 (-6.40-4.04)	0.341	1.68 (–4.63 to 8.00)	0.601
Readmissions ≤90 days	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Nancy grade 0	1 (Reference)		1 (Reference)	
Nancy grade 1	1.23 (0.56-2.72)	0.606	1.68 (0.65-4.32)	0.285
Nancy grade 2	1.22 (0.56-2.65)	0.617	1.20 (0.48-2.96)	0.699
Nancy grade 3	0.96 (0.42-2.21)	0.928	1.08 (0.40-2.95)	0.879
Nancy grade 4	1.32 (0.64-2.74)	0.451	1.87 (0.80-4.46)	0.161
Post-IPAA antibiotics	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Nancy grade 0	1 (Reference)		1 (Reference)	
Nancy grade 1	2.94 (1.10-7.86)	**0.031**	4.63 (1.33-16.04)	**0.016**
Nancy grade 2	2.14 (0.80-5.75)	0.132	3.24 (0.94-11.17)	0.063
Nancy grade 3	1.51 (0.52-4.34)	0.446	2.13 (0.58-7.80)	0.255
Nancy grade 4	1.88 (0.72-4.87)	0.195	3.07 (0.91-10.37)	0.071
Anastomotic leakage	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Nancy grade 0	1 (Reference)		1 (Reference)	
Nancy grade 1	4.19 (0.49-35.88)	0.191	3.45 (0.34-35.47)	0.298
Nancy grade 2	3.00 (0.34-26.40)	0.322	3.06 (0.32-29.72)	0.334
Nancy grade 3	1.50 (0.13-17.00)	0.743	1.35 (0.11-16.67)	0.815
Nancy grade 4	1.57 (0.17-14.38)	0.690	1.32 (0.12-14.01)	0.818
Abscess	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Nancy grade 0	1 (Reference)		1 (Reference)	
Nancy grade 1	1.59 (0.39-6.44)	0.517	5.12 (0.57-45.66)	0.144
Nancy grade 2	1.38 (0.34-5.57)	0.653	4.50 (0.51-29.65)	0.175
Nancy grade 3	0.73 (0.14-3.78)	0.709	2.35 (0.22-24.70)	0.476
Nancy grade 4	1.04 (0.26-4.07)	0.958	2.87 (0.32-25.44)	0.343
Time to first pouch complication	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Nancy grade 0	1 (Reference)		1 (Reference)	
Nancy grade 1	1.50 (0.89-2.55)	0.129	1.32 (0.72-2.43)	0.364
Nancy grade 2	1.26 (0.76-2.06)	0.368	1.26 (0.72-2.21)	0.417
Nancy grade 3	1.18 (0.70-2.01)	0.530	1.28 (0.69-2.37)	0.430
Nancy grade 4	1.09 (0.67-1.76)	0.726	1.23 (0.70-2.16)	0.480
Pouchitis	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Nancy grade 0	1 (Reference)		1 (Reference)	
Nancy grade 1	0.83 (0.41-1.70)	0.620	0.75 (0.33-1.71)	0.494
Nancy grade 2	1.19 (0.60-2.38)	0.615	0.89 (0.40-1.94)	0.762
Nancy grade 3	1.22 (0.59-2.51)	0.596	1.13 (0.49-2.59)	0.781
Nancy grade 4	0.81 (0.42-1.56)	0.531	0.80 (0.12-5.89)	0.865
Stenosis	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Nancy grade 0	1 (Reference)		1 (Reference)	
Nancy grade 1	0.77 (0.30-2.02)	0.599	1.56 (0.44-5.50)	0.488
Nancy grade 2	0.88 (0.35-2.20)	0.785	2.06 (0.60-7.01)	0.248
Nancy grade 3	0.89 (0.34-2.34)	0.814	2.23 (0.62-7.98)	0.218
Nancy grade 4	0.84 (0.35-1.98)	0.688	2.34 (0.71-7.68)	0.162
Fistula	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Nancy grade 0	1 (Reference)		1 (Reference)	
Nancy grade 1	1.10 (0.25-4.83)	0.896	1.59 (0.32-7.92)	0.570
Nancy grade 2	2.04 (0.54-7.78)	0.296	2.11 (0.50-8.93)	0.309
Nancy grade 3	0.73 (0.14-3.78)	0.709	0.95 (0.17-5.40)	0.952
Nancy grade 4	2.37 (0.67-8.47)	0.183	1.85 (0.44-7.74)	0.401

*Adjusted for age-group, sex, BMI, comorbidities, operation type and operations stages. Abbreviations: HR, hazard ratio; OR, odds ratio.
P<0.05 was significant.

doses and anti-TNF-α did not.[32] Similarly, Gainsbury et al found no association with short-term complications in patients treated with infliximab 12 weeks prior to IPAA.[2] Steroid doses of ≥20mg 6 weeks before surgery is assumed to increase postoperative morbidity;[6,33] however, we did not find preoperative systemic steroid treatment to be associated with pouch failure. Additionally, the ECCO recommendations state that thiopurines and cyclosporin do not increase risk of surgical complications, while results on anti-TNF-α are conflicting.[6]

Endoscopy frequency and latest Mayo score were not associated with pouch failure, although our definition did not differentiate between precolectomy and pre-IPAA endoscopies within 1 year prior to IPAA. This could impact the results for stage 3 and modified stage 2 patients in particular, as the latest Mayo score may reflect medically refractory UC treated with colectomy and possibly not inflammation leading up to IPAA. While severe disease activity and anatomical extension of UC has been found to increase risk of colectomy,[6,34] to our knowledge, the impact of macroscopic inflammation prior to IPAA on pouch complications has not been investigated elsewhere. Additionally, we only found endoscopic examination data in 67% of our patients, implying a gap of missing data.

The strengths in this study are the population size, the long follow-up, and the use of a continuous database including multiple decades. We used the validated and standardized Nancy Index for assessing disease activity, including rectal inflammation with good interobserver and intra-observer reliability.[22] This makes our results more transparent and comparable to other studies.

The primary limitation was the lack of a secondary pathology review, as data relied on the original examination. This entails possible observer bias and reduces the ability to independently verify histologic grading. A succinct pathology report may thus have led to less accurate Nancy grades. The same principal applies for data collected from patient records. Another limitation was the use of different electronic journal systems in the regions of Denmark, resulting in a cessation of data collection after termination or discharge from our department. Lastly, we did not collect patient-reported outcome data on pouch dysfunction through quality of life questionnaires, as pouch dysfunction may also have been the reason for pouch failure in some cases.

In conclusion, rectal inflammation did not impact pouch failure, time to pouch failure, postoperative complications or long-term pouch complications. Nor was any type of anti-inflammatory UC medicine, number of endoscopies, or latest Mayo Score prior to IPAA associated with pouch failure. Other recent studies found an association between histopathologic inflammation and pouch outcome. Collaborations between tertiary centers both nationally and internationally would be beneficial to increase population size and result power. Thus, the best time of pouch surgery is still based on clinical assessment, experience, and patient preference.

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REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies, providing: (1) an intuitive interface for validated data capture; (2) audit trails for tracking data manipulation and export procedures; (3) automated export procedures for seamless data downloads to common statistical packages; and (4) procedures for data integration and interoperability with external sources.

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Conflict of Interest

The authors declare no conflicts of interest.

Ethical Considerations

The Danish Patient Safety Authority (file no. 31-1521-57 and 20/37035) and the Danish Data Protection Agency (journal no. 20/3762) approved the study before initiation.

Data Availability

Data are available on request.

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Inflammatory Bowel Diseases 2026 32(1) 1–8
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