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Leading Off

Total Proctocolectomy vs Subtotal/total Colectomy for Neoplasia in Patients With Inflammatory Bowel Disease and Primary Sclerosing Cholangitis

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Background: Patients with inflammatory bowel disease (IBD) and primary sclerosing cholangitis (PSC) frequently undergo restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) for medically refractory disease or colonic dysplasia/neoplasia. Subtotal colectomy with ileosigmoid or ileorectal anastomosis may have improved outcomes but is not well studied. Due to increased risk for colorectal cancer in PSC-IBD, there is hesitancy to perform subtotal colectomy. We aim to describe the frequency of colorectal dysplasia/neoplasia following IPAA vs subtotal colectomy in PSC-IBD patients.

Methods: We completed a retrospective study from 1972 to 2022 of patients with PSC-IBD who had undergone total proctocolectomy with IPAA or subtotal colectomy. We abstracted demographics, disease characteristics, and endoscopic surveillance data from the EMR.

Results: Of 125 patients (99 IPAA; 26 subtotal), the indication for surgery was rectal sparing medically refractory disease (51% vs 42%), dysplasia (37% vs 30%) and neoplasia (11% vs 26%) in IPAA vs subtotal colectomy patients, respectively. On endoscopic surveillance of IPAA patients, 2 (2%) had low-grade dysplasia (LGD) in the ileal pouch and 2 (2%) had LGD in the rectal cuff after an average of 8.4 years and 12.3 years of follow-up, respectively. One (1%) IPAA patient developed neoplasia of the rectal cuff after 17.8 years of surgical continuity. No subtotal colectomy patients had dysplasia/neoplasia in the residual colon or rectum.

Conclusions: In patients with PSC-IBD, there was no dysplasia or neoplasia in those who underwent subtotal colectomy as opposed to the IPAA group. Subtotal colectomy may be considered a viable surgical option in patients with rectal sparing PSC-IBD if adequate endoscopic surveillance is implemented.

Lay Summary

We sought to evaluate the risk of developing dysplasia in patients with both inflammatory bowel disease and primary sclerosing cholangitis, following surgery with either total proctocolectomy with ileal pouch-anal anastomosis or subtotal/total colectomy with ileosigmoid or ileorectal anastomosis.

Key Words: inflammatory bowel disease, primary sclerosing cholangitis, dysplasia, colectomy

Introduction

Patients with primary sclerosing cholangitis (PSC) and inflammatory bowel disease (IBD), commonly termed PSC-IBD, often have a disease phenotype characterized by rectal sparing and backwash ileitis.[1] An estimated 70% of patients with PSC will develop IBD, and this cohort has an increased risk of colorectal dysplasia and neoplasia with worse overall survival.[1–6] Despite an expanding armamentarium of medical therapies, PSC-IBD patients frequently undergo surgery for medically refractory disease or to treat colonic dysplasia or neoplasia.

Since the 1990s, the surgery of choice in patients with PSC-IBD has been restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) to remove the inflamed organ and mitigate the risk of neoplasia.[7,8] Prior studies have demonstrated increased complications in patients with PSC-IBD who undergo IPAA with high rates of pouchitis, worse quality of life, and poor pouch function.[9–11] Subtotal colectomy with ileosigmoid (IS) or ileorectal (IR) anastomosis has been performed in patients with rectal sparing PSC-IBD, though it is unclear if it is a safe alternative with comparable outcomes.[12] In Scandinavia, the use of subtotal colectomy with ileorectal anastomosis has increased in recent years due to concern for reduced fertility following IPAA.[12,13] However, despite availability of high definition surveillance options, there is hesitancy to perform subtotal colectomy compared with IPAA due to perceived increased risk for colorectal cancer.[14]

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Key Messages

- **What is already known?** Patients with PSC-IBD have higher risk of colorectal cancer. Patients require surgery for medically refractory disease, dysplasia, or neoplasia. The preferred surgery is total proctocolectomy with IPAA, though patients have higher complications and worse quality of life. Subtotal colectomy with ileosigmoid or ileorectal anastomosis may be a better surgical option, but little is known about the risk of dysplasia/neoplasia.
- **What is new here?** In retrospective review of 125 patients, we found no evidence of dysplasia/neoplasia in those who underwent subtotal colectomy.
- **How can this study help patient care?** It is time for gastroenterologists, colorectal surgeons, and patients to begin a discussion about the best surgery for PSC-IBD patients.

Notably, clinical practice for endoscopic surveillance differs widely among gastroenterologists.[15,16] The 2021 International Ileal Pouch Consortium recommends diagnostic and surveillance pouchoscopy every 1 to 3 years for patients with PSC-IBD who have undergone IPAA, though there are inconsistent guidelines across various societies.[17] Currently, there are no surveillance guidelines for PSC-IBD patients who have undergone subtotal colectomy with IS/IR anastomosis.[17]

We aim to describe frequency of neoplastic, inflammatory, and surgical outcomes following IPAA vs subtotal colectomy with IS/IR in PSC-IBD patients.

Materials and Methods

Definitions

The diagnosis of IBD including Crohn's disease (CD) and ulcerative colitis (UC) was based on internationally accepted clinical diagnostic criteria, including endoscopic and histologic features. The extent of disease was described according to the Montreal classification.[18] The diagnosis of PSC was based on characteristic abnormal bile duct findings on cholangiography and/or histologic features on liver biopsy.[19,20]

Patient Cohort

We completed a retrospective review from January 1972 to January 2022 of adult patients 18 years of age and older from a large academic institution who were diagnosed with PSC-IBD and had undergone total proctocolectomy with IPAA or subtotal colectomy with IS/IR. Using standardized billing codes, a master system computer at a single academic institution searched for patients with PSC and IBD diagnoses with prior research authorization. Procedure codes for total proctocolectomy with IPAA and subtotal colectomy with IS/IR anastomosis were then utilized to identify PSC-IBD patients who had undergone surgery. This was followed by manual review of individual patient charts to confirm the diagnoses. We abstracted demographics (age, sex, race, smoking status) and disease characteristics from the electronic medical record (EMR).

Endoscopic Surveillance

All patients were required to have at least 1 postoperative flexible sigmoidoscopy or pouchoscopy with biopsies at our academic institution to be included in this study. Due to limitations in standardized endoscopic guidelines over time, we also evaluated number of years of follow-up. Variables included date of first postsurgical endoscopy with presence of pouchitis/colitis/cuffitis, severity of endoscopic inflammation, and medical management of inflammation. When dysplasia or neoplasia was found on postsurgical surveillance endoscopy, the date of the event, location, and histopathology (low-grade dysplasia, high-grade dysplasia, adenocarcinoma) were recorded.

Pouch Complications

Pouch dysfunction was defined as any new symptom (eg, diarrhea, urgency, incomplete evacuation, fever, abdominal pain, or hematochezia) that raised clinical concern leading to further testing or treatment. Complications were collected according to the 2021 International Ileal Pouch Consortium classification, which includes structural complications (pouch leaks, obstruction, other adverse events, pouch failure), inflammatory disorders (pouchitis, cuffitis, Crohn's-like disease of the pouch, diversion pouchitis), functional pouch disorders (irritable pouch syndrome, dyssynergic defecation, pouchalgia fugax, neuropathic pain), and neoplasia of the pouch.[17,21] A limited number of patients were evaluated for pouch dyssynergia using anorectal manometry or MRI defecography.[22]

Severity of pouch and prepouch inflammation was defined as mild, moderate, or severe, as documented in the endoscopic report. Subtypes of pouchitis were classified as acute antibiotic-responsive pouchitis (<4 episodes per year which respond to a 2-4 week course of antibiotics), chronic antibiotic-dependent pouchitis (≥4 episodes per year or persistent symptoms that require long-term continuous antibiotics or probiotics to maintain remission), or chronic antibiotic-refractory pouchitis (failure to respond to a 4-week course of antibiotic therapy, requiring prolonged treatment with oral or topical 5-aminosalicylate, corticosteroid, immunomodulator, or biologic therapy). No patients were on small molecule therapy. Date of first pouchitis episode was based on clinical suspicion or endoscopic finding. The first episode of pouchitis on pouchoscopy was classified using the Pouch Disease Activity Index (PDAI).[23] Data about medical management of pouchitis were classified as antibiotic, probiotic, 5-aminosalicylate, budesonide, corticosteroid, or biologic therapy.

Subtotal/total Colectomy Complications

Patients who underwent subtotal colectomy were noted to have IS or IR anastomosis. Postsurgical complications (abdominal/ventral hernia, adhesions, ileus, intra-abdominal abscess, small bowel obstruction) were reviewed, and details including date of complication, need for subsequent bowel surgery, and indication for subsequent surgery were collected.

Hepatobiliary Complications

Hepatobiliary complications from PSC were collected including date of liver transplant, recurrence of PSC posttransplant, date of retransplant (if applicable), and cholangiocarcinoma.

Statistical Analysis

Patient characteristics and clinical data were presented as mean ± standard deviation (SD), median and interquartile range (IQR), or frequency and percentage. Descriptive statistics were used to report findings from the dysplasia and neoplasia cohort due to low subject numbers. Kaplan-Meier estimates for survival were calculated for first postsurgical complication, first inflammatory complication, pouch excision, dysplasia, neoplasia, and overall survival.

Results

The initial data search identified 157 patients with billing code diagnoses of PSC and IBD who had undergone colectomy, and 125 patients were included in statistical analysis (Figure 1). A total of 32 patients were excluded due to absence of confirmed PSC and IBD diagnoses, inadequate postsurgical follow-up, or lack of bowel continuity surgery.

Demographics

Baseline characteristics including demographic data and disease information are summarized in Table 1. Of the 125 patients who met inclusion criteria, 99 patients had undergone restorative proctocolectomy with IPAA, and 26 patients had undergone subtotal colectomy with IS or IR anastomosis. Most patients were male (54.4%) and white (97.6%). Median age at IBD diagnosis was 22.7 years (IQR, 18.1-33.7) for the IPAA group, and 26.3 years (IQR, 20.4-37.2) for the subtotal colectomy group. Of the 84.8% of patients with UC, 87.7% underwent IPAA, and 12.3% underwent subtotal colectomy. Of the 15.2% of patients with CD, 31.6% underwent IPAA at outside hospitals, and 68.4% underwent subtotal colectomy. In the IPAA group, 15.1% were current/former smokers; and in the subtotal colectomy group, 23.1% were former smokers.

Surgery

The primary indication for surgery was rectal sparing medically refractory disease (51.5% vs 42.3%), dysplasia (37.4% vs 30.8%), and neoplasia (11.1% vs 26.9%) in IPAA vs subtotal colectomy patients, respectively. Median duration of IBD prior to surgery was 10 years, and median duration of PSC prior to surgery was 4 years. Thirty-nine patients were diagnosed with PSC following surgery. The majority of IPAA procedures performed were J pouch (97.0%) configuration. Of the 26 patients who underwent subtotal colectomy, 50% had IS anastomosis and 50% had IR anastomosis. Median GI follow up was 10.1 years. Overall survival was different between the IPAA and subtotal colectomy groups (Figure 2).

Dysplasia and Neoplasia

On endoscopic surveillance of IPAA patients, 2 (2%) developed low-grade dysplasia (LGD) in the ileal pouch, and 2 (2%) developed LGD in the rectal cuff after an average of 8.4 years and 12.3 years of follow-up, respectively (Table 2). The patients with LGD of the ileal pouch or rectal cuff had undergone surgery for rectal sparing medically refractory disease. Both patients who developed LGD of the ileal pouch had severe pouchitis requiring biologic therapy and concomitant *Clostridioides difficile*–related pouchitis. No patients had high-grade dysplasia. To manage the dysplasia, all 4 patients underwent endoscopic resection with continued surveillance. One (1%) IPAA patient who had undergone surgery for medically refractory disease was lost to follow-up and represented with neoplasia of the rectal cuff after 17.8 years of surgical continuity. This patient underwent chemotherapy/radiation followed by pouch excision, then unfortunately died from complications relating to cholangiocarcinoma. No patients who had undergone subtotal colectomy developed dysplasia or neoplasia in the residual colon or rectum. No patients who underwent IPAA or subtotal colectomy with a surgical indication of dysplasia/neoplasia had evidence of dysplasia/neoplasia on endoscopic surveillance.

Inflammatory Complications

Median time to first episode of pouchitis was 10.4 months for the IPAA group. The Kaplan-Meier estimates for survival-free from pouchitis was 25.3% at 5 years, 15.8% at 10 years, and

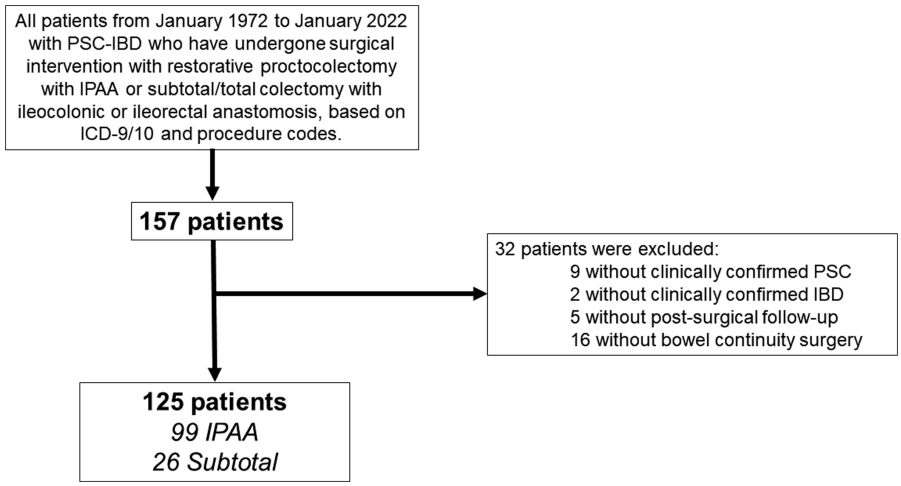

Figure 1. Screening of patients for study inclusion. Schematic outlining how patients were chosen for participation in the present study. Abbreviations: PSC-IBD, primary sclerosing cholangitis and inflammatory bowel disease; ICD, International Classification of Diseases; IPAA, ileal pouch-anal anastomosis.

Table 1. Demographics and baseline characteristics of patients with PSC-IBD and total proctocolectomy with ileal pouch-anal anastomosis (IPAA) vs subtotal colectomy with ileosigmoid or ileorectal anastomosis.

	Total Proctocolectomy With Ileal Pouch-Anal Anastomosis (*n* = 99)	Subtotal Colectomy With Ileosigmoid Or Ileorectal Anastomosis (*n* = 26)	*P*
Sex, Female	37 (37.4%)	11 (42.3%)	0.71 001
Race, White	96 (97.0%)	26 (100%)	0.66 791
Smoking status			
Never	84 (84.8%)	20 (76.9%)	0.48 541
Former	14 (14.1%)	6 (23.1%)	
Current	1 (1.0%)	0 (0%)	
IBD Diagnosis			<0.0001[1]
Ulcerative Colitis	93 (93.9%)	13 (50.0%)	
Crohn's Disease	6 (6.1%)	13 (50.0%)	
Age at IBD Diagnosis, median (range)	22.7 (2.3-56.3)	26.3 (7-53)	0.16 362
Ulcerative colitis			
Location			
- *E1*	0 (0%)	0 (0%)	
- *E2*	9 (9.7%)	7 (53.8%)	
- *E3*	84 (90.3%)	6 (46.2%)	
Crohn's disease			
Location			
- L1	0 (0%)	0 (0%)	
- L2	3 (50.0%)	0 (0%)	
- L3	3 (50.0%)	13 (100%)	
Behavior			
- B1	4 (66.7%)	8 (61.5%)	
- B2	1 (16.7%)	2 (15.4%)	
- B3	1 (16.7%)	1 (7.7%)	
- B2 and B3	0 (0%)	2 (15.4%)	
Perianal disease	2 (33.3%)	5 (38.5%)	
Age at PSC Diagnosis, median (range)	34.7 (13.5-71.3)	47.8 (19.8-69.8)	0.0118[2]
Indication for Colectomy			
Medically Refractory	51 (51.5%)	11 (42.3%)	
Dysplasia	37 (37.4%)	8 (30.8%)	
Neoplasia	11 (11.1%)	7 (26.9%)	
Surgery Type			
IPAA			
J pouch	96 (97.0%)		
Ileorectal		13 (50.0%)	
Ileosigmoid		13 (50.0%)	

[1]χ^2
[2]Wilcoxon rank sum test.
Abbreviations: PSC-IBD, primary sclerosing cholangitis and inflammatory bowel disease; IPAA, ileal pouch-anal anastomosis.

7.5% at 20 years (Figure 3). At first episode of endoscopic pouchitis (median 19.6 months), pouch inflammation was most often mild in severity (37.3%) followed by moderate (33.7%), and severe (21.7%). Prepouch inflammation was most often moderate in severity (45.9%) in comparison with mild (37.8%) or severe (13.5%). The median PDAI score was 7 (0-12 range), with a median subscore for endoscopy of 3 (0-6 range) at first pouchoscopy with evidence of pouchitis. Of the 84 patients (96.6%) that were treated with antibiotics for pouchitis, 12 (14.3%) had acute antibiotic-responsive pouchitis, 15 (17.9%) had chronic antibiotic-dependent pouchitis, and 41 (48.8%) had chronic antibiotic-refractory pouchitis. Antibiotics included ciprofloxacin (95.2%), metronidazole (86.9%), amoxicillin-clavulanic acid (51.2%), rifaximin (45.2%), vancomycin (42.9%), levofloxacin (36.9%), doxycycline (10.7%), tinidazole (5.9%), and

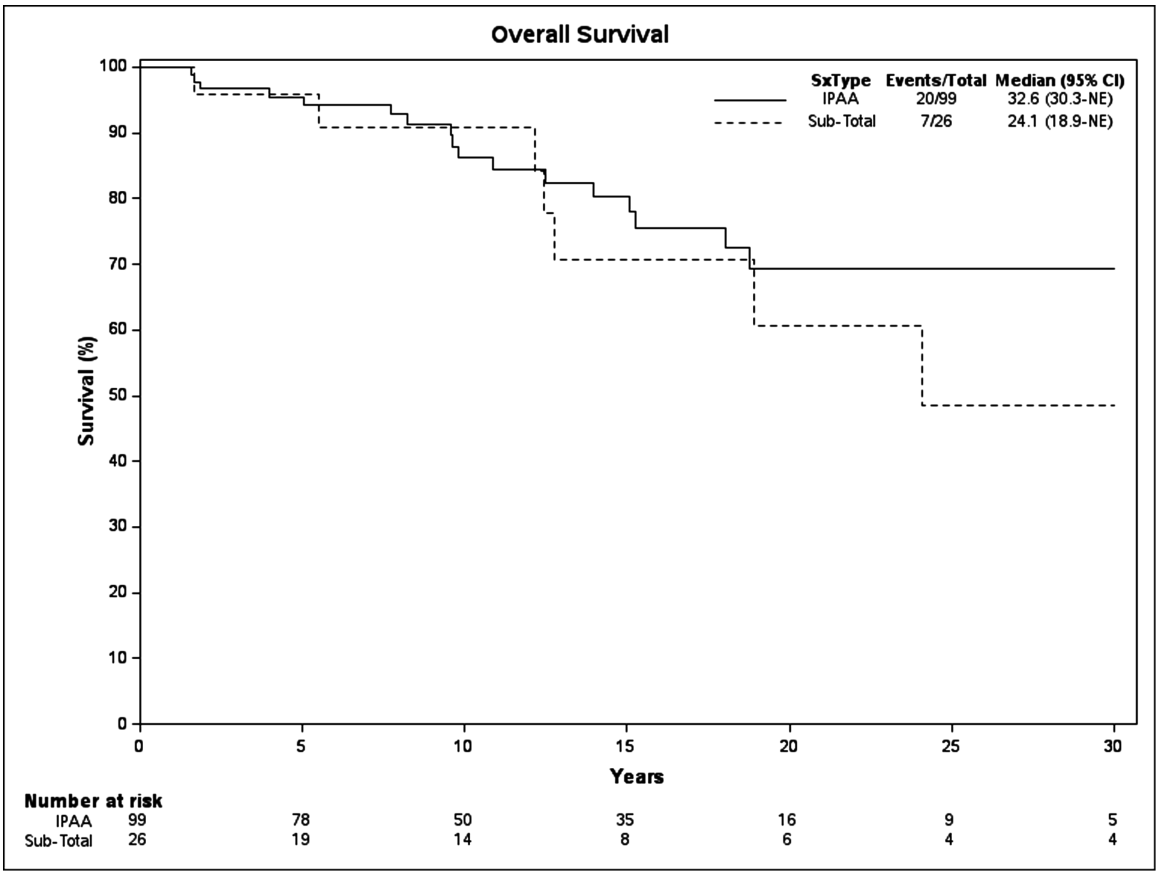

Figure 2. Kaplan-Meier curves for overall survival in PSC-IBD patients who have undergone restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) vs subtotal colectomy with ileosigmoid or ileorectal anastomosis. Abbreviation: PSC-IBD, primary sclerosing cholangitis and inflammatory bowel disease.

amoxicillin (4.8%). Among IPAA patients who developed pouchitis (n = 87), 18.4% (n = 16) required biologic therapy. The most frequently used biologic therapies were vedolizumab (56.3%), adalimumab (56.3%), infliximab (37.5%), and ustekinumab (25.0%). Among patients with pouchitis, 19 (21.8%) developed Crohn's-like disease of the pouch, with 63.1% requiring biologic therapy. Additionally, 23 (23.2%) patients developed *Clostridioides difficile*–related pouchitis.

Median time to first episode of colitis/proctitis was 38.9 months for the subtotal colectomy group. Sixteen subtotal colectomy patients developed colitis and required treatment with biologics (50.0%), immunomodulators (37.5%), prednisone (31.3%), budesonide (25.0%), 5-aminosalycilates (18.8%), and antibiotics (18.8%). The Kaplan-Meier estimates for survival-free from colitis was 61.6% at 5 years, 61.8% at 10 years, and 24.5% at 20 years (Figure 3).

Surgical Complications

Patients with IPAA experienced 7.5 surgical complications per 100 years (11.8 median follow-up years) including small bowel obstruction (n = 19), abscess (n = 14), anastomotic strictures (n = 11), hernia (n = 10), extrapouch fistula (n = 9), pouch-pouch fistula (n = 4), ileus (n = 4), hematoma (n = 4), penetrating Crohn's disease requiring surgery/procedure (n = 3), perianal fistula (n = 2), pouch leak (n = 1), and mucosal bridge (n = 1). Two patients required pouch revision surgery. Seven patients required pouch excision due to recurrent pouchitis (n = 3), prepouch fistula (n = 2), severe cuffitis (n = 1), and neoplasia of the rectal cuff (n = 1). Sixteen (39.0%) patients required additional bowel or pouch surgery. The Kaplan-Meier estimates for survival freedom from first postsurgery complication for the IPAA group was 62.9% at 5 years, 60.0% at 10 years, and 42.1% at 20 years (Figure 4). Subtotal colectomy patients experienced 2.7 surgical complications per 100 years (13.8 median follow-up years) including ileus (n = 2), abscess (n = 2), small bowel obstruction (n = 2), and hernia (n = 1). One subtotal colectomy patient developed perianal fistulizing disease and underwent end ileostomy. The Kaplan-Meier estimates for survival freedom from first postsurgery complication for the subtotal colectomy group was 71.8% at 5 years, 71.8% at 10 years, and 66.3% at 20 years (Figure 4).

Functional Pouch Complications

Fourteen (14.1%) patients were found to have pouch dyssynergia. This was noted in clinical documentation from the treating gastroenterologist, and diagnosis was not standardized; thus 3 patients were diagnosed with clinical findings on history and exam. Further investigation included anorectal manometry (n = 9) and MR defecography (n = 2).

Hepatobiliary Complications

Liver transplant due to PSC or cholangiocarcinoma was performed in 38 patients (30 IPAA, 8 subtotal colectomy). Of the 7 patients who had a liver transplant prior to IPAA,

Table 2. Outcomes in PSC-IBD patients who have undergone total proctocolectomy with ileal pouch-anal anastomosis (IPAA) vs subtotal colectomy with ileosigmoid or ileorectal anastomosis.

	Total Proctocolectomy With Ileal Pouch-Anal Anastomosis (n = 99)	Subtotal Colectomy With Ileosigmoid Or Ileorectal Anastomosis (n = 26)
Primary Outcomes		
Dysplasia		
Location		
Ileal Pouch	2 (2.0%)	
Rectal cuff	2 (2.0%)	
Rectum/Colon		0 (0%)
Neoplasia		
Location		
Ileal Pouch	0 (0%)	
Rectal cuff	1 (1.0%)	
Rectum/Colon		0 (0%)
Secondary Outcomes		
Surgical complications		
Number per 100 years	7.5	2.7
Inflammatory Complications		
Pouchitis or Colitis	87 (87.9%)	16 (61.5%)
Type of Pouchitis		
AARP	12 (14.8%)	
CADP	15 (17.9%)	
CARP	41 (48.8%)	
Crohn's-like disease of pouch	19 (21.8%)	
C. difficile pouchitis	23 (23.2%)	
Score for inflammation		
PDAI, median (range)	7 (0-12)	
Endoscopic score, median (range)	3 (0-6)	
Prepouch inflammation	36 (43.4%)	
Mayo Score for UC (n = 3)		
1 (mild)		1 (33.3%)
2 (moderate)		1 (33.3%)
3 (severe)		1 (33.3%)
SES-CD (n = 13)		
0-6 (inactive/mild)		6 (46.2%)
>6 (moderate/severe)		7 (53.8%)
Treatment (multiple)		
Antibiotics	84 (96.6%)	3 (18.8%)
Probiotics	35 (40.2%)	0 (0%)
Mesalamine	33 (37.9%)	5 (31.3%)
Budesonide	36 (41.4%)	4 (25.0%)
Prednisone	45 (51.7%)	5 (31.3%)
Biologics	16 (18.4%)	8 (50.0%)
Small molecules	0 (0%)	0 (0%)
Functional Complications		
Pouch dyssynergia	14 (14.1%)	

Abbreviations: PSC-IBD, primary sclerosing cholangitis and inflammatory bowel disease; AARP, acute antibiotic-responsive pouchitis; CADP, chronic antibiotic-dependent pouchitis; CARP, chronic antibiotic-refractory pouchitis; PDAI, Pouch Disease Activity Index; UC, ulcerative colitis; SES-CD, Simple endoscopic score for Crohn's disease.

4 patients required colectomies due to dysplasia. Of the 3 patients who had a liver transplant prior to subtotal colectomy, all required surgeries due to dysplasia (n = 1) or neoplasia (n = 2). Recurrence of PSC was found in 10 patients (8.0%). Three patients required a second liver transplant, and 1 patient required a third liver transplant. Eight patients had

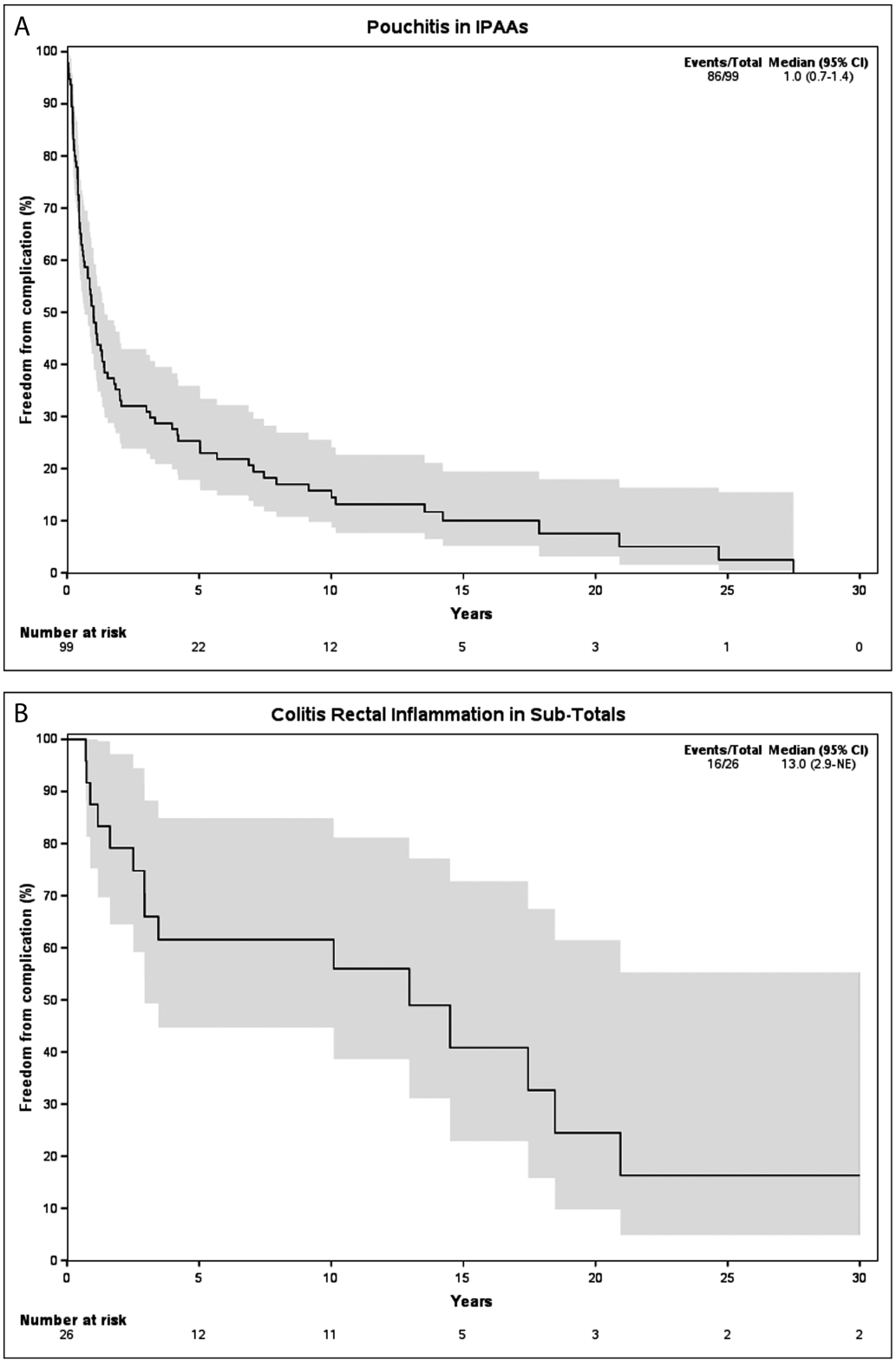

Figure 3. Kaplan-Meier curve for freedom from inflammatory complication (pouchitis, colitis) in PSC-IBD patients who have undergone (A) restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) and (B) subtotal colectomy with ileosigmoid or ileorectal anastomosis. Abbreviation: PSC-IBD, primary sclerosing cholangitis and inflammatory bowel disease.

a diagnosis of cholangiocarcinoma before undergoing IPAA ($n = 6$) or subtotal colectomy ($n = 2$). Thirty patients developed cholangiocarcinoma following IPAA ($n = 22$) or subtotal colectomy ($n = 8$).

Discussion

Ileal pouch-anal anastomosis has become the procedure of choice for restoration of intestinal continuity in patients with PSC-IBD. Despite improved frequency of surgical

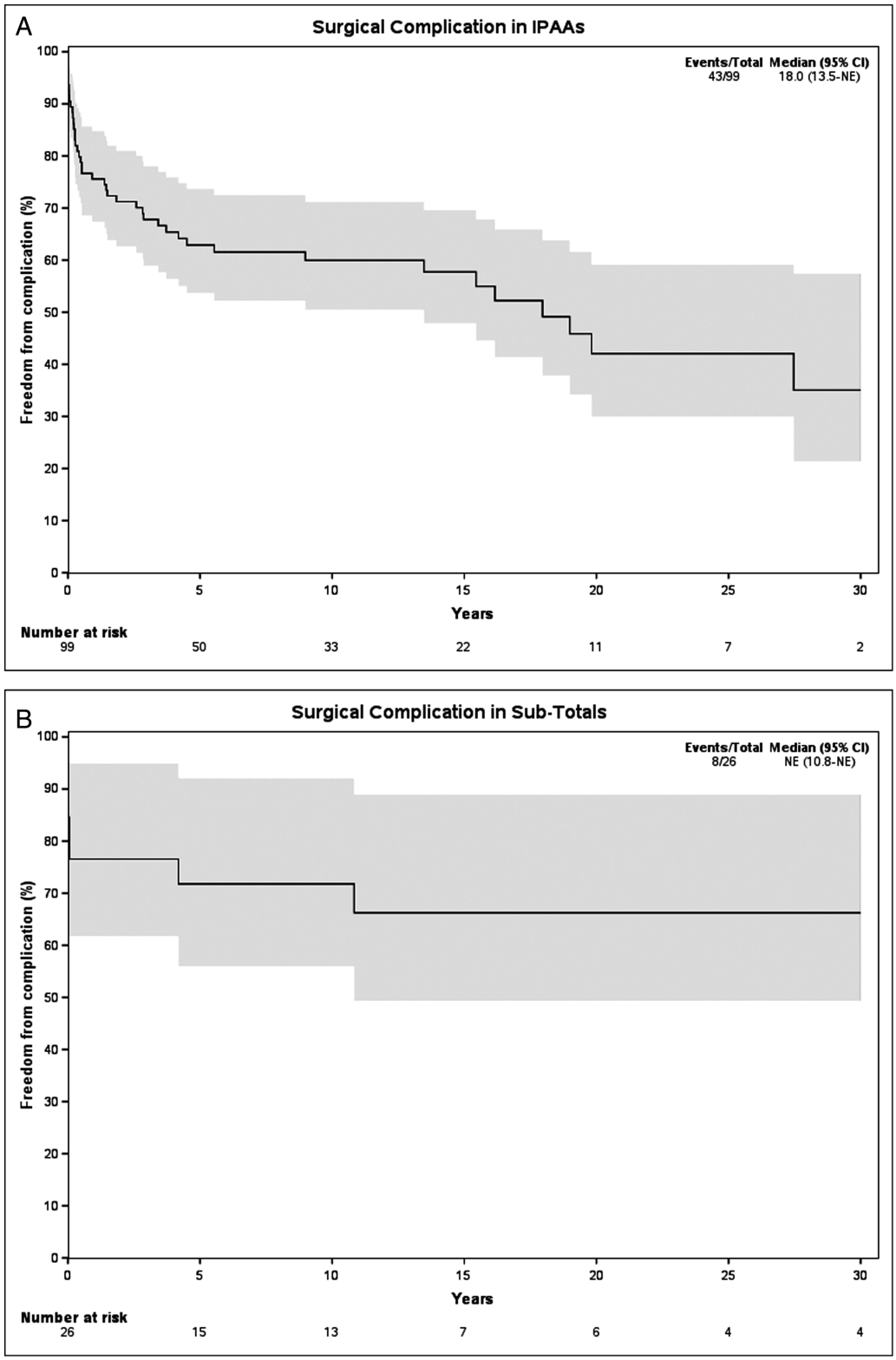

Figure 4. Kaplan-Meier curves for surgical complications in PSC-IBD patients who have undergone (A) restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) and (B) subtotal colectomy with ileosigmoid or ileorectal anastomosis. Abbreviation: PSC-IBD, primary sclerosing cholangitis and inflammatory bowel disease.

complications, 5% to 10% of patients may still require pouch excision for pouch leak, fistula, pouch failure, or Crohn's-like disease of the pouch.[21] Ileal pouch-anal anastomosis may not be the ideal surgery, as PSC-IBD patients often develop severe pouchitis, worse pouch function, and poor quality of life.[9–11,24] Female patients have added concern for reduced fertility after IPAA, though evidence suggests a lower impact if the rectum is left intact.[13] Given these difficulties associated

with IPAA, it is reasonable to consider an alternative surgery such as subtotal colectomy with IS/IR anastomosis if rectal sparing disease is present. Studies have shown improved functional outcomes, lower rates of surgical complications, and less impact on fertility for patients who have undergone subtotal colectomy.[25,26] As it is well known that patients with PSC-IBD are at increased risk for colorectal neoplasia, gastroenterologists and colorectal surgeons may be overly cautious about patients' long-term risk of developing neoplasia following surgery.[27] Therefore, it is important to understand if performing subtotal colectomy, leaving the rectum intact, increases the risk for neoplasia in the PSC-IBD patient.

In this retrospective referral center–based study, we did not observe dysplasia or neoplasia in PSC-IBD patients who underwent subtotal colectomy ($n = 26$). In PSC-IBD patients who underwent IPAA ($n = 99$), the occurrence of pouch dysplasia or neoplasia was relatively low (1%-2%) in keeping with other studies.[8] No patients who underwent surgery for dysplasia or neoplasia had evidence of dysplasia or neoplasia on postsurgery endoscopic surveillance. These findings suggest favorable neoplastic outcomes for PSC-IBD patients considering a subtotal colectomy, which is relevant given the high prevalence of rectal sparing in PSC-IBD patients.

In a prior study of 31 patients with PSC-IBD who had undergone surgery (14 IPAA, 7 subtotal colectomy with ileorectal anastomosis), 7 patients had colorectal cancer, though the study did not specify type of surgery patients with colorectal cancer had undergone.[28] Another study of 65 patients with PSC-IBD following IPAA were followed for a median of 6 years, and only 3 patients developed neoplasia.[29] Recently, in a large retrospective analysis of 1319 patients with IBD who had undergone IPAA, those with PSC ($n = 220$) were found to have a more than 5-fold increased risk of pouch neoplasia.[8] In a multicenter retrospective study of UC patients who underwent subtotal colectomy with ileorectal anastomosis, PSC was an independent risk factor for developing colorectal neoplasia, though only 13 (3.8%) patients had PSC, and 4 patients had a history of rectal cancer.[30] A systematic review estimates the incidence of malignancy in the residual rectum of IBD patients following subtotal colectomy to be 1.3%, although only 1 study accounted for rectal sparing.[31] In our study, due to low neoplasia rate following surgery ($n = 0$) in the subtotal colectomy PSC-IBD cohort, it is difficult to conclude the true risk of neoplasia.

Our study is consistent with estimated incidence of pouchitis (87.8%) and colitis/proctitis (61.5%) across reported studies. Some studies have shown higher rates of surgical complications in IPAA compared with subtotal colectomy, though this risk is not increased by presence of PSC.[12,25,26,32] In our study, IPAA patients experienced 7.5 surgical complications per 100 years (11.8 median follow-up years) compared with 2.7 surgical complications per 100 years (13.8 median follow-up years) in subtotal colectomy patients. Furthermore, 7 patients required pouch excision, highlighting the high morbidity associated with IPAA surgery. In a case-control study of 48 PSC-IBD patients (31 IPAA, 17 subtotal colectomy with ileorectal anastomosis), functional outcomes using the Oresland scale were worse in the subtotal colectomy group compared with IPAA, though rectal sparing was not noted; these symptoms were likely due to high rates of proctitis-driving symptoms of increased frequency and urgency.[12] Our study did not directly assess functional outcomes in either group.

Indication for surgery is an important consideration, as most patients (51.5% IPAA, 42.3% subtotal colectomy) in our study underwent colectomy due to rectal sparing medically refractory disease. This is surprising given the expanding availability of medical therapies, and higher rates of colectomy due to neoplasia in the literature. It may be beneficial to evaluate the impact of biologics on surgical indication in a future study. We could not ascertain information of location and focality of dysplasia/neoplasia for patients who underwent surgery outside our institution, which is a limitation of this study. Further studies are needed to determine when to consider subtotal colectomy in patients with isolated neoplasia or rectal sparing medically refractory disease.

Patients with PSC-IBD often undergo liver transplant, and while immunosuppression may permit milder IBD in some, more than 25% of patients may experience an IBD flare requiring medication escalation following transplant.[33,34] Additionally, severity of inflammation during the time of transplant may be a risk factor for flare following transplant.[35] Studies clearly demonstrated that liver transplant increases the risk for colorectal dysplasia or neoplasia, and although it can occur in quiescent disease, this risk is pronounced in those who have moderate to severe IBD following liver transplant.[36–38] The incidence of colorectal cancer in patients with PSC-IBD after liver transplant with an intact colon varies from 0 to 43.5 per 1000 persons per year.[39] The role immunosuppressive therapies play on increasing colorectal cancer risk following transplant is unclear, as research is conflicting.[40,41]

There are several limitations to this study. It is retrospective, which inherently relies on documentation available within the EMR over the long interval of 5 decades (1972-2022). However, we used rigorous data extraction protocols with strict criteria to categorize patients and confirm findings. Endoscopic surveillance interval for neoplasia is not standardized for patients with PSC-IBD following IPAA or subtotal colectomy, and therefore our findings were variable based on physician/patient preference and should be interpreted with caution. Given the lack of standardized endoscopic guidelines over time, we recognize that the inclusion criteria of at least 1 follow-up endoscopic exam is a limitation of the study. We accounted for number of years of follow-up to help clarify data interpretation. The availability of enhanced endoscopic imaging during surveillance colonoscopy over the last decade may also have influenced improved dysplasia detection. Similarly, patients may not always return to a referral center for surveillance that can easily be completed locally. As PSC is a disease with insidious onset, the date of diagnosis is driven by awareness of physicians. Similarly, as the subclinical phase of PSC-IBD is longer than those without PSC, the duration of IBD may be underestimated. This study was performed at a single academic institution, which may result in bias limiting the generalizability of the study. Additionally, not all surgeries were performed at our institution, and there was difficulty obtaining surgical information including patient or provider discussion for choosing subtotal colectomy vs IPAA, anastomosis type, and stages.

In conclusion, we did not observe an increase in dysplasia or neoplasia in our retrospective cohort of PSC-IBD patients with rectal sparing who underwent subtotal colectomy compared with IPAA. To improve surgical and functional outcomes, subtotal colectomy may be considered a viable surgical option in patients with rectal sparing PSC-IBD if endoscopic surveillance for dysplasia and neoplasia is implemented.

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Conflict of Interest

K.A.D. has no conflict of interest. P.S. has no conflicts of interest. G.F. has no conflicts of interest. W.S.H. has no conflicts of interest. N.P.M. has no conflicts of interest. N.C. .has no conflicts of interest. S.S. has no conflicts of interest. L.R. has no conflicts of interest.

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