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The Incidence of Pouch Neoplasia Following Ileal Pouch–Anal Anastomosis in Patients With Inflammatory Bowel Disease

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Abstract

Background: Ileal pouch–anal anastomosis (IPAA) is the standard restorative procedure following proctocolectomy in patients with inflammatory bowel disease (IBD) who require colectomy. However, removal of the diseased colon does not eliminate the risk of pouch neoplasia. We aimed to assess the incidence of pouch neoplasia in IBD patients following IPAA.

Methods: All patients at a large tertiary center with International Classification of Diseases–Ninth Revision/International Classification of Diseases–Tenth Revision codes for IBD who underwent IPAA and had subsequent pouchoscopy were identified using a clinical notes search from January 1981 to February 2020. Relevant demographic, clinical, endoscopic, and histologic data were abstracted.

Results: In total, 1319 patients were included (43.9% women). Most had ulcerative colitis (95.2%). Out of 1319 patients, 10 (0.8%) developed neoplasia following IPAA. Neoplasia of the pouch was seen in 4 cases with neoplasia of the cuff or rectum seen in 5 cases. One patient had neoplasia of the prepouch, pouch, and cuff. Types of neoplasia included low-grade dysplasia (n = 7), high-grade dysplasia (n = 1), colorectal cancer (n = 1), and mucosa-associated lymphoid tissue lymphoma (n = 1). Presence of extensive colitis, primary sclerosing cholangitis, backwash ileitis, and rectal dysplasia at the time of IPAA were significantly associated with increased risk of pouch neoplasia.

Conclusions: The incidence of pouch neoplasia in IBD patients who have undergone IPAA is relatively low. Extensive colitis, primary sclerosing cholangitis, and backwash ileitis prior to IPAA and rectal dysplasia at the time of IPAA raise the risk of pouch neoplasia significantly. A limited surveillance program might be appropriate for patients with IPAA even with a history of colorectal neoplasia.

Lay Summary

The incidence of pouch neoplasia in inflammatory bowel disease patients who have undergone ileal pouch–anal anastomosis (IPAA) is low. Extensive colitis, primary sclerosing cholangitis, and backwash ileitis prior to IPAA as well as rectal dysplasia at time of IPAA raise the risk of pouch neoplasia significantly.

Keywords: pouch neoplasia, ileal pouch–anal anastomosis, inflammatory bowel disease

Introduction

Restorative proctocolectomy with ileal pouch–anal anastomosis (IPAA) has become the surgical procedure of choice in patients with inflammatory bowel disease (IBD) who require colectomy.[1,2] Surgical intervention is a common modality used for IBD patients with medically refractory disease, poor tolerance of medications, and inflammatory-associated neoplasia. Colectomy substantially reduces the risk for development of colorectal cancer; however, this does not completely eliminate the risk for neoplasia of the pouch. Pouch neoplasia includes a spectrum of neoplastic changes ranging from dysplasia to adenocarcinoma. Dysplasia or cancer of the colectomy specimen has been described to be the strongest predictor of IPAA-related cancer.[3] There are a small number of cases reported, and thus the true incidence and natural history of pouch dysplasia, adenocarcinoma, or neoplasia following IPAA in IBD patients have not been fully characterized.[4]

There are several large studies regarding the incidence of pouch neoplasia. A 2014 study of 1200 patients with IBD and IPAA in the Netherlands over 20 years found that only 1.8% developed neoplasia and 1.3% developed adenocarcinoma.[5] Another study in 2010 of 3202 patients with IBD and

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Key Messages

- What is already known? The true incidence and natural history of pouch neoplasia following ileal pouch–anal anastomosis (IPAA) in inflammatory bowel disease patients has not been fully characterized. There are a small number of cases reported in the literature. As a result, there is no consensus on the necessity and potential interval of pouch surveillance.
- What is new here? Out of 1319 patients in this cohort, 10 (0.8%) developed neoplasia involving the pouch following IPAA.
- How can this study help patient care? The incidence of pouch neoplasia in this cohort of patients was low. A limited surveillance program might be appropriate for patients with IPAA tailored to the presence of risk factors identified in this study.

IPAA at Cleveland Clinic over 25 years (1984-2009) found 11 patients with cancer of the anal-transitional zone (ATZ) or pouch body with cumulative incidence for pouch neoplasia of 5.1% at 25 years.[6] Given the paucity of data regarding the risk of pouch dysplasia, there is no consensus on the necessity and potential interval of pouch surveillance.[7]

Pouch surveillance with random biopsies became routine previously, but it has since become apparent that dysplasia and cancer are rare.[8] A review of pouch surveillance guidelines from various societies demonstrated dissimilar and inconsistent recommendations.[9] Survey data have shown physicians also disagree regarding the need for pouch surveillance and the necessary screening interval, making surveillance practices highly variable.[10] It is not unreasonable to assume that factors that may contribute to a high-risk colon will also result in a high-risk pouch. Both the British Society of Gastroenterology[11] and the European Crohn's and Colitis Organization[12] recommend that high-risk patients (those with primary sclerosing cholangitis [PSC], previous colorectal neoplasia, atrophic mucosa, and refractory pouchitis) undergo annual surveillance pouchoscopy, whereas the recommendation for low-risk patients is to undergo pouchoscopy every 5 years. The American Society of Gastrointestinal Endoscopy[13] recommends considering yearly surveillance pouchoscopy in high-risk patients, but risk factors have not been well studied.

Lightner et al[14] performed an analysis of all adult patients who previously had IPAA for ulcerative colitis (UC) and underwent pouchoscopy between January 2010 and January 2020 at the Cleveland Clinic, in which 9398 pouchoscopy procedures were performed in 3672 patients. Thirteen patients were found to have biopsy-proven neoplasia at the time of pouchoscopy, all located at the ATZ. Seven had low-grade dysplasia (LGD), none had high-grade dysplasia (HGD), and 6 had invasive adenocarcinoma (4 in the ATZ and 2 in the pouch). All 6 patients were symptomatic with anal bleeding or pelvic pain at the time of pouchoscopy, had palpable lesions on digital rectal exam, and had visible lesions on pouchoscopy. Based on these results, surveillance pouchoscopy was not recommended in asymptomatic patients, as significant neoplasia following IPAA for UC was rare.[14]

In this retrospective study, we sought to determine the incidence of pouch neoplasia in IBD patients who have undergone IPAA at our institution as well as to identify potentially relevant risk factors for pouch neoplasia in this specific cohort.

Methods

Patient population

This retrospective study was approved by our center's Institutional Review Board. Using a search of the electronic medical record, we identified all patients ≥18 years of age who were evaluated at our institution with a diagnosis of IBD who underwent IPAA and had subsequent pouchoscopy between January 1981 and February 2020 using International Classification of Diseases–Ninth Revision and International Classification of Diseases–Tenth Revision diagnostic codes as well as procedure codes. The medical records of only patients who did not withdraw research authorization were included. This was followed by manual review of individual patient charts to confirm each diagnosis. In patients meeting inclusion criteria with a confirmed IBD diagnosis, clinical data were then abstracted for various demographic, clinical, endoscopic, and histopathological outcomes. The date of the first visit recorded for IBD diagnosis was recorded as the index date. Patients were excluded for the following reasons: <18 years of age at the time of last follow-up, did not have an ileoanal pouch, did not have a pouchoscopy on record, no confirmed IBD diagnosis on record, and no follow-up at our central institutional site following index visit.

Patient data

Patient data collected included age, sex, smoking history, and personal and family history of colorectal cancer.

Inflammatory bowel disease

IBD was diagnosed based on clinical diagnostic criteria as per the treating gastroenterologist and review of the medical record. Diagnosis was supported by characteristic endoscopic, radiographic, and/or histologic findings. Patients with an IBD diagnosis were then subcategorized as having Crohn's disease (CD), UC, or indeterminate colitis based on review of the medical record. The date of IBD diagnosis was defined as when a diagnosis was first described in the patient's medical record and confirmed histologically at our institution.

Disease characteristics included subtype of IBD and related complications such as presence of backwash ileitis and/or extensive colitis, personal history of PSC, age at surgery, indication for surgery, and duration of disease at time of surgery. For IPAA, the number of stages and anastomosis type were recorded. If IPAA was performed for dysplasia in the setting of IBD, the type of colonic dysplasia including LGD, HGD, or indeterminate dysplasia was recorded in addition to dysplasia type (visible or random), presence of rectal dysplasia, and focality in the colon (unifocal or multifocal).

Pouchoscopy data

Pouchoscopy variables included date of first pouchoscopy, indication for pouchoscopy, type of pouch present, endoscopic and/or histopathologic evidence of chronic pouchitis, severity of pouchitis if present, and/or presence of chronic cuffitis. Severity of pouchitis was defined as mild, moderate, or severe as documented in the endoscopic report.

Neoplasia

When neoplasia was found on pouchoscopy, the location and type of neoplasia as well as duration of IBD at detection of neoplasia were also noted. Following a diagnosis of

neoplasia, all subsequent pouchoscopy procedures with biopsy were recorded along with any additional pertinent surgical procedures and outcomes of neoplasia. Long-term data collected included the rate of pouch failure defined as need for pouch excision, presence of neoplasia on surgical pathology, and duration pouch remained in place.

Statistical analysis

Patient characteristics and clinical data were presented as mean ± SD, median and range, or frequency and percentage. Descriptive statistics were used to report findings from the neoplasia cohort. Categorical variables were reported as a unique count and percentage of the sample. Univariate analysis of clinical characteristics and associated risk of neoplasia were reported as hazard ratio (HR) with 95% confidence interval (CI), with a P value <.05 denoting statistical significance.

Results

The initial data search identified 3621 patients with suspected diagnoses of IBD who underwent surgical intervention. After manual review, 1319 patients were included in the final analysis, and 2302 were excluded due to absence of an ileoanal pouch, prior history of ileorectal anastomosis (IRA), no pouchoscopy on record, absence of confirmed diagnosis of IBD, follow-up at a noncentral institutional site, or pediatric age at last follow-up (Figure 1).

Demographics

Baseline characteristics including demographic data and median follow-up time are summarized in Table 1. In total, 1319 patients were included (43.9% women) with median age of 35.7 years at IPAA for medically refractory colitis, dysplasia, or adenocarcinoma of the colon. Most patients had UC (95.2%). Prior to IPAA, 188 (14.4%) had backwash ileitis, 581 (44.2%) had extensive colitis, and 185 (14.0%) had a personal history of colorectal neoplasia. A total of 220 patients (16.8%) had PSC. Seventy (5.3%) patients had a family history of colorectal cancer (CRC) and 377 (28.7%) patients had current or former tobacco use, as denoted in the electronic medical record.

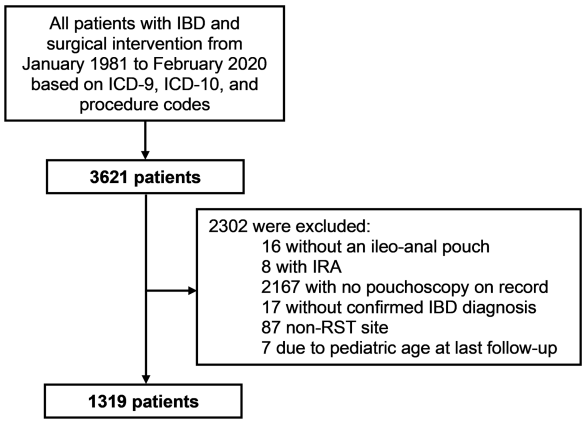

Figure 1. Screening of patients for study inclusion. Utilizing International Classification of Diseases–Ninth Revision (ICD-9) and International Classification of Diseases–Tenth Revision (ICD-10) diagnostic codes for inflammatory bowel disease (IBD), a master computer system at our institution was used to search for patients with the diagnosis of IBD who had research authorization. Procedure codes for ileal pouch–anal anastomosis (IPAA) were then utilized to identify IBD patients who underwent IPAA. A total of 2302 patients were excluded. IRA, ileorectal anastomosis; RST, Rochester.

Table 1. Baseline Demographics and Clinical Characteristics (N =1319).

Duration of follow-up, y	8.6 (1 day-41.1 years)
Age at IPAA (n = 1317), y	35.7 (8.0-82.4)
Female	577 (43.9)
IBD diagnosis before IPAA (n = 1313)	
UC	1250 (95.2)
CD	40 (3.0)
Indeterminate colitis	23 (1.8)
Presence of backwash ileitis before IPAA (n = 1309)	188 (14.4)
Presence of extensive colitis before IPAA (n = 1313)	581 (44.2)
Presence of neoplasia before IPAA (n = 1312)	185 (14.0)
Presence of primary sclerosing cholangitis before IPAA (n = 1313)	220 (16.8)
Family history of colorectal cancer (n = 1312)	70 (5.3)
Former/current tobacco use (n = 1313)	377 (28.7)
IPAA indication (n = 1232)	
Medially refractory	1053 (85.5)
Dysplasia or adenocarcinoma	179 (14.6)
No. of IPAA stages (n = 1313)	
2 or less	945 (72.0)
3	350 (26.7)
Unknown	18 (1.4)
Anastomosis type (n = 1177)	
Mucosectomy	190 (16.1)
Stapled without mucosectomy	907 (77.1)
Handsewn	80 (6.8)
Duration of disease at time of IPAA (n = 1311), y	4.0 (0.0-53.0)

Value are median (range) or n (%). Percentages were calculated on the basis of those with data available.
Abbreviations: CD, Crohn's disease; IBD, inflammatory bowel disease; IPAA, ileal pouch–anal anastomosis; UC, ulcerative colitis.

Surgery

Indications for IPAA included medically refractory IBD (85.5%) and colorectal dysplasia or CRC (14.6%). Two-step or less IPAA was performed in 72%, with 3-step (26.7%) IPAA performed less frequently. A stapled anastomosis without mucosectomy was performed in 77.1%, with mucosectomy alone (16.1%) and handsewn anastomosis (6.8%) performed less frequently. Median duration of IBD prior to IPAA was 4.0 years (Table 1).

For those who underwent IPAA for colorectal dysplasia or CRC, most patients had low-grade dysplasia (71.8%). Dysplasia was more often detected on random colon biopsies (58.8%) in comparison with visible dysplasia (41.2%). Rectal dysplasia was present in 2.1% of patients. When dysplasia

Table 2. Characteristics of Colorectal Dysplasia Prior to IPAA (N = 1319).

Type of colonic dysplasia prior to IPAA (n = 156)	
LGD	112 (71.8)
HGD	42 (26.9)
Indeterminate	2 (1.3)
Dysplasia type (n = 153)	
Visible	63 (41.2)
Random	90 (58.8)
Presence of rectal dysplasia (n = 1305)	27 (2.1)
Focality in colon (n = 155)	
Unifocal	88 (56.8)
Multifocal	67 (43.2)

Values are n (%).
Abbreviations: HGD, high-grade dysplasia; IBD, inflammatory bowel disease; LGD, low-grade dysplasia.

was detected, it was most often unifocal (56.8%) in comparison with multifocal (43.2%) prior to undergoing IPAA (Table 2).

Pouchitis and outcomes of neoplasia

Median duration of follow-up after IPAA was 8.6 years. Most patients had evidence of pouchitis (60.1%) at index pouchoscopy. Pouchitis was most often mild in severity (70.6%) in comparison with moderate (24.2%) or severe (5.2%). Chronic cuffitis was present in only 6.1% of patients (Table 3).

Out of 1319 patients, 10 (0.8%) developed pouch-associated neoplasia following IPAA. Median duration of time from IBD diagnosis to development of neoplasia was 32.5 years. Median duration of time from first stage of IPAA to neoplasia diagnosis was 12.3 years. Neoplasia of the pouch was seen in 4 cases with neoplasia of the cuff or rectum seen in 5 cases. One patient had neoplasia of the prepouch, pouch, and cuff. In total, LGD was seen in 7 cases, HGD in 1 case, CRC in 1 case, and mucosal-associated lymphoid tissue (MALT) lymphoma in 1 case. Four had resolution of neoplasia on follow-up pouchoscopy, 3 underwent pouch excision, 1 had persistent neoplasia, and 2 had unknown outcomes of neoplasia (Table 3). Of those with neoplasia involving the pouch, 3 had LGD and 1 had MALT lymphoma. Outcomes were variable for those with LGD of the pouch including pouch excision or persistent neoplasia, or resolution of neoplasia on follow-up pouchoscopy. Of those with neoplasia of the rectum or cuff, 4 had LGD and 1 had CRC. Outcomes for those with neoplasia of the rectum or cuff included resolution on follow-up pouchoscopy or pouch excision (see Supplement 1 for supporting content). A total of 109 patients underwent pouch excision (8.3%). Three (2.8%) had pouch excision for neoplasia, 2 (1.8%) of which had neoplasia present on surgical pathology (see Supplement 2 for supporting content).

Presence of extensive colitis prior to IPAA was significantly associated with a more than 4-fold increased risk of pouch neoplasia (HR, 4.14; 95% CI, 1.05-16.35; P = .0425). Presence of PSC prior to IPAA was significantly associated with a more than 5-fold increased risk of pouch neoplasia (HR, 5.65; 95% CI, 1.52-21.06; P = .0099). Presence of backwash ileitis prior to IPAA was significantly associated a more than 5-fold increased risk of pouch neoplasia (HR, 5.95; 95% CI, 1.58-22.31; P = .0082). Presence of rectal dysplasia at the time of IPAA was associated with a more than 8-fold increased risk of pouch neoplasia (HR, 8.91; 95% CI, 1.10-72.55; P = .0409). Sex, age at IPAA, former or current tobacco use, and family history of CRC were not significantly associated with an increased risk of pouch neoplasia (Table 4).

Table 3. Pouchitis and Outcomes of Pouch Neoplasia (N = 1319).

Presence of chronic pouchitis	793 (60.1)
Pouchitis severity at index pouchoscopy (n = 796)	
Mild	562 (70.6)
Moderate	193 (24.2)
Severe	41 (5.2)
Presence of chronic cuffitis	81 (6.1)
Presence of pouch neoplasia	10 (0.8)
Duration of IBD at diagnosis of pouch neoplasia (n = 10), y	32.5 (18.0-50.0)
Duration of time from first stage of IPAA to neoplasia diagnosis (n = 10), y	12.3 (1.6-38.1)
Neoplasia location (n = 10)[a]	
Prepouch	1 (10)
Pouch	4 (40)
Rectum/cuff	5 (50)
Pouch neoplasia type (n = 10)	
LGD	7 (70)
HGD	1 (10)
CRC	1 (10)
MALT lymphoma	1 (10)
Outcome of neoplasia (n = 10)	
Resolution on follow-up pouchoscopy	4 (40)
Surgical excision of pouch	3 (30)[b]
Unknown	2 (20)
Persistent neoplasia	1 (10)[c]

Values are n (%) or median (range).
Abbreviations: CRC, colorectal cancer; HGD, high-grade dysplasia; IBD, inflammatory bowel disease; IPAA, ileal pouch–anal anastomosis; LGD, low-grade dysplasia; MALT, mucosa-associated lymphoid tissue.
[a]One patient had involvement of the prepouch, pouch, and rectum/cuff with high-grade dysplasia but was only counted as having neoplasia of the prepouch.
[b]Two of the 3 patients with surgical excision of the pouch had neoplasia present on surgical pathology.
[c]No follow-up pouchoscopy was on record to evaluate for further persistence or resolution of neoplasia.

Discussion

Our study shows that the occurrence of pouch neoplasia in patients with IBD who have undergone IPAA is relatively low. Only 10 (0.8%) patients developed pouch neoplasia out of 1319, most of which included LGD (7 patients), followed by HGD (1 patient), CRC (1 patient), and MALT lymphoma (1 patient). These findings may potentially suggest a limited surveillance program in IBD patients who have undergone IPAA, tailored based on the presence of high-risk factors.

While the first IPAA was performed by Parks and Nicholls in 1978,[15] the first true de novo pouch-related adenocarcinoma was not reported until 1992.[16] Since then, several case reports, single-center case series, national registries, and

Table 4. Univariate Analysis of Clinical Characteristics on Risk of Neoplasia.

Clinical Characteristic	Hazard Ratio (95% CI)	*P* Value
Male	1.65 (0.41-6.61)	.4773
Age at IPAA, per 10 y	1.20 (0.69-2.10)	.5247
Presence of extensive colitis before IPAA	4.14 (1.05-16.35)	.0425
Presence of primary sclerosing cholangitis before IPAA	5.65 (1.52-21.06)	.0099
Former/current tobacco use	1.75 (0.47-6.51)	.4072
Presence of backwash ileitis before IPAA	5.95 (1.58-22.31)	.0082
Family history of colorectal cancer	1.74 (0.22-14.04)	.6012
Presence of rectal dysplasia at time of IPAA	8.91 (1.10-72.55)	.0409

Abbreviations: CI, confidence interval; IPAA, ileal pouch–anal anastomosis.

systematic reviews have documented varying estimates of pouch-related neoplasia and associated risk factors, although consistently reported rates less than the risk for de novo CRC.[4,6,17,18] Given that the overall risk of cancer following IPAA is unknown and that pouch cancer surveillance is controversial, it is important to understand the long-term risk of neoplasia in this group of patients. Surveillance strategies for the development of pouch dysplasia or CRC ultimately should be based on risk stratification. Several studies have outlined multiple risk factors for the development of pouch neoplasia in IBD including colorectal dysplasia and/or CRC identified before or at surgical intervention, atrophic or type C ileal mucosa, refractory pouchitis, and PSC.[19,20]

In patients with IBD, particularly UC, colectomy substantially reduces the risk of developing CRC. A systematic review of IBD patients who underwent IPAA showed a cumulative incidence of pouch dysplasia and carcinoma of 3.0% and 2.7%, respectively, after 20 years.[18] Of all cancers that develop in the pouch, most are adenocarcinomas (84%), although lymphoma and squamous cell carcinoma have also been described.[21] In IBD patients who have undergone IPAA, studies have described the overall cancer risk is comparable to the background population particularly given the rarity of pouch cancer following IPAA.[22] However, even though pouch adenocarcinoma is rare, the prognosis in these patients is quite poor,[23] which emphasizes the importance of surveillance in this patient population. Of those who develop adenocarcinoma after IPAA for UC, nearly two-thirds develop at the ATZ, with the remainder developing from the pouch mucosa.[24] In our neoplasia cohort, we demonstrated similar findings with neoplasia involving the cuff or rectum in 5 patients, followed by neoplasia involving the pouch in 4 patients and 1 patient with neoplasia involving the prepouch, pouch, and rectum/cuff. We also identified the presence of rectal dysplasia at the time of IPAA as a potential risk factor with a more than 8-fold increased risk of pouch neoplasia. However, given the small number of neoplasia events in this patient population, it is difficult to generalize this claim, as most patients underwent IPAA for medically refractory IBD (85.5%) in comparison with colorectal dysplasia or CRC (14.6%).

Interestingly, the benefit of routine surveillance for dysplasia in the pouch has been questioned, as the significance of LGD in the pouch is not always entirely clear.[25] In our neoplasia cohort, most patients had LGD. Additionally, most patients had endoscopic and histologic evidence of pouchitis at index pouchoscopy (60.1%). Low-grade dysplastic features on histopathology can be a physiologic response particularly in the setting of chronic pouchitis or cuffitis. This is further confirmed by resolution of neoplasia on follow-up pouchoscopy in almost half the patients in our neoplasia cohort, most of whom had neoplasia involving the rectum or cuff.

Several studies have outlined atrophic or type C ileal mucosa and refractory pouchitis as potential risk factors for pouch dysplasia.[19,20] Much of our study population had evidence of chronic pouchitis (60.1%), although we did not find this to be particularly associated with an increased risk of pouch neoplasia. However, we did describe the presence of extensive colitis prior to IPAA to be significantly associated with a more than 4-fold increased risk and presence of backwash ileitis prior to IPAA to be significantly associated a more than 5-fold increased risk of pouch neoplasia in this group. This may suggest that our patient population had more severe IBD at baseline, as most patients underwent IPAA for medically refractory IBD in comparison with colorectal dysplasia or CRC.

It is well known that patients with concomitant PSC and IBD are at an increased risk for CRC.[26] However, Imam et al[27] described 65 patients with PSC and IBD who underwent colectomy with IPAA and were followed for a median of 6 years. Only 3 patients developed evidence of neoplasia, suggesting that a more frequent pouch surveillance strategy may be unnecessary in this subset of patients.[27] In our study, a small subset of patients had a diagnosis of PSC prior to undergoing IPAA (16.8%). The presence of PSC prior to IPAA was significantly associated with a more than 5-fold increased risk of pouch neoplasia in our cohort. It is known that backwash ileitis and PSC often co-occur which may place these patients at increased risk of pouch-related neoplasia. However, it is difficult to conclude whether PSC is truly associated with an increased risk of pouch neoplasia in this cohort due to the low pouch neoplasia event rate.

While the rectal cuff is at theoretical increased risk of neoplasia, large studies report no difference in malignancy among patients who underwent a handsewn anastomosis with mucosectomy vs stapled anastomosis.[6,28] Additionally, large studies have also compared IPAA with other surgical approaches including IRA. Those who underwent IRA had a greater risk of developing neoplasia than those who underwent IPAA. Stapled anastomosis without mucosectomy was the most common anastomosis type (77.1%). This highlights the importance of considering specific, individualized surgical approaches and interventions in this patient population to minimize any potential future risk of neoplasia.[29,30]

Overall, our findings are similar to those described in other studies examining the risk of pouch neoplasia in IBD patients who have undergone IPAA. Our study highlights the risk of pouch neoplasia in a relatively large cohort of patients with IBD who have undergone IPAA, even though this risk is relatively low. Additionally, among the 109 patients in our study who underwent pouch excision, most of whom had pouch dysfunction, only 2 (1.8%) had neoplasia present on surgical pathology. However, making direct comparisons across

studies can be challenging, particularly given the low event rate of pouch-related neoplasia overall. The low occurrence of pouch neoplasia in this cohort makes it difficult to conclude whether these risk factors are truly associated with an increased risk of pouch neoplasia.

The limitations of this study include it being performed at a single tertiary referral center, which may result in bias, limiting the study's generalizability. This study also had limited follow-up (median 8.6 years), which may not capture the full spectrum of pouch neoplasia events following IPAA in this group. This was also a retrospective study, and as a result, there was significant reliance on documentation within the electronic medical record. However, we utilized a large patient database and identified all possible patients with IBD who underwent IPAA at our institution. Rigorous data extraction protocols and strict criteria were utilized to categorize patients and confirm case status.

Conclusions

The development of neoplasia in the ileoanal pouch following IPAA is uncommon. We identified the presence of extensive colitis, PSC, and backwash ileitis prior to IPAA as well as rectal dysplasia at the time of IPAA as potential factors that may raise the risk of pouch neoplasia in this group of patients. However, due to the low neoplasia event rate, it is difficult to determine the true impact of these factors on the risk for developing pouch-related neoplasia. With these findings, our data suggest that a limited surveillance program may be appropriate, especially for those with previously identified risk factors as outlined in the literature. Future studies should focus on a longer duration of follow-up and multicenter collaboration to better determine the natural history and epidemiology of pouch neoplasia in these patients. Such long-term studies will be useful in providing guidance regarding the optimal pouchoscopy surveillance strategy following IPAA in IBD patients.

Acknowledgments

This work has been approved by the appropriate ethical committees at Mayo Clinic Rochester and subjects gave prior research authorization.

Author Contribution

S.A.U.: literature search, data collection and interpretation, formation of figures and tables, and drafting of manuscript. B.P.C.: data collection, drafting of manuscript, and critical review of manuscript. M.F.J.: data collection and critical review of manuscript. C.N.D.: data collection and analysis and critical review of manuscript. J.E.E.: data collection and critical review of manuscript. W.S.H.: data collection and analysis and critical review of manuscript. L.E.R.: data interpretation and critical review of manuscript. E.V.L.: literature search, data interpretation, and critical review of manuscript. N.C.-P.: literature search, study design, data collection and interpretation, and critical review of manuscript.

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Conflict of Interest

L.E.R. has served on advisory boards for Janssen Pharmaceuticals and Fresenius Kabi. E.V.L. has served as a consultant for AbbVie, Amgen, Arena, Bristol Myers Squibb, Boehringer Ingelheim, CALIBR, Celgene, Celltrion Healthcare, Eli Lilly, Fresenius Kabi, Genentech, Gilead, Gossamer Bio, GlaxoSmithKline, Iterative Scopes, Janssen, Morphic, Ono Pharma, Pfizer, Protagonist, Sun Pharma, Surrozen, Takeda, and UCB; and received research support from AbbVie, Bristol Myers Squibb, Celgene/Receptos, Genentech, Gilead, Gossamer Bio, Janssen, Pfizer, Takeda, Theravance, and UCB. N.C.-P. has served as a consultant for Boston Scientific and Alexion Pharma. S.A.U., B.P.C., M.F.J., C.N.D., J.E.E., and W.S.H. disclose no conflicts.

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