Crohn's & Colitis 360, 2025, **7**, otaf001
https://doi.org/10.1093/crocol/otaf001
Advance access publication 7 February 2025
Observations and Research

Clinical Characteristics and Outcomes of Small Bowel Neoplasms in Crohn's Disease: A Case-Control Study

Siri A. Urquhart, MD,[*] Thomas C. Smyrk, MD,[†] William S. Harmsen, MS,[‡] Edward V. Loftus, Jr., MD,[*] John B. Kisiel, MD,[*] and Nayantara Coelho-Prabhu, MBBS[*]

[*]Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN, USA
[†]Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN, USA
[‡]Clinical Trials and Biostatistics, Mayo Clinic, Rochester, MN, USA

Address correspondence to: Nayantara Coelho-Prabhu, MBBS, Division of Gastroenterology and Hepatology, Mayo Clinic, 200 1st Street SW, Rochester, MN 55905, USA. Tel.: 507-284-2407 (coelhoprabhu.nayantara@mayo.edu).

Background: Patients with Crohn's disease (CD) who have ileal or any small bowel (SB) involvement are at increased risk of developing SB cancer. Due to the rarity of this complication of CD, we aimed to describe the clinical features, presentation, and of small bowel neoplasms (SBN) in patients with CD.

Methods: A case-control study was performed to include patients ≥18 years old with a diagnosis of CD with or without SBN at a single large referral center from January 1992 to May 2023. Patients were identified using bioinformatics and natural language processing tools, as well as anatomic pathology records. Two age- and sex-matched controls were identified for each case.

Results: In total, 54 patients with CD and SBN and 108 patients with CD without SBN were identified. Of the cases, most had ileal CD (55.6%) with stricturing (59.3%) phenotype. Median duration of CD prior to SBN diagnosis was 19.5 years. Nonpenetrating/nonstricturing behavior (odds ratio [OR], 9.23; 95% CI, 2.91-29.32; $P = .0008$) was significantly associated with an increased odds of SBN. History of tobacco use (OR, 0.27; 95% CI, 0.13-0.60; $P = .0011$) and IBD-associated colonic neoplasia (OR, 0.18; 95%, CI 0.4-0.85; $P = .0303$) were protective in development of SBN.

Conclusions: Nonpenetrating/nonstricturing CD appeared to raise SBN risk. History of tobacco use and colonic IBD-associated neoplasia are associated with reduced risk of SBN. Further studies with large sample sizes are needed to determine true incidence and risk factors associated with SBN in CD and assess potentially protective effects of early surgery.

Lay Summary

Nonpenetrating/nonstricturing and stricturing (only) Crohn's disease may be associated with increased odds of small bowel neoplasia, while penetrating disease did not seem to be a risk factor. History of tobacco use and inflammatory bowel disease-associated colorectal neoplasia showed reduced small bowel neoplasia risk.

Key Words: Crohn's disease, inflammatory bowel disease, ileal neoplasm, malignancy

Introduction

Although the small bowel (SB) accounts for approximately three-quarters of the length and 90% of the mucosal surface of the digestive tract, SB cancer is rare, accounting for an estimated 0.6% of all new cancer cases in the United States in 2020.[1,2] The Surveillance, Epidemiology, and End Results program recently estimated that its incidence has been increasing, with a study in the United States reporting an annual increase in incidence of 1.3%.[3,4] SB cancer has 5 major subtypes: adenocarcinoma, neuroendocrine tumor, sarcoma, gastrointestinal (GI) stromal tumor, and lymphoma, of which SB adenocarcinoma is the most common type.[2]

The first case of SB carcinoma in Crohn's disease (CD) was reported by Ginzburg in 1956.[5] Since that time, there have been numerous case reports, case series, retrospective reviews, and cohort studies which have sought to define the occurrence and incidence of small bowel neoplasm (SBN) in CD. SB adenocarcinoma and associated death are more common among patients with inflammatory bowel disease (IBD) compared with the general population.[6] The ileum is the most common site of CD involvement[7] and those who have ileal, or any small intestinal involvement are at a significantly increased risk of developing SB adenocarcinoma with a relative risk of 18-33.2 and standardized incidence ratio of 22. As compared with sporadic SB adenocarcinoma which occurs evenly distributed throughout the SB, SB adenocarcinoma in CD is primarily found in the ileum.[8]

The relative risk of developing carcinoma of the SB in patients with CD has been estimated to range from 6 to 320.[9–11] Jess et al. evaluated a population-based cohort of 374 patients from Copenhagen County, Denmark, with CD to determine the long-term risk of intestinal and extra-intestinal malignancies. The risk of SB cancer was increased more than 60-fold compared to the general population.[12] Estimates from a US cohort in Olmsted County, MN, have reported a 40-fold increase in risk of SB adenocarcinoma in a cohort of 692

Received for publication: August 30, 2024. Editorial Decision: December 10, 2024

patients with CD.[13] A meta-analysis of 5 population-based studies reported that the pooled relative risk of SB adenocarcinoma was 27.1 (95% CI, 3.4-66.7) compared with the general population.[14]

Despite the increased relative risk of SB adenocarcinoma in CD, the absolute risk remains low at 0.3 cases per 1000 patient-years, and thus screening or active surveillance is not currently recommended.[8,15] There are no current prospective studies to inform the value of surveillance, but case reports and series of SB adenocarcinoma are usually in patients who have not had prior resection, had long disease duration, and often presented with new obstructive symptoms.[16,17]

The prognosis for SB adenocarcinoma in patients with CD, particularly those with ileal or SB involvement, is generally poor but can vary based on several risk factors. Patients with CD-associated SB adenocarcinoma often present at an earlier stage compared to those with sporadic SB adenocarcinoma. This earlier detection can lead to better outcomes. For instance, Wieghard et al. found that patients with CD-associated SB adenocarcinoma had a better 5-year overall survival rate of 43% compared to 34% for de novo SB adenocarcinoma.[18] However, the cancer-specific survival was similar between the 2 groups.[18]

Fields et al. indicated that CD itself is not an independent risk factor for mortality in SB adenocarcinoma, with similar overall survival rates between Crohn's-associated and sporadic cases.[19] Factors such as younger age at diagnosis, tumor location in the ileum, and poorly differentiated tumors are more common in CD-associated SB adenocarcinoma, which can influence prognosis.[19] Despite these findings, the overall prognosis remains poor, with a 5-year overall survival rate of around 29% for CD-associated SB adenocarcinoma patients.[20] Advanced disease at diagnosis, lymph node involvement, and metastasis are common and significantly impact survival rates.[7] Common treatment options for SB adenocarcinoma in patients with CD, particularly those with ileal or SB involvement, include a combination of surgical resection, adjuvant chemotherapy, systemic chemotherapy for advanced disease, as well as emerging targeted and immunotherapy options.[21]

SB adenocarcinoma is typically reported as a complication in SB CD with chronic inflammation as a risk factor, especially among patients with long-term SB disease.[20] The prevalence is estimated at 0.08%-5% of patients with CD.[19,22–24] There have been several published case reports as well as multiple retrospective reviews and cohort studies which have attempted to define the occurrence of SB carcinoma in CD and potential risk factors.[16,25,26] Prior studies have suggested male predominance,[6,27] tobacco use, longstanding disease duration,[28–30] penetrating disease behavior,[6,31] prior SB resection,[27] or therapy for CD[27,32] as risk factors. These findings, however, are limited by small sample size.

Due to the lack of information on this rare, but fatal complication of CD, we sought to retrospectively review our institutional experience to better describe clinical features and presentation, outcomes, and incidence of SBN in patients with CD.

Materials and Methods

Patient Population

This retrospective study was approved by our Institutional Review Board. Using bioinformatics and natural language processing tools to search the electronic medical record, all adult (≥18 years old) patients were identified using ICD-9 and ICD-10 diagnostic codes for CD with SBN who underwent at least 1 endoscopic procedure at our institution between January 1992 and May 2023. This was followed by manual review of individual patients charts as permitted by Minnesota Health Records Act, 144.295, which allows patients to opt out of retrospective research.

In patients with a confirmed CD and SBN diagnosis, we then abstracted relevant demographic, clinical, radiographic, endoscopic, and histologic outcomes, including location and type of SBN. The date of first visit for IBD diagnosis (index) was recorded. We excluded patients without confirmed CD or SBN diagnosis; presence of SB neuroendocrine tumor or GI stromal tumor; absence of a diagnostic endoscopic procedure on file prior to SBN diagnosis; and less than 1 follow-up visit at our central institutional site following index visit.

Case-Control Definitions

For patients with CD and SBN, date of diagnosis, type and location of SBN, presenting symptom associated with SBN diagnosis, and outcomes were recorded. The comparison group was identified from well-annotated anatomic pathology database reports of patients with CD who underwent prior surgical intervention for SB CD. Two age- and sex-matched controls were identified for each case.

Patient and CD Characteristics

CD was diagnosed based on clinical diagnostic criteria as per the treating gastroenterologist and review of the medical record for confirmation of characteristic endoscopic, radiographic, and/or histologic findings. The date of IBD diagnosis was defined by the earliest pathologic confirmation at our institution.

CD characteristics included extent of disease involvement, disease behavior, medical therapies at the time of CD diagnosis, and history of prior SB stricture.

Related complications such as upper GI involvement or perianal disease, personal history of primary sclerosing cholangitis (PSC), former or current tobacco use, personal history of IBD-associated neoplasia, and prior CD-related surgery predating SBN diagnosis were abstracted.

Small Bowel Neoplasm

Location, type, and size of SBN were noted. The presenting symptoms associated with diagnosis of SBN were recorded in addition to the modality used to diagnose SBN—endoscopy, cross-sectional imaging, or at the time of surgery. Medical therapies used for the treatment of CD at the time of SBN diagnosis were noted. Additional SBN characteristics were abstracted including histologic grade, association with stricture or fistula, lymph node involvement, and presence of metastatic disease. Use of adjuvant chemotherapy for SBN was noted. Recurrence of SBN was recorded in addition to time to recurrence for this subset of patients.

Statistical Analysis

Patient characteristics and clinical data were presented as mean with standard deviation, median with range, or frequency with percentages. Descriptive statistics were used to report findings. Categorical variables were reported as a unique count and percentage of the sample. Univariate analysis of

clinical characteristics and associated risk of SBN were reported as odds ratios (ORs) with 95% CI and *P*-value < .05 denoting statistical significance. Statistical software used for analysis included SAS version 9.4 and R version 4.2.2.

Results

The initial data search identified 294 patients with suspected diagnoses of CD and SBN. After manual review, 54 patients were included in the final analysis, and 240 were excluded due to absence of CD and/or SBN diagnoses, neuroendocrine tumor diagnosis, absence of endoscopy on file prior to SBN diagnosis, and less than 1 follow-up visit at our central institutional site.

Controls (patients with CD without SBN diagnosis) were identified from well-annotated pathology records. All controls had prior surgical intervention for symptomatic CD (Figure 1).

Demographics

Baseline characteristics including demographic data and median follow-up time are summarized in Table 1. In total, 54 cases (patients with CD and SBN diagnoses) and 108 controls (patients with CD without SBN diagnosis) were identified. Of the cases (35.2% female), the median age at CD diagnosis was 34.1 years (range, 19.2-49.9 years). A majority of cases had ileal CD (55.6%) and stricturing disease behavior (59.3%), but only 3 (4.2%) had upper GI involvement and 11 (20.4%) had perianal disease. The presence of SB stricture prior to SBN neoplasm diagnosis was noted in 33 cases (61.1%) and 74 controls (68.5%). Seventeen cases (31.5%) had a prior IBD-related surgery predating SBN diagnosis. None of the cases had PSC. Two cases (3.7%) had a personal history of colonic IBD-associated neoplasia, and 5 cases (9.3%) had a family history of colorectal neoplasia. Sixteen cases (29.6%) had a history of tobacco use as outlined in the electronic medical record.

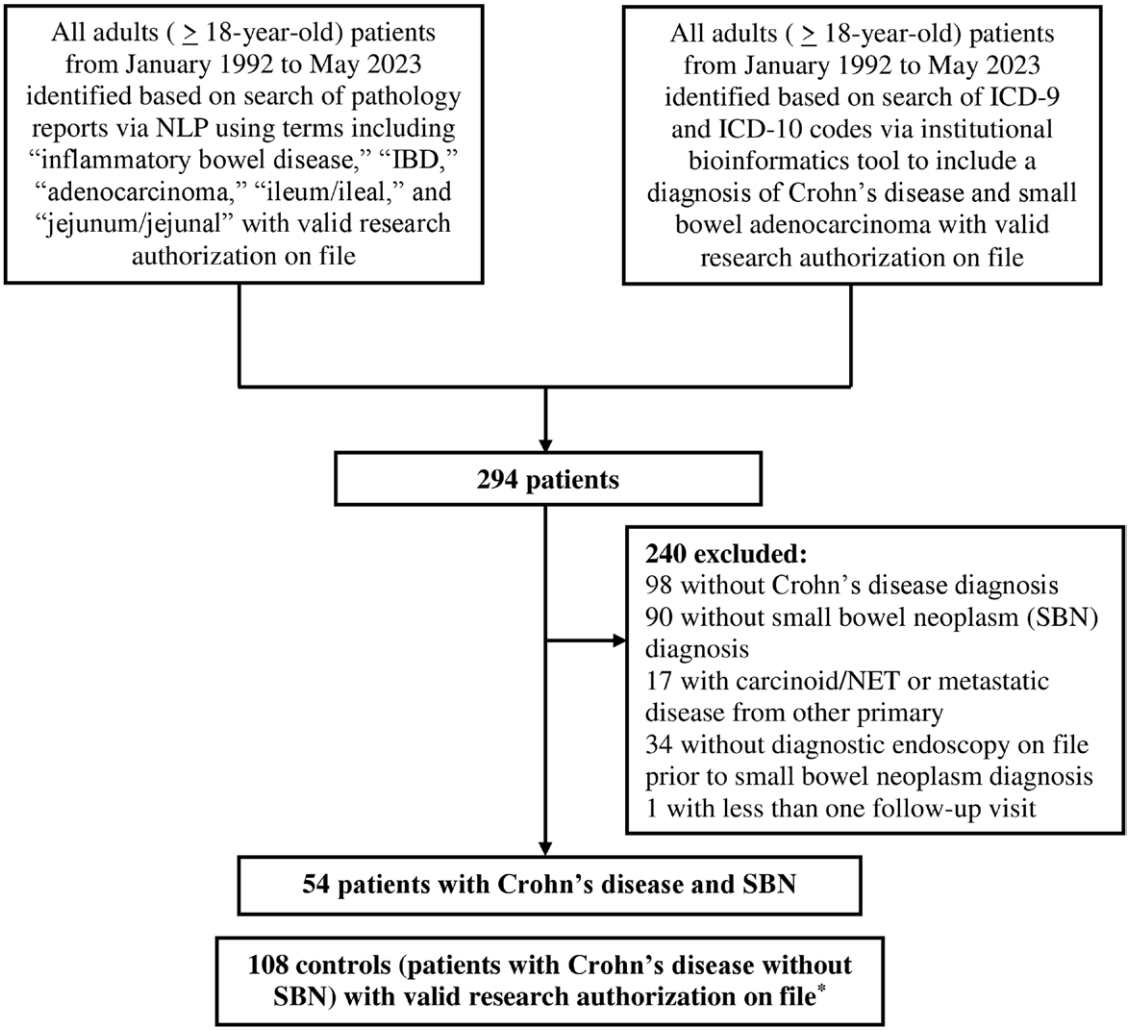

Figure 1. Screening of patients for study inclusion. Utilizing an anatomic pathology natural language processing, institutional bioinformatics search tool, and anatomic pathology records, all adult (≥18 years old) patients were identified using a combination of search terms including "inflammatory bowel disease," "IBD," "adenocarcinoma," "ileum/ileal," and "jejunum/jejunal" and ICD-9/ICD-10 codes for diagnoses of Crohn's disease and small bowel neoplasm who had a valid research authorization on file. A total of 240 patients were excluded. *Controls were identified from anatomic pathology records. All controls had prior surgery for small bowel Crohn's disease.

SBN Characteristics and Outcomes

The median age at SBN diagnosis was 56.5 years (range, 30-78 years) and median duration of CD at the time of SBN diagnosis was 19.5 years (range, 0 days to 53 years) (Table 2). Most patients had SB adenocarcinoma (87.0%) located in the ileum (75.9%). The most common presenting symptom associated with SBN diagnosis was obstruction (51.9%) followed by abdominal pain (25.9%). SBN was most often diagnosed at the time of surgery (61.1%), followed by endoscopy (9.7%) and cross-sectional imaging (9.7%). At the time of SBN diagnosis, patients were on several types of medical therapies for CD including immunomodulators (7.4%), biologic agents (7.4%), corticosteroids (5.6%), and 5-aminosalicylate agents (5.6%).

Fifty patients (92.6%) underwent surgical resection for management of SBN (Table 2). Twenty-one patients (38.9%) had lymph node involvement, and 22 patients (40.7%) had metastatic disease at the time of SBN diagnosis. Thirty-one patients (57.4%) received neoadjuvant chemotherapy. Eight patients (14.8%) had recurrence of SBN with median time to recurrence of 20 months.

There were significant associations between odds of nonstricturing/nonpenetrating (OR, 9.23; 95% CI, 2.91-29.32; $P = .0008$) and stricturing (OR, 3.05; 95% CI, 1.19-7.83; $P = 0.0008$) disease behavior being associated among cases with SBN relative to penetrating disease (OR, 1 (reference)) behavior (Table 3). There was a significant difference in the odds of history of tobacco use (OR, 0.27; 95% CI, 0.13-0.60; $P = .0011$) and history of colonic IBD-associated neoplasia (OR, 0.18; 95% CI, 0.4-0.85; $P = .0303$) and SBN. The associations between odds of CD extent or age at CD diagnosis and SBN were not significant.

Discussion

In this case-control study of patients with CD and SBNs, nonstricturing/nonpenetrating disease behavior was associated with an increased likelihood of developing SBN relative to penetrating disease behavior. Tobacco use and a history of colonic IBD-associated neoplasia may be protective against the development of SBN in the setting of CD. These findings may potentially suggest heightened

Table 1. Baseline demographics and clinical characteristics

	Case ($N = 54$)	Control ($N = 108$)
Female sex, *n* (%)	19 (35.2)	42 (38.9)
Former/current tobacco use, *n* (%)	16 (29.6)	62 (57.4)
Primary sclerosing cholangitis, *n* (%)	0 (0.0)	1 (0.9)
Personal history of IBD-associated neoplasia, *n* (%)[a]	2 (3.7)	17 (15.7)
Family history of colorectal neoplasia, *n* (%)	5 (9.3)	5 (4.6)
Age at Crohn's disease diagnosis (y)		
Median (range)	34.1 (19.2-49.9)	35.2 (22.7-51.4)
Extent of Crohn's disease involvement, *n* (%)		
Ileal	30 (55.6)	52 (48.1)
Colonic	2 (3.7)	1 (0.9)
Ileocolonic	22 (40.7)	55 (50.9)
Upper GI involvement, *n* (%)	3 (4.2)	4 (3.7)
Crohn's disease behavior, *n* (%)		
Nonstricturing/nonpenetrating	16 (29.6)	8 (7.4)
Stricturing	32 (59.3)	62 (57.4)
Penetrating	6 (11.1)	38 (35.2)
Perianal disease, *n* (%)	11 (20.4)	22 (20.4)
Crohn's disease treatment at time of Crohn's disease diagnosis, *n* (%)		
Corticosteroids	1 (1.9)	5 (4.6)
5-ASA	5 (9.3)	17 (15.7)
Immunomodulator monotherapy[b]	0 (0.0)	3 (2.8)
Biologic[c]	0 (0.0)	5 (4.6)
Unknown	48 (88.9)	78 (72.2)
History of small bowel stricture, *n* (%)	33 (61.1)	74 (68.5)
Prior IBD-related surgery prior to small bowel neoplasm diagnosis, *n* (%)	17 (31.5)	N/A
Duration of follow-up (y)		
Median (range)	3 (4 days to 26 years)	8 (6 days to 27 years)

Percentages were calculated on the basis of those with data available. Abbreviations: IBD, inflammatory bowel disease; GI, gastrointestinal; 5-ASA, 5-aminosalicylate; N/A, not applicable.
[a]Duration of time between IBD-associated neoplasia and small bowel neoplasm diagnosis was 5-7 years.
[b]Immunomodulators included azathioprine, methotrexate, or 6-mercaptopurine.
[c]Biologics included infliximab, adalimumab, certolizumab, natalizumab, vedolizumab, ustekinumab, and/or risankizumab.

Table 2. Small bowel neoplasm characteristics and outcomes

	Case ($N = 54$)
Age at small bowel neoplasm diagnosis (y)	
Median (range)	56.5 (30-78)
Duration of Crohn's disease at time of small bowel neoplasm diagnosis (y)	
Median (range)	19.5 (0 days to 53 years)[a]
Type of small bowel neoplasm, *n* (%)	
Adenocarcinoma	47 (87.0)
Signet ring	7 (13.0)
Location of small bowel neoplasm, *n* (%)	
Jejunum	9 (16.7)
Ileum	41 (75.9)
Ileocecal valve	4 (7.4)
Presenting symptom associated with diagnosis of small bowel neoplasm, *n* (%)	
Obstruction	28 (51.9)
Abdominal pain	14 (25.9)
Weight loss	5 (9.3)
Hematochezia	1 (1.9)
Anemia	2 (3.7)
Other[b]	3 (5.6)
Unknown	1 (1.9)
Diagnosis of small bowel neoplasm, *n* (%)	
Endoscopy	9 (16.7)
Cross-sectional imaging	9 (16.7)
At time of surgery	33 (61.1)
Unknown	3 (5.6)
Crohn's disease treatment at time of small bowel neoplasm diagnosis, *n* (%)	
Corticosteroids	3 (5.6)
5-ASA	3 (5.6)
Immunomodulator[c]	4 (7.4)
Biologic[d]	4 (7.4)
No treatment	3 (5.6)
Unknown	37 (68.5)
Outcome of small bowel neoplasm diagnosis, *n* (%)	
Surgical resection	50 (92.6)
Small bowel tumor size (cm)	
Median (range)	4 (0.3-25)
Histologic tumor grade of small bowel neoplasm, *n* (%)	
Grade 1	5 (9.3)
Grade 2	13 (24.1)
Grade 3	22 (40.7)
Grade 4	11 (20.4)
Unknown	2 (3.7)
Small bowel neoplasm associations, *n* (%)	16 (29.6)
Stricture	2 (3.7)
Fistula	4 (7.4)
Both	
Lymph node involvement at time of small bowel neoplasm diagnosis, *n* (%)	21 (38.9)
Metastatic disease at time of small bowel neoplasm diagnosis, *n* (%)	22 (40.7)
Adjuvant chemotherapy, *n* (%)	31 (57.4)
Recurrence of small bowel neoplasm, *n* (%)	8 (14.8)
Time to recurrence of small bowel neoplasm (months)	
Median (range)	20 (7-32)

Percentages were calculated on the basis of those with data available.
Abbreviation: 5-ASA, 5-aminosalicylate.
[a]2 patients had same date of diagnosis for both Crohn's disease and small bowel neoplasm.
[b]Other included perforation, appendicitis, and intra-abdominal abscess.
[c]Immunomodulator included azathioprine, methotrexate, or 6-mercaptopurine.
[d]Biologics included infliximab, adalimumab, certolizumab, natalizumab, vedolizumab, ustekinumab, and/or risankizumab.

surveillance and awareness of this rare and often poorly recognized complication of CD, tailored based on the presence of risk factors.

Numerous risk factors for developing SBN in CD have been proposed and studied in the literature. Long disease duration is a well-established risk factor for SBN in CD.[12,22] The risk of SBN may also be associated with anatomic location of CD.[16,33] For example, the OR of developing SB carcinoma was found to be much higher among 363 patients whose disease was confined to the SB (relative risk [RR] = 158.5) than among 507 patients with ileocolonic CD (RR = 83.8).[34] In our present study, SBN was often associated with longer disease duration; however, disease extent in the case and control groups was comparable, rendering this factor not statistically significant. Penetrating disease behavior did not seem to be a risk factor for SBN based on our cohort, but nonpenetrating/nonstricturing disease appeared to raise SBN risk (OR, 9.23; 95% CI, 2.91-29.32; $P = .008$). This may be a result of longer disease course prior to development of complications, undertreatment, or less likelihood of resection in these patients.

Protective factors against development of SBN in CD have been less frequently studied. In a study of 29 patients with CD and SB carcinoma, Piton et al. found that SB resection and prolonged use of salicylates may protect against SB carcinoma in CD patients.[35] In our study, tobacco use was found to be protective against SBN. All controls underwent surgical intervention for symptomatic CD, which is often the result of a more severe or refractory disease phenotype. About 57.4% of controls had former/current tobacco use in comparison to 29.6% of cases. Tobacco use is generally considered a risk factor for the development and progression of CD and its complications, including SBN. Smoking has been linked to more aggressive disease phenotypes, including structuring and penetrating disease,[36] which are risk factors for SB adenocarcinoma. These differences are the likely explanation for tobacco use being a protective factor against the development of SBN in this study. A history of IBD-associated colonic neoplasia was also found to be a protective factor in our study. More patients in the control group had a prior history of IBD-associated colonic neoplasia (15.7% vs 3.7%) and ileocolonic disease (50.9% vs 40.7%) in comparison to cases. Colonic neoplasia often leads to more intensive surveillance and management strategies that can mitigate the risk of SBN, which may account for this being a protective factor.

Table 3. Univariate conditional logistic model of clinical characteristics on risk of small bowel neoplasm

Clinical characteristc	Odds ratio (95% CI)	*P*-value
Crohn's disease extent		
Colonic	2.98 (0.25-35.12)	.3206
Ileocolonic	0.70 (0.34-1.41)	
Ileal	1.0 (reference)	
Crohn's disease behavior		
Nonstricturing/nonpenetrating	9.23 (2.91-29.32)	.0008
Stricturing	3.05 (1.19-7.83)	
Penetrating	1.0 (reference)	
History of small bowel stricture	0.73 (0.37-1.43)	.3539
Former/current tobacco use	0.27 (0.13-0.60)	.0011
History of IBD-associated neoplasia	0.18 (0.4-0.85)	.0303
Age at Crohn's disease diagnosis, per 10 years	0.87 (0.70-1.08)	.2093

Abbreviations: IBD, inflammatory bowel disease; CI, confidence interval.

There is also emerging data that early ileocecal resection for CD is associated with improved long-term outcomes compared with medical therapy[37–39] and may be utilized as a treatment strategy in select patients with stricturing or penetrating ileocolonic CD. Early surgery for SBN in patients with CD can mitigate chronic inflammation, reduce postoperative morbidity, decrease the need for emergency surgery, improve long-term outcomes, and enhance surveillance and management, leading to better overall patients outcomes. Early surgical intervention can remove segments of the bowel that are chronically inflamed, thereby reducing the ongoing inflammatory stimulus that can lead to dysplasia and subsequent adenocarcinoma. Chronic inflammation is a well-known risk factor for cancer development in CD.[31,32] Early surgery, particularly for luminal disease, is associated with lower rates of postoperative complications compared to surgery performed for complicated disease, such as strictures or fistulas. This can lead to better overall outcomes and reduced mortality.[40] By addressing disease complications early, elective surgery can prevent the need for emergency surgical interventions, which are associated with higher morbidity and mortality rates.[40,41] Early surgical resection has been associated with a lower cumulative risk of reoperation and reduced need for immunomodulators in the years following surgery. This suggests a more favorable long-term disease course and potentially better quality of life for patients.[41,42] Patients who undergo early surgery are often placed under more rigorous postoperative surveillance, which can facilitate early detection of any recurrent or new neoplastic lesions, thereby improving overall prognosis.[31,32]

There are also several limitations to our study. This retrospective study was conducted at a tertiary/quaternary referral center and included a time period spanning over several years from 1992 to 2024. A majority of this time predates current CD treatment options and goals of therapy to include mucosal healing. Treatment targets, guidelines, and diagnostic modalities (including imaging and endoscopic techniques) have also changed during this time period. It is important to note that while retrospective studies are a useful tool for exploring clinical outcomes, these can also be associated with several limitations including incomplete or missing data. As these types of studies often span long periods of time, medical practices, diagnostic criteria, treatments, and even patient populations may change over time, introducing variability and making it difficult to interpret trends or results. Therefore, this may result in findings that may not be relevant or generalizable to current clinical practices or patient populations. However, given the rarity and poor prognosis associated with this complication of CD, it is important to understand the potential risk factors associated with this complication to improve patient outcomes and fill gaps in current knowledge.

The inclusion of controls with prior surgical intervention for symptomatic CD was intended to capture a cohort of patients who have experienced a more advanced or severe form of disease. We recognize that using patients with a history of surgical intervention as controls could introduce potential bias. Surgical intervention for symptomatic CD is typically reserved for patients with more severe or refractory disease, which could make this group inherently different from those with milder forms of the disease. This could potentially affect the generalizability of the findings, as the controls may represent a patient population with more severe disease compared to those who have not undergone surgery. As a result, surgical intervention could not be evaluated as a potential and as a result, this could not be evaluated as a potential risk or protective factor in the development of SBN in patients with CD.

Conclusion

Nonpenetrating/nonstricturing and stricturing CD behavior appeared to raise SBN risk, while penetrating disease behavior did not seem to be a risk factor. This may be a result of longer disease course before the development of complications, less need for surgical resection, and/or possible undertreatment. A history of IBD-associated colonic neoplasia and former/current tobacco use were associated with reduced risk of SBN. Smoking predisposes to the development of stricturing and/or penetrating disease and neoplasia often results in more frequent surveillance. Further studies with large sample sizes are needed to determine true incidence and risk factors associated with SBN in CD and assess the potentially protective effects of early surgery.

Author Contributions

S.A.U.: Literature search, data collection and interpretation, formation of figures and tables, and drafting of manuscript. T.C.S.: Data collection and critical review of manuscript. W.S.H.: Data collection and analysis and critical review of manuscript. E.V.L.: Literature search, data interpretation, and critical review of manuscript. J.B.K.: Literature search, study design, data interpretation, and critical review of manuscript. N.C.-P.: Literature search, study design, data interpretation, and critical review of manuscript.

Funding

No specific funding or grant support received.

Conflicts of Interest

S.A.U.: Discloses no conflicts. T.C.S.: Discloses no conflicts. W.S.H.: Discloses no conflicts. E.V.L.: Consulting for AbbVie, Amgen, Astellas, Bristol-Myers Squibb, Boehringer Ingelheim, Celltrion Healthcare, Eli Lilly, Fresenius Kabi, Genentech, Gilead, GlaxoSmithKline, Iterative Scopes, Janssen, Morphic, Ono Pharma, Sun Pharma, Surrozen, Takeda, UCB. Research support from AbbVie, AstraZeneca, Bristol-Myers Squibb, Celgene/Receptos, Genentech, Gilead, Janssen, Takeda, and UCB. Shareowner Exact Sciences and Moderna. J.B.K.: Research funding and intellectual property licensed to Exact Sciences. N.C.-P.: Research funding from Fujifilm, Cook Endoscopy, and Alexion Pharma.

Ethical Considerations

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

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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