Detection rate and outcome of colonic serrated epithelial changes in patients with ulcerative colitis or Crohn's colitis

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SUMMARY

Background—Chronic ulcerative colitis (CUC) and colonic Crohn's disease (CD) increase colorectal neoplasia (CRN) risk. While sessile serrated polyp (SSP) is a known cancer precursor, serrated epithelial changes (SEC) are of uncertain prevalence and neoplastic risk.

Aim—To assess the serrated lesion detection rates in CUC and CD and documented incidence of subsequent CRN in a retrospective, single-centre cohort study.

Methods—Patients were identified by a central diagnostic index and pathology review confirmed SEC, SSP, CUC and CD diagnoses from 2006–12. Matched controls were identified from among all CUC and CD patients having colonoscopy during the second half of the time period. All were followed for incident CRN, estimated by the Kaplan–Meier method.

Results—Between 2006 and 2012, 79 SEC and 10 SSP cases were identified. Detection rates were estimated to be 10/1000 and 2/1000 patients, for SEC and SSP respectively, among 4208 unique CUC or CD patients having colonoscopy from 2010–12. With only 10 cases, SSP patients were not further analysed. Cumulative incidence of subsequent CRN at 1 and 3 years was 12% (95% CI, 0–30%) and 30% (3–57%), respectively, in SEC patients compared to 4% (0–12%) and 9% (0–23%), respectively, in CUC or CD controls ($P = 0.047$, log-rank). However, this statistical difference was not significant after patients were stratified for history of prior or synchronous dysplasia ($P = 0.09$).

Conclusions—Serrated epithelial changes and sessile serrated polyps are uncommonly detected by colonoscopy in chronic ulcerative colitis and Crohn's disease patients. Histology with changes

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SUPPORTING INFORMATION

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of serrated epithelium may be associated with risk of subsequent colorectal neoplasia, however further studies are needed to explore this relationship.

INTRODUCTION

Patients with both chronic ulcerative colitis (CUC) and Crohn's disease (CD) of the colon are at a two to three fold increased risk for development of colorectal cancer (CRC) in comparison to the general population.[1–3] Risk factors for the development of CRN in patients with inflammatory bowel diseases (IBD) include increased disease duration, extent, and age, along with comorbid primary sclerosing cholangitis (PSC).[4–13] By expert consensus, aggressive surveillance with white light colonoscopy or dye-enhanced chromoendoscopy with random colonic mucosal biopsies is recommended in patients with long-standing (8 years or greater) CUC and CD involving more than 1/3 of the colon.[11, 14–18]

It is widely accepted that the finding of dysplasia in IBD patients, whether in focal lesions or on random biopsy, warrants either heightened surveillance or prophylactic colectomy.[9–11, 14, 18–20] The same cannot be said about the finding of serrated lesions, as little is known about either the frequency or significance of such lesions in IBD. Lesions with serrated histology are frequently seen in the general population;[21–23] while this heterogenous group includes indolent distal hyperplastic polyps, other serrated lesions such as sessile serrated polyps (SSP, formerly sessile serrated adenoma) and traditional serrated adenomas (TSA) may be precursors in up to 30% of all sporadic CRC.[21, 24–28] Therefore, we are concerned that serrated lesions may play a greater role in IBD carcinogenesis than previously appreciated.

Serrated dysplastic lesions have been reported in mucosa adjacent to CRC in IBD patients.[29] Additionally, DNA markers including mutant *BRAF* and microsatellite instability, typical of the sessile serrated pathway, have been observed in CRCs of IBD patients, even without serrated histological changes.[26] Recently described in IBD,[30] serrated epithelial change (SEC) is a histological finding in which epithelial serrations are characteristically seen in the upper half of the crypt, as is typical of benign hyperplastic polyps.[24, 31] Early observations on the natural history of SEC in IBD are conflicting in their estimates of subsequent CRN risk. Parian, *et al.*, reported that nearly a third of patients with SEC developed subsequent CRN, including CRC;[30] however, Atwaibi and colleagues found no increase in neoplasia risk after adjusting for other clinical predictors.[31]

We measured the cross-sectional rate of diagnosis of serrated lesions in IBD patients, and then conducted a retrospective cohort study to measure rates of subsequent neoplasia in IBD patients with serrated lesions. We hypothesised that although these lesions are reported with increasing frequency, the outcomes of IBD patients with SEC may be influenced by known confounding risk factors including prior or synchronous adenomas.

METHODS

Patients

After Institutional Review Board approval, codes from the Systematised Nomenclature of Medicine Clinical Terms (SNOMED CT) were used to search a centralised pathology database at Mayo Clinic (Rochester, MN) between 2006 and 2012. Using the terms 'colon', 'active chronic colitis', 'inactive chronic colitis', and 'serrated change', potential cases of SEC and SSP were identified. Electronic records were reviewed by a single examiner to confirm CUC or CD, and to confirm the clinical pathologic diagnosis of SEC or SSP as the index lesion, excluding 'hyperplastic' polyps. While ileal resection or ileo-cecectomy for CD was permitted, patients with prior colonic surgery for dysplasia, CRC, or refractory CUC were excluded. Pathology slides from the index diagnosis from all of the remaining patients were all reviewed by a single expert GI pathologist (T. C. S.) to confirm SEC or SSP arising in chronic colitis.

To estimate the frequency of detection for serrated lesions in IBD, the total number of unique patients with CUC and CD undergoing colonoscopy from 2010 to 2012 was enumerated using American Medical Association Current Procedural Terminology (45378, 45380, 45381, 45382, 45384, 45385 and 45386) and International Classification of Diseases (9th Edition) codes (555, 555.1, 555.2, 555.9, 556, 556.1, 556.2, 556.3, 556.4, 556.5, 556.6, 556.8, 556.9). Because all SEC or SSP diagnoses were made by colonoscopy, and all were adults, IBD patients who underwent only flexible sigmoidoscopy were excluded, along with any patient who was not age 18 years or older at the time of endoscopy.

Data abstraction

A single individual extracted demographical data from the electronic medical record including gender, vital status, age at index and smoking history (current, former or past). IBD characteristics including disease type (CUC or CD), duration (in years from diagnosis), and disease extent (proximal or distal to splenic flexure) at index and at historical maximum, and the presence or absence of primary sclerosing cholangitis (PSC), were also abstracted. Colonoscopic data included type of index endoscopy (white light or chromoendoscopy), biopsy method (targeted or random) and the number of subsequent colonoscopies after index. Proximity of serrated lesions to adenomatous dysplasia was classified as 'adjacent' if it was found in the same of pathology specimen bottle. The date of the last colonoscopy or colectomy was used to determine length of follow-up for outcome analyses. The pathology record for each patient was also reviewed for prior adenomatous CRN, presence of synchronous adenomas at the time of SEC or SSP index diagnosis and the, development of subsequent CRN or CRC. To determine if SEC was more likely to segregate with clinical risk factors for CRN and to manually confirm the accuracy of search criteria, clinical variables were also abstracted on 50 IBD patients without SEC or SSP, randomly selected from the list of those undergoing colonoscopy between 2010 and 2012. SEC patients from 2006 to 2012 were frequency matched to 100 control IBD patients on disease type (CD vs. UC), disease extent (left-sided vs. extensive), disease duration (in years) and co-morbid primary sclerosing cholangitis. SEC and control groups were stratified by the presence of previous or synchronous CRN (yes/no) and followed for development of subsequent CRN,

CRC, or colectomy. End-points occurring within 3 months of the index diagnosis were excluded from the analysis to avoid misclassifying an index diagnosis as an end-point. All data were entered into a secure database by the same abstracter (D.H.J).

Statistical analysis

For patients in the outcome analysis, differences in baseline characteristics were assessed by the Wilcoxon rank-sum test for continuous variables; proportions were assessed by the chi-square or Fisher's exact test, where appropriate. Cumulative incidence of subsequent CRN, CRC or colectomy was estimated using the Kaplan–Meier method and reported with 95% confidence intervals (CI).

RESULTS

Detection rate and baseline characteristics

Figure 1 diagrams the flow of patients identified, excluded, re-classified and diagnosed. A total of 79 patients with SEC and 10 with SSP were identified and the number of cases was reported by year (Figure S1). A total of 4208 unique IBD patients underwent colonoscopy between 2010 and 2012. During the same time period, a total of 43 cases of SEC and 9 cases of SSP were found, for an estimated detection rate of 10 per 1000 (95% CI, 8–14) for SEC and 2 per 1000 (1–4) for SSP, respectively.

Median ages at index were 57 years [interquartile range, (IQR) 48–65] and 48 years (IQR 42–57) for the SEC and SSP groups respectively (Table 1). CUC was the predominant form of IBD in SEC (84%) but was less common among SSP cases (40%) ($P = 0.005$). Median disease duration was longer in the SEC group compared to the SSP group at 18 (IQR 10.5–29) and 9.5 (IQR 1.5–22.5) years, respectively. Overall, the median age at IBD diagnosis was 34 years (IQR 25.5–46.5) in SEC and 34.5 years (31–44.75) in SSP. Proportions of patients with extensive disease were similar, 77% in SEC and 70% in SSP. PSC was found in 23 of SEC patients (29%), but was not seen in the SSP cohort. CRN was diagnosed prior to ($n = 19$) or synchronous with ($n = 8$) index lesions in 27 of SEC patients (34%). Six of 27 (22%) had both prior and synchronous dysplasia at index. SEC occurred in the same side of the colon (proximal or distal to splenic flexure) as prior dysplasia in 8 of 19 (42%), and in 11 of 14 (79%) of those with synchronous lesions. In SSP patients, CRN was diagnosed prior to ($n = 2$) or synchronous with ($n = 4$) in 6 of the 10 patients (60%). All SSP lesions were visible and therefore targeted at index colonoscopy; however, only 38% of SEC patients were diagnosed with targeted biopsies, despite similar use of chromoendoscopy (20%) at index in each group. Because only 10 SSP patients were found during the entire study period, outcome analyses were not performed on this group.

The sub-set of IBD patients diagnosed with SEC between 2010 and 2012 was compared to a random sample of IBD patients who had colonoscopy during the same time period (Figure 1c, Table 2). A total of 52 records were reviewed to obtain 50 control patients, demonstrating high accuracy of the search criteria (kappa = 0.96). SEC patients were more likely to have clinical risk factors for CRN. They were older and had longer disease duration. PSC was also more common in SEC patients (28%, $n = 12/43$) compared to 6%

(3/50) controls ($P = 0.005$). A history of prior CRN, the development of subsequent CRN and rate of colectomy were not significantly different between the SEC group and controls.

Incidence of subsequent CRN

The full SEC cohort was then stratified into two groups: those with either prior or synchronous adenomatous dysplasia at index ($n = 27$) or none ($n = 52$). Further chart review excluded 26 patients from analysis of 'to time of subsequent CRN'; 19 were for lack of subsequent endoscopy (3 with prior or synchronous CRN and 16 with none) and 7 developed subsequent CRN within 3 months of index diagnosis (7 with prior or synchronous CRN and 0 with none), leaving a total of 53 SEC patients for analysis of incident CRN (Figure 1d). Control patients with at least one follow-up colonoscopy were matched and stratified by colorectal neoplasia history. CUC was the predominant IBD type. There were no significant differences in median age, sex distribution, IBD subtype, IBD extent, the duration of IBD, or the presence of PSC. Rates of past and current smoking were also similar with the majority of patients in each group being never smokers. Median follow-up to last colonoscopy or colectomy was 24 months (IQR, 16–47) among SEC patients and 31 months (IQR, 19–58) among controls ($P = 0.7$); there were no significant differences when patients were stratified by prior or synchronous CRN history (Table 3).

Fifteen of 53 (28%) SEC patients and 11 of 100 (11%) control patients developed subsequent CRN (Table 4). Among SEC patients, subsequent neoplasia arose in the form of unifocal LGD ($n = 8$), multifocal LGD ($n = 4$), SSA ($n = 1$), traditional serrated adenoma ($n = 1$) and HGD ($n = 1$). No cancers arose in patients with SEC. Ten subsequent lesions were endoscopically visible (91%). Among SEC patients, subsequent CRN occurred on the same side of the colon (proximal or distal to splenic flexure) as the index SEC lesion in only 5 of 11 (45%) cases. Among controls, the subsequent neoplastic lesions included unifocal LGD ($n = 6$), multifocal LGD ($n = 2$), SSA ($n = 1$), HGD ($n = 1$) and CRC ($n = 1$). The single control patient who developed cancer had no history of prior or synchronous CRN.

The cumulative incidence of subsequent CRN at 1 and 3 years was 12% (95% CI, 0–30%) and 30% (3–57%), respectively, in SEC patients was 4% (0–12%) and 9% (0–23%), respectively, in controls ($P = 0.047$, log-rank). However, this difference was not statistically significant following stratification for prior/synchronous CRN history. Thereafter, the cumulative incidence of subsequent CRN at 1 and 3 years was 25% (0–68%) and 60% (5–100%), respectively, in SEC patients with prior/synchronous CRN, and 17% (0–47%) and 31% (0–74%) respectively in controls with prior/synchronous CRN ($P = 0.09$). For those without prior/synchronous CRN, the 1 and 3 year incidence of subsequent CRN was 6% (0–21%) and 17% (0–44%), respectively, in SEC patients compared to 0% (0–0%) and 2% (0–8%), respectively in controls ($P = 0.1$) (Figure 2).

DISCUSSION

With recognition of the serrated pathway in CRC pathogenesis, accurate diagnosis and prognostic assessment of serrated lesions in IBD patients has potentially important clinical relevance. To the best of our knowledge, this is the first full-length report of detection rate and neoplastic risk in IBD patients with SEC. We found a low but increasing prevalence of

lesions with serrated morphology. When compared to control patients from our IBD population, patients in the SEC group were significantly more likely to have conventional risk factors for CRN, including long-standing IBD and PSC. A history of prior or synchronous CRN was associated with a significantly greater cumulative incidence of subsequent CRN. After stratifying for CRN history, the impact of SEC on subsequent neoplasia risk was not statistically significant.

Excluding hyperplastic polyps, serrated lesions now account for up to 13–19% of all sporadic polyps removed at screening colonoscopy, and are encountered more often in the proximal colon and in association with increasing age.[23] Based on diagnostic records at our single centre, the number of serrated lesions diagnosed in IBD patients appears to have risen since 2009 (Figure S1), but the detection rate for these lesions appears to be substantially lower than in the sporadic population at our institution.[23] Because of small numbers in the IBD cohort, this trend should be viewed with caution. Historically, serrated lesions were missed or misclassified in the sporadic setting.[23] As SSPs are reported with increasing frequency, there has been a concordant decrease in the frequency of hyperplastic polyps, suggesting that reclassification may contribute in part to this trend.[23] Based on our findings, serrated lesions are reported less frequently in IBD patients than in sporadic patients at our institution. It is not clear whether serrated lesions in IBD are truly less common or have been historically missed by colonoscopy or by pathology.

Serrated epithelial changes lesions were most frequently found in patients with other conventional risk factors for CRN. This suggests that SEC may represent mucosal injury response, identify patients with significant cumulative inflammatory burden or serve as a marker of future dysplasia. Forty per cent of SEC was identified by chromoendoscopy and targeted biopsies, commonly ordered at our institution for surveillance of IBD patients with prior CRN. While chromoendoscopy may be valuable in detecting flat lesions in IBD[32] it may also result in over-diagnosis of indolent lesions. Because most lesions appear to have been endoscopically visible, at least by enhanced techniques, we have avoided use of the term 'flat serrated change' coined by previous authors.

Limited data are available for comparison. The current literature contains only two case series, published in abstract form, which differ in the assessment of neoplastic risk attributable to SEC.[30, 31] Atwaibi, *et al.*, did not find increased development of subsequent CRN in IBD patients with SEC compared to IBD controls[31], but also did not report on neoplasia history of study patients. Parian, *et al.*, in contrast, found that SEC was significantly associated with both concomitant and subsequent dysplasia.[30] Subsequent dysplasia frequently occurred in the same anatomical location as SEC,[30] a finding we did not confirm. The full reports of these observations have not yet been published, limiting comparisons among study methodology. Future studies of serrated lesions in IBD patients will benefit from a full pathologic review to avoid potential misclassification, a significant problem in serrated lesion diagnosis.[33] Our data are internally consistent; the cumulative incidence of CRN among patients with a history of adenomatous dysplasia in the present study is similar to rates observed in patients with polypoid adenomatous dysplasia history in a prior study from our institution.[34]

We acknowledge several important limitations to this study. The number of patients studied was relatively small but was assembled from all available cases after a rigorous selection process. The sample size may have been underpowered to detect significant effects in multivariate comparisons. Additionally, the detection rate of serrated lesions in IBD patients was estimated from coding and billing records. Because of this, it is possible that we may have missed potential cases. However, all potential case patients were confirmed after review by a senior GI pathologist to ensure appropriate classification. It is also possible that neoplasia history or endpoints were missed or misclassified. To avoid this, we were conservative to include indefinite dysplasia among prior CRN, despite the potential to weaken the differences among groups. Additionally, any CRN found within 3 months of index was not considered for analysis. This minimised the likelihood of counting the index as an endpoint, or including a lesion that was missed at the index colonoscopy. We were also careful to exclude patients with prior history of HGD or CRC from analysis as these patients already met an endpoint that would mandate a significant change in management. We accounted for the variable duration of follow-up among patients by use of the Kaplan–Meier method to measure our pre-defined study endpoint; longer term follow-up is critical to validate these observations. There also appear to be limitations to histology as a stand-alone surveillance tool among high-risk individuals; a control patient developed CRC without any prior dysplasia history. Therefore, new tools, such as molecular markers, should be systematically studied for incremental value in neoplastic risk stratification of SEC lesions in IBD patients.[24, 35]

In summary, these early observations suggest that patients with SEC appear to have other high-risk clinical features, including extensive disease, long-standing disease duration and PSC. As a group, these patients are thus at high risk of subsequent adenomatous CRN; however, much of this risk may be influenced by other risk factors, especially a history of prior adenomatous dysplasia, or adenomatous dysplasia which is synchronous to SEC. Examination of larger studies will be needed to better estimate the effect size of SEC histology on risk of subsequent CRN to inform surveillance guidelines. Additionally, we found low rates of detection of SSP lesions among patients with IBD. Therefore, these results should serve as a catalyst to improve endoscopic recognition of adenomas and SSP, and improve phenotypic and molecular risk stratification of IBD patients at risk for CRN.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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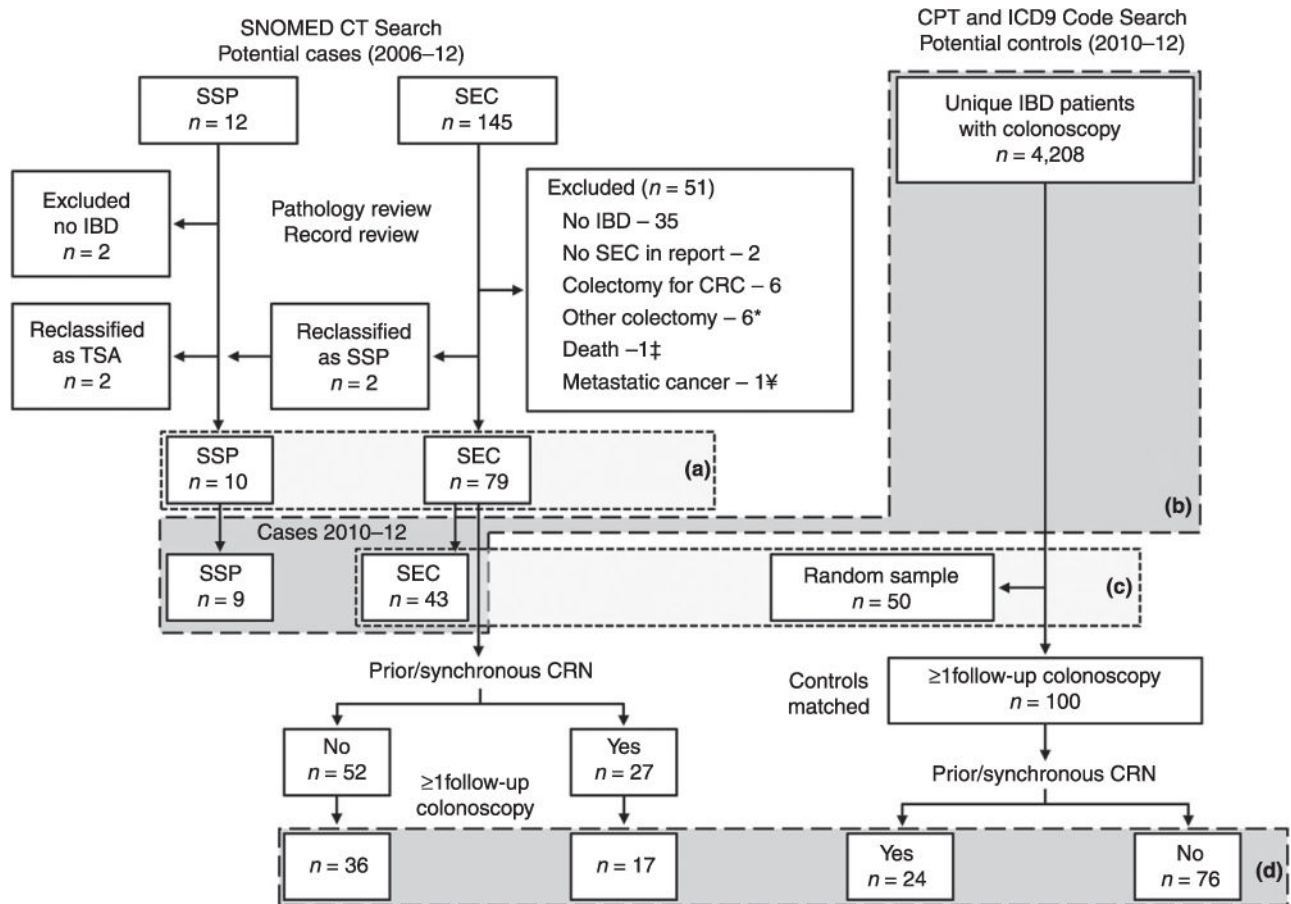
Figure 1.
Flow diagram of patient selection: (a) Characteristics of chronic colitis patients with serrated epithelial changes (SEC) or sessile serrated polyp (SSP), 2006–12 (Table 1); (b) patients included in detection rate calculation; (c) characteristics of serrated epithelial change (SEC) patients and randomly selected control IBD patients undergoing colonoscopy between 2010–12 (Table 2); (d) patients included in time to event analysis (Tables 3, 4 and Figure 2); SNO-Med, systematised nomenclature of medicine; CPT, current procedural terminology (American Medical Association); ICD-9, international classification of diseases (9th Edition); SEC, serrated epithelial change; SSP, sessile serrated polyp; IBD, inflammatory bowel disease; TSA, traditional serrated adenoma. * Non-dysplastic indications; † Immediately after index - Lymphoma; ¥ Ovarian cancer metastatic to the colon.
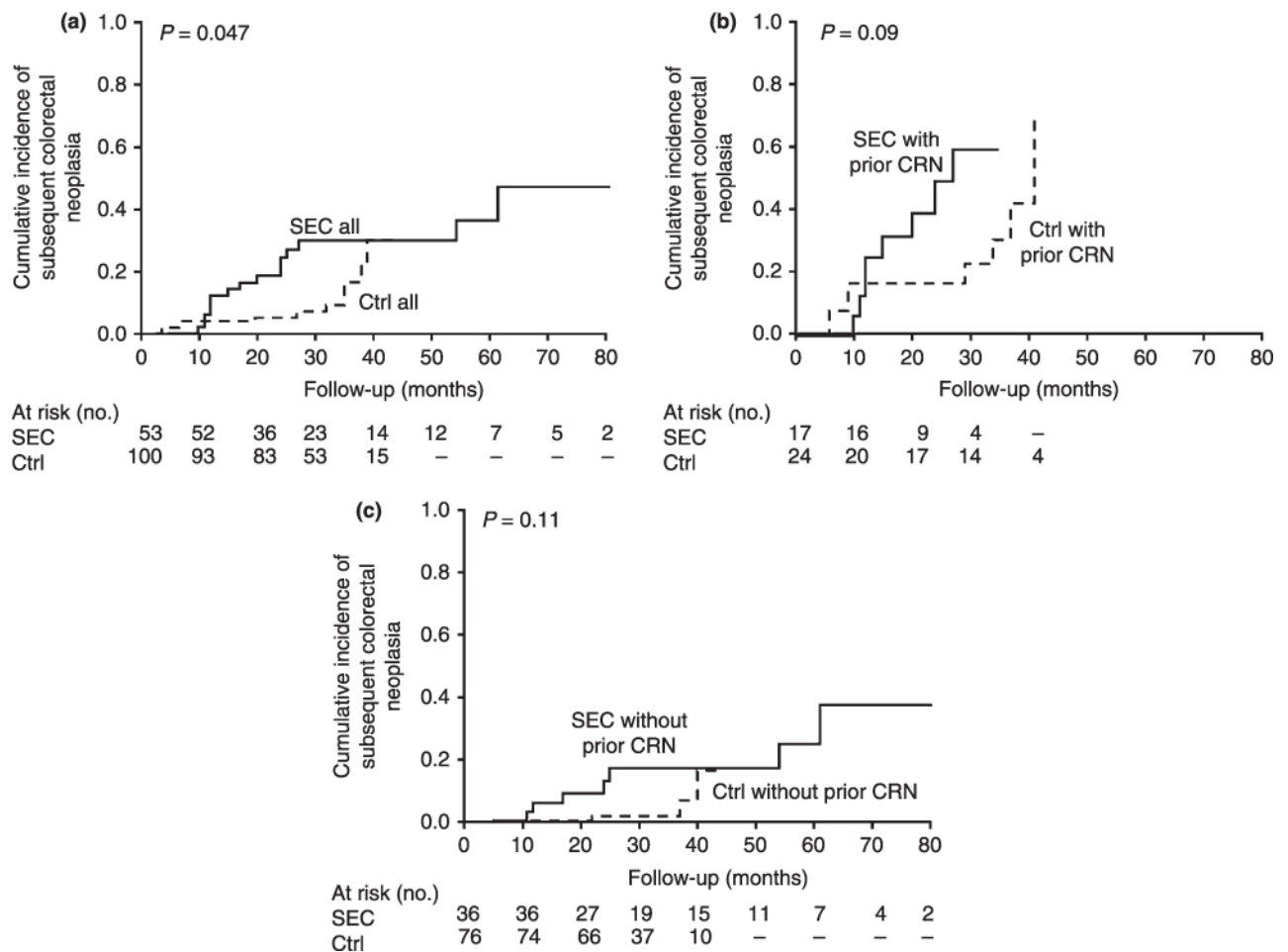
Figure 2.
Cumulative incidence of subsequent colorectal neoplasia (CRN) for: (a) All serrated epithelial change patients (—SEC all) compared to IBD controls (- - Ctrl all); (b) serrated epithelial change patients with a history of prior or synchronous CRN (— SEC with prior CRN) compared to IBD controls with prior CRN (- - Ctrl with prior CRN); and (c) serrated epithelial change patients without history of prior or synchronous CRN (— SEC without prior CRN) compared to IBD controls without prior colorectal neoplasia (- - Ctrl without prior CRN).

Table 1

Characteristics of chronic colitis patients with serrated epithelial change (SEC) or sessile serrated polyp (SSP), 2006–12

	SEC	SSP
N	79	10
Median age, years (IQR)	57 (48–64.75)	48 (41.5–57.25)
Males (%)	49 (62%)	7 (70%)
CUC (%)	66 (84%)	4 (40%)
Median IBD duration at index, years (IQR)	18 (10.5–29)	9.5 (1.5–22.5)
Extensive disease (%)	61 (77%)	7 (70%)
PSC (%)	23 (29%)	0 (0%)
Prior or synchronous CRN (%)	27 (34%)	6 (60%)
Targeted index biopsy (%)	30 (38%)	10 (100%)
Chromoendoscopy at index (%)	16 (20%)	2 (20%)

CUC, chronic ulcerative colitis; PSC, primary sclerosing cholangitis; CRN, colorectal neoplasia.

Table 2

Characteristics of serrated epithelial change (SEC) patients and control IBD patients undergoing colonoscopy between 2010–12

	SEC	Control	*P*-value
N	43	50	–
Median age years (IQR)	58 (47–64)	42 (27.25–60.5)	**0.0014**
Males (%)	22 (51%)	23 (46%)	0.68
CUC (%)	34 (79%)	28 (56%)	**0.03**
Median IBD duration at index, years (IQR)	20 (12–29.5)	7 (3.25–15.75)	**<0.001**
Extensive disease (%)	34 (79%)	37 (74%)	0.63
Prior CRN (%)	15 (35%)	9 (18%)	0.10
Subsequent CRN (%)	7 (16%)	4 (8%)	0.33
Colectomy (%)	4 (9%)	2 (4%)	0.41
PSC (%)	12 (28%)	3 (6%)	**0.005**
Smoking (%)			
Current	2 (5%)	7 (14%)	0.17
Past	17 (40%)	10 (20%)	**0.04**
Never	23 (53%)	30 (60%)	0.54
Unknown	1 (2%)	3 (6%)	0.62

IBD, inflammatory bowel disease; CUC, chronic ulcerative colitis; PSC, primary sclerosing cholangitis; CRN, colorectal neoplasia. Bold values emphasize statistically significant *P* values.

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Table 3

Characteristics of patients included in incidence of subsequent colorectal neoplasia (CRN) analysis

	History of prior or synchronous CRN							
	Without				With			
	SEC	Control	*P*-value		SEC	Control	*P*-value	
N	36	76	–		17	24	–	
Median age years (IQR)	58 (49–64)	54 (51–58)	0.2		59 (51–69)	60 (55–62)	0.9	
Males (%)	22 (61%)	40 (53%)	0.4		11 (65%)	10 (42%)	0.2	
CUC (%)	31 (86%)	57 (75%)	0.2		15 (88%)	18 (75%)	0.4	
Median IBD duration at index, years (IQR)	19 (14–30)	20.5 (11–29)	0.7		14 (10–26)	17.5 (9–22)	0.7	
Extensive disease (%)	30 (83%)	63 (83%)	1.0		12 (71%)	21 (88%)	0.2	
Colectomy (%)	2 (6%)	4 (5%)	1.0		3 (18%)	1 (4%)	0.3	
PSC (%)	11 (31%)	16 (21%)	0.3		4 (24%)	3 (13%)	0.4	
Smoking (%)								
Current	3 (8%)	4 (5%)	0.7		1 (6%)	1 (4%)	1.0	
Past	12 (33%)	17 (22%)	0.3		5 (29%)	12 (50%)	0.2	
Never	21 (58%)	53 (70%)	0.3		10 (59%)	11 (46%)	0.5	
Unknown	0 (0%)	2 (3%)	0.6		1 (6%)	0 (0%)	0.4	
Median follow-up, months (IQR)	31 (19–57)	29 (14–37)	0.2		20 (12–29)	32 (7–37)	0.07	

SEC, serrated epithelial change; IQR, interquartile range; CUC, chronic ulcerative colitis; IBD, inflammatory bowel disease; PSC, primary sclerosing cholangitis.

Table 4

Subsequent colorectal neoplasia events

Neoplasia history	Subsequent CRN	Synchronous lesion	Prior lesion[*]
SEC			
Prior or synchronous CRN			
-Prior only	*N* = 5		
	Unifocal LGD (3)	–	Unifocal LGD (3)
	Multifocal (LGD and SSP)	–	Unifocal LGD
	Multifocal LGD	–	Multifocal LGD
-Prior and synchronous	*N* = 2		
	Unifocal LGD	Unifocal LGD	Unifocal LGD
	Multifocal (HGD and LGD)	Multifocal indefinite	Multifocal indefinite
-Synchronous only	*N* = 1		
	Multifocal LGD	Multifocal LGD	–
None	*N* = 7		
	Unifocal LGD (4)	–	–
	Unifocal TSA	–	–
	Unifocal SSP	–	–
Control			
-Prior CRN	*N* = 8		
	Unifocal LGD (5)	–	Unifocal LGD (5)
	Multifocal LGD (2)	–	Multifocal LGD (2)
	Unifocal HGD	–	Unifocal LGD TVA
None	*N* = 3		
	Unifocal LGD	–	–
	SSP	–	–
	CRC	–	–

SEC, serrated epithelial changes; CRN, colorectal neoplasia; LGD, low grade dysplasia; SSP, sessile serrated polyp; HGD, high grade dysplasia; TSA, traditional serrated adenoma; TVA, tubulovillous adenoma; CRC, colorectal carcinoma.

[*] In patients with multiple prior lesions, most recent is reported.