HHS Public Access

Author manuscript

Dig Dis Sci. Author manuscript; available in PMC 2021 January 01.

Published in final edited form as:

Dig Dis Sci. 2020 January ; 65(1): 111–118. doi:10.1007/s10620-019-05754-9.

Interval Colorectal Cancer in Inflammatory Bowel Disease: The Role of Guideline Adherence

Kristin E. Burke, MD, MPH,
Division of Gastroenterology, Massachusetts General Hospital, Boston, MA, USA

Harvard Medical School, Boston, MA, USA

Jennifer Nayor, MD,
Division of Gastroenterology, Brigham and Women's Hospital, Boston, MA, USA

Emily J. Campbell, MPH,
Department of Medicine, Massachusetts General Hospital, Boston, MA, USA

Ashwin N. Ananthakrishnan, MD,
Division of Gastroenterology, Massachusetts General Hospital, Boston, MA, USA

Harvard Medical School, Boston, MA, USA

Hamed Khalili, MD, MPH,
Division of Gastroenterology, Massachusetts General Hospital, Boston, MA, USA

Harvard Medical School, Boston, MA, USA

James M. Richter, MD
Division of Gastroenterology, Massachusetts General Hospital, Boston, MA, USA

Harvard Medical School, Boston, MA, USA

Abstract

Background: Factors associated with interval colorectal cancer (CRC) development in the inflammatory bowel disease (IBD) population remain unclear.

Corresponding Author: Kristin E. Burke, MD, MPH, Division of Gastroenterology, Massachusetts General Hospital, 55 Fruit Street, Boston, MA 02114, Telephone: 617.726.7933, Fax: 617.726.3080, KEBURKE@mgh.harvard.edu.

Specific author contributions:

Kristin E. Burke – Study conception and design, data acquisition, drafting manuscript, critically revising manuscript
Jennifer Nayor – Data acquisition, critically revising manuscript
Emily J. Campbell – Data acquisition, critically revising manuscript
Ashwin N. Ananthakrishnan – Analysis and interpretation of data, critically revising manuscript
Hamed Khalili – Study conception and design, critically revising manuscript
James M. Richter – Study conception and design, analysis and interpretation of data, critically revising manuscript

Disclosures:

Kristin E. Burke, Jennifer Nayor, and Emily J. Campbell have no conflicts of interest to disclose. Ashwin N. Ananthakrishnan served on the scientific advisory board of Abbvie, Takeda, and Merck. Hamed Khalili receives consulting fees from Abbvie, Takeda, and Samsung Bioepis. James M. Richter is a consultant for Shire Pharmaceuticals.

Aims: Amongst a cohort of patients with interval CRC, we aimed to evaluate IBD characteristics, colonoscopy quality indicators, and surveillance guideline adherence.

Methods: We performed a retrospective review of IBD- and non-IBD-associated interval CRCs diagnosed between January 2007 and December 2014 within a large U.S. healthcare system. We evaluated risk factors for CRC amongst patients with IBD. We assessed adherence to surveillance guidelines according to the American Society for Gastrointestinal Endoscopy (IBD surveillance) and the U.S. Multi-Society Task Force on Colorectal Cancer (polyp surveillance). We compared colonoscopy quality measures between patients with and without IBD.

Results: Amongst 5345 cases of colonic adenocarcinoma, we detected 15 IBD-associated cases of interval CRC, and 230 non-IBD-associated cases of interval CRC. Compared to patients without IBD, IBD patients were younger (54.5 vs. 70.4 years; $p<0.0001$) and experienced a shorter interval between index colonoscopy and CRC diagnosis (20.7 vs. 35.1 months; $p=0.0009$). Fifty three percent (8/15) of interval CRCs in IBD patients were detected within surveillance guidelines. All IBD patients with interval CRC detected after guideline surveillance interval had high-risk features, including active inflammation, previous low-grade or indefinite dysplasia, multiple pseudopolyps on index colonoscopy, or a first-degree relative with CRC. There were no differences in colonoscopy quality measures between patients with and without IBD.

Conclusions: This study stresses the importance of strict short-interval surveillance for IBD patients with high-risk features, including active inflammation on index colonoscopy.

Keywords

Surveillance; Guidelines; Crohn’s disease; Ulcerative colitis; Interval colorectal neoplasia

INTRODUCTION

Colorectal cancer (CRC) surveillance for the patient with inflammatory bowel disease (IBD) presents a special challenge to the practicing gastroenterologist. The risk of colorectal neoplasia in patients with IBD is increased 2–5 times that of age-matched controls based on population-based studies[1–5] and is cited to account for approximately 10–15% of deaths in IBD patients.[6] A 2001 meta-analysis of 54,478 patients with ulcerative colitis across 116 studies described an overall prevalence of 3.7%, with an increasing cumulative probability of cancer with each decade of disease duration.[4] A 2007 meta-analysis of 60,122 patients with Crohn’s disease across 34 studies identified an increased relative risk of CRC of 2.4%, with a strong correlation between location of diseased colon segment and location of colon cancer.[2] In a recent study of CRC outcomes, presence of inflammatory bowel disease was associated with an increased risk of death (hazard ratio, 1.45; 95% CI, 1.29–1.63), compared to sporadic CRC, with particularly worse 5-year survival in individuals under 50 years old with inflammatory bowel disease.[7] These statistics present an imperative to optimize CRC prevention in the IBD population.

Based on these risks, current American Society for Gastrointestinal Endoscopy (ASGE) colorectal cancer surveillance guidelines for IBD recommend the first screening colonoscopy 8 years after disease diagnosis or at the time of diagnosis of PSC, with subsequent surveillance colonoscopies every 1–3 years.[8] Guidelines additionally set a 1-year

surveillance interval for patients with high-risk features, including primary sclerosing cholangitis; a history of dysplasia; active disease, stricture, or multiple pseudopolyps on index colonoscopy; or a family history of CRC in a first-degree relative.[8]

These high-risk features do have a mechanistic basis. Inflamed mucosa transforms into dysplastic tissue under the stress of positive inflammatory regulatory signals, including toll-like receptors and chemokines, and loss of negative regulators, such as IL-10 and transforming growth factor-β.[9] As such, clinical markers of prolonged inflammation, including age at IBD diagnosis, disease duration, and extent of disease (pancolitis for ulcerative colitis and ≥ 50% of colonic involvement for Crohn's disease), are the greatest risk factors for IBD-associated colorectal neoplasia.[10, 11] Inflammation severity is another risk factor for development of colorectal neoplasia in IBD, both at the endoscopic and histologic levels.[12] Pseudopolyp formation, which denotes previous severe inflammation, has been associated with an increased risk of neoplasia in two previous studies, with increased odds of up to 2.5 (95% CI 1.4 – 4.6).[13, 14] Based on accumulation of these factors, the risk of colorectal neoplasia in patients with ulcerative colitis approximates 2% following 10 years of disease, 8% following 20 years of disease, and 18% following 30 years of disease.[4] The risk is less dramatic, but remains proportionately elevated for patients with Crohn's disease. Concurrent primary sclerosing cholangitis (PSC) presents the highest risk for development of IBD-associated colon cancer.[15,16]

Despite guidelines, interval colorectal cancers, cancers that develop before the next recommended surveillance colonoscopy, do occur. In a recent study of 1273 individuals with inflammatory bowel disease undergoing a routine surveillance program in the Netherlands, 1.3% (17 individuals) developed colorectal cancer.[17] All but 5 cancers were attributed to inadequate colonoscopy quality, inadequate surveillance interval, or inadequate management of previous dysplasia. However, in a population subject to frequent endoscopic procedures, the relative contributions of colonoscopy quality and guideline adherence for high-risk IBD features in development of interval colorectal cancer have not been explored.

In a cohort of 245 patients with interval colorectal cancer, we aim to further understand drivers for interval colorectal neoplasia in the IBD population, with specific attention to the roles of colonoscopy quality and high risk clinical IBD features. We describe features associated with interval colorectal neoplasia in the IBD population and assess adherence to ASGE guidelines for cancer surveillance in this population. These guidelines have the most stringent intervals amongst international IBD surveillance guidelines,[8, 18–21] providing a conservative basis for assessment of the role of guideline adherence in development of interval colorectal cancer. We compare non-IBD risk factors (such as cecal intubation rate and preparation) for interval CRC amongst patients with and without IBD.

METHODS

Study Cohort

Utilizing an electronic pathology database, we identified 5345 diagnoses of colonic adenocarcinoma between January 1, 2007 and December 31, 2014 at two large U.S. academic medical centers and an affiliated community hospital. Amongst these, based on

prior studies of interval colorectal cancer, patients who underwent index colonoscopy between 6 months and 5 years before diagnosis of colonic adenocarcinoma were assessed for endoscopist and guideline-recommended follow-up and included in analysis.[22, 23] This cohort has been previously described.[24] Patients with interval CRC were assessed for a history of IBD. For IBD patients, we recorded disease characteristics, including type and location of disease; age at diagnosis; past and current IBD therapies at time of colon cancer diagnosis; presence of pseudopolyps, stricture, or active inflammation on index colonoscopy; previous history of indefinite, low-grade, or high-grade dysplasia; and smoking status. For all patients with interval CRC, we assessed for personal history of colon cancer, family history of colon cancer in a first-degree relative, and presence of a hereditary colon cancer syndrome.

We reviewed the index colonoscopy (the last colonoscopy performed) prior to each case of interval CRC. We recorded the procedure date, the indication, the performing endoscopist, the bowel preparation quality (modified Aronchick Assessment with fair and poor prep considered inadequate), cecal intubation, and the number, size, and location of polyps. For IBD patients, we also noted whether random or targeted surveillance biopsies were performed. We utilized colonoscopy reports, progress notes, and patient results letters to determine the endoscopist-recommended interval follow-up. We reviewed pathology reports from the index colonoscopy to determine polyp histology and presence and location of inflammation. We reviewed pathology from the time of colon cancer diagnosis for date of diagnosis, histologic diagnosis, and location of the cancer.

Assessment of Guideline Adherence

We utilized the ASGE[8] guidelines regarding the role of endoscopy in IBD to determine endoscopic surveillance intervals for patients with IBD (table 1). For all patients with ≥ 8 years of extensive or left-sided disease and no additional high-risk features, we used a surveillance colonoscopy interval of 3 years, consistent with the most lenient interval recommended by the ASGE. We used a surveillance interval of 1 year for all patients with primary sclerosing cholangitis; findings of dysplasia, active inflammation, pseudopolyps, or stricture on index colonoscopy; and first-degree relative with CRC at age < 50.

Appropriate interval follow-up for non-IBD surveillance purposes was determined based on the 2012 U.S. Multi-Society Task Force on Colorectal Cancer surveillance guidelines. The guideline recommendations for each finding are listed in table 1. Interval colon cancer surveillance guidelines are based on of the National Comprehensive Cancer Network.[25] Guideline recommendations are listed in table 1. Patients without documentation regarding colonoscopy preparation, cecal intubation, endoscopist-recommendation of interval follow-up, and polyp pathology were excluded from analysis regarding adherence to guidelines.

Statistical Analysis

We performed descriptive analysis of patients with IBD diagnosed with interval CRC using proportions and means. Index colonoscopy characteristics and non-IBD associated risk factors for CRC were separately analyzed in IBD and non-IBD patients. Categorical variables were described using number and percent, and were compared between groups

using chi-squared tests. Continuous variables were reported as means and standard deviations, and were compared between interval colon cancer patients with and without IBD using t-tests, as all data met criteria for normality.

For IBD and non-IBD patients, we divided cases of interval CRC into two groups: those that were detected before or at (including up to 90 days after) the guideline surveillance interval, and those that were detected at least 90 days after the guideline surveillance interval. We also assessed whether interval CRCs were detected before or at (including up to 90 days after) the endoscopist-recommended surveillance interval. We compared the proportion of patients with and without IBD in each window using chi-squared tests.

We performed all statistical analysis using SAS Studio (SAS Institute Inc., Cary, NC). For all comparative analysis, we considered a two-sided p-value < 0.05 as statistically significant.

Ethical Considerations

This study was approved by the Massachusetts General Hospital Institutional Review Board.

RESULTS

Amongst 39,644 surveillance colonoscopies, 5,345 colon cancers were diagnosed between January 1, 2007, and December 31, 2014. Of these, 245 (4.6%) were interval colorectal cancers. Fifteen of 245 (6.1%) interval CRCs occurred in patients with IBD, while 230 of 245 (93.9%) occurred in patients without IBD. The incidence of interval colorectal cancer was 0.69% (15 cases / 2184 IBD surveillance colonoscopies) in the IBD population and 0.61% (230 cases / 37,460 surveillance colonoscopies) in the non-IBD population.

The disease characteristics of IBD patients with interval CRC are in table 2. Ten of 15 (66.7%) IBD patients had a diagnosis of ulcerative pancolitis. The remainder (5/10; 33.3%) carried a diagnosis of Crohn's disease with either colonic (40.0%) or ileocolonic (60.0%) distribution. Patients had an average IBD duration of 21.1 (SD 12.2) years. Only one patient had concurrent primary sclerosing cholangitis. Two patients had a personal history of colon cancer and two patients had a family history of colon cancer in a first-degree relative. Overall, disease appeared mild, as only 4/15 (26.7%) patients were on biologic therapy at the time of CRC diagnosis. However, 12/15 (80.0%) had active disease, both endoscopically and histologically, at time of index colonoscopy. Five patients had a history of indefinite (2), low-grade (2), or high-grade (1) dysplasia within 5 years of the index colonoscopy.

All IBD patients with interval colorectal cancer underwent index surveillance colonoscopy by white light endoscopy. Thirteen of 15 (86.7%%) individuals underwent random surveillance biopsies, while 1/15 (6.7%) underwent targeted biopsies alone, and 1/15 (6.7%) had both random and targeted biopsies.

On histologic review of the interval colonic adenocarcinoma, 11/15 patients with IBD were confirmed to have IBD-associated CRC on the basis of chronic inflammation at the site of malignancy with or without other foci of low- or high-grade dysplasia either near the adenocarcinoma site or elsewhere in the colon. Two IBD patients were diagnosed with

sporadic colorectal cancer based on pathology. In the remaining two patients, histologic review was unable to differentiate between adenocarcinoma arising from an area of IBD-associated polypoid dysplasia or a sporadic polyp. Ten of 11 patients with confirmed IBD-associated CRC had active IBD at the site of malignancy on index colonoscopy.

Table 3 presents analysis comparing interval between index colonoscopy and CRC diagnosis, age of CRC diagnosis, and known non-IBD-related risk factors for colorectal cancer in patients with and without IBD. As compared to patients without IBD, patients with IBD were significantly younger at age of interval CRC diagnosis (54.5 vs. 70.4; $p<0.0001$). IBD patients also experienced a shorter time from index colonoscopy to interval CRC diagnosis (20.7 months vs. 35.1 months; $p=0.0009$). Both IBD and non-IBD patients experienced similar index colonoscopy quality, as measured by rates of cecal intubation and adequate preparation. They also had similar rates of previous colorectal cancer and family history of colorectal cancer. No patients with IBD carried a diagnosis of a hereditary polyposis syndrome.

Adherence to ASGE IBD-related surveillance guidelines is presented in table 4. A total of 8/15 (53.3%) interval CRCs were detected within surveillance guidelines. Only 2/12 (16.7%) patients with active inflammation on index colonoscopy experienced interval CRC detection within the recommended surveillance window. Only 1/5 (20%) patients with a history of dysplasia within the past 5 years underwent surveillance colonoscopy within 1 year. Neither of the two patients with a family history of CRC underwent 1-year surveillance. Only 1/3 (33.3%) patients with multiple pseudopolyps underwent interval surveillance within 1 year.

The proportion of patients diagnosed before or within the guideline cancer surveillance interval (8/15) was not significantly different than the proportion of non-IBD patients diagnosed before or within the guideline interval (144/230; $p=0.487$). Only 9/15 patients with IBD had a clear, documented endoscopist interval follow-up recommendation at the time of index colonoscopy. Seven of 15 (46.7%) IBD patients were diagnosed with interval CRC before or within the endoscopist-recommended interval. This was not significantly different than the 137/230 (59.3%) non-IBD patients diagnosed before or within the endoscopist-recommended interval ($p=0.336$).

DISCUSSION

In this U.S. multicenter study of interval colorectal cancer involving two academic hospitals and a community-based affiliated hospital, patients with IBD were diagnosed with interval colorectal cancer at a significantly younger age and with a significantly shorter interval from index colonoscopy as compared to patients without IBD. The preponderance of IBD patients with interval colorectal cancer had active disease at the time of index colonoscopy. We found no significant differences in colonoscopy quality measures, including cecal intubation rate and preparation quality, amongst patients with and without IBD.

In our cohort, only 53.3% of patients were diagnosed with interval CRC within the ASGE surveillance window, specifically due to non-adherence to surveillance guidelines for the

subset of non-PSC patients with high-risk features. Our stratified analysis by high-risk features shows that the largest opportunity for improvement is in the surveillance of patients with active disease at time of index colonoscopy. Eighty percent (12/15) of patients with IBD had active disease at the time of their index colonoscopy, 75% (9/12) of whom were diagnosed with interval CRC on colonoscopy that occurred after the 12-month ASGE surveillance guideline interval recommendation. Though the ASGE guidelines are the most stringent of international IBD surveillance guidelines for surveillance of patients with active IBD,[8, 18–21] presence of active inflammation in the majority of IBD patients in our interval CRC population and detection of most cancers outside of the ASGE window support this degree of rigorous surveillance and improved methods of surveillance in this population.

Active disease has been associated with an increased risk of dysplasia in past studies.[12, 26–28] In a case control study of patients with ulcerative colitis, Rutter et al. demonstrated a correlation between both colonoscopic (OR 2.5; P<0.001) and histologic (OR 5.1; P<0.001) inflammation and risk of neoplasia.[28] Rubin et al. also demonstrated multivariable-adjusted increased odds of colorectal cancer of 3.68 (p=0.001) in ulcerative colitis patients with active histologic inflammation as compared to controls, when adjusted for family history of CRC, medications, smoking status, and PSC.[27] A prospective cohort study of patients with ulcerative colitis undergoing dysplasia surveillance demonstrated an advanced neoplasia hazard ratio of 3.4 (95% CI 1.1–10.4) in patients with an increased binary histologic activity score as compared to those without.[12]

The mechanistic basis for progression to colorectal cancer in patients with active IBD is well defined. Inflammatory and dysbiotic signals exert a field effect on constantly re-epithelializing and chronically inflamed tissue, leading to dysplasia.[9, 29] Dysplastic tissue progresses to CRC through molecular pathways including chromosomal instability, microsatellite instability, and the CpG island methylator phenotype (CIMP) pathway.[9, 30–32] In addition to accelerating dysplasia, active inflammation may also hide dysplastic lesions that would otherwise be visible with modern endoscopic techniques.[33, 34] Strict adherence to surveillance of patients with active disease on index colonoscopy is an important component of dysplasia surveillance.

Like patients with active inflammation, only 20% of patients with previous indefinite (2), low-grade (2), or high-grade dysplasia (1) were diagnosed with interval CRC within the 1-year guideline interval. It remains uncontested in the literature that close follow-up of dysplasia is paramount.[16, 33–36] Due to the field effect of inflammation, the presence of dysplasia could indicate the presence of synchronous lesions that may be equivalent to or higher grade than the dysplasia found.[37, 38] Fortunately, advanced imaging techniques, including high-definition endoscopy and chromoendoscopy, have led to the ability to visualize most dysplasia.[33, 34] The recommended management of flat high-grade dysplasia remains surgery, while patients with indefinite or low-grade dysplasia, especially if completely resected, may continue close surveillance with either high-definition endoscopy or chromoendoscopy.[34, 37] Part of this study period occurred prior to the routine use of high-definition imaging for dysplasia surveillance, but emphasizes the importance of strict surveillance.

Our study has many strengths. First, we leveraged a large multicenter cohort from academic institutions that specialize in IBD care to determine the impact of factors on the endpoint of interval colorectal cancer diagnosis, rather than intermediary dysplasia. Studies of interval cancer are critical because they directly evaluate the most concrete clinical endpoint of screening. Second, we were able to utilize colonoscopy quality indicators, including preparation quality and cecal intubation rates amongst patients with interval colorectal cancer both with and without IBD, to evaluate both IBD and non-IBD related risk factors for interval colorectal cancer. Lastly, through our electronic health record, we were able to assess documented provider-recommended interval follow-up to determine if patient or provider factors influenced non-adherence to surveillance guidelines.

Our results must be interpreted within the limitations of our study design. To the benefit of our patients, we identified very few interval colorectal cancers in patients with IBD. Though all patients appeared to be long-term patients within the participating institutions, an intervening colonoscopy performed at an outside institution may have been missed. Colonoscopies were also not graded to objectively assess endoscopic disease severity; as such, disease activity was categorized on a binary basis. Though degree of endoscopic and histologic disease activity is less relevant when interpreting American colorectal cancer surveillance guidelines in IBD,[8, 21] it is a cornerstone of surveillance intervals in European guidelines,[18–20] possibly limiting the generalizability of these findings. Many cases of IBD-associated CRC in this cohort were diagnosed prior to the current American and European guidelines, and would have been found in adherence with previous guideline recommendations. This discrepancy further supports the current guidelines and the need for close surveillance of IBD patients with high-risk features.

In summary, IBD patients with interval colorectal cancer had a significantly younger age of onset and decreased time from index colonoscopy to time of interval CRC diagnosis as compared to patients without IBD. Our findings support active inflammation as an important risk factor for interval colorectal cancer in IBD patients, with opportunity for earlier detection of colorectal cancer or dysplasia through improved surveillance of patients with recent active disease.

ACKNOWLEDGEMENTS

Grant Support:

This work was supported by the National Institute of Diabetes and Digestive and Kidney Diseases at the National Institutes of Health [F32 DK115134 to KEB and K23 DK099681 to HK]; This work was also supported by a career development award from American Gastroenterological Association (AGA) to HK.

REFERENCES

1. Winther KV, Jess T, Langholz E, et al. Long-term risk of cancer in ulcerative colitis: a population-based cohort study from Copenhagen County. Clin Gastroenterol Hepatol 2004;2:1088–95. [PubMed: 15625654]
2. von Roon AC, Reese G, Teare J, et al. The risk of cancer in patients with Crohn's disease. Dis Colon Rectum 2007;50:839–55. [PubMed: 17308939]
3. Bernstein CN, Blanchard JF, Kliewer E, et al. Cancer risk in patients with inflammatory bowel disease: a population-based study. Cancer 2001;91:854–62. [PubMed: 11241255]

4. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut 2001;48:526–35. [PubMed: 11247898]
5. Jess T, Rungoe C, Peyrin-Biroulet L. Risk of colorectal cancer in patients with ulcerative colitis: a meta-analysis of population-based cohort studies. Clin Gastroenterol Hepatol 2012;10:639–45. [PubMed: 22289873]
6. Jewel Samadder N, Valentine JF, Guthery S, et al. Colorectal Cancer in Inflammatory Bowel Diseases: A Population-Based Study in Utah. Dig Dis Sci 2017.
7. Bogach J, Pond G, Esckicioglu C, et al. Age-Related Survival Differences in Patients With Inflammatory Bowel Disease-Associated Colorectal Cancer: A Population-Based Cohort Study. Inflamm Bowel Dis 2019.
8. American Society for Gastrointestinal Endoscopy Standards of Practice C, Shergill AK, Lightdale JR, et al. The role of endoscopy in inflammatory bowel disease. Gastrointest Endosc 2015;81:1101–21 e1–13. [PubMed: 25800660]
9. Sebastian S, Hernandez V, Myrelid P, et al. Colorectal cancer in inflammatory bowel disease: results of the 3rd ECCO pathogenesis scientific workshop (I). J Crohns Colitis 2014;8:5–18. [PubMed: 23664897]
10. Guagnozzi D, Lucendo AJ. Colorectal cancer surveillance in patients with inflammatory bowel disease: What is new? World J Gastrointest Endosc 2012;4:108–16. [PubMed: 22523611]
11. Gillen CD, Walmsley RS, Prior P, et al. Ulcerative colitis and Crohn's disease: a comparison of the colorectal cancer risk in extensive colitis. Gut 1994;35:1590–2. [PubMed: 7828978]
12. Gupta RB, Harpaz N, Itzkowitz S, et al. Histologic inflammation is a risk factor for progression to colorectal neoplasia in ulcerative colitis: a cohort study. Gastroenterology 2007;133:1099–105; quiz 1340–1. [PubMed: 17919486]
13. Velayos FS, Loftus EV Jr., Jess T, et al. Predictive and protective factors associated with colorectal cancer in ulcerative colitis: A case-control study. Gastroenterology 2006;130:1941–9. [PubMed: 16762617]
14. Rutter MD, Saunders BP, Wilkinson KH, et al. Cancer surveillance in longstanding ulcerative colitis: endoscopic appearances help predict cancer risk. Gut 2004;53:1813–6. [PubMed: 15542520]
15. Broome U, Lofberg R, Veress B, et al. Primary sclerosing cholangitis and ulcerative colitis: evidence for increased neoplastic potential. Hepatology 1995;22:1404–8. [PubMed: 7590655]
16. Fumery M, Dulai PS, Gupta S, et al. Incidence, Risk Factors, and Outcomes of Colorectal Cancer in Patients With Ulcerative Colitis With Low-Grade Dysplasia: A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol 2017;15:665–674 e5. [PubMed: 27916678]
17. Mooiweer E, van der Meulen-de Jong AE, Ponsioen CY, et al. Incidence of Interval Colorectal Cancer Among Inflammatory Bowel Disease Patients Undergoing Regular Colonoscopic Surveillance. Clin Gastroenterol Hepatol 2015;13:1656–61. [PubMed: 25956835]
18. Excellence NIfHaC. Colonoscopic Surveillance for Prevention of Colorectal Cancer in People with Ulcerative Colitis, Crohn's Disease or Adenomas London, 2011.
19. Annese V, Daperno M, Rutter MD, et al. European evidence based consensus for endoscopy in inflammatory bowel disease. J Crohns Colitis 2013;7:982–1018. [PubMed: 24184171]
20. Cairns SR, Scholefield JH, Steele RJ, et al. Guidelines for colorectal cancer screening and surveillance in moderate and high risk groups (update from 2002). Gut 2010;59:666–89. [PubMed: 20427401]
21. Farraye FA, Odze RD, Eaden J, et al. AGA technical review on the diagnosis and management of colorectal neoplasia in inflammatory bowel disease. Gastroenterology 2010;138:746–74, 774 e1–4; quiz e12–3. [PubMed: 20141809]
22. Lieberman DA, Rex DK, Winawer SJ, et al. Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2012;143:844–857. [PubMed: 22763141]
23. Erichsen R, Baron JA, Stoffel EM, et al. Characteristics and survival of interval and sporadic colorectal cancer patients: a nationwide population-based cohort study. Am J Gastroenterol 2013;108:1332–40. [PubMed: 23774154]

24. Nayor J, Saltzman JR, Campbell EJ, et al. Impact of physician compliance with colonoscopy surveillance guidelines on interval colorectal cancer. Gastrointest Endosc 2017;85:1263–1270. [PubMed: 27889548]
25. Engstrom PF, Arnoletti JP, Benson AB 3rd, et al. NCCN Clinical Practice Guidelines in Oncology: colon cancer. J Natl Compr Canc Netw 2009;7:778–831. [PubMed: 19755046]
26. Brackmann S, Andersen SN, Aamodt G, et al. Relationship between clinical parameters and the colitis-colorectal cancer interval in a cohort of patients with colorectal cancer in inflammatory bowel disease. Scand J Gastroenterol 2009;44:46–55. [PubMed: 18609187]
27. Rubin DT, Huo D, Kinnucan JA, et al. Inflammation is an independent risk factor for colonic neoplasia in patients with ulcerative colitis: a case-control study. Clin Gastroenterol Hepatol 2013;11:1601–8 e1–4. [PubMed: 23872237]
28. Rutter M, Saunders B, Wilkinson K, et al. Severity of inflammation is a risk factor for colorectal neoplasia in ulcerative colitis. Gastroenterology 2004;126:451–9. [PubMed: 14762782]
29. Choi CR, Bakir IA, Hart AL, et al. Clonal evolution of colorectal cancer in IBD. Nat Rev Gastroenterol Hepatol 2017;14:218–229. [PubMed: 28174420]
30. Konishi K, Shen L, Wang S, et al. Rare CpG island methylator phenotype in ulcerative colitis-associated neoplasias. Gastroenterology 2007;132:1254–60. [PubMed: 17408633]
31. Olaru AV, Cheng Y, Agarwal R, et al. Unique patterns of CpG island methylation in inflammatory bowel disease-associated colorectal cancers. Inflamm Bowel Dis 2012;18:641–8. [PubMed: 21830278]
32. Chakrabarty S, Varghese VK, Sahu P, et al. Targeted sequencing-based analyses of candidate gene variants in ulcerative colitis-associated colorectal neoplasia. Br J Cancer 2017.
33. Leifeld L, Rogler G, Stallmach A, et al. White-Light or Narrow-Band Imaging Colonoscopy in Surveillance of Ulcerative Colitis: A Prospective Multicenter Study. Clin Gastroenterol Hepatol 2015;13:1776–1781 e1. [PubMed: 25952309]
34. Laine L, Kaltenbach T, Barkun A, et al. SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease. Gastrointest Endosc 2015;81:489–501 e26. [PubMed: 25708752]
35. Choi CH, Ignjatovic-Wilson A, Askari A, et al. Low-grade dysplasia in ulcerative colitis: risk factors for developing high-grade dysplasia or colorectal cancer. Am J Gastroenterol 2015;110:1461–71; quiz 1472. [PubMed: 26416190]
36. Sengupta N, Yee E, Feuerstein JD. Colorectal Cancer Screening in Inflammatory Bowel Disease. Dig Dis Sci 2016;61:980–9. [PubMed: 26646250]
37. Farraye FA, Odze RD, Eaden J, et al. AGA medical position statement on the diagnosis and management of colorectal neoplasia in inflammatory bowel disease. Gastroenterology 2010;138:738–45. [PubMed: 20141808]
38. Kiran RP, Khoury W, Church JM, et al. Colorectal cancer complicating inflammatory bowel disease: similarities and differences between Crohn's and ulcerative colitis based on three decades of experience. Ann Surg 2010;252:330–5. [PubMed: 20622662]

Table 1:

Guideline intervals for colonoscopy surveillance in patients with a history of inflammatory bowel disease, colorectal cancer, and previous polyps.

Personal History of Inflammatory Bowel Disease	
History	**Interval Recommendation**
≥ 8 years of left-sided or extensive disease	1–3 years
Primary Sclerosing Cholangitis	1 year
Active inflammation	1 year
History of dysplasia	1 year
Family history of colorectal cancer in first-degree relative < 50	1 year
Multiple pseudopolyps	1 year
Stricture	1 year

No personal history of inflammatory bowel disease or colon cancer	
Finding	**Interval Recommendation**
Normal Colonoscopy, no FH colon cancer	10 years
Normal Colonoscopy, colon cancer in 1st-degree relative	5 years
Adenomas	
1–2 less than 10 mm	5 years
3–10 less than 10 mm	3 years
Any adenoma > 10 mm	3 years
Personal history of polyposis syndrome	1 year
Inadequate preparation (fair or poor)	1 year
Incomplete colonoscopy (did not reach cecum)	Immediate Repeat

Personal History of Colon Cancer	
History	**Interval Recommendation**
First colonoscopy after colectomy for cancer diagnosis	1 year
Index colonoscopy within 4 years of original cancer diagnosis	3 years
Index colonoscopy over 4 years from cancer diagnosis	5 years

Table 2:

Disease characteristics of patients with inflammatory bowel disease diagnosed with interval colon cancer (N=15)

Disease Characteristics	Value
Type of Inflammatory Bowel Disease	
Ulcerative colitis, n (%)	10 (66.7)
Crohn's disease, n (%)	5 (33.3)
Disease Extent (Ulcerative colitis)	
Pancolitis, n (%)	10 (100.0)
Disease location (Crohn's disease)	
Colonic, n (%)	2 (40.0)
Ileocolonic, n (%)	3 (60.0)
Age of IBD diagnosis, mean (SD)	33.5 (11.3)
Primary Sclerosing Cholangitis, n (%)	1 (6.7)
Disease duration at CRC diagnosis, mean (SD)	21.1 (12.2)
Active disease at time of index colonoscopy, n (%)	12 (80.0)
Pseudopolyps on index colonoscopy, n (%)	3 (20.0)
Stricture on index colonoscopy, n (%)	1 (6.7)
Low-grade or indefinite dysplasia on colonoscopy prior to CRC diagnosis, n (%)	4 (26.7)
High-grade dysplasia on colonoscopy prior to CRC diagnosis, n (%)	1 (6.7)
Therapy at time of CRC diagnosis, n (%)	
Anti-Tumor necrosis factor	4 (26.7)
Thiopurine	2 (13.3)
5-ASA	9 (60.0)
Prednisone	1 (26.7)
Previous maintenance medications, n (%)	
Anti-Tumor necrosis factor	0 (0.0)
Thiopurine	4 (26.7)
5-ASA	4 (26.7)
Smoking, n (%)	
Never	11 (73.3)
Past	4 (26.7)
Current	0 (0.0)

Table 3:

Comparison of index colonoscopy and non-inflammatory bowel disease risk factors for interval colorectal cancer in patients with and without inflammatory bowel disease

	IBD	Non-IBD	P
Female, n (%)	4 (26.7)	103 (44.6)	0.18
Age at index colonoscopy, mean (SD)	52.8 (15.6)	67.5 (11.7)	<0.0001
Age of CRC diagnosis, mean (SD)	54.5 (15.7)	70.4 (11.8)	<0.0001
Time from index colonoscopy to cancer diagnosis (months), mean (SD)	20.7 (14.1)	35.1 (16.1)	0.0009
Indication for index colonoscopy			
Screening, n (%)	10 (66.7)	67 (29.1)	0.002
Surveillance, n (%)	3 (20.0)	103 (44.8)	0.06
Diagnostic, n (%)	2 (13.3)	60 (26.1)	0.27
Cecum intubated, n (%)	14 (93.3)	210 (92.1)	0.86
Adequate prep, n (%)	10 (76.9)	154 (75.1)	0.88
Personal History of CRC, n (%)	2 (13.3)	38 (16.5)	0.75
HNPCC or FAP[1], n (%)	0 (0.0)	7 (3.0)	0.49
Family history CRC, n (%)	2 (13.3)	23 (10.0)	0.67

[1]HNPCC = Hereditary nonpolyposis colorectal cancer, FAP = Familial Adenomatous Polyposis

Table 4:

Adherence to ASGE inflammatory bowel disease surveillance guidelines[8] amongst patients with inflammatory bowel disease

History	Surveillance colonoscopies within ASGE guidelines – Proportion (%)
≥ 8 years of left-sided or extensive disease (without additional high-risk features)	3/3 (100.0)
Primary Sclerosing Cholangitis	1/1 (100.0)
Active inflammation	2/12 (16. 7)
History of dysplasia within the past 5 years	1/5 (20.0)
Family history of colorectal cancer in first-degree relative < 50	0/2 (0.0)
Multiple pseudopolyps	1/3 (33.3)
Stricture	1/1 (100.0)