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Colorectal Cancer in Inflammatory Bowel Disease: Risk Factors and Surveillance Modalities, Experience of A Gastroenterology Department

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Abstract

Ulcerative colitis and Crohn's disease have an approximately 2-3-fold increased risk of colorectal cancers. The risk factors most frequently associated with the risk of these cancers in inflammatory bowel disease are those indicative of chronic inflammation, primary sclerosing cholangitis, previous dysplasia, and a family history of colorectal cancers. The pace of CRC surveillance in this population will be determined by the presence of these risk factors, and the surveillance modality is based on colonoscopy with chromoendoscopy and targeted biopsies. In the absence of staining, systematic biopsies can be performed.

Keywords: Ulcerative colitis, colorectal cancers, inflammatory bowel disease, chromoendoscopy.

INTRODUCTION

It is now widely accepted that patients with long-standing chronic inflammatory bowel disease (IBD) have a higher risk of colorectal cancer (CRC) than the general population. This risk varies according to several factors, such as the existence of chronic inflammation, extent of disease, primary sclerosing cholangitis (PSC), personal history of dysplasia and family history of CRC in a first-degree relative. It is important to identify these risk factors so that patients can be offered personalized monitoring adapted to their level of risk.

MATERIALS AND METHODS

This is a retrospective study reporting 7 cases of digestive cancers occurring during IBD out of a total of 1628 IBD cases followed in our department, over a period of the 21-years study extended from January 2002 to January 2023. All our patients benefited from endoscopic and histological surveillance and surgical treatment.

RESULTS

In our study, 7 cases of colorectal cancer due to IBD were reported, representing 0.4% of patients followed up for IBD in department, with an average age of 52.5 years and extremes of age ranging from 40 to 60 years. The sex ratio was 2.5, with a clear female predominance (5 women and 2 men).

Our patients have no particular antecedents, in particular no smoking, no history of associated primary sclerosing cholangitis, and no personal or family dysplasia or neoplasia.

Most of our patients (6) were being followed for ulcerative colitis (UC), all treated with aminosalicylates, and one patient was being followed for pancolic crohn's disease (CD) treated with immunosuppressants.

The risk factors found in our series were the extent of lesions and duration of evolution: 6 patients had pancolic disease (5 UC and 1 MC), and one patient had UC in the left recto-colon. The duration of disease progression was greater than 10 years in all our patients.

All our patients benefited from total colonoscopy, which revealed the presence of ulcerative processes in 4 cases (one rectal process (Figure 1) and 3 colonic processes), two cases of left colonic stenosis (Figure 2) and colonic pseudopolyps in one patient (Figure 3).

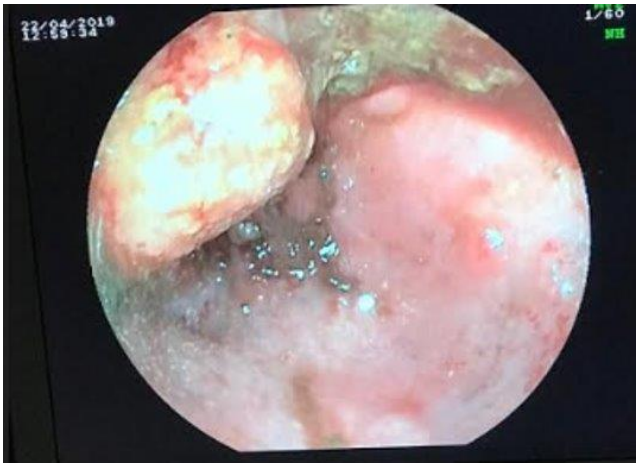

Figure 1: Ulcerative process of the upper rectum on UC

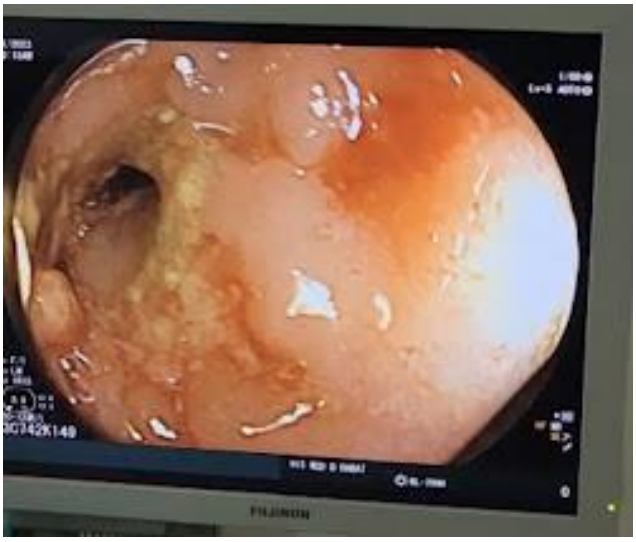

Figure 2: High-grade dysplastic colonic stenosis in crohn's disease

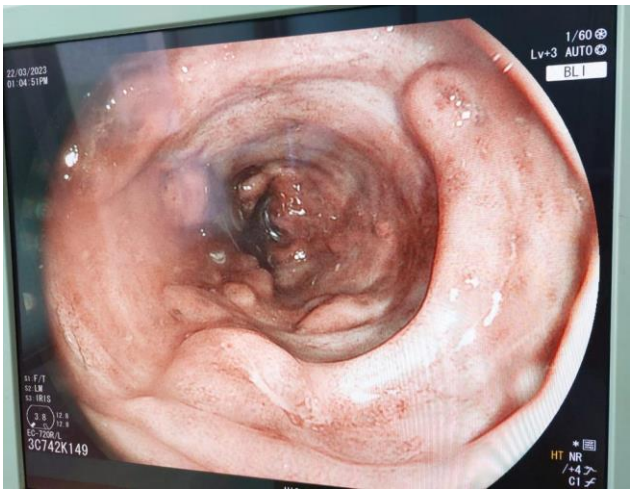

Figure 3: Inflammatory pseudopolyps as high-grade dysplasia in UC

Anatomopathological studies of per-endoscopic biopsies revealed colonic adenocarcinoma in 3 cases, mucosal colloid adenocarcinoma of the rectum in one case, and high-grade dysplastic lesions in 3 cases.

All our patients benefited from total colectomy, adjuvant chemotherapy was indicated in 3 patients and neoadjuvant radio-chemotherapy in one. Progression was favorable in all cases, with an average follow-up of around ten years.

DISCUSSION

Bowel cancers associated with crohn's disease (CD and ulcerative colitis (UC) represent only a small proportion of all bowel cancers, around 0.4% [1]. They affect young patients known to have IBD.

UC and long-standing Crohn's disease colitis have an approximately 2-3-fold increased risk of CRC, with estimates varying according to study, time period and individual risk factors [2, 3]. Fortunately, it appears that CRC rates are declining over time, probably due to improved medical treatment and colonoscopic screening and surveillance, nevertheless, CRC remains a cause of mortality and a reason for colectomy in this population.

A 2001 meta-analysis of studies prior to the era of improved medical treatment and endoscopic imaging and management reported an overall CRC prevalence in any UC patient of 3.2%, with a cumulative CRC risk of 2%, 8% and 10%, depending on the study. More recent studies suggest that this risk is lower, in the order of 1%, 3% and 7% at 10, 20 and 30 years [4].

Data from Asia-Pacific populations, where the increase in IBD incidence is more marked than in Western populations, show an increased risk of CRC in patients with IBD-induced colitis. A meta-analysis of 31,287 UC patients from 44 studies in Asian countries revealed a pooled prevalence of CRC of 0.85%, with a cumulative risk of 0.02%, 4.8% and 13.9% at 10, 20 and 30 years [5].

The risk factors most frequently associated with the risk of CRC occurrence in IBD are those indicative of chronic inflammation (extensive disease, histological inflammation, cumulative inflammatory load - which incorporates duration of disease and severity of inflammation), primary sclerosing cholangitis (PSC), previous dysplasia, extent of disease and a family history of CRC in a first-degree relative. Risk factors for CRC can be classified as patient- and disease-related [6].

Patient-Related Factors

Data are mitigated as to whether increasing age is in itself a risk factor for CRC, independently of the background risk of sporadic CRC unrelated to IBD in older age groups [6]. The increased risk associated with younger versus older age of IBD onset (variably defined in studies, but generally with an age cut-off of 30 years) reported in previous studies, more likely reflects disease duration and cumulative inflammation over time, as opposed to accelerated carcinogenesis in younger-onset IBD [6].

In a meta-analysis of 11 cohort studies using multivariable analyses, men showed a significantly 1.50-1.58-fold higher risk of CRC than women. The same meta-analysis reported no significant association between race and CRC risk based on 2 cohort studies [7].

Although smoking is an established risk factor for CRC, it is not systematically associated with an increased risk of CRC-associated IBD [6].

A family history of CRC is an established risk factor for CRC in IBD patients, based on multivariable analyses of case-control and cohort studies [7]. This increased risk appears to be relevant irrespective of first or second degree, although having a first-degree relative with CRC diagnosed before the age of 50-55 confers the highest risk.

Disease-Related Factors

The type of IBD (UC vs CD) has not been consistently associated with a differential risk of recto-colonic neoplasia [6]. The risk of CRC in patients with only rectitis due to IBD is similar to that in the general population, and these patients should not be included in surveillance in the absence of disease extension.

The most relevant disease-related factors are: extent and duration of colitis, and concomitant history of PSC. Extensive disease is associated with a significantly 2-3-fold higher risk of IBD-associated neoplasia, compared with intermediate-extension CD and left-sided UC, both of which are still associated with a high risk of colorectal neoplasia compared with rectitis due to IBD alone [7].

Patients with IBD and concomitant PSC have an estimated 3- to 5-fold higher independent risk of CRC than patients without concomitant PSC [7-9]. The reasons for this phenomenon have not been elucidated, but may include changes in bile acid metabolism, altered intestinal or biliary microbiota and systemic immunological alterations that predispose to colon and biliary cancers in such patients. Patients with IBD and concomitant PSC often present with quiescent clinical and histological IBD, but a high prevalence of CRC at the time of PSC diagnosis [6]. Accordingly, all international gastroenterology societies recommend that CCR monitoring should begin at the time of PSC diagnosis, with a closer monitoring interval.

Anatomical structural alterations of the colon, including stenosis and inflammatory pseudopolyps, have also been associated with an increased risk of CRC in previous studies, but these associations, particularly pseudopolyps, have not been confirmed in more robust recent analyses that control for histological inflammation and other relevant confounding factors [7, 10, 11].

Histological inflammation, more than endoscopic inflammation, is a major risk factor for CRC. Patients with concomitant PSC are an exception, as they often have minimal histological colonic inflammation despite having some of the highest CRC risk rates. One factor that continues to be used in risk stratification algorithms to determine surveillance in patients is the

severity of inflammation at the previous colonoscopy [6].

Once pathologically confirmed dysplasia is detected, the patient should be considered at particularly high risk. Patients with high-grade dysplasia are at particularly high risk of prevalent or incident CRC within a short period of time, which amply justifies total colectomy.

The frequency of CRC surveillance in this population will be determined by the presence of these risk factors. In practice Perform a baseline colonoscopy for any colonic IBD that has progressed for more than 6-8 years, then establish a schedule of colonic dysplasia screening according to individual risk level (Table I). The recommendation not to start screening and surveillance until 8-10 years after disease onset comes from an older meta-analysis of 19 studies of heterogeneous design, which reported the cumulative risk of CRC 10, 20 and 30 years after disease onset as 2%, 8% and 18%. Another meta-analysis limited to population-based cohort studies reported a cumulative CRC risk of 2.6% and 6.6% after 10 to 20 and > 20 years of IBD, respectively, with a cumulative incidence of 21% after 20 years of extensive disease [6].

Table I : Pace of CRC screening colonoscopies in IBD (6)

Table 1. US-based and International Guidance for Colonoscopic Surveillance in Inflammatory Bowel Disease

Guideline and methodology	Screening initiation, years after symptom onset[a]	Surveillance intervals	Risk categories
US-based guidelines (ACG, ASGE) and clinical practice update (AGA)			
ACG 2019 GRADE	8–10 years	1–2 years	Annual surveillance in PSC, otherwise every 1–3 years based on the number of risk factors for CRC and findings from the previous colonoscopy, albeit with no discrete risk-categorization groups
ASGE 2015 GRADE	8 years	1–3 years	Annual surveillance in PSC, "active" inflammation,[a] anatomic abnormality (stricture, multiple pseudopolyps), history of dysplasia, CRC in FDR. Acknowledge that optimal surveillance interval is otherwise not defined.
AGA 2021 (clinical practice update) Expert consensus	8–10 years	1–5 years	Annual surveillance: PSC, moderate or severe inflammation (any extent), CRC in FDR aged <50, dense pseudopolyposis, history of invisible dysplasia or higher-risk visible dysplasia within the past 5 years Every 2–3 years: mild inflammation (any extent), strong family history of CRC (but not FDR aged <50 years), features of previous severe colitis (moderate pseudopolyps, extensive mucosal scarring), history of invisible dysplasia or higher-risk visible dysplasia >5 years ago, history of lower-risk visible dysplasia <5 years ago. Every 5 years: continuous disease remission since last colonoscopy with mucosal healing on current exam, plus either ≥2 consecutive exams without dysplasia or minimal historical colitis extent.
European-based guidelines			
ECCO 2017 (UC only) Expert consensus	8 years	High: 1 year; Intermediate: 2–3 years; Not intermediate or high: 5 years	High-risk: extensive colitis with severe active inflammation, stricture or dysplasia detected within the past 5 years, PSC, or CRC in FDR aged <50 years; Intermediate-risk: extensive colitis with mild-moderate active inflammation, pseudopolyps, or CRC in FDR aged >50 years
BSG 2019 GRADE	8 years	High: 1 year; Intermediate: 3 years; Low: 5 years	High risk: Same as ECCO except moderate-severe active endoscopic/histologic inflammation; Intermediate risk: Same as ECCO except mild active endoscopic/histologic inflammation; Low risk: extensive colitis with no active endoscopic/histologic inflammation, left-side colitis, or Crohn's colitis <50% colon.
NICE 2011 NICE guideline protocol	10 years	High: 1 year; Intermediate: 3 years; Low: 5 years	High, intermediate, and low risk: same as BSG
German 2019 (UC only) Expert consensus	8 years	High: 1 year; Intermediate: 2–3 years; Low: 4 years	High risk: Same as ECCO Intermediate risk: Same as ECCO Low risk: No criteria for high- or intermediate-risk

Regarding screening modalities in practice according to ECCO 2013 recommendations, Colonoscopy in remission period (more profitable for the endoscopist and for the pathologist) with chromoendoscopy and targeted biopsies is the reference examination for colorectal cancer screening with the rationale of looking on the flat or raised mucosa for dysplasia as a marker and precursor of cancer, In the absence of staining, systematic biopsies can be performed: 4 on each quadrant every 10 cm (placed in separate pots) over the entire colonic frame (i.e. 40 biopsies), Virtual staining (NBI, FICE, iScan) has not proved effective in detecting dysplasia, Preparation must be perfect with meticulous inspection and preferably with High Definition equipment [12]. If dysplasia is detected on a random biopsy with no visible lesion, a new colonoscopy with chromoendoscopy should be performed at 3 months. Finally, both low-grade and high-grade dysplasia must be confirmed by a second independent pathologist [13].

CONCLUSION

The occurrence of colorectal cancer in patients with IBD is the main fear of both patients and physicians, and screening remains a major challenge, based on colonoscopy with chromoendoscopy and targeted biopsies of visible lesions. The frequency of surveillance in this population will be determined by the presence of certain risk factors.

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