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EDITORIAL

Colorectal cancer surveillance in patients with inflammatory bowel disease: What is new?

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Abstract

Several studies assessing the incidence of colorectal cancer (CRC) in inflammatory bowel disease (IBD) patients have found an increased risk globally estimated to be 2 to 5 times higher than for the general population of the same age group. The real magnitude of this risk, however, is still open to debate. Research is currently being carried out on several risk and protective factors for CRC that have recently been identified in IBD patients. A deeper understanding of these factors could help stratify patient risk and aid specialists in choosing which surveillance program is most efficient. There are several guidelines for choosing the correct surveillance program for IBD patients; many present common characteristics with various distinctions. Current recommendations are far from perfect and have important limitations such as the fact that their efficiency has not been demonstrated through randomized controlled trials, the limited number of biopsies performed in daily endoscopic practice, and the difficulty in establishing the correct time to begin a given surveillance program and maintain a schedule of surveillance. That being said, new endoscopic technologies should help by replacing random biopsy protocols with targeted biopsies in IBD patients, thereby improving the efficiency of surveillance programs. However, further studies are needed to evaluate the cost-effectiveness of introducing these techniques into daily endoscopic practice.

Key words: Colonoscopy; Colorectal cancer; Crohn's disease; Dysplasia; Inflammatory bowel disease; Ulcerative colitis

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INTRODUCTION

Several epidemiological studies have demonstrated an increased risk of colorectal cancer (CRC) in patients with inflammatory bowel disease (IBD)[1] globally estimated to be 2 to 5 times higher than in the general population of the same age group[2]. While the risk of CRC in both ulcerative colitis (UC) and Crohn's disease (CD) involving the colon seems to be similar, the magnitude of this risk has yet to be determined since results from different studies are heterogeneous in terms of geographical, temporal, and methodological variables. Furthermore, the risk of CRC is not the same for all patients. Several risk factors have been clearly identified, including an earlier onset of IBD, longer duration of colitis, and more extensive disease, along with others that have not been universally confirmed[3]. While the commonly accepted

hypothesis of an increased risk of CRC in IBD patients has prompted medical society guidelines to endorse cancer prevention strategies[4-8], current recommendations are still far from perfect and tend to miss a significant number of smaller mucosal lesions. In addition, because current surveillance programs in IBD patients imply repeated colonoscopies and multiple biopsies, they are both laborious and time-consuming. This has provoked ongoing discussions regarding the efficacy of such strategies and ways to improve them. In particular, new endoscopic technologies may prove useful for overcoming these problems by reducing the number of biopsies needed and the overall examination time.

In this article we discuss several aspects of endoscopic surveillance for CRC in IBD patients including an update on the new endoscopic technologies currently available.

EPIDEMIOLOGY OF CRC IN IBD

Several studies assessing the incidence of CRC in IBD patients have found an increased risk for developing this malignant neoplasm in comparison to control subjects. Indeed, CRC accounts for approximately 10%-15% of all deaths in IBD patients[9]. However, the real magnitude of their increased risk for the disease is still under debate because of discrepancies between previous and current epidemiological data.

In one of the earliest cohort studies of 3117 patients with UC (diagnosed from 1922 to 1983) from the Uppsala region in Sweden, the incidence of CRC was 5.7 times higher (95% CI: 4.6-7.0) than the normal rate, as reported in another Swedish population-based study. Considering both UC and CD, a Canadian cohort study of 5529 patients with IBD followed between 1984 and 1997 and included in the Manitoba Health database found a similar increase in the incidence of CRC in UC and CD[10]. In the particular case of rectal cancer, the incidence ratio was higher than that of the general population in UC patients, but not in CD patients. A meta-analysis of 116 studies involving 54 478 patients reported that the overall prevalence of CRC in UC patients was 3.7%; this increased to 5.4% in cases with pancolitis[1]. Two other meta-analyses involving CD patients demonstrated an increased risk of CRC, including an increased risk for developing small bowel and extraintestinal cancer along with lymphoma[11,12]. The overall relative risk of CD patients for developing CRC was 2.5 (1.3-4.7), which increased to 4.5 (1.3-14.9) in patients with colonic disease and decreased to 1.1 (0.8-1.5) in isolated ileal disease[12].

In contrast with these results, the magnitude of risk in recent population-based studies appears to be much smaller and often restricted to specific geographic areas: A study of 692 patients from Olmsted County, Minnesota, USA analyzed between 1940 and 2001 showed that the standardized incidence ratio for CRC was not statistically higher in patients with UC and CD as compared to the non-affected population. In fact, the only statistically higher risk was a two-fold increase in cases of extended UC[13]. Other population-based studies conducted in Hungary and Denmark have reported either no increased risk or only a modestly higher risk of CRC in patients with UC and CD[14,15]. The prevalence of CRC in UC patients in the Asia-Pacific region ranges from 0.3%-1.8%[16] and more recently, a nationwide study of the Korean Association for the Study of Intestinal Diseases (KASID) found a cumulative incidence of UC-associated CRC comparable to that of western countries[17]. There are similar data regarding the risk of CRC in patients with CD[18]. However, further long-term data on the cumulative risk attributable to UC and CD are required in the Asia-Pacific region.

The most recent data from St. Mark's Hospital surveillance program seems to indicate that disease duration is a main risk factor, with the cumulative incidence of CRC or dysplasia being 7.7% at 20 years and 15.8% at 30 years[19]. In any event, these incidence rates are lower than those cited in the aforementioned meta-analysis[1].

Taking all these data into account, it is obvious that the results present a great deal of heterogeneity. This may be due in part to the geographic variations in the incidence of CRC in different countries. In the United States and the United Kingdom, the annual risk of CRC has been estimated to be 4-5 cases per 1000 person-years for patients with IBD, whereas the risk seems to be considerably lower in patients living in Scandinavia and other countries (2 cases per 1000 person-years). The reason for this geographic heterogeneity is still unclear, but several factors may be involved, including genetic factors, diet, use of chemoprevention, improved surgical treatments, increased colonoscopic surveillance, or a combination thereof. Globally, the prevalence of CRC in all countries studied is around 3.7% among UC patients, with a crude annual incidence rate ranging from approximately 0.06% to 0.16% (a relative risk of 1-2.75)[20].

The observed heterogeneity in the results may also be partly due to changes in incidence rates over time, with a progressive reduction in these rates in more recent studies. It must be taken into consideration that these new data come from an era that includes better surveillance methods, more widespread use of medicines to control inflammation even during asymptomatic periods in order to maintain remission of the disease, and other variables that might lower the risk of CRC in IBD patients, which would explain changes in incidence rates[21].

Finally, the results are bound to be influenced by the fact that different studies follow different methods for calculating the risk. This makes comparisons between studies extremely difficult. For example, many studies report the cumulative risk of developing CRC in a given population of IBD patients without stratifying the patients on the basis of various risk factors, while others report a standardized incidence ratio without providing information on the lifetime risk[22].

SPORADIC AND IBD-ASSOCIATED CRC

Independent from epidemiological data, CRC associated

with IBD presents particular characteristics that differentiate it from sporadic CRC, which suggests the need for more specific surveillance programs in IBD patients. In colitis-related CRC, for example, the development of multiple synchronous malignancies is more common; moreover, adenomatous polyps do not always precede the appearance of a malignant neoplasm, as occurs in sporadic cases. In fact, carcinogenesis in the inflamed colon seems to follow a different sequence of genetic alterations than that observed in sporadic cancers in the normal colon[23]. Whereas the former is characterized by an "inflammation-dysplasia-carcinoma" sequence, the latter involves an "adenoma-sequence"[24]. This complicates the detection of IBD-associated CRC with the standard surveillance program because in most cases the dysplastic lesions appear as flat lesions. Dysplasia itself can occur within or near plaque-like lesions or raised polypoid masses, defined as a dysplasia-associated lesion or mass (DALM). However, the definition for DALM has evolved over time, and a new entity-the adenoma-like mass (ALM)-has just recently been proposed. Both are considered risk factors for developing CRC in IBD, with the likelihood of finding concurrent colon cancer at the time of colectomy being 42% with high-grade dysplasia and 19% with low-grade dysplasia[25]. Finally, while the rate at which colitic mucosa progresses to dysplasia and ultimately to CRC is unknown, it is believed to be more rapid than the progression of adenomas to CRC in the non-IBD population[26].

RISK FACTORS FOR DEVELOPING CRC IN IBD PATIENTS

Several risk and protective factors for the development of CRC in IBD patients have been identified and discussed (Table 1). These are summarized below.

The extent and duration of colonic disease, the coexistence of primary sclerosing cholangitis (PSC), and a family history of sporadic CRC have all been confirmed as risk factors in several different studies.

One of the most important risk factors is disease duration. While this is somewhat complex to establish, the onset of symptoms is generally used to define when the disease begins. The risk of UC-associated CRC starts to increase after 7 years of extensive colonic disease (left-sided disease and pancolitis)[27]. With regard to CD patients, the median duration of disease prior to the diagnosis of CRC was similar to that observed in UC patients (15 years and 18 years, respectively). The approximate cumulative incidence of CRC in patients with left-sided disease or pancolitis is 2% at 10 years, 8% after 20 years, and 18% 30 years after the onset of IBD[1]. However, in contrast with these figures, the recent St. Mark's Hospital surveillance program identified a constant cancer incidence rate which only increased after a disease duration of at least 40 years, putting into question the recommendation to increase surveillance intensity in those patients with a longer disease duration[19].

Table 1 Confirmed risk factors and proposed protective factors for developing colorectal cancer in inflammatory bowel disease patients

Confirmed risk factors	Protective factors under investigation
Extent of colitis[27]	5-ASA treatment[75-77]
UC pancolitis	
UC left-sided colitis	
CD colitis (> 50%)	
Disease duration[19]	UDCA treatment[78-80]
Association with PSC[39-41]	Folate supplementation[82-84]
Family history of CRC[37,38]	Colectomy[81]
Active inflammation[34]	Maintaining of remission
Pseudopolyps	Mucosal healing
Strictures	Histological healing
Degree of histological inflammation	

5-ASA: 5-aminosalicylate; UDCA: Ursodeoxycholic acid; UC: Ulcerative colitis; CD: Crohn's disease; PSC: Primary sclerosing cholangitis; CRC: Colorectal cancer.

The extent of mucosal inflammation has also been correlated with the risk of developing CRC. In fact, while patients with extensive disease (pancolitis and left-sided colitis) have an increased risk of developing CRC, patients with only proctitis or proctosigmoiditis do not. Starting a specific surveillance program in this group of patients is thus not recommended[28]. It should be noted that the extent of the disease may change over time in any individual with UC or CD[29], which may make it advisable to continue with a strategy based on the maximum documented extent of disease. In addition, while some studies have shown that the presence of backwash ileitis is associated with multiple tumors, at present there is not enough evidence to confirm it as a risk factor for CRC in IBD patients[30].

The severity of inflammation is another important risk factor for IBD-associated CRC, even at a microscopic level. Two studies have demonstrated a frequency of CRC that was double that expected in patients with post-inflammatory polyps, which constitute a marker of severity of inflammation (OR 2.5; 95% CI: 1.4-4.6)[31-33]. Several studies have indicated that CRC can arise in areas of the colon that are endoscopically normal, but which exhibit histological alterations. In these studies, neoplasia was not detected in areas of the colon not involved with the inflammatory process[34]. However, it is not clear whether this increased risk is due to a higher misdiagnosis of dysplastic polyps, which are difficult to distinguish from benign pseudopolyps, or to a real, independent risk factor involving the presence of pseudopolyps and the inflammatory response. Additionally, other markers of inflammation, including the presence of strictures, have been found to be independently associated with an increased risk for developing CRC, although the relationship is complex. For example, in patients with CD, colonic strictures are a consequence of the transmural inflammatory process and are not a risk factor in the development of CRC. In contrast, colonic strictures in UC patients are considered to be a risk factor for developing

Table 2 Summary of the main differences in the recommendations for colorectal cancer surveillance programs in inflammatory bowel disease patients

Guidelines	Remission	Beginning of surveillance	Surveillance schedule	Random biopsy protocol	New endoscopic technique recommended
U.K. 2002[7]	Necessary	8-10 yr (pancolitis) 15-20 yr (left-sided colitis)	3 yr (2° decade) 2 yr (3° decade) 1 yr (4° decade)	Recommended	Not mentioned
AGA 2003[8]	Not mentioned	8 yr (pancolitis) 15 yr (left-sided colitis)	Every 1-2 yr	Recommended	Not mentioned
ACG 2004[5]	Necessary	8-10 yr	Every 1-2 yr	Recommended	Not mentioned
ECCO 2008[4]	Necessary	8 yr (pancolitis) 15 yr (left-sided colitis)	2 yr (1°-2° decade) - 1 yr (3° decade)	Recommended	Chromoendoscopy
BSG 2010[6]	Necessary	10 yr	- 3 yr lower risk - 2 yr intermediate risk - 1 yr higher risk	Recommended	Chromoendoscopy

AGA: American Gastroenterological Association; ACG: American College of Gastroenterology; UK: United Kingdom; ECCO: European Crohn's and Colitis Organization; BSG: British Society of Gastroenterology.

the disease[35]. Moreover, cancers associated with a stricture seem to be diagnosed at a more advanced stage than those not associated with strictures[36].

Having a family history of sporadic CRC is also a risk factor for developing cancer; indeed, IBD patients with a first-degree relative with CRC have twice the risk of developing the disease than those who do not[37]. Moreover, if a first-degree relative suffered from CRC before the age of 50 years, the risk of IBD patients for developing CRC increases nine-fold[38]. The presence of a first-degree relative with IBD, however, does not increase the risk of healthy family members for developing CRC[38].

The association between UC and PSC was first described in 1965[39]. A case-control study observed a cumulative risk for CRC of 9% after 10 years from the diagnosis of the disease, 21% after 20 years, and 50% after 25 years, in comparison to the risk of UC patients without associated PSC (2%, 5%, and 10%, respectively). These results indicate that the association of both diseases constitutes a strong risk factor[40]. Moreover, the risk remains higher even after a liver transplant for the treatment of PSC[41].

Finally, some studies have shown some genetic polymorphisms associated with the risk of CRC in patients with IBD, particularly in patients with UC[42,43]. However, more studies are needed to confirm these data and to find a specific biomarker useful to identify the high risk patients for progression to CRC.

ENDOSCOPIC SCREENING

A surveillance program that includes a colonoscopic examination is the best approach currently available to prevent the development of CRC in both the general population and IBD patients[4-8,44,45]. There are several guidelines for recommending a specific surveillance program in IBD patients; these guidelines present some similarities along with various distinctions. The overall strategy, highlighting some of the differences, can be summarized as follows (Table 2)[4-8]: (1) while almost all of the guidelines are in agreement that the screening colonoscopy should be performed on patients during clinical remission of the disease in order to avoid confusing inflammatory changes with dysplasia, several guidelines make no clear reference to this point. In any event, a surveillance procedure should not be unduly delayed if remission cannot be achieved; (2) all guidelines are in agreement that surveillance colonoscopies should be started 8-10 years after the onset of symptoms for patients with left-sided or extensive colitis as well as for those with CD colitis. However, the statements published by the European Crohn's and Colitis Organization (ECCO), and the guidelines of the American Gastroenterological Association (AGA) and public health officials in the United Kingdom distinguish between beginning surveillance in patients with pancolitis (8-10 years) and in those with left-sided colitis (15-20 years); (3) all guidelines are in agreement about the need for following regular surveillance schedules after the initial colonoscopy; however, there is no agreement about the interval time. The latest British Society of Gastroenterology (BSG) guidelines suggest for the first time that regular colonoscopies should be carried out either annually or every 3 years or 5 years depending on the presence of additional risk factors. The BSG groups patients into three categories. The first category is for high-risk patients (dysplasia in the past 5 years declining surgery, PSC/transplant PSC, family history of CRC in a first degree relative aged 50 or under, or extensive colitis with moderate/severe active endoscopic/histological inflammation), in which colonoscopies should be conducted annually. In patients with intermediate risk (post-inflammatory polyps, family history of CRC in a first degree relative aged 50 years and above, or extensive colitis with mild active endoscopic/histological inflammation), a colonoscopy should be conducted every 3 years. In patients with a lower risk (left-sided colitis, CD colitis with less than 50% of the colonic mucosal surface affected by the disease, or extensive colitis with no active endoscopic/histological inflammation), colonoscopies should be conducted

every 5 years. In contrast, the ECCO statements recommend performing a colonoscopy every two years during the first 20 years of the disease and then annually. The United Kingdom guidelines recommend performing a colonoscopy every three years in the second decade after the onset of symptoms, every two years in the third decade, and annually by the fourth decade of disease. Finally the AGA guidelines recommend performing a colonoscopy every 1-2 years without the further specifications included in the American College of Gastroenterology (ACG) guidelines; (4) all the aforementioned guidelines agree that colonoscopic surveillance should be performed annually in patients with PSC from the moment of the PSC diagnosis; (5) all guidelines agree that two to four random biopsy specimens should be taken with a jumbo forceps every 10 cm along the entire colon, with additional samples being taken in suspicious areas. Particular attention should be placed on taking 4-quadrant biopsy specimens every 5 cm in the lower sigmoid and rectum due to the increased risk for cancer development in this area; (6) only the two recent BSG guidelines and the ECCO statement recommend the use of chromoendoscopy to collect targeted biopsies of abnormal areas without following the aforementioned biopsy protocol; (7) full colonoscopies are always recommended because approximately a third of UC-associated CRCs develop in the proximal colon[46]; and (8) although there is no clear evidence that pouch surveillance is beneficial, it is recommended in the BSG guidelines. It is possible to offer a surveillance program to these patients as follows: patients undergoing colectomy could be subjected to a sigmoidoscopy of pouch/rectal mucosa every year in the case of "high risk patients" (previous rectal dysplasia, dysplasia/cancer at the time of pouch surgery, PSC, type-C mucosa of pouch with persistent atrophy and severe inflammation) and of every 5 years in "low risk patients" (those lacking any high risk factors), taking four proximal and four distal pouch biopsies.

All of the currently available surveillance programs have some limitations, as discussed below.

EFFICACY OF SURVEILLANCE

Even though a surveillance protocol is recommended in all currently available guidelines for IBD patients, no randomized studies to date have documented a reduction in the risk of developing or dying from CRC because of surveillance colonoscopy. An evidence-based review of previously published studies concluded that there was no clear evidence that surveillance colonoscopy prolongs survival in patients with extensive UC[47]. However, indirect evidence suggests that surveillance reduces the risk of death due to IBD-associated CRC in a cost-effective manner[48-50]. Moreover, there is evidence that cancer can generally be detected at an earlier stage in patients who undergo surveillance colonoscopy and that these patients have a correspondingly better prognosis. In fact, the five-year survival rate after a CRC diagnosis in IBD patients was 100% in a group of patients undergoing a surveillance program, compared to 74% in the non-surveillance group[51]. In addition, more tumors were found at an early stage in the surveillance group.

BIOPSY PROTOCOL

Random biopsies visualize less than 1% of the total colonic mucosa surface area and can thus lead to a large sampling error. In one study, the probability of detecting dysplasia was 90% if 33 biopsies were taken and 95% if 56 biopsies were taken[52]. The use of jumbo forceps increases the detection rate of random biopsies and is recommended in all CRC surveillance protocols. From a practical point of view, obtaining 6 samples from each of the 6 segments of the colon (right colon, transverse colon, descending colon, sigmoid colon, and proximal and distal rectum), or alternatively 4 samples from each of the 8 colonic segments (cecum, ascending colon, hepatic flexure, transverse colon, spleen flexure, descending colon, sigma, and rectum) allows practitioners to analyze 36 or 32 biopsy samples in only 6 or 8 biopsy containers, respectively, and has thus been employed by some experts in an effort to reduce costs.

The need to follow an extensive biopsy protocol in each exploration seems to limit the daily application of such surveillance programs in clinical practice. Several studies indicate the phenomenon of "under sampling" in routine clinical practice as well as the fact that the majority of gastroenterologists do not follow the international guideline recommendations when performing endoscopic surveillance in IBD. In the United Kingdom, more than 50% of the gastroenterologists surveyed obtained fewer than 10 colonic mucosal biopsies per endoscopic surveillance examination[53]. In a study carried out in the United States, only 18% of surveillance examinations yielded 20 or more mucosal biopsy specimens[54], while only 54% of gastroenterologists in the United States reported obtaining at least 31 biopsy specimens during surveillance exams[55]. In the Netherlands, a recent study showed that only 27% of gastroenterologists approached the recommended number of 33 random biopsies[56]. The limited performance of biopsies results in a significant number of surveillance failures that may consequently increase the surveillance sampling error; this represents a real problem in daily endoscopic practice.

BEGINNING A SURVEILLANCE PROGRAM

The ECCO statement and the guidelines from the AGA and the United Kingdom all recommend commencing surveillance after 8-10 years of disease in cases of CD or extensive colitis and after 15-20 years of disease in cases of left-sided UC. While starting surveillance beforehand is not generally recommended, the evidence on which this practice is based is poor[1]. In fact a recent study demonstrates that a substantial proportion of all IBD-associated CRC (20%) occurs in the first decade of

IBD, just before the BSG and AGA guidelines suggest starting colonic surveillance[57]. The diagnosis of CRC is thus delayed or missed in 17%-28% of patients when surveillance is conducted strictly according to formal guidelines. This shows that in fact we do not know how to predict with certainty the rate of tumor growth in patients with IBD. In order to choose the correct moment to begin a surveillance program, we should consider not only the extent and duration of the disease, but also the presence of other risk factors. The surveillance guidelines based upon disease duration and extent must therefore be expanded, taking into account other risk factors such as severity of the disease, family history of CRC, and the presence of pseudopolyps, none of which have been incorporated in the current surveillance guidelines, even though these factors could help identify those patients who need to start a surveillance program.

NEW ENDOSCOPIC TECHNOLOGY

Most published studies point out the need to develop and use new endoscopic technology in order to reduce the number of random biopsies performed while improving the diagnosis rate of pre-malignant dysplastic lesions. The possibility of collecting targeted biopsies is an attractive alternative for increasing the efficiency of dysplasia detection.

Chromoendoscopy

This technique involves spraying a dye (indigo carmine or methylene blue) onto the colonic mucosa to enhance the visualization of subtle mucosal changes suggestive of neoplasia that are not visible with the white light of standard endoscopy. Several studies have shown a higher dysplasia detection rate for high-magnification chromoendoscopic colonoscopy than for conventional optical colonoscopy with random biopsies[58-60]. The use of high-magnification chromoendoscopy increases the diagnostic yield for dysplastic lesions 3 to 4.5-fold[20,61]. Comparable diagnostic yields have been obtained with both methylene blue and indigo carmine[62,63]. The drawback is that this technique is time consuming and requires an endoscopist experienced in identifying the various suspicious mucosal patterns. Moreover, a recent study found that both dysplasia and cancer were endoscopically visible in most UC patients, suggesting that these pathologies may be reliably identified during scheduled examinations[64]. Nevertheless, this is the only technique that is actually recommended in the latest guidelines for CRC surveillance programs in patients with IBD instead of random biopsy collection. Future research will be needed to assess the real utility and cost-effectiveness of chromoendoscopy in IBD-associated CRC surveillance programs.

Other newer endoscopic techniques

Only scant data are available on the use of newer endoscopic techniques for the detection of dysplasia in IBD patients. Thus far, none of these techniques have been recommended in the current available guidelines on CRC surveillance in IBD patients.

Some studies have investigated the utility of chromoendoscopy with confocal endomicroscopy, which basically constitutes an *in-vivo* histology technique after intravenously injecting 2.5-5 mL of fluorescein 10%. Confocal chromoscopic endomicroscopy was superior to chromoendoscopy alone for detecting intraepithelial neoplasia[65]. The diagnostic yield for intraepithelial neoplasia when endomicroscopy-targeted biopsies were performed was 2.5 times greater than that obtained with chromoendoscopy-guided biopsies alone and 4.75 times greater than that for conventional colonoscopy with random biopsies[65,66]. The most important limitation of this technique is the interobserver variability in interpreting real-time histology; this drawback is magnified when the gastroenterologist is less experienced in histological interpretation. Future studies are needed to identify the precise role of this technique in IBD surveillance programs.

Another alternative is the miniprobe-based endomicroscopy technique. After the miniprobe is pleaded is pleaded correct? through a 2.8 mm work channel of any standard videoendoscope, the laser unit generates a confocal image with a high frame rate per second. Studies comparing this technique with others are currently being evaluated and there are no available data with regard to IBD patients[67].

Narrow band imaging (NBI) is another innovative technique that can provide clear imaging of the microvascular mucosal structure as a result of the differential optical absorption of light by hemoglobin[68]. The images are similar to those obtained through chromoendoscopy, but without dye. Some studies have demonstrated that NBI and conventional chromoendoscopic techniques showed equal sensitivity and specificity in the differentiation of neoplastic and non-neoplastic lesions[69,70]. Although both techniques seem superior to conventional colonoscopy, a recent study demonstrated that the efficacy of NBI did no better than conventional colonoscopy in detecting patients with neoplasia[71].

Another promising technique is fluorescence endoscopy, which assesses intraepithelial neoplasia after topical or systemic sensitization with 5-ALA. After the application of 5-ALA, this substance is intracellularly converted into the fluorophore, protoporphyrin Ⅸ, which selectively accumulates in neoplastic tissue and is then detectable as a reddish spot when illuminated with blue monochromatic light. A small study showed an excellent sensitivity for this technique, ranging from 87% to 100% after local sensitization, in detecting dysplastic lesions in IBD patients[72]. Other innovative endoscopic techniques are currently under evaluation, including that of optical coherence tomography, which is an optical analogue to endoscopic ultrasound with an imaging depth of 2 mm. Two studies have analyzed the feasibility of this method for differentiating the transmural inflammation in CD from patterns of active UC[73,74], but no data are available to date with regard to CRC surveillance programs.

Further studies are needed before the introduction of these new technologies into clinical practice can be definitively recommended.

CONCLUSION

Studies on the prevalence and incidence of CRC in patients with IBD are heterogeneous in terms of geographical, temporal, and methodological variables, but we can conclude that patients with IBD exhibit an increased risk for developing CRC. The mechanism of carcinogenesis seems to follow distinct rules in comparison to that of sporadic CRC and is not yet completely understood or predictable. This justifies the special attention these patients receive in the form of a specific surveillance program, although no randomized studies have documented a reduction in the risk for developing or dying from CRC with the use of surveillance colonoscopy. In the future, IBD patients should be categorized according to confirmed risk factors in order to individualize CRC surveillance programs in terms of when to start them and at what intervals surveillance should be carried out. New endoscopic technologies should be helpful in reducing the number of random biopsies performed by increasing the targeted biopsy protocol, thereby improving the efficiency of a given surveillance program. However, further studies are needed to assess the cost-effectiveness and advantages of these techniques in clinical practice.

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