REVIEW
243  Endoscopic ultrasound in oncology: An update of clinical applications in the gastrointestinal tract
Valero M, Robles-Medranda C

MINIREVIEWS
255  Endoscopic recommendations for colorectal cancer screening and surveillance in patients with inflammatory bowel disease: Review of general recommendations
Huguet JM, Suárez P, Ferrer-Barceló L, Ruiz L, Monzó A, Durá AB, Sempere J

ORIGINAL ARTICLE
Retrospective cohort study
263  Endoscopic resolution and recurrence of gastric antral vascular ectasia after serial treatment with argon plasma coagulation
Garg S, Aslam B, Nickl N

Observational Study
267  Utility of the balloon-overtube-assisted modified over-the-wire stenting technique to treat post-sleeve gastrectomy complications
Ponte A, Pinho R, Proença L, Silva J, Rodrigues J, Sousa M, Silva JC, Carvalho J

Randomized Controlled Trial
273  Multicenter randomised controlled trial comparing the high definition white light endoscopy and the bright narrow band imaging for colon polyps
Singh R, Cheong KL, Zorrón Cheng Tao Pu L, Mangira D, Koay DSC, Kee C, Ng SC, Rerknimitr R, Aniwan S, Ang TL, Goh LK, Ho SH, Lau JYW

CASE REPORT
282  Bladder urothelial carcinoma extending to rectal mucosa and presenting with rectal bleeding
Aneese AM, Manuballa V, Amin M, Cappell MS
ABOUT COVER

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World Journal of Gastrointestinal Endoscopy (World J Gastroint Endosc, WJGE, online ISSN 1948-5190, DOI: 10.4253) is a peer-reviewed open access (OA) academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians. WJGE covers topics concerning gastroscopy, intestinal endoscopy, colonoscopy, capsule endoscopy, laparoscopy, interventional diagnosis and therapy, as well as advances in technology. Emphasis is placed on the clinical practice of treating gastrointestinal diseases with or under endoscopy.

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INDEXING/ABSTRACTING

World Journal of Gastrointestinal Endoscopy is now indexed in Emerging Sources Citation Index (Web of Science), PubMed, and PubMed Central.

FLYLEAF

I-III Editorial Board

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NAME OF JOURNAL
World Journal of Gastrointestinal Endoscopy

ISSN
ISSN 1948-5190 (online)

LAUNCH DATE
October 15, 2009

FREQUENCY
Monthly

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PUBLICATION DATE
June 16, 2017

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Endoscopic recommendations for colorectal cancer screening and surveillance in patients with inflammatory bowel disease: Review of general recommendations

Jose María Huguet, Patricia Suárez, Luis Ferrer-Barceló, Lucía Ruiz, Ana Monzó, Ana Belén Durá, Javier Sempere

Screening for colorectal cancer (CRC) in patients with inflammatory bowel disease (IBD) is recommended by all scientific societies. However, there are differences in the recommendations they make regarding screening and surveillance. We address a series of questions that come up in the daily clinical practice of a physician. The first two questions that are raised are: (1) Who should be offered screening for CRC? and (2) When should the first colonoscopy be performed? The next step is to decide who should undergo endoscopic surveillance and at what intervals they should be performed. Chromoendoscopy is emerging as the recommended endoscopic technique for screening and surveillance. The terminology for describing lesions detected with endoscopy is also changing. The management of visible lesions or non-visible dysplasia is also a motive for the review. We end the review by addressing the follow-up for endoscopically resected lesions. These questions often cannot be answered easily due to the varying degrees of evidence available; therefore, we have made some general recommendations based on those made by the various guidelines and consensuses. The first screening colonoscopy should be offered 8 years after an IBD diagnosis and we recommend that patients be stratified according to the individual risk for each for endoscopic surveillance intervals.

Key words: Colitis surveillance; Colitis screening; Chromoendoscopy; Colorectal cancer; Inflammatory bowel disease

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Core tip: There is a worldwide consensus among all scientific societies regarding the recommendation
of screening for colorectal cancer in patients with inflammatory bowel disease (IBD). However, there are differences between the various recommendations that they make regarding the screening and surveillance that must be performed with these patients. We have reviewed the guidelines and consensuses from around the world on this subject and extracted some simple, general recommendations that can be used by all physicians who treat patients of this type. The first screening colonoscopy should be offered 8 years after a IBD diagnosis and we recommend that patients be stratified according to the individual risk for each for endoscopic surveillance intervals.

Huguet JM, Suárez P, Ferrer-Barceló L, Ruiz L, Monzó A, Durá AB, Sempere J. Endoscopic recommendations for colorectal cancer screening and surveillance in patients with inflammatory bowel disease: Review of general recommendations. World J Gastrointest Endosc 2017; 9(6): 255-262 Available from: URL: http://www.wjgnet.com/1948-5190/full/v9/i6/255.htm DOI: http://dx.doi.org/10.4253/wjge.v9.i6.255

INTRODUCTION

There is a worldwide consensus among all scientific societies regarding the recommendation of screening for colorectal cancer (CRC) in patients with inflammatory bowel disease (IBD) [1-19]. This should be carried out by means of colonoscopy. The optimal timing for the performance of the colonoscopy, as far as possible, is during the remission phase and with appropriate colonic cleansing. The objective is to detect potentially resectable premalignant lesions (dysplasia) and CRC in the early stages, which gives a better prognosis. Since the introduction of endoscopic screening techniques, the risk of CRC in IBD does not appear to have decreased, but CRC-related mortality has decreased [19].

However, there are differences among the various recommendations of the scientific societies about the screening and surveillance which must be performed with these patients. The reasons for this are the different dates of publication of these consensuses and the fact that, in some aspects, there is no clear evidence that can be applied. In addition, adherence to the guidelines is not always optimal, and this was demonstrated in a recent Japanese study in which only 63% of the respondents stated that they started screening between seven to ten years after onset of ulcerative colitis (UC), while up to 20% initiated it at three years or less [21], thus not conforming to the Guidelines for the management of UC in Japan [19].

The objective of this review is to address all the recommendations of the scientific societies regarding the screening and surveillance of CRC in IBD, so that the opportunity to formulate recommendations based on the guidelines and consensuses of the various scientific societies can be made available throughout the world. For our revision, we selected every scientific society whether local, national or international who ever published one or several papers with recommendations about the screening and surveillance process of the CRC in patients with IBD (Table 1). To make our recommendations we followed these criteria: (1) publishing date of the guide (stronger as more recent the date was); (2) number of scientific societies that supported the recommendations; and (3) agreement of at least 70% of the authors (5 out of 7) to add a recommendation to the list. The present review is structured as a series of questions which the physician poses in his or her daily clinical practice, followed by our recommendation with a subsequent review of the evidence available in the published guidelines and consensuses.

TO WHOM SHOULD CRC SCREENING BE OFFERED?

Our recommendation: Screening for CRC should be offered to the following patients with IBD: Patients with UC regardless of its extent; Patients with Crohn’s disease (CD) which affects at least 1/3 of the colon or with complex perianal disease; Patients with an ileo-anal pouch; Patients with indetermined or unclassified colitis (IC). The endoscopy should preferably be performed in clinical-biological remission situations and should allow an estimation of the individual risk of CRC, as well as the extent of the disease.

All scientific societies agree on this point [1-19] without exception, in offering screening to patients with IBD. NZGG (New Zealand Guidelines Group) recommends a risk-benefit assessment for patients with significant associated comorbidities and for patients over 75 years of age for whom screening risks may outweigh the
WHEN SHOULD THE FIRST SCREENING COLONOSCOPY BE PERFORMED?

Our recommendation: The first screening colonoscopy should be offered 8 years after a CD or UC diagnosis. For a diagnosis of primary sclerosing cholangitis (PSC), colonoscopy should be performed as soon as possible. With an ileo-anal pouch, it should be performed one year after the surgical intervention. Patients with first-degree relatives who have been diagnosed with CRC at an age of less than 50 should be offered the first endoscopy 10 years before the age of the family member when affected by CRC or eight years after diagnosis of IBD (whichever occurs earlier).

Most scientific societies recommend performing the first endoscopy between eight and ten years after the diagnosis or onset of symptoms. North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) recommends starting screening 1 year earlier than other protocols. The 2013 ECCO guidelines for UC[5] management bring this first colonoscopy forward to six to eight years from the onset of symptoms. However, ECCO recommends starting the screening at eight years in its 2013 endoscopy guideline[1], as do CCA[6], American Society for Gastrointestinal Endoscopy (ASGE)[7], American Gastroenterological Association (AGA)[15] and Asia-Pacific in its CD guideline[23]. However, BSG[5], Asociación Colombiana de Gastroenterología (ACOG)[17] and NICE[13] recommend initiating the first screening endoscopy ten years after the diagnosis. Yet other scientific societies delay the initiation of screening depending on whether it is a left-side colitis or pancolitis[12]. The rest recommend the first screening at between eight and ten years after diagnosis or the onset of symptoms[1,3,6,7,9,11,12,13,15,18]. For a PSC diagnosis, there is a consensus that the first endoscopy should be performed when the disease is detected and, as we will see later, there is no doubt that there should be annual colonoscopy[1,3,7,9,11,13,15,18]. None of the guidelines or consensuses specify when the first endoscopy should be performed for an ileo-anal pouch, although there is more consensus regarding the subsequent follow-up.

There is a consensus that there is an added risk factor for CRC in patients with IBD who have a family history of CRC. However, CCA is the only society that makes a specific recommendation, indicating that if there is a family history of CRC, screening should begin before eight years after the diagnosis of the disease[6]. It also indicates that, in those young patients whose only additional risk factor is having a first-degree relative with CRC at less than 50 years of age, the screening should be performed ten years before the age of the affected family member at the time of diagnosis[6].

WHO SHOULD BE OFFERED ENDOSCOPIC SURVEILLANCE?

Our recommendation: After endoscopic screening, endoscopic follow-up should be performed for all patients except for those with ulcerative proctitis, CD with involvement of less than 1/3 of the colon, and those in which the risks outweigh the possible benefits.

This aspect is addressed by the majority of the guidelines, and there is a general consensus about not performing endoscopic surveillance for CRC screening in patients with proctitis or with CD of minimal extent[1,6,7,9,11,12,13,15,18], as their risk of developing neoplasia is very low. AGA also excludes patients with procotosigmoiditis from follow-up[15]. Only the ECCO-Elderly[22], NICE[13] and NZGG[16] guidelines refer to the need for balancing the risks and benefits of performing endoscopic surveillance for elderly patients and those with significant comorbidities or with a short life expectancy.

SHOULD THE SAME ENDOSCOPIC SURVEILLANCE INTERVALS BE FOLLOWED FOR ALL PATIENTS?

Our recommendation: No. We recommend that patients be stratified according to the individual risk for each.

The most recently published guidelines and consensuses recommend stratifying patients with IBD who will be included in an endoscopic surveillance programme according to individual risk[1,3,7,11,13,15,17,18]. In this way, we will be able to offer a more individualised endoscopic follow-up to each patient.

ARE THERE INDIVIDUAL RISK FACTORS THAT ALLOW US TO STRATIFY ENDOSCOPIC SURVEILLANCE?

Our recommendation: Yes.

In patients with left-sided UC or pancolitis and CD which affects at least 1/3 of the colon, having any of the following must be considered high risk factors: PSC, extensive involvement, moderate-severe active inflammation sustained over time (endoscopic or histological), first-degree relative with CRC at an age of less than 50, stenosis or dysplasia detected during the previous five years. Any of the following should also be
considered as intermediate risk factors: Extensive colitis with mild or moderate sustained active inflammation (endoscopic or histological), the occurrence of inflammatory polyps or having a first-degree relative with CRC at an age of greater than 50. A diagnosis of IBD at a young age should be taken into account as a relative risk factor (due to the long duration of the disease).

The following should be considered high-risk factors in cases where there is an ileo-anal pouch: Dysplasia or previous CRC, PSC, type C mucosa in the pouch (persistent atrophy and severe inflammation).

The most recent recommendations coincide in establishing some risk factors for the development of CRC in patients with IBD. The following are risk factors according to ECCO, NZGG, BSG and ACPGBI, CCA, ASGE, American College of Gastroenterology (ACG), Crohn’s and Colitis Foundation of America (CCFA), NICE, AGA, World Gastroenterology Organization (WGO), ACOG and SVG: PSC, extensive involvement, moderate–severe active inflammation sustained over time (endoscopic or histological), first-degree relative with CRC at an age of less than 50, and stenosis or dysplasia detected during the previous five years

If ileo-anal pouch: Dysplasia or previous CRC, PSC, type C mucosa in the pouch (persistent atrophy and severe inflammation). They also agree that a liver transplant for PSC does not eliminate the risk of CRC. There is no consensus in the guidelines regarding whether the onset of IBD at a very young age should be considered a risk factor. In relation to this, AGA considers that the screening should be performed on these patients more for the duration of the disease than for its appearance at a young age. However, according to BSG, CCFA, WGO and SVG, the appearance of IBD at a young age should be considered a high risk factor. The following are considered intermediate risk factors according to ECCO, NZGG, BSG and ACPGBI, NICE, and ACOG: Extensive colitis with mild or moderate sustained inflammatory activity (endoscopic or histological), the occurrence of inflammatory polyps, and a first-degree relative with CRC at an age of above 50.

On the other hand, ECCO, BSG and ACPGBI, CCA and SVG consider the following to be high risk factors for patients with an ileo-anal pouch: Dysplasia or previous CRC, PSC, type C mucosa in the pouch (persistent atrophy and severe inflammation).
there are no risk factors, a colonoscopy should be performed every five years[1,5,6,18].

WHAT IS THE RECOMMENDED ENDOSCOPIC TECHNIQUE FOR SCREENING AND SURVEILLANCE?

Our recommendation: Chromoendoscopy with endoscopic resection or taking biopsies directed at visible lesions is the technique of choice. If this is not possible, high-definition video-colonoscope should be used and four biopsies taken for every ten cm of the colon.

The consensuses published in recent years coincide in pointing out that chromoendoscopy with endoscopic resection or taking biopsies directed at visible lesions is the preferred surveillance technique, as it increases the number of dysplastic lesions that can be detected[1,5,7,8,25]. Although it is true that this technique increases the time required for the exploration, the analysed studies conclude that it is more cost-effective than white-light colonoscopy. The principal disadvantages to its performance are that it requires thorough intestinal preparation and more time to complete the exploration, and the endoscopist must be specifically trained[25]. The guidelines of AGA[24], BSG[5], NICE[13], ECCO[1] and CCFA[11] support this technique if done properly by expert endoscopists. This technique may improve the detection of flat dysplasia and help ensure the complete resection of polypoid or minimally elevated lesions. Therefore, it could be of value in the follow-up of high-risk patients[1,3-7,24].

When chromoendoscopy is not available, or a suitable expert is not available, or if its performance is hindered due to significant inflammation, pseudopolyps, poor preparation or poorly visualised mucosal areas, then the taking of random biopsies in addition to biopsies targeting any suspected lesions appears to be a reasonable alternative[1,3-5,7], but it must be taken into account that the detection of neoplasias is inferior to that of chromoendoscopy[1]. For cases in which white-light colonoscopy are used, the high-definition colonoscopy are preferred to the standard colonoscopy, as the visualisation is better. When using a standard endoscope, the use of chromoendoscopy is preferred over white-light[25]. Although there is no evidence regarding the quantity of biopsies to be taken, some guidelines recommend taking at least four biopsies from each segment of the colon every ten cm[1,4]. In the recently published SCENIC Consensus (Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in IBD Patients: International Consensus Recommendations)[25], there is no clear agreement among experts regarding the quantity of biopsies to take or the manner in which they should be taken.

Narrow-band imaging has not been shown to increase the detectability of dysplasia during endoscopy[1,7,25]. More studies are needed to evaluate the effectiveness of Narrow-band imaging as well as other techniques such as the use of autofluorescence or microscopic confocal endoscopy[1,5,6,24,25].

HOW IS CHROMENDOSCOPY PERFORMED?

Our recommendation: Use 0.04% to 0.1% methylene blue or between 0.1% to 0.03% indigo carmine. Perform cecal intubation and apply a dye to the colon mucosa as the endoscope is removed, if possible using a catheter spray. Examine one segment before apply colorant in the next. Normally 0.1% methylene blue or 0.03% to 0.1% indigo carmine is used. Cecal intubation should be performed using a white-light endoscope. The colonic mucosa should then be stained by spray aspirating the excess fluids and carefully evaluating the mucosa. Once the lesion is localised, chromoendoscopy helps to delimit it, assess its size and borders and perform techniques that help rule out submucosal invasion[1,7,8,25].

DOES THE OCCURRENCE OF DYSPLASIA REQUIRE CONFIRMATION?

Our recommendation: The occurrence of dysplasia must be confirmed by a second pathologist. Histopathological analysis is qualitative and consequently has a high inter-observer variability, especially in low grade dysplasia and in inflamed mucosa. Therefore, there is a general consensus that the occurrence of dysplasia should be confirmed by an independent expert gastrointestinal pathologist[1,4-7,11,15,18,21,25].

WHAT TERMINOLOGY SHOULD WE USE TO DESCRIBE LESIONS DETECTED WITH ENDOSCOPY?

Our recommendation: The terms “dysplasia-associated lesion or mass” (DALM) and “flat lesions” should be discontinued. We should be using the modified Paris Classification in which lesions are divided into visible dysplasia and invisible dysplasia depending on whether the biopsy has been taken from a lesion visualised in the colonoscopy or not. Visible dysplasia is divided into polypoid and non-polypoid depending on whether or not the lesion protrudes from the lumen ≥ 2.5 mm. The descriptions of visible lesions should also include mention of whether they are ulcerated and whether the borders are easily distinguished from the surrounding mucosa.

The ECCO guideline[1] insists on discontinuing the terms “DALM” and “flat lesions” and using the Paris Classification[26]. It also differentiates between endoscopically visible and non-visible lesions. The ASGE[7] guideline adds to the above the importance of distinguishing whether the lesions are located in an area affected by colitis, whether or not the borders...
Lesion without protrusion above the mucosa
Lesion not attached to the mucosa by a stalk: Entire
Lesion attached to the mucosa by a stalk

**Definition**

- **Lesion’s border is discrete and can be distinguished from surrounding mucosa**
- **Lesion with at least a portion depressed below the level of the mucosa**
- **Lesion protruding from the mucosa into the lumen**
- **Lesion’s border is not discrete and cannot be distinguished from surrounding mucosa**

**Terminology for reporting findings**[25].

| Term                  | Definition                                                                 |
|-----------------------|-----------------------------------------------------------------------------|
| Visible dysplasia     | Dysplasia identified on targeted biopsies from a lesion visualised at colonoscopy |
| Polypoid              | Lesion protruding from the mucosa into the lumen ≥ 2.5 mm                   |
| Pedunculated Sessile  | Lesion attached to the mucosa by a stalk                                   |
| Sessile               | Lesion not attached to the mucosa by a stalk: Entire base is contiguous with the mucosa |
| Nonpolypoid           | Lesion with little (< 2.5 mm) or no intrusion above the mucosa              |
| Superficially elevated| Lesion with protrusion but < 2.5 mm above the lumen (less than the height of the closed cup of a biopsy forceps) |
| Flat                  | Lesion without protrusion above the mucosa                                  |
| Depressed             | Lesion with at least a portion depressed below the level of the mucosa      |
| General descriptors   | Ulcerated Ulceration (fibrous-appearing base with depth) within the lesion |
| Border                | Distinct border Lesion’s border is discrete and can be distinguished from surrounding mucosa |
| Indistinct border     | Lesion’s border is not discrete and cannot be distinguished from surrounding mucosa |
| 2 Invisible dysplasia | Dysplasia identified on random (non-targeted) biopsies of colon mucosa without a visible lesion |

Lesions that are endoscopically visible and well-defined, irrespective of their location and degree of dysplasia or whether or not there is involvement by colitis, should be endoscopically resected by an expert endoscopist, and biopsies should be taken of the adjacent mucosa[1,5,7,11,15,25]. The ASGE guideline also recommends preparing tattoo and photo-documentation of the resected lesions. They also suggest colectomy as a possibility to discuss with the patient, if the completely excised lesion exhibits high-grade dysplasia (HGD)[27]. If complete resection is anatomicopathologically confirmed, and there is no dysplasia in the adjacent mucosa or elsewhere in the colon, the indication is close endoscopic follow-up. If the described conditions are not met, the treatment would be total colectomy.

### HOW SHOULD NON-VISIBLE DYSPLASIA BE INITIALLY MANAGED?

**Our recommendation:** Dysplasia which is not endoscopically visible but found in serial biopsies of the colon must be confirmed by an independent pathologist after the performance of a chromoendoscopy by an expert endoscopist. If confirmed, management will depend on the degree of dysplasia.

**As for the management of invisible dysplasia, that which is detected in random colon biopsies, the quality of the evidence in the recommendations is very low[27].** The ECCO[1] and ASGE guidelines[7] and the SCENIC Consensus[25] indicate repeating colonoscopy with chromoendoscopy, regardless of the degree of dysplasia, by an expert endoscopist to confirm that there is no endoscopically visible lesion, and taking random biopsies to rule out the occurrence of synchronous dysplasia. If an endoscopically visible lesion is detected after this examination, and there is no more dysplasia elsewhere, they recommend endoscopic resection.

### HOW SHOULD NON-VISIBLE DYSPLASIA BE MANAGED IN RELATION TO THE DEGREE OF DYSPLASIA?

**Our recommendation:** Endoscopically non-visible HGD is an indication for colectomy. The management of low-grade, invisible dysplasia should be agreed upon in a multidisciplinary committee and with the patient, with colectomy or endoscopic follow-up being the two possible options.

In the event that HGD or adenocarcinoma is detected without a visible lesion, surgery is the recommended option[1,5,7,15]. If low-grade dysplasia without a visible lesion is detected in the second chromoendoscopy performed by an expert, the degree of agreement among the guidelines is lower. It must be a multidisciplinary decision and discussed with the referring surgeon.

**How should a visible lesion be managed?**

Our recommendation: Visible lesions which are well delimited, with no evidence of dysplasia in the mucosa adjacent to the lesion and without synchronous dysplasia, should be resected endoscopically regardless of the degree of dysplasia.

Lesions that are endoscopically visible and well-defined, irrespective of their location and degree of dysplasia or whether or not there is involvement by colitis, should be endoscopically resected by an expert endoscopist, and biopsies should be taken of the adjacent mucosa[1,5,7,11,15,25]. The ASGE guideline also recommends preparing tattoo and photo-documentation of the resected lesions. They also suggest colectomy as a possibility to discuss with the patient, if the completely excised lesion exhibits high-grade dysplasia (HGD)[27]. If complete resection is anatomicopathologically confirmed, and there is no dysplasia in the adjacent mucosa or elsewhere in the colon, the indication is close endoscopic follow-up. If the described conditions are not met, the treatment would be total colectomy.
patient\textsuperscript{1,4,5,7,11,15,25}. Colectomy is recommended if low-grade dysplasia is multifocal, but the recommendations are more conservative for low-grade, unifocal dysplasia, and a closer annual endoscopic follow-up may be offered\textsuperscript{1,5,7,11,15,25}.

The New Zealand Guidelines Group\textsuperscript{4} advocates offering colectomy to all patients who are found to have dysplasia, and performing close endoscopic follow-up only in those who refuse or are unfit for surgical treatment.

**HOW SHOULD ENDOSCOPICALLY RESECTED LESIONS BE FOLLOWED?**

Our recommendation: The follow-up for resected lesions in healthy mucosa which is not affected by colitis should be the same as that for sporadic adenomas. Lesions which are endoscopically resected in areas affected by colitis should be examined endoscopically at three months, and annually thereafter.

There is a strong consensus that the management of lesions detected in mucosal areas not affected by colitis should be the same as that of sporadic adenomas\textsuperscript{1,3,7,11,15,25}. As for lesions located in areas where there is or has been active inflammation, which have been endoscopically resected and in which there is no dysplasia of the surrounding mucosa, the follow up should be close. The ECCO guideline\textsuperscript{7} recommends performing an endoscopy at three months, and if there is no dysplasia, to change to annual endoscopic follow-up, preferably with chromoendoscopy. ASGE\textsuperscript{7} recommends an initial examination at between one to six months and then changing to annual monitoring. The SCENIC Consensus\textsuperscript{23,25} distinguishes between polypoid and non-polypoid lesions. For polypoid lesions, it advises follow up at three to six months and then annually if they are sessile, large and excised in a fragmented manner. However, for those smaller polyps excised en bloc, it advises immediate annual follow-up. As for non-polypoid dysplastic lesions, they recommend monitoring at three to six months (the risk of CRC is greater, and it is more difficult to ensure that the polypectomy has been complete).

**SUMMARY OF OUR RECOMMENDATIONS**

CRC screening should be offered to patients with IBD (UC, IC, CD affecting at least 1/3 of the colon or with complex perianal disease and to patients with an ileo-anal pouch). The first screening colonoscopy should be offered eight years after a diagnosis of CD or UC; at one year after the surgical construction of an ileo-anal pouch, or at the time of the diagnosis of PSC. It should be kept in mind that subsequent endoscopic surveillance should be performed on all patients except for those with ulcerative proctitis, CD with involvement of less than 1/3 of the colon and those for which the risks far outweigh the possible benefits. We recommend patient stratification according to the individual risk of each patient in order to determine more individualised follow-up intervals. The technique of choice for endoscopic surveillance is chromoendoscopy with endoscopic resection or biopsy of visible lesions. Regarding the terminology to be used, we should use the modified Paris Classification and abandon terms such as “DALM” and “flat lesions”. Regarding the management of lesions, we should differentiate between visible and invisible lesions. Visible lesions which are well delimited, with no evidence of dysplasia in the mucosa adjacent to the lesion and without synchronous dysplasia, should be resected endoscopically regardless of the degree of dysplasia. Dysplasia which is not endoscopically visible but found in serial biopsies of the colon must be confirmed by an independent anatomical pathologist after the performance of a chromoendoscopy by an expert endoscopist. If this is confirmed, management will depend on the degree of dysplasia. Endoscopically non-visible HGD is an indication for colectomy. The management of low-grade invisible dysplasia should be agreed upon in a multidisciplinary committee and with the patient, with colectomy or endoscopic follow-up being the two possible options. The follow-up for resected lesions in healthy mucosa which is not affected by colitis should be the same as that for sporadic adenomas. However, lesions which are endoscopically resected in areas affected by colitis should be examined endoscopically at three months, and annually thereafter.

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