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# Surveillance of long-standing colitis: The role of image-enhanced endoscopy



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#### АВЅТ Я А С Т

Patients with long-standing inflammatory bowel disease of the colon are at an increased risk of developing colorectal carcinoma. Surveillance programs have been implemented with the aim of detecting neoplastic lesions in an early stage. Due to limitations of conventional white light endoscopy, several new techniques to enhance the detection of dysplastic lesions in this setting have been explored. These advanced endoscopic techniques use a variety of methods to improve visualization, such as pancolonic dyespraying (chromoendoscopy), optical filters (narrow-band imaging) and autofluorescence of mucosal tissue (autofluorescence imaging). At present, most guidelines have adopted chromoendoscopy as the preferred method for surveillance, based on several controlled studies. It is currently unknown if widespread implementation of chromoendoscopy will lead to an improved clinical outcome.

This review explores the current evidence on image-enhanced endoscopic techniques used in the detection of neoplastic lesions in patients with long standing colitis.

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Abbreviations: IEE, image enhanced endoscopy; WLE, white light endoscopy; HD-WLE, high-definition white light endoscopy; CE, chromoendoscopy; NBI, narrow-band imaging; FICE, Fujinon intelligent color enhancement; AFI, Autofluorescence imaging; ADR, adenoma detection rate; IN, intraepithelial neoplasia; CRC, colorectal cancer; IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis.

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#### Introduction

Patients with inflammatory bowel disease (IBD) are at an increased risk of developing colorectal cancer (CRC) [1-3]. This association has been shown for both ulcerative and Crohn's colitis [4] with cumulative risks estimated to amount to 18% for a disease duration of 30 years [3]. More recent population-based studies show a less distinct risk for the general IBD population [5-8], possibly owing to improved and more effective therapeutic regimens, the effects of surveillance or different kinds of bias in the early reports. Presently, the risk of CRC in the whole IBD population is estimated to be increased with a standardized incidence ratio of 1.7 [5]. The highest risk is encountered in patients cared for in referral centers, patients with a longer disease duration and/or extensive colitis and in patients diagnosed before the age of 30, a concomitant diagnosis of primary sclerosing cholangitis (PSC) and a family history of CRC [9–13]. Recently, we created a prediction rule for IBD-associated CRC, based on the presence of PSC, extensive colitis and post-inflammatory polyps, which was found to reliably distinguish patients with a high or low risk of developing CRC [14].

Endoscopic characterization of dysplastic lesions in colonic mucosa affected by IBD can be challenging, owing to the variable appearance of precancerous lesions. Mucosal abnormalities relating to colitis, both inflammatory and post-inflammatory (e.g. scarring or inflammatory polyps), may also cause difficulty in differentiating benign from dysplastic lesions. In addition, the occurrence of nonpolypoid dysplasia with minimal or no elevation, which is considered a frequently encountered phenotype in IBD [15], further hampers identification of dysplasia in this setting.

Until recently, endoscopically raised lesions containing dysplasia were termed dysplasia-associated lesions or masses (DALMs). Early studies reported high cancer rates in association with the occurrence of DALMs and therefore colectomy was advocated in these cases [16,17]. More recently, polyps with dysplasia found in an area of inflammation that have an endoscopic resemblance to sporadic adenomas (adenoma-like masses or ALMs) were described [18,19]. Several studies have shown that endoscopic resection of ALMs is feasible and safe if patients are closely followed-up thereafter [20–22].

Due to improvements in endoscopes, different classification of lesions and changes in management decisions, several authors have suggested to abandon the DALM/ALM-nomenclature [23,24]. In addition, it is now widely acknowledged that nearly all dysplastic lesions are endoscopically visible [25,26]. Hence, for lesions in an area affected by inflammation, clinicians are increasingly pursuing a classification based on endoscopic resectability. Lesions that are both completely resectable and have negative biopsies from surrounding mucosa may indicate a better prognosis, in which case management can be based on endoscopic techniques rather than colectomy [21,23].

Despite the ongoing debate on the true risk of IBD-associated neoplasia, there is a widely held consensus on the need for surveillance in patients with long-standing and extensive IBD of the colon. Most major guidelines state that surveillance should be initiated 8–10 years after diagnosis, or immediately when coexistent PSC is diagnosed. Depending on additional risk stratification, surveillance intervals may vary between 1 and 5 years [27–32].

Until now, a direct link between early detection of dysplasia and a decrease in CRC-related mortality has not been evidently shown. A Cochrane systematic review was only able to include three studies that had a comparison group that had not received surveillance [33]. Although in these studies CRCs tended to be detected at an earlier stage, no clear effect on patient survival was shown. However, more recent retrospective studies have reported improved survival rates for patients undergoing surveillance [34,35]. Although a high percentage of interval CRCs, as observed in a British cohort followed for more than 30 years [7], might hamper the effectiveness of surveillance, a recent study on interval CRCs reported far lower incidence rates [36].

Until recently, the established method for surveillance had been the combination of standard white light endoscopy and taking random biopsies. Traditionally, this involved taking 4-quadrant biopsies every 10 cm along the colon, aimed at retrieving a minimum of 33 biopsies [37]. This strategy has recently been found to be largely ineffective, with one estimated episode of dysplasia detected for every 1505 random biopsies taken [38]. This finding, and the notion that almost all IBD-associated dysplastic lesions are in fact endoscopically visible [25,26], prompted updates of several guidelines in which the use of an image enhanced endoscopy technique (i.e. chromoendoscopy) was advocated.

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