REVIEW

Endoscopic surveillance strategies for dysplasia in ulcerative colitis

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ABSTRACT

Ulcerative colitis (UC) is a chronic inflammatory bowel disorder with an increased risk of colorectal cancer (CRC). This has led to the implementation of surveillance programmes to minimise this risk. Overall, these proactive programmes in association with better medical therapies have reduced the incidence of CRC in this population. Specific populations remain at increased risk, such as younger age at diagnosis, primary sclerosing cholangitis, colonic strictures and pseudopolyps. The majority of gastrointestinal international societies favour chromoendoscopy with targeted biopsies or random biopsies. The aim of this review is to present the current literature on dysplasia surveillance, the methodology and endoscopic technology available to assess dysplasia in UC.

Key points:

- ▶ Ulcerative colitis (UC) is a chronic inflammatory bowel disorder that is associated with an increased risk of colorectal cancer.
- ▶ Surveillance programmes are promoted to screen for dysplasia in patients with longstanding UC. Better outcomes are obtained with early diagnosis.
- ▶ Screening intervals differ based on risk factors and presence of inflammation.
- ▶ Most international societies support chromoendoscopy with targeted biopsies for dysplasia surveillance. However, it has technical limitations and longer procedural time.
- ▶ Other endoscopic modalities are being evaluated, but more research is required in inflammatory bowel disease population.

INTRODUCTION

Ulcerative colitis (UC) is a chronic idiopathic inflammatory bowel disease (IBD) with a relapsing and remitting course that increases the risk of patients developing colorectal cancer (CRC) when compared with the general population. There is now strong evidence that chronic mucosal inflammation is a main driver of the CRC risk.¹ The cumulative CRC risk in UC, regardless of disease extent, was initially estimated to be 2%, 8% and 18% after 10, 20 and 30 years of disease, respectively, in a 2001 meta-analysis.² A meta-analysis of population-based cohort studies demonstrated a 2.4-fold increased risk of CRC in UC (95% CI 2.1 to 2.7), which represented an overall CRC occurrence of 1.6% during the first 14 years of follow-up.³ The North California data 1998–2010 comparing CRC in the IBD versus general population showed a 1.6-fold higher risk of CRC in IBD, with an overall incidence of CRC in IBD being 60% higher than that of the general population.⁴ However, a 2012 Danish population-based study

determined that the CRC risk among patients with UC was comparable with that of the general population over a 30-year period (RR 1.07; 95% CI 0.95 to 1.21).⁵ Overall, recent population-based studies have shown a declining CRC risk, which has been attributed to improved control of inflammation, the possible chemopreventive effect of 5-ASAs, immunomodulators, biologics and improved colonoscopy surveillance in detection of early colonic neoplasia.^{3–9} Nevertheless, synchronous tumours are more common in IBD than in sporadic CRC and patients with IBD overall tend to develop CRC at a younger age and have lower survival rates than patients with non-IBD CRC.¹⁰

Risk factors for the development of CRC in IBD include younger age at diagnosis, longer duration and extent of disease, family history of CRC, chronic colonic mucosal inflammation, presence of colonic strictures, pseudopolyps and a shortened colon (table 1).^{11–14} In addition, patients with UC with concomitant

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Table 1 Recommendations for dysplasia surveillance in UC by major international societies

Society	Surveillance intervals	Recommended technique
ECCO (2017) ⁴⁸	<p>Neither intermediate nor high risk: every 5 years</p> <p>Intermediate risk: every 2–3 years</p> <ul style="list-style-type: none"> ▶ Extensive colitis with <i>mild</i> or <i>moderate</i> active inflammation ▶ Post-inflammatory polyps <ul style="list-style-type: none"> – CRC in a FDR >50 <p>High risk: every year</p> <ul style="list-style-type: none"> ▶ Extensive colitis with <i>severe</i> active inflammation ▶ Stricture or dysplasia within 5 years ▶ PSC (including post-OLT) <ul style="list-style-type: none"> – CRC in a FDR <50 	<ul style="list-style-type: none"> ▶ CE with targeted biopsies ▶ Random biopsies (4 every 10 cm) with targeted biopsies of visible lesions if CE is not available; but WLE is inferior to CE in dysplasia detection ▶ When performing surveillance with WLE, HD is recommended rather than SD
SCENIC (2015) ¹⁷	N/A	<ul style="list-style-type: none"> ▶ Surveillance with WLE, HD is <i>recommended</i> rather than SD ▶ Surveillance with SD colonoscopy, CE is <i>recommended</i> rather than WLE ▶ Surveillance with HD colonoscopy, CE is <i>suggested</i> rather than WLE ▶ NBI is not suggested in place of WLE (SD or HD) or CE
ASGE (2015) ⁴⁹	<p>Every 1–3 years</p> <ul style="list-style-type: none"> ▶ If mucosa is endoscopically and histologically normal on first two surveillance colonoscopies, the interval can be lengthened <p>Annual surveillance</p> <ul style="list-style-type: none"> ▶ Active inflammation ▶ History of dysplasia ▶ Anatomical abnormality (stricture, multiple pseudopolyps) ▶ PSC ▶ CRC in a FDR 	<ul style="list-style-type: none"> ▶ CE with pancolonial dye spraying and targeted biopsies, consider two biopsies from each colon segment for histological staging ▶ Random biopsies with targeted biopsies of any suspicious lesions if CE is not available or if the yield of CE is reduced by significant inflammation, pseudopolyps or poor preparation ▶ Pancolitis: 4 biopsies every 10 cm from caecum to rectum, for minimum of 33 biopsies ▶ No pancolitis: 4 biopsies every 10 cm limited to greatest extent of endoscopic or histological involvement documented by any colonoscopy
ESGE (2014) ⁵⁰	N/A	<ul style="list-style-type: none"> ▶ Pancolonial CE (0.1% methylene blue or 0.1%–0.5% indigo carmine) with targeted biopsies
BSG (2011) ⁵¹	<p>Low risk: every 5 years</p> <ul style="list-style-type: none"> ▶ Extensive colitis with <i>no</i> active (endoscopic or histological) inflammation ▶ Left-sided colitis <p>Intermediate risk: every 3 years</p> <ul style="list-style-type: none"> ▶ Extensive colitis with <i>mild</i> active (endoscopic or histological) inflammation ▶ Post-inflammatory polyps ▶ CRC in a FDR >50 <p>High risk: every year</p> <ul style="list-style-type: none"> ▶ Extensive colitis with <i>moderate</i> to <i>severe</i> active (endoscopic or histological) inflammation ▶ Stricture within 5 years ▶ Dysplasia within 5 years who declined surgery ▶ PSC (including post-OLT) ▶ CRC in a FDR <50 	<ul style="list-style-type: none"> ▶ Pancolonial CE with targeted biopsies ▶ 2–4 random biopsies from every 10 cm of the colorectum with targeted biopsies of visible lesions if CE is not used

Continued

Table 1 Continued

Society	Surveillance intervals	Recommended technique
Cancer Council of Australia ⁵² (2011)	Every year: <ul style="list-style-type: none"> ▶ Active disease ▶ PSC ▶ CRC in a FDR <50 ▶ Colon stricture ▶ Inflammatory polyps ▶ Shortened colon ▶ Previous dysplasia Every 3 years <ul style="list-style-type: none"> ▶ Inactive UC extending proximal to sigmoid colon without any of the above risk factors and CRC in a FDR >50 Every 5 years <ul style="list-style-type: none"> ▶ Two previous colonoscopies that were macroscopically and histologically normal 	<ul style="list-style-type: none"> ▶ CE with targeted biopsies obtained from visible lesions or strictures ▶ Random non-targeted biopsies from each colon segment and from raised lesions with WLE, if CE is unavailable
AGA (2010) ²³	Extensive or left-sided colitis should begin surveillance within 1 to 2 years after initial screening endoscopy. Optimal surveillance interval not defined Every 1–3 years <ul style="list-style-type: none"> ▶ After two negative examinations (no dysplasia or cancer) More frequent surveillance <ul style="list-style-type: none"> ▶ CRC in a FDR ▶ Active endoscopic or histologic inflammation ▶ Anatomical abnormality (foreshortened colon, stricture, inflammatory pseudopolyps) Every year <ul style="list-style-type: none"> ▶ PSC 	<ul style="list-style-type: none"> ▶ Random 4-quadrant biopsy from each anatomical section of the colon are recommended ▶ CE with targeted biopsies is considered an accepted alternative to WLE for experienced endoscopists
ACG (2010) ⁵³	<ul style="list-style-type: none"> ▶ Annual or biannual surveillance 	<ul style="list-style-type: none"> ▶ Multiple biopsies at 10 cm intervals

ACG, American College of Gastroenterology; AGA, American Gastroenterology Association; ASGE, American Society for Gastrointestinal Endoscopy; BSG, British Society of Gastroenterology; CE, chromoendoscopy; CRC, colorectal cancer; ECCO, European Crohn's and Colitis Organisation; ESGE, European Society of Gastrointestinal Endoscopy; FDR, first-degree relative; HD, high-definition; NBI, narrow-band imaging; OLT, orthotopic liver transplantation; PSC, primary sclerosing cholangitis; SCENIC, Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients: International Consensus Recommendations; SD, standard definition; WLE, white-light endoscopy.

primary sclerosing cholangitis (PSC) carry an increased risk of developing colorectal neoplasia (OR 2.98; 95% CI 1.54 to 5.76) and cancer (OR 3.01; 95% CI 1.44 to 6.29).¹⁵ In light of these findings, surveillance colonoscopies are strongly recommended as they have been shown to increase detection of neoplastic lesions and subsequently improve survival through the detection of early stage CRC.¹² Technological advancements in endoscopic imaging, such as high-definition (HD), chromoendoscopy (CE) and dye-less virtual chromoendoscopy (VCE) like narrow-band imaging (NBI), have improved the optical diagnosis and outcomes of dysplasia surveillance in IBD. This review will discuss the supporting literature and technological advances available in clinical practice for the surveillance of dysplasia in long-standing UC.

Endoscopic surveillance

The data highlight the importance of endoscopic surveillance in patients with UC with

inflammation proximal to the rectum; however, there are no randomised controlled trials that demonstrate a mortality benefit. A 2017 Cochrane review of five observational studies concluded that surveillance in long-standing IBD may reduce the development of both CRC and CRC-associated mortality through early detection (OR 0.58; 95% CI 0.19 to 0.69), although the quality of evidence was very low.¹⁶ The observed survival benefit may, however, be explained by detection of earlier stage CRC that resulted in improved outcomes of the surveillance group. Similarly, a retrospective cohort study of 149 patients found that a 5-year CRC-related survival rate in the surveillance group was 100% compared with 74% in the non-surveillance group ($p=0.042$), with earlier tumour stages found in the surveillance group ($p=0.004$).¹⁷ Other population-based cohort and case-control studies have also shown this reduction in colitis-associated mortality.^{18–20}

All guidelines recommend screening patients with UC with a history of endoscopic and/or histological evidence of inflammation extending proximal to the rectum. The initiation of a surveillance colonoscopy programme is recommended no later than 8 years following a diagnosis or onset of IBD symptoms, and at a time of diagnosis in patients with PSC.

Societies differ in regards to timing of surveillance intervals and optimal method of detecting dysplasia. In terms of surveillance intervals, the American gastrointestinal societies (American College of Gastroenterology, American Gastroenterological Association, American Society for Gastrointestinal Endoscopy) endorse screening every 1–3 years, whereas the European and Australian guidelines (European Crohn's and Colitis Organization, British Society of Gastroenterology, Cancer Council of Australia) prefer a risk-stratified approach based on high-risk factors. The recently published SCENIC International Consensus support the use of CE and targeted biopsies as opposed to high-definition colonoscopy and random four-quadrant biopsies every 10 cm in screening CRC.²¹ Furthermore, the majority of other international gastrointestinal societies support the same conclusion, despite low quality of evidence. A summary of risk factors for the development of CRC in patients with IBD and recommended surveillance by various international societies have been included in [table 1](#).

Random versus targeted biopsies

Dysplasia was initially thought to be flat and invisible, hence, the principle of performing a colonoscopy with random four-quadrant biopsies every 10 cm. For an adequate surveillance examination, it has been shown that 33 random biopsy specimens are required to detect dysplasia with 90% sensitivity.^{22,23} This random biopsy approach, however, has a low yield of dysplasia detection, is costly and time consuming, with low adherence by gastroenterologists in the community. Furthermore, a retrospective review of a tertiary IBD centre showed adequate biopsy sampling for surveillance in only 53.7% of patients with UC and 54.2% of patients with colonic CD despite good adherence to surveillance guidelines overall (75.6% in UC, 82.1% in colonic CD).²⁴ A retrospective analysis performed by van den Broek *et al* evaluated the yield of random biopsies during a 10-year surveillance programme with UC and found that neoplasia was identified in 0.2% of random biopsies while 94% of lesions were endoscopically visible.²⁵

There is indeed mounting evidence to suggest targeted biopsies should be used with CE and high-definition white-light endoscopy (HD-WLE) over random sampling. A Japanese multicentre randomised controlled trial of 246 patients with UC showed that HD-WLE targeted and random biopsies (11.4% vs 9.3%, $p=0.617$) detected similar rates of dysplasia, with targeted biopsies being more cost-effective and

time-effective.²⁶ A prospective cross-over study of 150 patients with IBD comparing HD-WLE with random biopsy, HD-WLE with targeted biopsies and CE with targeted biopsies revealed that a significantly higher number of dysplasias was detected with CE with targeted biopsies.²⁷ The Canadian study of Gasia *et al* supports targeted biopsies whether one is using HD-WLE, CE or VCE.²⁷ However, a recently published prospective study from France performed 1000 consecutive surveillance colonoscopies and compared targeted and random sampling; their result showed 20% of dysplastic lesions found were only detected on random biopsies. Subsequent multivariate analysis highlighted that patients with high-risk features such as personal history of dysplasia, concurrent PSC and shortened colon may in fact benefit from the use of random biopsies along with targeted ones due to the higher dysplasia rates, even when using CE; however, further data would be needed to confirm these findings.²⁸

Standard definition versus high-definition white-light endoscopy

SCENIC guidelines state HD-WLE is preferred over standard definition white-light endoscopy (SD-WLE), where a better image quality is beneficial given most dysplasia is visible.²¹ Nevertheless, a randomised controlled trial in a non-IBD population showed higher adenoma detection rate with HD-WLE over SD-WLE.²⁹ Subsequently, Subramanian *et al* performed a retrospective analysis of surveillance colonoscopies to compare the yield of dysplasia detection by SD-WLE with HD-WLE in patients with long-standing IBD. The study demonstrated significantly more dysplasia detection with HD-WLE in comparison with SD-WLE and with HD-WLE with targeted biopsies. The adjusted prevalence ratio for HD-WLE dysplasia detection was 2.21 (95% CI 1.09 to 4.45) and with targeted biopsies was 2.99 (95% CI 1.16 to 7.79).³⁰ Technology, nevertheless, does not replace the fact that the quality of the examination is increased with optimal bowel preparation and longer withdrawal time.³¹

Chromoendoscopy

Multiple studies compared CE and WLE as seen in [table 2](#). Kiesslich *et al* conducted the original randomised control trial of 165 patients with UC who were randomised to undergo SD-WLE or CE using 0.1% methylene blue. The study showed that the number of patients with dysplasia did not differ statistically as to whether they received CE or not (13 vs 6); however, more dysplastic lesions were found with CE (32 vs 10; $p=0.004$), as well as more dysplasia in flat mucosa (24 vs 4; $p=0.001$).³² Rutter *et al* completed a cross-over study of patients with long-standing UC, starting with SD-WLE with targeted and random biopsies and sequential CE with targeted biopsies in 100 patients. Dysplasia was found

Table 2 Chromoendoscopy vs white-light endoscopy studies

Authors (year)	Design	Dye	Number of patients	Patients with dysplasia	Comparison endoscopy	Dysplasia detection rate
Kiesslich <i>et al</i> (2003) Germany ³²	Randomised	MB 0.1%	165	13	SD-WLE	32 vs 10 DL
Matsumoto <i>et al</i> (2003) Japan ⁵⁴	Prospective cohort	IC 0.2%	57	12	SD-WLE	86% vs 38% sensitivity
Rutter <i>et al</i> (2004) UK ³³	Prospective cohort/crossover	IC 0.1%	100	7	SD-WLE	9 vs 2 DL
Hurlstone <i>et al</i> (2005) UK ⁵⁵	Prospective cohort	IC 0.5%	700	81	SD-WLE	69 vs 24 DL
Kiesslich <i>et al</i> (2007) Germany ⁵⁶	Randomised	MB 0.1%	153	15	SD-WLE	19 vs 4 DL
Marion <i>et al</i> (2008) USA ⁵⁷	Tandem colonoscopy	MB 0.1%	102	19	SD-WLE	17 vs 3 patients with DL
Günther <i>et al</i> (2011) Germany ⁵⁸	Randomised	IC 0.1%	150	6	SD-WLE	6 vs 0 patients with DL
Hlavaty <i>et al</i> (2011) Slovakia ⁵⁹	Tandem colonoscopy	IC 0.4%	20	7	SD-WLE	7 vs 0 DL
Picco <i>et al</i> (2013) USA ⁶⁰	Crossover	IC 0.2%	75	16	HD-WLE	22 vs 10 DL
Freire <i>et al</i> (2014) Portugal ⁶¹	Randomised, parallel-group	MB 0.1%	72	6	SD-WLE	7 vs 6 DL
Mohammed <i>et al</i> (2015) UK ³⁷	Randomised, parallel-group	IC 0.2%	103	11	HD-WLE	14 vs 6 DL
Carballal <i>et al</i> (2016) Spain ⁶²	Crossover	IC 0.4%	350	N/A	SD/HD-WLE	94 vs 40 DL
Iacucci <i>et al</i> (2016) Canada ⁶³	Randomised	IC 0.03% or MB 0.04%	180	22	HD-WLE	42 vs 27
Park <i>et al</i> (2016) Korea ⁶⁴	Randomised	IC	210	N/A	HD-WLE	20.6% vs 12.0%

CE, chromoendoscopy; DL, dysplastic lesion; HD-WLE, high-definition white-light endoscopy; IC, indigo carmine; MB, methylene blue; SD-WLE, standard definition white-light endoscopy.

in two biopsies under SD-WLE versus seven biopsies in targeted CE protocol ($p=0.06$).³³ Recently, a meta-analysis of three studies comparing CE versus SD-WLE in patients with UC was completed and showed that CE has increased dysplasia-detection rates over WLE with an OR of 2.47 per patient (95% CI 1.32 to 4.6; $p=0.005$) and OR 3.73 per lesion (95% CI 2.2 to 6.33; $p<0.00001$).³⁴ Meanwhile, Iannone *et al* showed CE was superior to SD-WLE only, as there was no diagnostic benefit for CE over HD-WLE, in a systematic review of 10 randomised controlled trials.³⁵ Real-life data from Mooiweer *et al* showed no increase in dysplasia detection with CE versus WLE with targeted or random biopsies.³⁶ Yet, the reported Spanish real-life experience with CE reports a higher diagnostic yield in CE over either WLE.³⁷ Therefore, low-quality data support the superiority of CE over SD-WLE; however, there were not enough data to suggest that CE is preferred over HD-WLE.³⁸ A significant element against CE is that it can be more time consuming than other modalities. Furthermore, CE uptake may be affected by the concern regarding learning of the new technique; however, a study by Caballal *et al* showed a comparable dysplasia detection rate between expert

and non-expert endoscopists using CE and report no significant learning curve effect.

CE consists of the application of diluted methylene blue or indigo carmine (concentration of 0.1% to 0.5%) during the withdrawal period with the use of a foot pump or via a spray catheter, to improve identification and characterisation of lesions. Indigo carmine is not absorbed by the mucosa, unlike methylene blue. Targeting the antigravity aspects of the bowel allow for more efficient coating of the lumen; suction of pools of excess dye allows for careful mucosal examination. In CE, the bowel preparation must be optimal, where any remaining residue should be removed during colonoscopy insertion. The disease must be in remission to ensure adequate differentiation between active inflammation and dysplasia, at the risk of potentially producing false-positive results.³⁹ The modified Paris classification should be used to define any lesion or dysplasia encountered during colonoscopy, characterising it as polypoid (sessile or pedunculated) or non-polypoid (slightly elevated, flat, depressed).⁴⁰ The pit pattern should then be assessed using the Kudo classification (types I–V) to predict the histological diagnosis of the lesion.⁴¹ Defining lesion borders will

Table 3 Narrow-band imaging (NBI) vs other modalities

Authors (year)	Design	Number of patients	Patients with dysplasia	Comparison endoscopy	Dysplasia detection rate
Dekker <i>et al</i> (2007) Netherlands ⁶⁵	Randomised crossover	42	8	SD-WLE	9 vs 12 DL
van den Broek <i>et al</i> (2011) Netherlands ⁶⁶	Randomised crossover	48	9	HD-WLE	13 vs 11 DL
Pellisé <i>et al</i> (2011) Spain ⁶⁷	Randomised crossover	60	12	CE (IC 0.5%)	10 vs 12 DL
Feitosa <i>et al</i> (2011) Brazil ⁶⁸	Randomised, parallel-group	16	0	CE (N/A)	0 vs 3 DL
Ignjatovic <i>et al</i> (2012) UK ⁶⁹	Randomised, parallel-group	112	10	HD-WLE	5 vs 7 DL
Bisschops <i>et al</i> (2012) Belgium ⁷⁰	Randomised	108	22	CE (MB 0.1%)	18.5% vs 16.7% DL
Efthymiou <i>et al</i> (2013) Australia ⁷¹	Crossover	44	10	CE (MB 0.1%)	17 vs 20 DL
Leifeld <i>et al</i> (2015) Germany ⁷²	Crossover	159	22	HD-WLE	31 vs 30 DL
Watanabe <i>et al</i> (2016) Japan ⁷³	Randomised	263	N/A	CE (IC)	11.9% vs 10.7% DL
Bisschops <i>et al</i> (2018) Belgium/Canada ⁴³	Randomised	131	14	CE (MB 0.1%)	21 vs 31 DL

CE, chromoendoscopy; DL, dysplastic lesion; HD-WLE, high-definition white-light endoscopy; IC, indigo carmine; MB, methylene blue; SD-WLE, standard definition white-light endoscopy.

be critical to determine if it is endoscopically resectable. Following a polypectomy or endoscopic mucosal resection, biopsies of the resection margins should be taken to ensure completeness of the resection.⁴²

Virtual chromoendoscopy

Virtual or dye-less CE (NBI [Narrowband Imaging; Olympus], i-Scan [Pentax], FICE [Fuji Intelligent Chromo-Endoscopy]) is an imaging technique where the white light projected is filtered which narrows the wavelength towards blue and green light. Blue light has a shallow penetration depth into the mucosa and is the main colour absorbed by haemoglobin, which allows for detailed examination of the mucosa and superficial vasculature. A meta-analysis of four studies comparing WLE and NBI in patients with UC showed no statistical difference between the groups, with an OR per-patient analysis of 0.97 (95% CI 0.62 to 1.53; $p=0.91$) and OR for per-lesion analysis of 0.94 (95% CI 0.63 to 1.4; $p=0.68$); the use of HD endoscopy did not alter these results.³⁰ Moreover, a multicentre prospective randomised controlled trial of 131 patients with UC by Bisschops *et al* found no difference in dysplasia detection rates between HD-CE and NBI; however, NBI had reduced procedure time compared with CE.⁴³ A recent meta-analysis by Har-Noy *et al* found no difference in the diagnostic yield between CE and NBI ($n=104$, per-patient analysis OR 1.0 [95% CI 0.51 to 1.95], per-lesion analysis OR 1.29 [95% CI 0.69 to 2.41]).³⁰ A summary of NBI studies is found in table 3. Meanwhile, iSCAN has very limited data and FICE has not been studied in clinical trials in the

IBD population. Iacucci *et al* evaluated high-definition iSCAN against CE and HD-WLE in a randomised non-inferiority trial of 270 patients with IBD and concluded that iSCAN and HD-WLE were non-inferior to CE.⁴⁴

NBI is not yet supported by guidelines as it has not been shown to be superior to WLE, although it seems to be similar to CE. The SCENIC consensus guidelines in particular have concluded virtual CE should not replace CE at this time.

Endoscopic modalities under investigation

Autofluorescence imaging (AFI) is based on the detection of natural tissue fluorescence emitted by endogenous molecules (fluorophores) such as collagen and porphyrins. Differences in fluorescence emissions between normal and neoplastic tissue after exposure to short-wavelength light translates into normal mucosa appearing green and dysplasia appearing purple. Van den Broek *et al* performed a small prospective pilot trial with a randomised cross-over design of WLE biopsies versus AFI-targeted biopsies and, promisingly, showed higher detection in AFI group.⁴⁵ However, Vleugels *et al* recently published a multicentre prospective randomised controlled trial comparing CE and AFI in a cohort of 210 patients with long-standing UC ($n=105$ AFI); the mean number of detected dysplastic lesions per patient was 0.13 (SD 0.37) for AFI and 0.37 (SD 1.02) for CE (relative dysplasia detection rate 0.36 [80% CI 0.21 to 0.61]). They subsequently concluded AFI should not be further investigated for surveillance in UC.⁴⁶

Confocal laser endomicroscopy is a novel technique that allows the real-time in vivo histological characterisation of lesion found during endoscopy. It is used for targeted lesion assessment only, and must be combined with another technique such as WLE or CE, hence it usually requires longer procedure times.^{38 47} It remains mainly experimental and the data for its use are very limited.

Endocytoscopy requires pretreatment with a mucolytic agent and staining with dyes such as methylene blue, and then a probe-based system is used allowing for ×1400 magnification and histological assessment. However, this has not been assessed in dysplasia surveillance in IBD as of yet.

CONCLUSION

UC is a chronic inflammatory disorder associated with an increased risk of dysplasia and colorectal cancer. As such, surveillance endoscopy programmes have been established to prevent this outcome, despite limited evidence. Technological advances have created opportunities for evaluation of dysplasia in the patient with UC, despite much debate over the best methodology to follow. Overall, CE with targeted biopsies seems to offer a higher rate of dysplastic lesion detection, although with longer procedure time. However, random biopsies, in addition to targeted ones, may be considered in patients with high-risk features. Further studies are required to better define the optimal surveillance modality.

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REFERENCES

- Flores BM, O'Connor A, Moss AC. Impact of mucosal inflammation on risk of colorectal neoplasia in patients with ulcerative colitis: a systematic review and meta-analysis. *Gastrointest Endosc* 2017;86:1006–11.
- Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. *Gut* 2001;48:526–35.
- Jess T, Simonsen J, Jørgensen KT, *et al.* Decreasing risk of colorectal cancer in patients with inflammatory bowel disease over 30 years. *Gastroenterology* 2012;143:375–81.
- Herrinton LJ, Liu L, Levin TR, *et al.* Incidence and mortality of colorectal adenocarcinoma in persons with inflammatory bowel disease from 1998 to 2010. *Gastroenterology* 2012;143:382–9.
- Lutgens MWMD, van Oijen MGH, van der Heijden GJMG, *et al.* Declining risk of colorectal cancer in inflammatory bowel disease: an updated meta-analysis of population-based cohort studies. *Inflamm Bowel Dis* 2013;19:789–99.
- Velayos FS, Terdiman JP, Walsh JM. Effect of 5-aminosalicylate use on colorectal cancer and dysplasia risk: a systematic review and Metaanalysis of observational studies. *Am J Gastroenterology* 2005;100:1345–53.
- Choi C-HR, Rutter MD, Askari A, *et al.* Forty-year analysis of colonoscopic surveillance program for neoplasia in ulcerative colitis: an updated overview. *Am J Gastroenterol* 2015;110:1022–34.
- Bonovas S, Fiorino G, Lytras T, *et al.* Systematic review with meta-analysis: use of 5-aminosalicylates and risk of colorectal neoplasia in patients with inflammatory bowel disease. *Aliment Pharmacol Ther* 2017;45:1179–92.
- Carrat F, Seksik P, Colombel J-F, *et al.* The effects of aminosalicylates or thiopurines on the risk of colorectal cancer in inflammatory bowel disease. *Aliment Pharmacol Ther* 2017;45:533–41.
- Ording AG, Horváth-Puhó E, Erichsen R, *et al.* Five-year mortality in colorectal cancer patients with ulcerative colitis or Crohn's disease: a nationwide population-based cohort study. *Inflamm Bowel Dis* 2013;19:800–5.
- Fumery M, Pineton de Chambrun G, Stefanescu C, *et al.* Detection of dysplasia or cancer in 3.5% of patients with inflammatory bowel disease and colonic strictures. *Clin Gastroenterol Hepatol* 2015;13:1770–5.
- Lutgens M, Vermeire S, Van Oijen M, *et al.* A rule for determining risk of colorectal cancer in patients with inflammatory bowel disease. *Clin Gastroenterol Hepatol* 2015;13:148–54.
- Beaugerie L, Itzkowitz SH. Cancers complicating inflammatory bowel disease. *N Engl J Med* 2015;372:1441–52.
- Beaugerie L, Svrcek M, Seksik P, *et al.* Risk of colorectal high-grade dysplasia and cancer in a prospective observational cohort of patients with inflammatory bowel disease. *Gastroenterology* 2013;145:166–75.
- Zheng H-H, Jiang X-L. Increased risk of colorectal neoplasia in patients with primary sclerosing cholangitis and inflammatory bowel disease: a meta-analysis of 16 observational studies. *Eur J Gastroenterol Hepatol* 2016;28:383–90.
- Bye WA, Nguyen TM, Parker CE, *et al.* Strategies for detecting colon cancer in patients with inflammatory bowel disease. *The Cochrane Library* 2017;13.
- Lutgens MWMD, Oldenburg B, Siersema PD, *et al.* Colonoscopic surveillance improves survival after colorectal cancer diagnosis in inflammatory bowel disease. *Br J Cancer* 2009;101:1671–5.
- Löfberg R, Broström O, Karlén P, *et al.* Colonoscopic surveillance in long-standing total ulcerative colitis—15-year follow-up study. *Gastroenterology* 1990;99:1021–31.
- Eaden J, Abrams K, Ekbom A, *et al.* Colorectal cancer prevention in ulcerative colitis: a case-control study. *Aliment Pharmacol Ther* 2000;14:145–53.
- Ananthakrishnan AN, Cagan A, Cai T, *et al.* Colonoscopy is associated with a reduced risk for colon cancer and mortality in patients with inflammatory bowel diseases. *Clin Gastroenterol Hepatol* 2015;13:322–9.
- 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.
- Rubin CE, Haggitt RC, Burmer GC, *et al.* DNA aneuploidy in colonic biopsies predicts future development of dysplasia in ulcerative colitis. *Gastroenterology* 1992;103:1611–20.
- 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.

- 24 Singh K, Al Khoury A, Kurti A, *et al.* High adherence to surveillance guidelines in IBD results in low CRC and dysplasia rates, while rates of dysplasia and cancer are low before the suggested start of surveillance. Results from a tertiary IBD center. *J Crohns Colitis* 2019;jjz066.
- 25 van den Broek FJC, Stokkers PCF, Reitsma JB, *et al.* Random biopsies taken during colonoscopic surveillance of patients with longstanding ulcerative colitis: low yield and absence of clinical consequences. *Am J Gastroenterol* 2014;109:715–22.
- 26 Watanabe T, Ajioka Y, Mitsuyama K, *et al.* Comparison of Targeted vs Random Biopsies for Surveillance of Ulcerative Colitis-Associated Colorectal Cancer. *Gastroenterology* 2016;151:1122–30.
- 27 Gasia MF, Ghosh S, Panaccione R, *et al.* Targeted biopsies identify larger proportions of patients with colonic neoplasia undergoing high-definition colonoscopy, dye chromoendoscopy, or electronic virtual chromoendoscopy. *Clin Gastroenterol Hepatol* 2016;14:704–12.
- 28 Moussata D, Allez M, Cazals-Hatem D, *et al.* Are random biopsies still useful for the detection of neoplasia in patients with IBD undergoing surveillance colonoscopy with chromoendoscopy? *Gut* 2018;67:616–24.
- 29 Rastogi A, Early DS, Gupta N, *et al.* Randomized, controlled trial of standard-definition white-light, high-definition white-light, and narrow-band imaging colonoscopy for the detection of colon polyps and prediction of polyp histology. *Gastrointestinal Endoscopy* 2011;74:593–602.
- 30 Subramanian V, Ramappa V, Telakis E, *et al.* Comparison of high definition with standard white light endoscopy for detection of dysplastic lesions during surveillance colonoscopy in patients with colonic inflammatory bowel disease. *Inflamm Bowel Dis* 2013;19:350–5.
- 31 Barclay RL, Vicari JJ, Doughty AS, *et al.* Colonoscopic withdrawal times and adenoma detection during screening colonoscopy. *N Engl J Med* 2006;355:2533–41.
- 32 Kiesslich R, Fritsch J, Holtmann M, *et al.* Methylene blue-aided chromoendoscopy for the detection of intraepithelial neoplasia and colon cancer in ulcerative colitis. *Gastroenterology* 2003;124:880–8.
- 33 Rutter MD *et al.* Pancolonic indigo carmine dye spraying for the detection of dysplasia in ulcerative colitis. *Gut* 2004;53:256–60.
- 34 Har-Noy O, Katz L, Avni T, *et al.* Chromoendoscopy, narrow-band imaging or white light endoscopy for neoplasia detection in inflammatory bowel diseases. *Dig Dis Sci* 2017;62:2982–90.
- 35 Iannone A, Ruospo M, Wong G, *et al.* Chromoendoscopy for surveillance in ulcerative colitis and Crohn's disease: a systematic review of randomized trials. *Clin Gastroenterol Hepatol* 2017;15:1684–97.
- 36 Mooiweer E, van der Meulen-de Jong AE, Ponsioen CY, *et al.* Chromoendoscopy for surveillance in inflammatory bowel disease does not increase neoplasia detection compared with conventional colonoscopy with random biopsies: results from a large retrospective study. *Am J Gastroenterol* 2015;110:1014–21.
- 37 Mohammed N, Kant R, Abid F, *et al.* 446 high definition white light endoscopy (Hdwle) versus high definition with Chromoendoscopy (Hdce) in the detection of dysplasia in long standing ulcerative colitis: a randomized controlled trial. *Gastrointest Endosc* 2015;81.
- 38 Bessissow T, Dulai PS, Restellini S, *et al.* Comparison of endoscopic dysplasia detection techniques in patients with ulcerative colitis: a systematic review and network meta-analysis. *Inflamm Bowel Dis* 2018;24:2518–26.
- 39 Flynn AD, Valentine JF. Chromoendoscopy for dysplasia surveillance in inflammatory bowel disease. *Inflamm Bowel Dis* 2018;24:1440–52.
- 40 Inoue H, Kashida H, Kudo S, *et al.* The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach and colon. *Gastrointest Endosc* 2003;58:S3–43.
- 41 Kudo S, Tamura S, Nakajima T, *et al.* Diagnosis of colorectal tumorous lesions by magnifying endoscopy. *Gastrointest Endosc* 1996;44:8–14.
- 42 Kaltenbach T, Sandborn WJ. Endoscopy in IBD: advances in dysplasia detection and management. *Gastrointest Endosc* 2017;86:962–71.
- 43 Bisschops R, Bessissow T, *et al.* Chromoendoscopy vs NBI in ulcerative colitis: a prospective RCT. *Gut* 2018;67:1087–94.
- 44 Iacucci M, Kaplan GG, Panaccione R, *et al.* A randomized trial comparing high definition colonoscopy alone with high definition dye spraying and electronic virtual chromoendoscopy for detection of colonic neoplastic lesions during IBD surveillance colonoscopy. *Am J Gastroenterol* 2018;113:225–34.
- 45 van den Broek FJC, Fockens P, van Eeden S, *et al.* Endoscopic tri-modal imaging for surveillance in ulcerative colitis: randomised comparison of high-resolution endoscopy and autofluorescence imaging for neoplasia detection; and evaluation of narrow-band imaging for classification of lesions. *Gut* 2008;57:1083–9.
- 46 Vleugels JLA, Rutter MD, Ragunath K, *et al.* Chromoendoscopy versus autofluorescence imaging for neoplasia detection in patients with longstanding ulcerative colitis (FIND-UC): an international, multicentre, randomised controlled trial. *Lancet Gastroenterol Hepatol* 2018;3:305–16.
- 47 Naymagon S, Marion JF, Lewis J. Surveillance in inflammatory bowel disease: chromoendoscopy and digital mucosal enhancement. *Gastrointest Endosc Clin N Am* 2013;23:679–94.
- 48 Magro F, Gionchetti P, Eliakim R, *et al.* Third European evidence-based consensus on diagnosis and management of ulcerative colitis. Part 1: definitions, diagnosis, extra-intestinal manifestations, pregnancy, cancer surveillance, surgery, and ileo-anal pouch disorders. *J Crohn's Colitis* 2017;11:649–70.
- 49 Shergill AK, Lightdale JR, Bruining DH, *et al.* The role of endoscopy in inflammatory bowel disease. *Gastrointest Endosc* 2015;81:1101–21.
- 50 Kamiński M, Hassan C, Bisschops R, *et al.* Advanced imaging for detection and differentiation of colorectal neoplasia: European Society of (ESGE) guideline. *Endoscopy* 2014;46:435–57.
- 51 Mowat C, Cole A, Windsor A, *et al.* Guidelines for the management of inflammatory bowel disease in adults. *Gut* 2011;60:571–607.
- 52 Party C, ed. *Clinical practice guidelines for surveillance colonoscopy in adenoma follow-up: following curative resection of colorectal cancer; and for cancer surveillance in inflammatory bowel disease*. Sydney, Australia: Cancer Council of Australia, 2011.
- 53 Kornbluth A, Sachar DB, Practice Parameters Committee of the American College of Gastroenterology. Ulcerative colitis practice guidelines in adults: American College of Committee. *Am J Gastroenterol* 2010;105:501–23.
- 54 Matsumoto T, Nakamura S, Jo Y, *et al.* Chromoscopy might improve diagnostic accuracy in cancer surveillance for ulcerative colitis. *Am J Gastroenterol* 2003;98:1827–33.
- 55 Hurlstone D, Sanders D, Lobo A, *et al.* Indigo carmine-assisted high-magnification chromoscopic colonoscopy for the detection and characterisation of intraepithelial neoplasia in ulcerative colitis: a prospective evaluation. *Endoscopy* 2005;37:1186–92.
- 56 Kiesslich R, Goetz M, Lammersdorf K, *et al.* Chromoscopy-guided endomicroscopy increases the diagnostic yield of intraepithelial neoplasia in ulcerative colitis. *Gastroenterology* 2007;132:874–82.

- 57 Marion JF, Wayne JD, Present DH, *et al.* Chromoendoscopy-targeted biopsies are superior to standard colonoscopic surveillance for detecting dysplasia in inflammatory bowel disease patients: a prospective endoscopic trial. *Am J Gastroenterol* 2008;103:2342–9.
- 58 Günther U, Kusch D, Heller F, *et al.* Surveillance colonoscopy in patients with inflammatory bowel disease: comparison of random biopsy vs. targeted biopsy protocols. *Int J Colorectal Dis* 2011;26:667–72.
- 59 Hlavaty T, Huorka M, Koller T, *et al.* Colorectal cancer screening in patients with ulcerative and Crohn's colitis with use of colonoscopy, chromoendoscopy and confocal endomicroscopy. *Eur J Gastroenterol Hepatol* 2011;23:680–9.
- 60 Picco MF, Pasha S, Leighton JA, *et al.* Procedure time and the determination of polypoid abnormalities with experience: implementation of a chromoendoscopy program for surveillance colonoscopy for ulcerative colitis. *Inflamm Bowel Dis* 2013;19:1913–20.
- 61 Freire P, Figueiredo P, Cardoso R, *et al.* Surveillance in ulcerative colitis: is chromoendoscopy-guided endomicroscopy always better than conventional colonoscopy? A randomized trial. *Inflamm Bowel Dis* 2014;20:2038–45.
- 62 Carballal S, Maisterra S, López-Serrano A, *et al.* Real-life chromoendoscopy for neoplasia detection and characterisation in long-standing IBD. *Gut* 2018;67:70–8.
- 63 Iacucci M, Gasia MF, Akinola O, *et al.* 624 final results of a randomized study comparing high definition colonoscopy alone with high definition dye spraying and electronic virtual Chromoendoscopy using iSCAN for detection of colonic neoplastic lesions during IBD surveillance colonoscopy. *Gastroenterology* 2016;150.
- 64 Park SJ, Kim H-S, Yang D-H, *et al.* Tu2086 high definition Chromoendoscopy with water-jet versus high definition white light endoscopy in the detection of dysplasia in long standing ulcerative colitis: a multicenter prospective randomized controlled study. *Gastroenterology* 2016;150.
- 65 Dekker E, van den Broek F, Reitsma J, *et al.* Narrow-band imaging compared with conventional colonoscopy for the detection of dysplasia in patients with longstanding ulcerative colitis. *Endoscopy* 2007;39:216–21.
- 66 van den Broek F, Fockens P, van Eeden S, *et al.* Narrow-band imaging versus high-definition endoscopy for the diagnosis of neoplasia in ulcerative colitis. *Endoscopy* 2011;43:108–15.
- 67 Pellisé M, López-Cerón M, Rodríguez de Miguel C, *et al.* Narrow-band imaging as an alternative to chromoendoscopy for the detection of dysplasia in long-standing inflammatory bowel disease: a prospective, randomized, crossover study. *Gastrointest Endosc* 2011;74:840–8.
- 68 Feitosa F, Carlos A, Nogueira JG, *et al.* Narrow-band imaging and chromoendoscopy for the detection of colonic dysplasia in inflammatory bowel disease: a prospective and randomized study. *Inflamm Bowel Dis* 2011;17:S14–S15.
- 69 Ignjatovic A, East JE, Subramanian V, *et al.* Narrow band imaging for detection of dysplasia in colitis: a randomized controlled trial. *Am J Gastroenterol* 2012;107:885–90.
- 70 Bisschops R, Bessissow T, Baert FJ, *et al.* 506 Chromo-Endoscopy versus narrow band imaging in ulcerative colitis: a prospective randomized controlled trial. *Gastrointest Endosc* 2012;75:AB148–148.
- 71 Efthymiou M, Allen PB, Taylor ACF, *et al.* Chromoendoscopy versus narrow band imaging for colonic surveillance in inflammatory bowel disease. *Inflamm Bowel Dis* 2013;19:2132–8.
- 72 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;13:1776–81.
- 73 Watanabe K, Nishishita M, Shimamoto F, *et al.* 722 comparison between Newly-Developed narrow band imaging and Panchromoendoscopy for surveillance colonoscopy in patients with longstanding ulcerative colitis: a prospective multicenter randomized controlled trial, navigator study. *Gastrointest Endosc* 2016;83.