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#### **ORIGINAL ARTICLE**

### Serrated adenoma prevalence in inflammatory bowel disease surveillance colonoscopy, and characteristics revealed by chromoendoscopy and virtual chromoendoscopy

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**BACKGROUND:** Sessile or nonpolypoid neoplastic lesions, including sessile serrated adenomas (SSAs), are difficult to detect in patients with inflammatory bowel disease (IBD).

**OBJECTIVES:** To assess the prevalence and endoscopic features of SSA in IBD patients undergoing surveillance colonoscopy using novel endoscopic techniques.

METHODS: Histology results of biopsies from a cohort of 87 patients (47 men; median age 51.4 years; median duration of disease 16.9 years; ulcerative colitis [n=40], Crohn disease [n=43], ischemic colitis [n=4]) with longstanding colonic IBD undergoing surveillance colonoscopy were reviewed. Lesions of dysplasia (adenoma-like mass, or dysplasia-associated lesion or mass), SSAs, adenoma-like polyps, hyperplastic polyps and inflammatory polyps were identified. Surveillance colonoscopy using high-definition alone, or with iScan (Pentax, USA) dye-sprayed or virtual chromoendoscopy was performed. Lesion characteristics were described before histological diagnosis.

RESULTS: Fourteen SSAs were detected in 87 (11%) IBD patients. The endoscopic characteristics of SSA lesions were: nonpolypoid appearance (86%), predominant localization in the proximal colon (79%), >6 mm in size (79%), cloudy cover (64%), Kudo pit pattern modified type IIO (86%) and irregular spiral vascular pattern (79%). Among the 44 SSAs and hyperplastic polyps found in the present study, the above characteristics of SSA at colonoscopy had a sensitivity of 92.86% (95% CI 66.06% to 98.8%) and specificity of 93.33% (95% CI 77.89% to 98.99%) in predicting a histological diagnosis of SSA (positive predictive value 86.67%, negative predictive value 96.55%).

**CONCLUSION:** SSAs are a common finding at surveillance colonoscopy in IBD and have several characteristic features. Further studies are needed to evaluate the natural history of these lesions in IBD patients.

**Key Words:** High-definition iScan virtual and dye chromoendoscopy; Inflammatory bowel disease; Sessile serrated adenoma

The risk of developing dysplasia and colorectal cancer in patients with longstanding inflammatory bowel disease (IBD) is well recognized (1-4). Random biopsies during white-light standard-definition colonoscopy (33 to 50 biopsies) with or without dye spraying chromoendoscopy (CE) has been the recommended strategy in North America to detect dysplastic lesions in patients with IBD (5). Several studies have shown that CE-guided targeted biopsies are more accurate in detecting dysplasia in patients with longstanding IBD (6-9) compared with white-light endoscopy (WLE). In fact, a recent consensus guideline (10) endorsed the use of CE as the standard surveillance colonoscopy in these patients.

La prévalence d'adénome dentelé lors des coloscopies de surveillance de la maladie inflammatoire de l'intestin et les caractéristiques révélées par chromoendoscopie standard ou virtuelle

**HISTORIQUE:** Les lésions néoplasiques sessiles ou non polypoïdes, y compris les adénomes dentelés sessiles (ADS), sont difficiles à déceler chez les patients atteints d'une maladie inflammatoire de l'intestin (MII).

**OBJECTIFS :** Évaluer la prévalence et les caractéristiques endoscopiques de l'ADS chez les patients atteints d'une MII qui subissent une coloscopie de surveillance au moyen de nouvelles techniques endoscopiques.

MÉTHODOLOGIE: Des chercheurs ont analysé les résultats histologiques des biopsies d'une cohorte de 87 patients (47 hommes; âge médian de 51,4 ans; durée médiane de la maladie de 16,9 ans; colite ulcéreuse [n=40], maladie de Crohn [n=43], colite ischémique [n=4]) atteints d'une MII du côlon de longue date qui avaient subi une coloscopie de surveillance. Des lésions de dysplasie (masse adénomateuse ou lésion ou masse associée à la dysplasie), d'ADS, de polypes adénomateux, de polypes hyperplasiques et de polypes inflammatoires avaient été constatées. Une coloscopie de surveillance à haute définition, seule ou accompagnée d'une chromoendoscopie à coloration standard ou virtuelle iScan (Pentax, États-Unis), avait été effectuée. Les caractéristiques des lésions étaient décrites avant le diagnostic histologique.

RÉSULTATS: Quatorze ADS ont été décelés chez 87 patients atteints d'une MII (11 %). Les caractéristiques endoscopiques des lésions d'ADS étaient une apparence non polypoïde (86 %), un foyer prédominant dans le côlon proximal (79 %), une dimension de plus de 6 mm (79 %), une opacité (6 4%), un motif ulcéreux de Kudo modifié de type IIO (86%) et des motifs vasculaires irréguliers en spirale (79 %). Sur les 44 ADS et polypes hyperplasiques relevés dans la présente étude, les caractéristiques précédentes d'ADS à la coloscopie avaient une sensibilité de 92,86 % (95 % IC 66,06 % à 98,8 %) et une spécificité de 93,33 % (95 % IC 77,89 % à 98,99 %) pour prédire un diagnostic histologique d'ADS (valeur prédictive positive de 86,67 %, valeur prédictive négative de 96,55 %).

**CONCLUSION :** Les ADS sont des observations courantes lors des coloscopies de surveillance des MII et possèdent plusieurs caractéristiques. D'autres études s'imposent pour en évaluer l'évolution naturelle chez les patients atteints d'une MII.

The new generation of high-definition (HD) endoscopes with electronic filter technology provide minute details of colonic mucosal and vascular patterns, and may identify subtle flat, multifocal, polypoid, and pseudopolypoid neoplastic and non-neoplastic lesions (11-13). In addition, the newly developed iScan (Pentax, Japan) technology uses a digital contrast method to enhance mucosal and vascular patterns, and enhances endoscopic images. Advantages of electronic virtual CE over traditional CE include its convenience, lower cost and straightforward reversibility (14-17).

Emerging evidence has shown that serrated adenomas are also associated with longstanding IBD colitis, which may contribute to the

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development of colorectal cancer (18). Recently, the 'serrated neoplasia pathway' in IBD was defined according to morphological and molecular characteristics, and appears to be involved in IBD-related colorectal oncogenesis. The penultimate stage in the progression to carcinoma of this pathway are serrated polyps including hyperplastic polyps (HPs), traditional serrated adenomas and the more recently described sessile serrated adenomas (SSAs). Furthermore, some categories of serrated polyps previously classified as HPs are actually the precursors of serrated adenoma (19-21). However, these lesions may be overlooked during endoscopy due to their flat morphology, indefinite margins and cloudy pale colour, and they are often covered by mucus. Moreover, due to the morphological similarity with HPs, most detected SSAs are left in situ when they are misinterpreted by colonoscopists as clinically irrelevant HPs (22-26).

There is uncertainty regarding the real prevalence of SSA in IBD patients with known high risk for developing dysplasia. The endoscopic features of SSA in IBD are subtle and easily missed. Thus, in the present study, we aimed to assess the prevalence and characteristics of SSA detected in IBD patients undergoing surveillance endoscopies using novel digital endoscopic modalities.

#### **METHODS**

#### Study design

The present analysis was a retrospective cohort study performed at a single tertiary referral centre. All histology was reviewed by two gastrointestinal pathologists (XG and SU), and all colonoscopies were performed by a single experienced operator (MI) who was well trained in novel endoscopic techniques in IBD.

#### **Patients**

All patients diagnosed with inactive (Mayo subscore 0 to 1 and Harvey-Bradshaw <4) longstanding ulcerative colitis (UC) or Crohn disease (CD) (27,28) at the IBD clinic at the University of Calgary (Calgary, Alberta) from September 2011 to November 2013 were identified and enrolled in the study. All procedures were performed using HD iScan virtual CE or dye CE at the discretion of the endoscopist. During the study period, there was no clinical preference or specific recommendation for one of the two techniques. Exclusion criteria were: previous history of sporadic colon cancer; reported allergy to dye spray; liver cirrhosis; blood coagulation disorders; moderate to severe disease activity; inability to complete colonoscopy because of poor bowel preparation or patient intolerance; and pregnancy.

The extent of IBD was described according to the Montreal classification and clinical-endoscopic disease activity was determined using the Mayo score for UC, Harvey-Bradshaw and SES-CD for CD (27-30). Focal findings and abnormalities outside of markedly inflamed mucosa were classified according to the pit pattern classification of Kudo and Paris (31,32), and the routine practice of the endoscopist (MI) .

The Calgary Laboratory Services and the Conjoint Health Research Ethics Board of the University of Calgary approved the study.

#### Colonoscopic assessment

All colonoscopies were performed using an EPK-I (Pentax EC-3490Fi; Pentax, Japan) processor with HD alone, HD-iScan virtual CE using the three iScan settings in sequence from set 1 to set 3, devoting a mean time of 20 s for each single iScan setting or HD dye CE, in which methylene blue 0.2% was sprayed in a segmental fashion for the entire withdrawal procedure. The methylene blue dye was sprayed using a catheter through the working channel of the endoscope, according to routine practice.

#### iScan technology

The iScan is a new digital virtual CE system developed by Pentax, Japan. It is a postprocessing imaging technology that analyzes endoscopic images in real time, and consists of three types of algorithms: surface enhancement (SE), contrast enhancement and tone enhancement, each of

which can be selected by pressing a preassigned button on the handpiece of the endoscope. SE enhances light-dark contrast by obtaining luminance intensity data for each pixel. With SE, the difference in luminance intensity between the pixels of interest and the surrounding pixels is analyzed and the edge components are enhanced. Contrast enhancement digitally adds blue colour to relatively dark areas. The iScan system can provide detailed analysis based on vessel (iScan v), mucosal pattern (iScan p) or surface architecture (iScan SE), (16,29). The vascular pattern, surface architecture and mucosal pattern can characterize inflammation and colonic neoplastic lesions (13-15).

#### Biopsy protocol

Mucosal abnormalities were analyzed with regard to location (anatomy and distance from the anus [in cm]), morphology (polypoid, flat or depressed) and size using the Paris classification (31). The Paris classification divides lesions into three main categories: I – protruding lesions (Is sessile or Ip pedunculated); II – nonprotruding and nonexcavated lesions (IIa flat elevated, IIb completely flat and IIc slightly depressed); and III – excavated lesions (31).

For each lesion, mucosal pit pattern was characterized according to the Kudo classification (32). On withdrawal of the colonoscope from the cecum to the anus, sequential targeted biopsy specimens from targeted areas of suspected dysplasia (circumscribed lesions with irregular surface) were obtained. Any suspicious lesions detected during examination were sampled or immediately removed. This conforms to current guidelines for targeted biopsies of detected lesions.

#### Histological assessment

A comprehensive histological assessment was performed by two gastrointestinal histopathologists (XG and SU) who were blinded to the endoscopic findings. Pathology classification of inflammatory activity were graded using the Harpaz New York Mount Sinai score into no inflammation, mild to moderate inflammation, or severe inflammation. Neoplastic changes were classified according to the recently revised Vienna classification (33-35).

An SSA was defined as a serrated lesion with irregular dilated crypts, including dilation of the base of the crypts, which often have a boot, L or inverted T shape.

#### Statistical analysis

Interobserver agreement was calculated using the Fleiss kappa measurement. Interobsever and intraobserver agreement were expressed using the kappa coefficient: a kappa value <0.20 indicates poor agreement, 0.20 to 0.40 fair, 0.41 to 0.60 moderate, 0.61 to 0.80 good and 0.81 to 1.0 excellent. The study was observational and not powered to show superiority of any specific technique.

#### RESULTS

#### Patient demographic characteristics and procedure indications

A cohort of 87 consecutive IBD patients (47 [54%] male), median age 51.4 years (range 23 to 86 years), median duration of disease (UC [n=40], CD [n=43], ischemic colitis [n=4]) 16.9 years with longstanding (≥8 years) colonic IBD undergoing surveillance colonoscopy was included for study analysis. The demographic characteristics of the patients are summarized in Table 1.

At the discretion of the endoscopist (MI), a specialist in IBD colonoscopy, 24 (27.6%) patients underwent surveillance using HD colonoscopy alone, 35 (40.2%) using HD-iScan virtual CE and 28 (32.2%) using HD dye CE (Table 2).

#### Prevalence of SSA in the surveillance cohort

Fourteen SSAs were noted in 10 of 87 (11%) IBD patients, accounting for 19% of all lesions detected. None of the IBD patients with SSAs had a family history of colon cancer or personal history of polyps or dysplastic lesions.

TABLE 1
Demographic characteristics in each group of inflammatory bowel disease (IBD) patients

	Endoscopy					
	HD alone	HD + CE	HD iScan* + DCE (n=28)			
Characteristic	(n=24)	(n=35)				
Male sex	15 (62.5)	15 (42.8)	17 (60.7)			
Age, years, mean ± SD	47.62±14.46	51.94±11.07	54.11±14.48			
Ulcerative colitis/Crohn disease/ischemic colitis, n/n/n	10/13/1	18/14/3	12/16/-			
Pancolitis	7 (70)	10 (55.5)	8 (66.7)			
Left-sided colitis	3 (30)	8 (44.4)	4 (33.3)			
Duration of IBD, years, mean ± SD	15.58±7.88	18.31±8.94	13.75±8.5			
Treatment with mesalazine	6 (25)	14 (40)	12 (42.9)			
Treatment with immunosuppressants	5 (21)	4 (11.4)	5 (17.9)			
Treatment with biological	4 (17)	5 (14.3)	5 (17.9)			
Combination treatment	2 (8)	3 (8.5)	1 (3.5)			
No treatment	7 (33.3)	8 (22.8)	4 (14.2)			
Family history of colorectal cancer	3 (12.5)	2 (5.7)	1 (3.5)			
Personal history of colorectal adenoma	7 (33.3)	5 (14.3)	9 (32.1)			
Primary sclerosing cholangitis	5 (21)	3 (8.5)	1 (3.5)			

Data presented as n (%) unless otherwise indicated. \*Pentax, Japan. CE Chromoendoscopy; DCE Dye sprayed CE; HD High definition

TABLE 2
Baseline characteristics of colonic lesions in inflammatory bowel disease patients

_		Endoscopy	
	HD alone	HD + CE	HD + iScan* DCE
Characteristic	(n=24)	(n=28)	(n=35)
Serrated adenoma	2 (8.3)	5 (17.8)	6 (17.1)
Hyperplastic polyps	13 (54.1)	7 (25.0)	10 (28.5)
Inflammatory polyps	7 (29.1)	8 (28.6)	3 (8.6)
Tubular adenoma	2 (8.3)	6 (21.4)	3 (8.6)
DALM/ALM	1 (4.1)	-	-
Intraepithelial neoplasia	_	_	_

Data presented n (%) unless otherwise indicated. \*Pentax, Japan. ALM Adenoma-like mass; CE Chromoendoscopy; DALM Dysplasia-associated lesion or mass; DCE Dye-sprayed CE; HD High definition

#### Endoscopic features of SSA

Eleven (79%) of the SSA lesions were localized in the proximal colon (five in the ascending colon, three in the cecum, one in the appendix and two in the hepatic flexure). Most were nonpolypoid lesions type IIb (86%) and ≥6 mm in size (78%) with indefinite margins. The Kudo pit pattern was type IIO in 12 (86%) and the vascular pattern appeared as spiral and irregular in 11 (79%) (Table 3). The other two SSAs were localized in the sigmoid colon. They were sessile, <6 mm in size and with Kudo pit pattern type I. The interobserver agreement was calculated (kappa coefficient 0.86). The intraobserver agreement was also graded as excellent, with a kappa coefficient of 0.90.

The classical features of SSA on HD white-light colonoscopy were nonpolypoid, covered by mucus and cloudy-appearing lesions. However, on HD iScan virtual CE, additional features characterized SSA such as Kudo pit pattern type II or IIO with indefinite margins and spiral isolated vessels. Similarly, with HD dye CE, characteristic features of SSA as above were found (Figures 1 to 4). In the present study, among the 44 SSAs and HPs, the above characteristics of SSA at colonoscopy had a sensitivity of 92.86% (95% CI 66.06% to 98.8%) and specificity of 93.33% (95% CI 77.89% to 98.99%) in predicting a histological diagnosis of SSA. The positive predictive value of endoscopic features of SSA was 86.67% (95% CI 59.55% to 97.95%) and the negative predictive value was 96.55% (95% CI 82.17% to 99.42%).

Of the SSAs, detection according to technique were: two in the HD group (8%); six in the HD-iScan virtual CE group (17%); and six in the HD dye CE with methylene blue (21%).

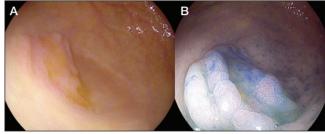


Figure 1) A High-definition colonoscopy showing flat lesion covered with mucus with irregular indefinite margins at the base of the appendix. B High-definition + dye chromoendoscopy with 0.2% methylene blue characterize and enhance the Kudo pit pattern type IIO and the edge of the lesion

#### Prevalence of other lesions at surveillance colonoscopy

Eleven adenomatous polyps were detected: two (8%) in the HD group, three (9%) in the HD iScan virtual CE group and six (21%) in the HD dye CE group. Thirty hyperplastic polyps were detected, 23 (77%) of which were localized in the left colon, mainly in the sigmoid colon. Only one patient had a dysplastic-associated lesion or mass (Table 2, Figure 4). This was a 44-year-old woman with longstanding Crohn's colitis and primary sclerosing cholangitis who underwent colectomy.

#### **DISCUSSION**

We report that SSAs may be detected in a significant proportion of IBD patients who undergo surveillance colonoscopy. Novel endoscopic techniques, such as iScan, virtual CE and dye-sprayed CE, may help in the detection of these lesions, although these findings require confirmation in a randomized controlled study.

In the present study, the prevalence of serrated sessile lesions located in IBD colitic mucosa was 16% in patients who underwent surveillance colonoscopy. The incidence of serrated sessile lesions was high in our population. However, this finding may not be generalizable to all gastroenterology practice because IBD patients were recruited from a tertiary care centre that specializes in dysplasia surveillance. The detection rates of SSA may vary according to centre, but is reported to be approximately 6% in average-risk patients undergoing screening colonoscopies for colorectal cancer detection (36). Thus, population-based studies are necessary to establish the incidence of SSA in IBD patients undergoing colonoscopy. A significant variable may be the experience of the colonoscopist in recognizing SSAs because they may otherwise be misintepreted as HPs.

TABLE 3
Baseline characteristics and endoscopic features of serrated adenoma in patients with inflammatory bowel disease

Age, years,		Localization		Size		Paris classification		Kudo pit pattern		
Female sex	median	UC/CD/IC	Right colon	Left colon	<6 mm	>6 mm	Is	llb*	I	IIO
7	50	5/6/2	11	2	2	11	3	10	1	12

Data presented as n. \*Completely flat nonprotruding nonexcavating lesion. CD Crohn disease; IC Ischemic colitis; Is Sessile protruding lesion; UC Ulcerative colitis

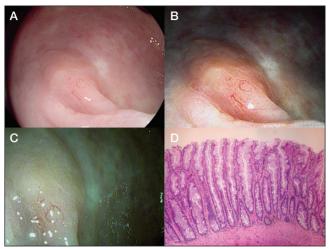


Figure 2) A to C High-definition + iScan (Pentax, Japan) virtual chromoendoscopy showing flat lesion with indefinite margins and irregular spiral vessels. D Histological examination revealing serrated adenoma (hematoxylin and eosin stain, original magnification ×100)



Figure 3) A to D High-definition iScan (Pentax, Japan) virtual chromoendoscopy showing Kudo pit pattern type IIO. E Histological examination revealing serrated adenoma (hematoxylin and eosin stain, original magnification ×100)

Serrated lesions exist in the inflammatory mucosa of IBD and are associated with a characteristic molecular profile. The appearance of the *BRAF* mutation is the early molecular change at the HP stage followed by microsatellite instability at the carcinoma stage (19,20). Rubio et al (18) assessed the histological phenotype of the dysplastic lesion juxtaposing colorectal carcinomas in 100 consecutive colectomy specimens from 50 patients with IBD and in 50 control (non-IBD) patients. They reported that 81.2% of the dysplastic lesions juxtaposing IBD carcinomas were villous or serrated adenoma, but only 55.1% in control cases. In particular, serrated adenoma accounted for nearly 29% of the noninvasive dysplastic lesions arising in IBD carcinomas but only 3% in control specimens.

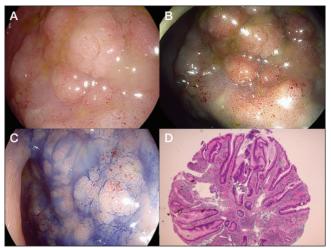


Figure 4) A and B High-definition iScan (Pentax, Japan) virtual chromoendoscopy showing dysplasia-associated lesion or mass with mixture of Kudo pit pattern types IIIL-IV. C High-definition with dye chromoendoscopy with 0.2% methylene blue better characterize details in the edge of the lesions and pit pattern. D Histological examination showing low-grade intraepithelial neoplasia (hematoxylin and eosin stain, original magnification ×40)

In our case cohort study, the percentage of SSA detection was high. Recently, Johnson et al (37) retrospectively assessed serrated lesion detection rates in IBD and documented incidence of subsequent colorectal neoplasia in single-centre cohort study. They reported that serrated epithelial changes and sessile serrated polyps are uncommonly detected in IBD patients. An underestimation of detection of these lesions may be due, in part, to the use of WLE and random biopsies in performing surveillance colonoscopy in IBD patients, which could easily miss these lesions due to lack of recognition of characteristic features. In addition, because HPs have traditionally been considered to be nonprogressive lesions with no malignant potential (37), they are often ignored and not biopsied or removed by endoscopists. Most of the previous studies using novel filter-enhanced technologies, such as narrow-band imaging (NBI), were mostly based on the endoscopists' experience and, in most of the circumscribed sigmoid or rectal flat lesions with a regular mucosal pit pattern (Kudo types I and II) and with a weak vascular intensity on NBI, were considered to be HPs and often did not undergo biopsy (38-43). However, using novel endoscopic techniques, the endoscopic features of SSAs are very similar to HPs and require experience to differentiate.

More of our patients had SSA detected by HD-iScan virtual CE (17%) and by dye-sprayed CE (21%) than by HD endoscopy alone (8%). However, it cannot be concluded from the present study whether novel endoscopic techniques are better at detecting SSAs because the sample size was small and the study was not randomized. Unfortunately, these lesions are often subtle in appearance at endoscopy and pose challenges for endoscopic detection and removal, especially in IBD colitic mucosa, in which the mucosa often appears atrophic with scars and pseudopolyps.

The new generation of HD endoscopes with electronic filter technology have the potential to improve neoplasia detection and may contribute to reducing random biopsies by obtaining targeted biopsies for histological evaluation. HD endoscopy offers resolution superior to

standard endoscopy and may significantly improve the detection and characterization of intraepithelial neoplasia in UC (11,12).

Conventional CE is the oldest and simplest method to improve the diagnosis of subtle epithelial changes and flat dysplastic lesions, and can improve characterization of margins that often can be difficult or impossible to detect using WLE. Several prospective randomized trials using methylene blue or indigo carmine for pan-CE in patients with longstanding UC have shown the unique benefit of CE in increasing the detection of intraepithelial neoplasia in IBD patients (5-9). HD-virtual CE, also known as dyeless CE, is a recently introduced image-enhancement technique.

There is controversy about the real role of NBI in dysplasia detection in UC patients. A recent study suggested that NBI offers no advantage over dye CE in IBD surveillance (38,41,43).

iScan remains a relatively unexplored technology in surveillance colonoscopy in IBD patients. However, it is a promising technique for differentiating neoplastic from non-neoplastic lesions of the colon. Hoffman et al (13) demonstrated that iScan was also able to predict neoplasia as precisely as dye CE, with an accuracy of 89% to 97%. Recently, in a prospective, randomized, back-to-back trial evaluating the utility of iScan in screening colonoscopy, Hong et al (15) demonstrated that iScan may fail to improve adenoma detection rates and the prevention of missed polyps; however, iScan appears to be effective for real-time histological prediction of polyp pathology compared with conventional HD white-light colonoscopy.

Finally, we have characterized and, for the first time, described the endoscopic findings of serrated adenoma in IBD patients using the iScan technique. SSAs tend to occur more often in the right colon compared with HPs; with a diameter exceeding 10 mm; with the type IIO pit pattern proposed by Kimura et al (23), which correspond to 'dilation of crypts'; and colouration may be yellowish due to mucin. They also have a cloud-like surface and indistinct borders that were predictive features on both HD-WLE and NBI, whereas

#### REFERENCES

- Eaden JA, KR Abrams, JF Mayberry. The risk of colorectal cancer in ulcerative colitis: A meta-analysis. Gut 2001;48:526-35.
- 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.
- 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
- Lutgens MW, van Oijen MG, van der Heijden GJ, 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.
- Francis A. Farraye, Robert D. Odze, Jayne Eaden, et al. AGA medical position statement on the diagnosis and management of colorectal neoplasia in inflammatory bowel disease. Gastroenterology 2010;138:738-45.
- Rutter M, Bernstein C, Matsumoto T, et al. Endoscopic appearance of dysplasia in ulcerative colitis and the role of staining. Endoscopy 2004;36:1109-14.
- Rutter MD, Saunders BP, Schofield G, et al. Pancolonic indigo carmine dye spraying for the detection of dysplasia in ulcerative colitis. Gut 2004;53:256-60.
- 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.
- Marion JF, Waye 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.
- Konijeti GG, Shrime MG, Ananthakrishnan AN, et al. Cost-effectiveness analysis of chromoendoscopy for colorectal cancer surveillance in patients with ulcerative colitis. Gastrointest Endosc 2013;S0016-5107.
- Mowat C, Cole A, Windsor A, et al. Guidelines for the management of inflammatory bowel disease in adults. Gut 2011;60:571-607.

dark spots and an irregular shape were predictive characteristics solely on NBI (24-26). However, these endoscopic vascular pattern findings (Figures 1 to 4) need to be validated.

The current study had several limitations. First, it was performed in a single referral tertiary academic centre and by one expert endoscopist. Additionally, the sample size of the study populations was not sufficiently large to detect subtle differences in dysplasia detection rates and to differentiate Crohn's colitis from UC. The study was observational and not powered to show superiority of any specific technique in diagnosing SSA in IBD. Thus, an appropriately randomized controlled trial comparing these dysplasia surveillance modalities is required to establish which is most effective.

Furthermore, a larger sample size is needed to better understand and characterize the morphology of the SSA in IBD patients compared with non-IBD patients. In the future, these data may aid endoscopists in recognizing and characterizing SSA in IBD patients, and facilitate real-time endoscopic therapeutic decisions.

#### CONCLUSION

Emerging evidence suggests that SSAs are common colonic lesions in IBD patients. It is possible that, as in non-IBD patients, these may be involved in the oncongenic pathway of colorectal cancer in IBD patients. SSAs are considered to be preneoplastic lesions, even if they do not show dysplasia at histology. Unfortunately, these lesions are often overlooked due to endoscopic features that are similar to HPs. Similar to dye CE, iScan CE has the potential to efficiently perform detailed characterization of the lesions and enable endoscopic targeting of biopsies or endoscopic therapeutic management.

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- Subramanian V, Mannath J, Ragunath K, et al. Meta-analysis: The diagnostic yield of chromoendoscopy for detecting dysplasia in patients with colonic inflammatory bowel disease. Aliment Pharmacol Ther 2011;33:304-12.
- SubramanianV, 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.
- Kodashima S, Fujishiro M. Novel image-enhanced endoscopy with i-Scan technology. World J Gastroenterol 2010;16:1043-9.
- Hoffman A, Kagel C, Goetz M, et al. Recognition and characterization of small colonic neoplasia with high-definition colonoscopy using i-Scan is as precise as chromoendoscopy. Dig Liver Dis 2010;42:45-50.
- Hong S.N, Choe WH, Lee JH, et al. Prospective, randomized, back-to-back trial evaluating the usefulness of i-Scan in screening colonoscopy. Gastrointest Endosc 2012;75:1011-21.
- 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;10:885-90.
- Efthymiou M, Allen PB, Taylor AC, et al. Chromoendoscopy versus narrow band imaging for colonic surveillance in inflammatory bowel disease. Inflamm Bowel Dis 2013;19:2132-8.
- 18 Rubio CA, Befrits R, Jaramillo E, et al. Villous and serrated adenomatous growth bordering carcinomas in inflammatory bowel disease. Anticancer Res 2000;20:4761-4.
- Bossard C, Denis MG, Bezieau S, et al. Involvement of the serrated neoplasia pathway in inflammatory bowel disease-related colorectal oncogenesis Oncol Rep 2007;18:1093-7.
- O'Brien MJ, Yang S, Mack C, et al. Comparison of microsatellite instability, CpG island methylation phenotype, BRAF and KRAS status in serrated polyps and traditional adenomas indicates separate pathways to distinct colorectal carcinoma end-points. Am J Surg Pathol 2006;30:1491-501.

- Chaubert P, Benhattar J, Saraga E, et al. K-ras mutations and p53 alterations in neoplastic and non-neoplastic lesions associated with longstanding ulcerative colitis. Am J Pathol 1994;144:767-75.
- Ishigooka S, Nomoto M, Obinata N, et al. Evaluation of magnifying colonoscopy in the diagnosis of serrated polyps. World J Gastroenterol 2012;18:4308-16.
- Kimura T, Yamamoto E, Yamano HO, et al. A novel pit pattern identifies the precursor of colorectal cancer derived from sessile serrated adenoma. Am J Gastroenterol 2012;107:460-9.
- Kahi CJ, Li X, Eckert GJ, Rex DK. High colonoscopic prevalence of proximal colon serrated polyps in average-risk men and women. Gastrointest Endosc 2012;75:515-20.
- Hazewinkel Y, López-Cerón M, East JE, et al. Endoscopic features of sessile serrated adenomas: Validation by international experts using high-resolution white-light endoscopy and narrow-band imaging Gastrointest Endosc 2013;7:916-24.
- Iacucci M, Xianyong G, Love J, et al. Novel irregular vascular pattern features of serrated adenoma detected by high-definition iScan endoscopic technique. Gastrointest Endosc 2014;79:182-4.
- Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for midly to moderately active ulcerative colitis: A randomized study. N Engl J Med 1987;317:1625-9.
- D'Haens G, Sandborn WJ, Feagan BG, et al. A review of activity indices and efficacy endpoints for clinical trials of medical therapy in adults with ulcerative colitis. Gastroenterology 2007;132:763-86.
- Montreal World Congress of Gastroenterology. Montreal classification. Can J Gastroenterol 2005;19:5-36.
- Daperno M, D'Haens G, Van Assche G, et al. Development and validation of a new, simplified endoscopic activity score for Crohn's disease: The SES-CD. Gastrointest Endosc 2004;60:505-12.
- 31. Participants in the Paris Workshop. The Paris endoscopic classification of superficial neoplastic lesions: Esophagus, stomach, and colon. Gastrointest Endosc 2003;58:S3-43.
- Kudo S, Tamura S, Nakajima T, et al. Diagnosis of colorectal tumorous lesions by magnifying endoscopy. Gastrointest Endosc 1996;44:8-14.
- Itzkowitz SH, Harpaz N. Diagnosis and management of dysplasia in patients with inflammatory bowel diseases. Gastroenterology 2004;126:1634-48.

- Riddell RH, Goldman H, Ransohoff DF, et al. Dysplasia in inflammatory bowel disease: Standardized classification with provisional clinical applications. Hum Pathol 1983;14:931-68.
- 35. Schlemper RJ, Riddell RH, Kato Y, et al. The Vienna classification of gastrointestinal epithelial neoplasia. Gut 2000;47:251-5.
- Payne SR, Church TR, Wandell M, et al. Endoscopic detection of proximal serrated lesions and pathologic identification of sessile serrated adenomas/polyps very on the basis of center. Clin Gastroenterol Hepatol 2014:12:1119-26.
- Johnson DH, Khanna S, Smyrk TC, et al. Detection rate and outcome of colonic serrated epithelial changes in patients with ulcerative colitis or Crohn's colitis. Aliment Pharmacol Ther 2014;39:1408-17.
- Dekker E, van den Broek FJ, Reitsma JB, 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.
- van den Broek FJ, 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.
- 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;10:885-90.
- Efthymiou M, Allen PB, Taylor AC, et al. Chromoendoscopy versus narrow band imaging for colonic surveillance in inflammatory bowel disease. Inflamm Bowel Dis 2013;19:2132-8.
- 42. 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;74:840-84.
- 43. Pellisé M, Fernández-Esparrach G, Cárdenas A, et al. Clinical impact of wide-angle, high-resolution endoscopy in the diagnosis of colorectal neoplasia in a non-selected population: A prospective randomized controlled trial. Gastroenterology 2008;135:1062-8.

















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