REVIEW

Clin Endosc 2023;56:563-577
https://doi.org/10.5946/ce.2023.070
pISSN: 2234-2400 • eISSN: 2234-2443

Open Access

CLINICAL ENDOSCOPY

Current status of image-enhanced endoscopy in inflammatory bowel disease

Young Joo Yang

Department of Internal Medicine, Chuncheon Sacred Heart Hospital, Hallym University College of Medicine, Chuncheon, Korea

In inflammatory bowel disease (IBD), chronic inflammation leads to unfavorable clinical outcomes and increases the risk of developing colorectal neoplasm (CRN); thereby highlighting the importance of endoscopically evaluating disease activity as well as detecting and characterizing CRN in patients with IBD. With recent advances in image-enhanced endoscopic (IEE) technologies, especially virtual chromoendoscopy (VCE) platforms, this review discusses state-of-the-art IEE techniques and their applicability in assessing disease activity and surveillance colonoscopy in patients with IBD. Among various IEE, VCE demonstrated the capacity to identify quiescent disease activity. And endoscopic remission defined by the new scoring system using VCE platform better predicted clinical outcomes, which may benefit the tailoring of therapeutic strategies in patients with IBD. High-definition dye-chromoendoscopy (HD-DCE) is numerically superior to high-definition white light endoscopy (HD-WLE) in detecting CRN in IBD; however, discrepancy is observed in the statistical significance. VCE showed comparable performance in detecting dysplasia to HD-WLE or DCE and potential for optical diagnosis to differentiate neoplastic from nonneoplastic lesions during surveillance colonoscopy. Applying these novel advanced IEE technologies would provide opportunities for personalized medicine in IBD and optimal treatment of CRN in patients with IBD.

Keywords: Chromoendoscopy; Colorectal neoplasms; Image-enhanced endoscopy; Inflammatory bowel diseases; Virtual chromoendoscopy

INTRODUCTION

Endoscopic examination is crucial for managing inflammatory bowel disease (IBD) to assess disease activity and detect neoplastic lesions. In IBD, mucosal inflammation is associated with unfavorable long-term outcomes including complications, flares, surgeries, and increased risk of bowel damage. Endoscopic healing is recommended as a long-term treatment target based on the selecting therapeutic targets in IBD II recommendation.[1,2] Therefore, meticulous evaluation of disease activity and treatment response with endoscopy is becoming increasingly important to optimize therapeutic strategies. Additionally, patients with long-standing ulcerative colitis (UC) and colonic Crohn's disease (CD) have an increased risk of developing colorectal neoplasia (CRN) compared with the general population.[3,4] However, detecting and characterizing CRN in IBD remain difficult because CRN frequently presents as flat or subtle morphologies that can be easily missed, and inflamed or regenerative mucosal changes prevent the identification of CRN in patients with IBD. In the last decade, endoscopic technologies have progressed and various image-enhanced endoscopy (IEE) techniques, including the recently developed advanced virtual chromoendoscopy (VCE), have enabled a more comprehensive and accurate evaluation of mucosal inflammation and detection of dysplasia. In this review, we provide an overview of the application of IEE in the assessment of disease activity as well as identification and characterization of CRN in patients with IBD.

Received: March 5, 2023 **Revised:** June 18, 2023 **Accepted:** June 22, 2023

Correspondence: Young Joo Yang
Department of Internal Medicine, Chuncheon Sacred Heart Hospital, Hallym University College of Medicine, 77 Sakju-ro, Chuncheon 24253, Korea
E-mail: yjyang@hallym.ac.kr

IMAGE-ENHANCED ENDOSCOPY

Dye-chromoendoscopy

Dye-chromoendoscopy (DCE) refers to endoscopic techniques that use a contrast dye (indigo carmine) or an absorptive agent (methylene blue or crystal violet) to enhance contrast and mucosal visualization. This enables endoscopists to delineate abnormalities such as morphological changes, lesion borders, surface pit patterns, or size of suspicious lesions.[5] Indigo carmine is a widely used contrast dye in DCE. It is not absorbed by the mucosal gland but pools in the pits and innominate grooves, highlighting the pit pattern and mucosal structure, such as irregular mucosal depression, abrupt cutting, or swelling of the fusion folds. Adverse reactions such as bradycardia, hypertension, nausea, vomiting, and rarely, bronchospasm and hives may occur following indigo carmine administration. However, these reactions occur with intravenous administration, and almost no side effects have been observed when a small amount is used for DCE. Methylene blue and crystal violet are used in the absorptive method to stain epithelial cells. Thus, the area surrounding the pit is stained, whereas the pit remains unstained and appears white, enabling accurate visualization of the pit pattern. Methylene blue also differentiates mucosal lesions from normal mucosa based on the degree of staining uptake. Normal mucosa exhibits a diffuse homogeneous dark blue appearance following the methylene blue administration, whereas abnormal mucosal lesions with inflammation or dysplastic changes appear light blue or pink as unstained or heterogeneously stained. This allows the detection of CRN or determination of the extent of inflammation in patients with IBD. Methylene blue is safe for use in humans. Although concerns have been raised regarding the possibility of oxidative damage to DNA owing to photosensitization by white light endoscopy (WLE) after absorption by cells, these concerns have not been clinically proven. There is no evidence that the risk of cancer is increased in patients undergoing DCE using methylene blue.

According to the "SURFACE" guidelines, which describe the process of performing DCE in patients with UC, DCE can be performed as follows.[5,6] (1) Strict patient selection: DCE is ideal for patients with clinical remission and mucosal healing but avoided in patients with active disease, if possible. (2) Unmask the mucosal surface: excellent bowel preparation is essential, and mucus or residual fluid in the colon must be removed during insertion. (3) Reduce peristaltic waves: antispasmodics can be administered, if necessary, to reduce blind spots due to spasms or haustral folds. (4) Full-length staining of the colon: pan-chromoendoscopy is recommended over focal staining. (5) Augmented detection with dyes: before the procedure, 0.1% to 0.5% indigo carmine, 0.05% to 0.5% methylene blue, or 0.05% to 0.2% crystal violet dye solution is needed and usually about 80 to 100 mL dye solution is used per procedure. To prepare 0.1% indigo carmine solution, 5 mL of 0.4% indigo carmine is diluted with 15 mL of water. To achieve a final concentration of 0.1%, 5 mL of 1% methylene blue is diluted with 45 mL water.[7] Different concentrations of dyes can be utilized depending on the purpose of the examination; for instance, a lower concentration is used for detection, whereas a higher concentration is used for characterizing the lesions. After cecal intubation, the colonic mucosa is meticulously inspected, and the lumen is dyed in a segmental fashion (every 20–30 cm) by withdrawing the colonoscope in a spiral fashion using a dye spray catheter or pump jet. It is important to use appropriate pressure while applying the dye using a catheter, as bleeding due to excessive injection pressure hinders the inspection of suspicious lesions. Direct injection of indigo carmine via a biopsy valve using a syringe can reduce the injection pressure and prevent bleeding. Additionally, it is crucial to apply a minimal amount of dye to prevent dye accumulation in depressed areas. After waiting for a few seconds for the dye to pool onto the mucosal surface, excess pools of indigo carmine are suctioned, and the mucosa is scrutinized. Indigo carmine staining persists for a few minutes and subsequently vanishes owing to dilution. Methylene blue requires approximately 60 seconds for absorption and the lesion can be examined for up to 20 minutes once stable staining occurs. (6) Crypt architecture analysis: pit pattern classification should be performed for all suspicious lesions. Types I and II indicate nonneoplastic lesions, whereas types III and V indicate neoplastic lesions, including carcinomas. (7) Endoscopic targeted biopsy: suspicious lesions with mucosal alterations should be biopsied, especially circumscribed lesions with stained types III–V pit patterns.

Virtual chromoendoscopy

VCE is widely used in endoscopic units to enhance the details of mucosal and vascular patterns without dye application. VCE includes various optical technologies such as narrow-band imaging (NBI; Olympus), iSCAN (Pentax), flexible imaging color enhancement (FICE; Fujinon), and blue laser light/linked color imaging (BLI/LCI; Fujifilm). Unlike a direct image acquired using standard WLE, which is obtained as a red-green-blue (RGB)

image using the full visible wavelength range (400–700 nm), in NBI, shorter wavelengths of light between 415 nm and 540 nm (a narrow band of blue and green light) passing through an optical filter are absorbed by hemoglobin. Thus, the blood vessels appear dark, and the contrast in the mucosal layer is increased. This enables the assessment of precious mucosa and vascular patterns.[8] Moreover, iSCAN, FICE, and BLI/LCI recreate virtual images using digital post-processing software.[9,10] iSCAN has three modes set by the endoscopist for each condition using a touch screen: surface enhancement (SE), tone enhancement (TE), and contrast enhancement (CE). SE mode facilitates lesion detection by controlling illumination intensity. CE mode facilitates the identification and demarcation of lesions by digitally adding blue color to the relatively darker areas. In TE mode, the frequencies of RGB color are altered and combined with images in new color schemes. This enhances the visualization of the mucosal structure, vascular patterns, and subtle color changes, and helps characterize the lesions.[10,11] Unlike iSCAN, which enhances per-pixel luminosity using white light, the recently developed iSCAN-optical enhancement (iSCAN-OE) increases overall transmittance of the hemoglobin absorption spectrum using an optical filter. FICE enables the visualization of tissue characteristics and vessels through signal processing, which extracts spectral images of specific wavelengths from white light. However, FICE poses difficulties in providing high-contrast images of microvessels under white light, which led to the development of BLI/LCI.[12] The BLI system comprises a light source and a processor that creates high-contrast images by enhancing blue-violet light while reducing white light components. Although LCI utilizes the same illumination spectrum as BLI, it increases color contrast, resulting in a reddish color becoming redder and a whitish color becoming whiter; thereby maintaining natural tones. Therefore, LCI facilitates the detection of lesions and inflammation. Table 1 summarizes the mechanisms, strengths, and weaknesses of the available IEE techniques.

ENDOSCOPIC EVALUATION FOR DISEASE ACTIVITY

Endoscopic healing is a clinical parameter for predicting favorable outcomes and treatment targets for optimized medical therapy. However, some discrepancies exist between endoscopic and histological activity. Persistent histological inflammation is frequently observed in patients with endoscopic healing, which suggests the limitations of endoscopic evaluation of disease activity in patients with IBD.[13,14] The limitations of endoscopic evaluation in capturing disease activity in patients with IBD may be attributed to two factors. First, current endoscopic scoring systems were developed using standard definition (SD)-WLE, which may not be sufficiently sensitive to detect subtle patchy changes in mucosal inflammation. Second, the current definition of endoscopic healing remains unclear. The lower end of the endoscopic inflammation assessment score was used to define endoscopic healing, which may have led to an inaccurate reflection of the actual state of mucosal inflammation. Therefore, several advanced IEE techniques have recently been adopted to accurately assess disease activity of IBD.

Kudo et al.[15] evaluated the performance of the NBI system to predict histological inflammation. They differentiated mucosal vascular pattern (MVP) into normal or distorted under conventional colonoscopy as well as clear or obscure under the NBI system. Comparing MVP to the histologic findings for inflammation, obscure MVP examined using NBI showed a significantly higher association with acute inflammatory cell infiltrates (26% vs. 0%, p=0.0001), goblet cell depletion (32% vs. 5%, p=0.0006), and basal plasmacytosis (2% vs. 21%, p=0.006) than clear MVP.[17] Additionally, the shape of the capillary vessels with magnified NBI in patients with UC in remission correlated with the histologic findings, such that the blood vessels shaped like vines (BV-V) demonstrated higher pathological activity than that of honeycomb-like blood vessels (BV-H).[16] Blood vessels shaped like bare branches (BV-BB) significantly predicted relapse at 12 months (odds ratio [OR], 14.2; 95% confidence interval [CI], 3.3–60.9]. However, because blue light with a wavelength of approximately 415 nm is mostly absorbed by hemoglobin, the NBI system poses some challenges in assessing vascular patterns in patients with moderate or severe disease activity accompanying intramucosal hemorrhage.[10,15]

In a randomized controlled trial (RCT), Neumann et al.[17] compared disease activity and extent assessed using VCE, especially iSCAN, with those assessed using high-definition (HD)-WLE based on histological results in UC patients with mild or inactive activity. iSCAN showed a higher endoscopic prediction of inflammatory extent (92.31% vs. 48.71%, p=0.0009) and activity (89.74% vs. 53.85%, p=0.066) than that of HD-WLE. Iacucci et al.[18] designed an endoscopic scoring system with iSCAN, which was combined with the scores for mucosal and vascular patterns. This scoring system showed a good correlation with Mayo endoscopic subscore [MES] (rs=0.86; 95% CI,

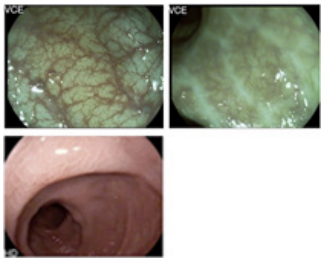
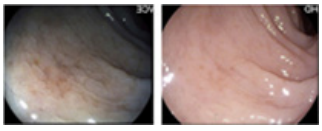
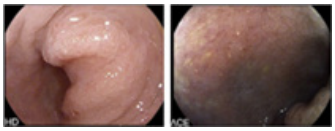
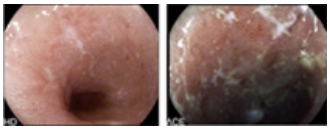
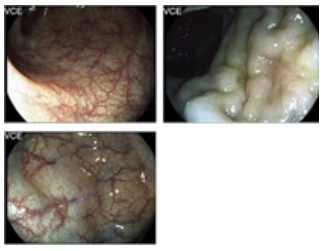
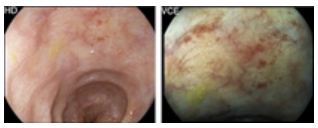
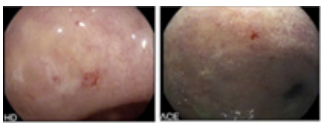
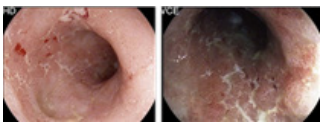
Table 1. Summary for currently available IEE techniques

IEE technique	Mechanism	Strength	Weakness
Dye-chromoendoscopy			
Absorptive dye: crystal violet, methylene blue	Enable to inspect details of cellular surface as the dye is absorbed by epithelial cells.	Enhance the detection of mucosal abnormalities such as inflammation or dysplastic changes based on the degree of stain uptake and differentiation of dysplastic changes through precious observation of pit pattern.	(1) Additional costs for the equipment needed for dye spraying. (2) Time consuming procedure. (3) Incomplete or uneven mucosal dye coverage. (4) Need for experience to interpret the suspicious lesion.
Contrast dye: indigo carmine	Emphasize irregularities of mucosal surface by being pooled in pit or innominate groove without absorption.	Facilitate to demarcate mucosal abnormalities.	
Virtual chromoendoscopy			
NBI	Use two narrow-band of blue (415 nm) and green light (540 nm), which are absorbed by hemoglobin in blood vessels to enhance mucosal surface and capillary patterns.	(1) Easily be activated at a push of a button. (2) Helpful for inspecting the mucosal vascular pattern.	(1) Poor illumination intensity of the first generation NBI system leads to dark and harsh images, especially in GI tract with a wide lumen. (2) Need training to achieve competence for analyzing surface and vascular patterns. (3) Disagreement between observers in diagnosis using NBI.
FICE	Computed spectral image processing that reconstructs dedicated wavelengths resulting in improved visualization of mucosal structures and microvasculature	Improve analysis of pit pattern and mucosal junction between normal and pathologic lesion.	(1) Difficulty in providing high-contrast images of microvessels under white light. (2) Difficulty to choose FICE channel according to clinical cases. (3) Require advanced endoscopic technologies and experience.
iSCAN	Digital post-processing image enhancement technology, which provides digital contrast to endoscopic images using three functions: surface enhancement, contrast enhancement, and tone enhancement.	(1) Enhance the visualization of the mucosal structure, vascular patterns, subtle color changes. (2) Facilitate detection and characterization of the lesions. (3) Red remains the predominant blood vessel color, unlike NBI.	(1) Need further validation. (2) Require additional cost to install platform, advanced endoscopic technologies, and experience.
BLI	Enhance blue-violet light and simultaneously reduce white light components using semiconductor laser beam to create high contrast images.	(1) Emphasize the contrast between blood vessels and surrounding tissues. (2) Brighter than NBI.	(1) Limitations to increase the contrast of vessels in submucosa compared with NBI. (2) Images are slightly darker.
LCI	Based on BLI technique, expand the color range of reddish and whitish colors to generate brighter images compared to WLE images.	(1) Improve the recognition of slight differences in mucosal color compared to conventional WLE by reallocating the acquired color information to a color space. (2) Special training is not required because LCI images are similar to the color enhanced images of WLE images.	Need further validation.

IEE, image-enhanced endoscopy; NBI, narrow-band image; GI, gastrointestinal; FICE, flexible imaging color enhancement; BLI, blue light images; LCI, linked color images; WLE, white light endoscopy.

0.79–0.91; $p<0.0001$) and histologic activity assessed by New York Mount Sinai system (NYMS) histologic scoring system (rs=0.65; 95% CI, 0.49–0.76; $p<0.0001$). Furthermore, iSCAN detected abnormal mucosal and vascular patterns in 30.4% and 73.9% of patients with an MES of 0, respectively. This demonstrated its potential for identifying residual inflammation and subtle histologic changes. Using iSCAN-OE with magnification, the same research group demonstrated that the new iSCAN-OE score had a good relationship with two histological scores, extent, chronicity, activity, plus additional findings [ECAP] (r=0.70; 95% CI, 0.52–0.81; $p<0.0001$) and the Robarts histopathology index [RHI] (r=0.61, $p<0.01$). They accurately detected mucosal inflammation, identified by ECAP or RHI with an accuracy of 80% and 68%, respectively.[19] Based on these results, the Paddington international virtual chromoendoscopy score (PICaSSO) was developed using iSCAN to redefine mucosal (elongated crypts, scars, microerosions, erosions, and ulcerations) and vascular changes (spare vessel, a vessel with dilatation, and intramucosal or luminal bleeding) from 0 to 15 to assess inflammation (Table 2).[20-22] Endoscopic remission, defined as a score <3 of PICaSSO, had a good correlation with various histologic scores such as RHI, Nancy histological index (NHI), Villanacci simple score, Geboes score (GS), and ECAP. Moreover, endoscopic remission of PICaSSO indicates favorable long-term outcomes at 6 (hazard ratio [HR], 0.19; 95% CI, 0.11–0.33) and 12 months (HR, 0.22; 95% CI, 0.13–0.34), similar to histologic remission in a real-life multicenter prospective study.[22] Additionally, endoscopic remission evaluated by PICaSSO alone using iSCAN showed comparable predictive ability for certain clinical outcomes, such as hospitalization, colectomy,

Table 2. Paddington international virtual chromoendoscopy score

Mucosal architecture			
0. No mucosal defect.	**I. Microerosion or crypt abscess.**	**II. Erosions size <5 mm.**	**III. Ulcerations size >5 mm.**
(A) Continuous/regular crypts.	1: Discrete.	1: Discrete.	1: Discrete.
(B) Crypts not visible (scar).	2: Patchy.	2: Patchy.	2: Patchy.
(C) Discontinuous and or dilated/ elongated crypts.	3: Diffuse.	3: Diffuse.	3: Diffuse.
			
Vascular architecture			
0. Vessels without dilatation.	**I. Vessels with dilatation.**	**II. Intramucosal bleeding.**	**III. Luminal bleeding.**
(A) Roundish following crypt architecture.	(A) Roundish with dilatation.	(A) Roundish with dilatation.	(A) Roundish with dilatation.
(B) Vessels not visible (scar).	(B) Crowded or tortous superficial vessels with dilatation.	(B) Crowded or tortous superficial vessels with dilatation.	(B) Crowded or tortous superficial vessels with dilatation.
(C) Sparse (deep) vessels without dilatation.			
			

and medication change with a combination of endoscopic and histologic remission at follow-up over 12 months.[23] In contrast, ulcerative colitis endoscopic index of severity (UCEIS) with histologic remission was more favorable for predicting certain clinical outcomes than UCEIS alone. Although PICaSSO was initially developed with the iSCAN platform, it had a good correlation with RHI and NHI when used with NBI (ρ=0.83; 95% CI, 0.751–0.902 and ρ=0.79; 95% CI, 0.678–0.87) or BLI/LCI (ρ=0.65; 95% CI, 0.482–0.781 and ρ=0.63; 95% CI, 0.472–0.754)/(ρ=0.65; 95% CI, 0.486–0.775 and ρ=0.63; 95% CI, 0.486–0.754) platforms, respectively.[24] Additionally, the accuracies for predicting histologic remission of PICaSSO with NBI or BLI/LCI was comparable with the current scoring system, such as MES, UCEIS. Recent advances in artificial intelligence have led to the development of a novel VCE-convolutional neural network (CNN) model that can assess endoscopic remission and predict histologic remission as well as the risk of disease flare.[25] The PICaSSO multicenter study used 1,090 endoscopic videos of 283 patients with UC for training, validation, and testing. Endoscopic activity was graded using UCEIS during HD-WLE, and PICaSSO during iSCAN 1–3. This CNN system detected endoscopic remission (PICaSSO≤3) with a sensitivity of 79%, specificity of 95%, and area under the receiver operator curve (AUROC) of 0.94, as well as predicting histological remission with an accuracy of 80% to 85%.

To evaluate the diagnostic capability of LCI in detecting mucosal inflammation in UC, Uchiyama et al.[26] categorized LCI patterns into three categories: A, no redness; B, redness with visible vessels; and C, redness without visible vessels. The LCI index had a good correlation with the histopathological Matts score and better predicted non-relapsed rates within 30 months after LCI examination (p=0.0055) than MES (p=0.0632). A retrospective Japanese study demonstrated that LCI could better identify histological mucosal inflammation (defined by GS 2–3) by detecting redness in the colonic mucosa, and better predict relapse in UC than WLE.[27] These findings suggest that LCI can be a useful tool for detecting mucosal inflammation in patients with IBD. However, in a recent meta-analysis of 12 studies that compared the correlation between endoscopy (MES, UCEIS, PICaSSO) and histological disease activity scores (GS, NHI, RHI, NYMS) across SD-WLE, HD-WLE, and VCE in patients with UC, endoscopic activity scores demonstrated a strong correlation with histologic scores regardless of the endoscopic platform.[28] However, subgroup analysis revealed that histologic remission was more accurately predicted by VCE than by WLE. Considering the results of current studies, VCE could help identify histologic remission or predict clinical outcomes in patients in an endoscopically quiescent state. PICaSSO demonstrated its potential as a reliable and accurate scoring system for endoscopic assessment using various VCE platforms in patients with IBD. Table 3 summarizes representative studies evaluating disease activity in IBD using IEE.[15-19,22-27]

ENDOSCOPIC EVALUATION FOR THE DETECTION OF CRN

Patients with UC and colonic CD are at an increased risk of developing CRN, including carcinoma.[3,4] However, chronic inflammation and a wide range of morphologic features of CRN, such as subtler and flat lesions, hamper accurate detection and treatment of CRN.[29] To enhance the identification of CRN, the Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients: International Consensus Recommendations (SCENIC) guidelines recommends using HD-WLE or SD-DCE rather than SD-WLE alone, and suggested HD-DCE for surveillance colonoscopy in patients with IBD.[29] With recent advances in resolution and virtual modalities, various IEE techniques, including DCE, NBI, iSCAN, and FICE, were studied to determine whether they can detect CRN in patients with IBD. Several studies compared CRN detection rates between HD-DCE and HD-WLE. A randomized trial by Alexandersson et al.[30] demonstrated that the CRN detection rate of HD-DCE was more significant than that of HD-WLE alone (11% vs. 5%, p=0.03) and superiority of HD-DCE was also confirmed in the RCT by Wan et al.[31] However, a multicenter prospective randomized trial by Yang et al.[32] that enrolled 210 patients with long-standing UC reported that although the detection rate was numerically higher in the HD-DCE group, HD-DCE was not significantly superior to HD-WLE in detecting CRN (5.6% vs. 3.9%, p=0.749). Recent meta-analyses reported that the CRN detection performance of DCE was better than that of SD-WLE alone, whereas the CRN detection performance of DCE was comparable with that of HD-WLE, especially in the subgroup analysis confined to RCTs.[33,34]

When comparing NBI to conventional WLE, including HD-WLE, for detecting CRN in patients with long-standing UC, several studies have reported that NBI does not improve the detection of CRN. In a randomized crossover study that included 42 patients with UC, the CRN detection rate of NBI was com-

Table 3. Representative studies evaluating disease activity assessment in IBD using IEE

Study	Study design	Study population	Aim	Colonoscope technique	Outcomes
Kudo et al. (2009)[15]	Single center prospective study	30 Inactive or mild UC (157 colorectal segments)	To assess correlation between MVP and the histologic grade of inflammation	Conventional vs. NBI colonoscopy	Obscure MVP under NBI colonoscopy was associated with acute inflammatory cell infiltrates (26% vs. 0%, p=0.0001), goblet cell depletion (32% vs. 5%, p=0.0006), and basal plasmacytosis (2% vs. 21%, p=0.006).
Sasanuma et al. (2018)[16]	Single center prospective study	52 UC: left-sided or total-colitis type UC and achieved clinical remission with an endoscopic Mayo score of 0 or 1	To assess the relationships of magnified NBI with histological disease activity and prognosis	White light vs. magnified NBI	Magnified NBI findings such as blood vessels shaped like vines showed a good relationship with pathological findings (p<0.01).
Neumann et al. (2013)[17]	Prospective randomized controlled study	78 Mild or inactive IBD (36 UC, 42 CD)	To assess whether iSCAN has the potential to enhance assessment of disease severity and extent compared to HD-WLE	HD-WLE, VCE (iSCAN)	iSCAN significantly improved the diagnosis of the severity (53.85% vs. 89.74%) and extent (48.71% vs. 92.31%) of mucosal inflammation in patients with IBD. Average duration of the examination was comparable between HD-WLE and iSCAN (18 min vs. 20.5 min).
Iacucci et al. (2015)[18]	Single center retrospective cohort study	78 UC	To create a more refined histological and endoscopic criteria based on this novel technique in order to redefine inflammatory activity and mucosal healing	HD-VCE (iSCAN), WLE	Of those with Mayo endoscopic subscore of 0, 30.4% had an abnormal mucosal pattern and 73.9% of them had an abnormal vascular pattern on iSCAN.
Iacucci et al. (2017)[19]	Single center prospective cohort study	41 UC and 9 control	To investigate the use of iSCAN-OE in the assessment of inflammatory changes in UC	VCE (iSCAN-OE)	iSCAN-OE accurately identified mucosal inflammation with the accuracy of 68% to 80% and correlated well with ECAP (r=0.70, p<0.001) and RHI (r=0.61, p<0.01).
Iacucci et al. (2021)[22]	Multicenter prospective international study	307 UC	To establish the performance and relationship between PICaSSO and other endoscopic scores (MES, UCEIS) with several histological scores (RHI, NHI, ECAP, Geboes, Villanacci) and their association with HR	HD-WLE, iSCAN 1–3	The PICaSSO score (r=0.76–0.79) correlated strongly with multiple histological indices than either MES (r=0.68–0.73) or UCEIS (r=0.71–0.74).
			To evaluate whether PICaSSO was predictor of specified clinical outcomes including hospitalization colectomy, or initiation or changes in medical therapy, (steroids, immunomodulators, and biologics)		PICaSSO score ≤3 predicted better specified clinical outcomes at 6 and 12 months than PICaSSO >3 (HR 0.19 and 0.22, respectively), similar to histologic remission.

(Continued to the next page)

Table 3. Continued

Study	Study design	Study population	Aim	Colonoscope technique	Outcomes
Nardone et al. (2022)[23]	Multicenter prospective study	302 UC	To investigate the performance of the combination of endoscopic and histologic remission for predicting specified clinical outcomes (hospitalization, colectomy, or initiation or changes in medical therapy) over 6 and 12 months in comparison with endoscopic remission alone by using the new VCE-PICaSSO along with several endoscopic (MES, UCEIS) and histological scores (RHI, NHI)	HD-WLE, iSCAN 1–3	Endoscopic remission by VCE-PICaSSO alone was similar to combined endoscopic and histologic remission for predicting specified clinical outcomes at 12 months (HR 0.42 and HR 1.03, for RHI and NHI, respectively).
Cannatelli et al. (2022)[24]	Multicenter prospective study	159 UC	To evaluate the reproducibility of the PICaSSO with the NBI, LCI/BLI platforms	NBI, LCI/BLI	The PICaSSO score can be consistently and accurately reproduced with NBI (RHI: r=0.83, accuracy 0.808 for HR, NHI: r=0.79, accuracy 0.821 for HR) and LCI/BLI (RHI: r=0.65/0.65, NHI: r=0.63/0.64, accuracy 0.827/0.79 for HR).
Iacucci et al. (2023)[25]	Multicenter retrospective study	1,090 Endoscopic videos from 283 UC	To develop an AI tool to distinguish ER/activity, and predict histology and risk of flare from WLE and VCE videos	HD-WLE, iSCAN 1–3	The AI system accurately distinguished ER using WLE (UCEIS ≤1) and VCE (PICaSSO≤3) videos with 72% and 79% sensitivity, 87% and 95% specificity, and AUROC of 0.85 and 0.94, respectively. The prediction of HR was similar between WLE and VCE videos (accuracies ranging from 80% to 85%).
Uchiyama et al. (2017)[26]	Single center pilot study	52 UC (193 area assessed by LCI)	The efficacy of LCI for diagnosing mucosal inflammation	LCI	Endoscopic LCI classification and LCI index can subdivide samples with the same Mayo endoscopic subscore (MES 0: 41.8% with LCI-B [redness with visible vessels], 4.6% with LCI-C [redness without visible vessels]; MES 1: 34.6% with LCI-B, 60.5% with LCI-C). Non-relapse rates significantly correlated with LCI classification (p=0.0055), but not with MES (p=0.0632).
Matsumoto et al. (2021)[27]	Single center retrospective study	72 UC in remission	To investigate the clinical utility of LCI for the evaluation of endoscopic activity and prediction of relapse	HD-WLE, LCI	LCI findings were significantly correlated with GS (GS 0 or 1: 89% of WLI–/LCI–, GS 2 or 3:42% of WLI-/LCI+, p<0.01). Non-relapse rates were significantly correlated with WLE/LCI classification (group B [WLE–/LCI+]/C [WLE+/LCI+], p=0.0067), but not with MES (p=0.079).

IBD, inflammatory bowel disease; IEE, image-enhanced endoscopy; UC, ulcerative colitis; MVP, mucosal vascular pattern; NBI, narrow-band image; CD, Crohn's disease; HD-WLE, high definition white light endoscopy; VCE, virtual chromoendoscopy; iSCAN-OE, iSCAN-optical enhancement; PICaSSO, Paddington international virtual chromoendoscopy score; MES, Mayo endoscopic score; UCEIS, UC endoscopic index of severity; RHI, Robarts histopathology index; NHI, Nancy histological index; ECAP, extent, chronicity, activity, plus score; HR, hazard ratio; BLI, blue light images; LCI, linked color images; AI, artificial intelligence; ER, endoscopic remission; AUROC, area under the receiver operator curve; GS, Geboes score.

parable with that of conventional colonoscopy (19% vs. 17%, p=0.71).[35] Although more suspicious lesions were observed (52 vs. 28, p=0.03) and more targeted biopsies were performed (148 vs. 85) during NBI than conventional WLE, this did not result in an actual increase in the detection rate of CRN. Another crossover RCT that included 25 patients with UC reported a comparable detection rate of CRN between NBI and HD-WLE (82% vs. 73%, p=1.00).[36] However, this study found that nonneoplastic lesions were detected more frequently using NBI than HD-WLE, suggesting that NBI may have limited accuracy in differentiating neoplastic and nonneoplastic mucosa. Furthermore, HD-NBI was compared with HD-DCE for detecting CRN using targeted biopsy in two RCTs. In a crossover RCT that enrolled 60 patients with colonic IBD, HD-NBI demonstrated a similar detection rate for intraepithelial neoplasia (20% vs. 18.3%, p=0.43).[37] Although withdrawal time was significantly reduced with HD-NBI than that with HD-DCE (15.74 vs. 26.87, p<0.01), missed intraepithelial neoplastic lesions were more common with HD-NBI than HD-DCE; however, the differences were not significant (31.8% vs. 13.6%, p=0.20). Another RCT that enrolled 131 patients with UC also showed that the CRN detection rate of HD-NBI was comparable to that of HD-DCE (21.5% vs. 21.2%, p=0.96); however, total procedure time was significantly shorter with HD-NBI than that with HD-DCE (25.0 vs. 32.5, p<0.001).[38]

CRN detection by iSCAN was also compared with that of HD-WLE or DCE. Iacucci et al.[39] evaluated CRN detection using iSCAN, HD-WLE, and HD-DCE in 270 patients with long-standing inactive IBD for surveillance colonoscopy. In this randomized non-inferiority trial, the CRN detection rate of iSCAN was not inferior to that of HD-DCE. The CRN detection rate of HD-WLE was not inferior to that of iSCAN or HD-DCE (18.9% vs. 11.1% vs. 17.8%, p=0.91), indicating that HD-WLE alone was adequate for detecting CRN in this study. Recently, Kandiah et al.[40] demonstrated that the CRN detection rates with targeted biopsy were not significantly different between iSCAN and HD-WLE in an RCT that enrolled 188 patients with long-standing IBD (14.9% vs. 24.2%, p=0.14). Additionally, only one biopsy among the 6,751 non-targeted biopsies confirmed CRN, which suggested that targeted biopsy with iSCAN or HD-WLE is a good strategy for surveillance colonoscopy in patients with IBD. Recent meta-analyses have reported that CRN detection using VCE was comparable to that of DCE or HD-WLE.[41,42] In a meta-analysis of 11 RCTs comparing VCE, including AF, FICE, iSCAN, and NBI with DCE and SD or HD-WLE in detecting CRN, the CRN detection of VCE was equivalent to that of DCE or HD-WLE in a per-patient analysis.[41] In contrast, the CRN detection of VCE was inferior to that of HD-WLE and comparable to that of DCE in a per-dysplasia analysis.[41] In another meta-analysis that assessed the effectiveness of different IEE techniques (SD or HD-WLE, DCE, AFI, and VCE including NBI, iSCAN, and FICE) for identifying CRN in patients with IBD, the CRN detection of DCE was better than that of SD-WLE.[42] DCE showed significantly equivalent efficacy in identifying patients with CRN and the total number of CRN when compared with those of HD-WLE and VCE, although DCE numerically outperformed HD-WLE and VCE. However, procedure time was significantly longer (9.63 minutes) in DCE than in VCE, particularly NBI.

Based on previous studies, DCE was significantly superior to SD-WLE. Additionally, a trend favoring DCE over HD-WLE was observed; however, the statistical significance was inconsistent. Several meta-analyses have reported that HD-WLE is not inferior to DCE. VCE, including NBI and iSCAN, failed to improve CRN detection in patients with IBD. However, VCE showed significantly non-inferior performance compared to HD-WLE and DCE, although DCE showed numerically superior performance. VCE have several advantages over DCE. VCE reduced procedure time and cost of dye application. Moreover, it is free of uneven dye staining, which hampers accurate mucosal observation.[43] The recently updated SCENIC guidelines recommend DCE for surveillance colonoscopy in patients with IBD if SD-WLE is used. HD-WLE alone is also recommended, considering the disadvantages of DCE application. VCE or DCE is an acceptable method for surveillance colonoscopy in patients with IBD if HD colonoscopy is used; however, it should be performed by well-trained endoscopists. Additionally, targeted biopsy is sufficient if patients do not present with any high-risk features of CRN development, such as a previous history of neoplasia, tubular colon shape, or primary sclerosing cholangitis.[44] This recommendation is also supported by European Society of Gastrointestinal Endoscopy (ESGE) guidelines and expert opinion.[45,46] Table 4 summarizes the representative studies for CRN detection in IBD using IEE.[30-32,35-40]

ENDOSCOPIC EVALUATION FOR CHARACTERIZATION OF CRN

Chronic inflammation in IBD leads to mucosal distortion and subsequent regenerative changes, which interrupts the adap-

Table 4. Representative studies for colorectal neoplasia detection in IBD using IEE

Study	Study design	Study population	Colonoscope technique	Outcomes
Alexandersson et al. (2020)[30]	Single center prospective randomized controlled study	305 IBD (186 UC, 116 CD, 3 indeterminate colitis)	HD-DCE vs. HD-WLE	The dysplastic detection rate was significantly higher in HD-DCE than in HD-WLE (11.2% vs. 4.6%, p=0.032).
Wan et al. (2020)[31]	Multicenter randomized controlled study	122 Long-standing UC	HD-WLE with target biopsy (WLT) vs. HD-WLE with random biopsy (WLR) vs. HD-DCE with target biopsy (CET)	The number of colonoscopies with a diagnosis of dysplasia was significantly higher in WLR (8.1% vs. 1.9%, p=0.014) and CET (9.7% vs. 1.9%, p=0.004) than in WLT.
Yang et al. (2019)[32]	Multicenter prospective randomized controlled study	210 Long-standing UC	HD-WLE with random biopsy (HDWL-R) vs. HD-DCE with target biopsy (HDCE-T)	No significant difference in the colitis associated dysplasia detection rate between HDCE-T and HDWL-R (3.9% vs. 5.6%, p=0.749). No significant difference in the median time for colonoscopy withdrawal between HDWL-R and HDCE-T (17.6 min vs. 16.5 min, p=0.212).
Dekker et al. (2007)[35]	Prospective, randomized, crossover study	42 Long-standing UC	NBI vs. conventional colonoscopy	No significant difference in neoplasia detection between NBI and conventional colonoscopy.
van den Broek et al. (2011)[36]	Randomized crossover trial	48 UC	NBI vs. HD-WLE	No significant difference in neoplasia detection between NBI and HD-WLE (69% vs. 81%, p=0.727).
Pellisé et al. (2011)[37]	Prospective, randomized, crossover study	61 Inactive colonic IBD (42 UC, 19 CD)	HD-DCE vs. HD-VCE (NBI)	The withdrawal time was significantly longer in DCE than in NBI (26.87 min vs. 15.74 min, p<0.01), but there was no significant difference in intraepithelial lesion detection between DCE and NBI.
Bisschops et al. (2018)[38]	Multicenter prospective randomized controlled study	131 long-standing UC	HD-VCE (NBI) vs. HD-DCE	The total procedural time is shorter in NBI than in DCE (25.0 min vs. 32.5 min, p<0.001), but there was no significant difference in neoplasia detection rate between DCE and NBI (21.2% vs.21.5%; OR, 1.02; p=0.964).
Iacucci et al. (2018)[39]	Single center prospective randomized controlled study	270 Inactive IBD (129 UC, 136 CD, 5 indeterminate colitis)	HD-WLE vs. HD-DCE vs. HD-VCE (iSCAN)	iSCAN or HD-WLE is not inferior to dye spraying colonoscopy for detection of colonic neoplastic lesions (WLE 18.9%, DCE 17.8%, VCE 11.1%, p= 0.91).
Kandiah et al. (2021)[40]	Multicenter randomized controlled study	188 IBD (131 UC,57 CD)	HD-WLE vs. HD-VCE (iSCAN-OE mode 2)	No significant difference in neoplasia detection (24.2% vs.14.9%, p=0.14) and withdrawal time (24 min vs. 25.5 min, p=0.216) between HD-WLE and iSCAN OE2.

IBD, inflammatory bowel disease; IEE, image-enhanced endocopy; UC, ulcerative colitis; CD, Crohn's disease; HD-DCE, high definition dye-chromoendoscopy; HD-WLE, high definition white light endoscopy; NBI, narrow-band image; HD-VCE, high definition-virtual chromoendoscopy; OR, odds ratio; iSCAN-OE, iSCAN-optical enhancement.

tation of Kudo pit pattern, as well as prediction of histology and invasiveness of CRN.[39] Moreover, the proportion of CRN confirmed by histology among suspicious lesions is approximately 15% during colitis surveillance, which poses difficulty in discriminating neoplastic lesions from nonneoplastic and regenerative changes.[38,47] Several studies assessed the endoscopic features and predictors to differentiate CRN using DCE to enhance CRN characterization in IBD. Sugimoto et al.[48] demon-

strated that flat or superficial elevated lesions, red discoloration, and left-side location were associated with high-grade dysplasia (HGD) using DCE as well as NBI with magnifying colonoscopy, if necessary. Furthermore, pit pattern I or II was not observed in HGD, whereas pit pattern IV and pit pattern III_L were frequently detected in superficial elevation and flat lesions, respectively. Carballal et al.[47] reported that proximal location (OR, 1.86; 95% CI, 1.02–3.40; p=0.04), Kudo pit pattern III–V (OR, 5.05; 95% CI, 2.58–9.88; p=0.001), polypoid morphology (OR, 2.80; 95% CI, 1.57–5.01; p=0.001), and loss of the innominate lines (OR, 1.95; 95% CI, 1.06–3.58; p=0.003) were associated with CRN in IBD. In contrast, a recent retrospective study that used DCE to identify CRN reported that Kudo pit pattern ≥III had a low correlation with CRN with an area under the curve (AUC) of 0.649.[49] However, Kudo pit patterns I and II presented a high negative predictive value of 92% even for non-experts, indicating that it can be used to select lesions for target biopsy.[49]

When VCE was assessed to characterize CRN in patients with IBD, Matsumoto et al.[50] showed that the tortuous surface pattern observed by magnifying NBI might be useful for identifying CRN during surveillance colonoscopy for UC. A pilot study by Bisschops et al.[51] evaluated the diagnostic accuracy and interobserver agreement of Kudo pit pattern using HD-DCE or non-magnified HD-NBI to assess CRN in UC surveillance. They found that Kudo III_L, III_s, IV, or V pit patterns had a sensitivity of 77% for identifying CRN. This study also found that HD-NBI had significantly better interobserver agreement for distinguishing between neoplastic and nonneoplastic pit patterns than HD-DCE (κ=0.653 vs. 0.495, p<0.001). However, overall interobserver agreement for any pit pattern was better in HD-DCE than that in HD-NBI (κ=0.322 vs. 0.224, p<0.001).[51] Moreover, when surveillance colonoscopy was performed using HD-WLE, HD-DCE, and iSCAN, Kudo pit pattern II, III–IV, and V (OR, 21.50; 95% CI, 8.65–60.10) also significantly increased CRN prediction with right side location (OR, 6.52; 95% CI, 1.98–22.5).[39] To effectively distinguish neoplastic lesions from nonneoplastic lesions using advanced endoscopic technologies, a new endoscopic classification of visual characteristics, the Frankfurt advanced chromoendoscopic IBD lesions (FACILE), was developed and validated.[52] FACILE was generated through uni- and multivariate analysis of various endoscopic features including morphology (polypoid, nonpolypoid), surface architecture (roundish, villous-regular, villous-irregular, and irregular/nonstructural), vessel architecture (nonvisible, regular, and irregular/nonstructural) as well as inflammation within the lesion (yes or no) observed by HD-WLE, DCE, and VCE, including iSCAN and NBI. Irregular vessel architecture (OR, 3.49; 95% CI, 1.74–7.10), nonpolypoid lesion (OR, 3.13; 95% CI, 1.32–7.25), irregular surface patterns (OR, 8.89; 95% CI, 3.21–25.96), and signs of inflammation within the lesions (OR, 2.42; 95% CI, 1.24–4.79) were significant predictors of CRN. Additionally, the sensitivity, specificity, and AUC of this classification for predicting CRN were 94%, 51%, and 0.76, respectively. Recently, Cassinotti et al.[53] evaluated the differentiation performance of FICE using Kudo classification; the sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio of the Kudo classification were 91%, 76%, 3.8, and 0.12, respectively. From this study, the authors further studied new endoscopic classification (FICE-KUDO/IBD) specific for FICE, the modified Kudo classification, and included pit patterns and inflammatory markers to differentiate visible colonic lesions. Comparing the performance of FICE-KUDO/IBD with that of SD-WLE, FICE-KUDO/IBD classification was more accurate in identifying neoplastic lesions, with a sensitivity of 93% and specificity of 97%. Furthermore, FICE-KUDO/IBD had a significantly better nonpolypoid lesions detection rate than SD-WLE (8 vs. 7, p=0.016).[54] Table 5 summarizes the representative studies characterizing CRN in IBD using IEE.[47-51,53,54]

CONCLUSIONS

Precise endoscopic assessment of disease activity is fundamental for the optimal treatment of IBD. Furthermore, accurate detection and optical diagnosis of suspicious neoplastic lesions during surveillance colonoscopy are crucial to avoid unnecessary biopsies and reduce surgical treatment due to delayed carcinoma diagnosis in patients with IBD. With recent progress in IEE technologies, VCE platforms such as NBI, iSCAN, FICE, and BLI/CLI systems were developed and adopted in colonoscopic examinations to improve the performance of endoscopic assessments in patients with IBD. Although advanced VCE technologies such as NBI have limitations in evaluating vascular surface patterns in patients with hemorrhage, VCE shows potential for predicting histological remission and clinical outcomes in patients in an endoscopically quiescent state. Additionally, several studies, including meta-analyses, have reported that HD-DCE, HD-VCE, and HD-WLE have comparable performances in detecting CRN during surveillance colonoscopy, although a trend favoring DCE over HD-WLE was observed. Moreover, VCE showed the possibility of dif-

Table 5. Representative studies for characterization of CRN in IBD using IEE

Study	Study design	Study population	Colonoscope technique	Outcomes
Carballal et al. (2018)[47]	Multicenter prospective cohort study	350 IBD (273 UC, 72 CD, 5 indeterminate colitis)	SD or HD-DCE	DCE with target biopsy is superior to WLE for dysplasia detection (57.4% incremental yield for DCE). Endoscopic characteristics predictive of dysplasia were proximal location, loss of innominate lines, polypoid morphology and Kudo pit pattern III–V.
Sugimoto et al. (2017)[48]	Single center retrospective study	39 HGD from 31 UC	DCE, NBI±magnifying	Flat/superficial elevated lesions (48.7%/30.8%) and red discoloration (79.5%) were associated with HGD.
Aladrén et al. (2019)[49]	Multicenter retrospective study	709 Examinations from 569 IBD (458 UC, 102 CD, 9 indeterminate colitis)	DCE	The correlation between dysplasia and Kudo pit patterns predictors of dysplasia (≥III) was low, with AUC of 0.649. Endoscopic activity (OR, 2.692), Paris 0–Is classification (OR, 2.751), and right colon localization (OR, 2.033) were risk factors for dysplasia detection, while rectum (OR, 0.421) or sigmoid localization (OR, 0.445) were protective against dysplasia.
Matsumoto et al. (2007)[50]	Single center cross sectional study	296 Sites from 46 UC	NBI with magnifying	The tortuous surface patterns were associated with dysplasia (vs. honeycomb-like or villous patterns: 8% vs. 0.4%, p=0.003).
Bisschops et al. (2017)[51]	Multicenter retrospective study	50 Images from 27 UC	HD-DCE, HD-NBI	The agreement for differentiating neoplastic from nonneoplastic lesions is significantly better for NBI in comparison with HD-DCE (k=0.653 vs. 0.495, p<0.001). The assessment of pit pattern I or II with non-magnified HD-DCE or NBI has a high negative predictive value (88%) to rule out neoplasia.
Cassinotti et al. (2019)[53]	Single center prospective study	204 Lesions from 59 UC	FICE	FICE can help to predict the histology of raised lesions in UC (SE 91%, SP 76%, and positive and negative LR 3.8, and 0.12). A new classification of pit patterns, based on fibrin cap as a marker of inflammation, improved the diagnostic performance (SE 91%, SP 93%, and positive and negative LR 13, and 0.10).
Cassinotti et al. (2020)[54]	Single center prospective observational parallel study	100 UC	FICE, SD-WLE	FICE with a modified Kudo classification adapted for IBD is more accurate than standard WLE in differentiation of visible lesions (SE 93% vs. 64%, p=0.065; SP 97% vs. 86%, p=0.002, positive-LR 28.3 vs. 4.5, p=0.001; negative LR 0.07 vs. 0.42, p=0.092; NPV 99% vs. 96%, p=0.083).

CRN, colorectal neoplasm; IBD, inflammatory bowel disease; IEE, image-enhanced endoscopy; UC, ulcerative colitis; CD, Crohn's disease; SD-WLE, standard definition-white light endoscopy; HD-WLE, high definition white light endoscopy; DCE, dye-chromoendoscopy; HGD, high-grade dysplasia; NBI, narrow-band image; AUC, area under the curve; OR, odds ratio; FICE, flexible imaging color enhancement; SE, sensitivity; SP, specificity; LR, likelihood ratio; NPV, negative predictive value.

ferentiating nonneoplastic lesions from neoplastic lesions. To establish IEE techniques, especially VCE, as standard-of-care in managing IBD, to tailor therapeutic strategies, and to detect and manage CRN earlier in patients with IBD, growing evidence of the widespread application of IEE technologies in a large IBD population is warranted.

Conflicts of Interest

The author has no potential conflicts of interest.

Funding

None.

ORCID

Young Joo Yang https://orcid.org/0000-0001-6325-1104

REFERENCES

1. Neurath MF, Travis SP. Mucosal healing in inflammatory bowel dis-

eases: a systematic review. Gut 2012;61:1619–1635.
2. Ungaro RC, Yzet C, Bossuyt P, et al. Deep remission at 1 year prevents progression of early Crohn's disease. Gastroenterology 2020; 159:139–147.
3. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. Gut 2001;48:526–535.
4. Freeman HJ. Colorectal cancer risk in Crohn's disease. World J Gastroenterol 2008;14:1810–1811.
5. Kiesslich R, Neurath MF. Chromoendoscopy in inflammatory bowel disease. Gastroenterol Clin North Am 2012;41:291–302.
6. Kiesslich R, Neurath MF. Chromoendoscopy: an evolving standard in surveillance for ulcerative colitis. Inflamm Bowel Dis 2004; 10:695–696.
7. Rutter M, Bernstein C, Matsumoto T, et al. Endoscopic appearance of dysplasia in ulcerative colitis and the role of staining. Endoscopy 2004;36:1109–1114.
8. Deepak P, Fowler KJ, Fletcher JG, et al. Novel imaging approaches in inflammatory bowel diseases. Inflamm Bowel Dis 2019;25:248–260.
9. Nardone OM, Cannatelli R, Ghosh S, et al. New endoscopic tools in inflammatory bowel disease. United European Gastroenterol J 2022;10:1103–1112.
10. Iacucci M, Furfaro F, Matsumoto T, et al. Advanced endoscopic techniques in the assessment of inflammatory bowel disease: new technology, new era. Gut 2019;68:562–572.
11. Kodashima S, Fujishiro M. Novel image-enhanced endoscopy with i-scan technology. World J Gastroenterol 2010;16:1043–1049.
12. Morimoto Y, Kubo M, Kuramoto M, et al. Development of a new generation endoscope system with lasers "LASEREO". Fujifilm Res Dev 2013;58:1–6.
13. Bessissow T, Lemmens B, Ferrante M, et al. Prognostic value of serologic and histologic markers on clinical relapse in ulcerative colitis patients with mucosal healing. Am J Gastroenterol 2012;107:1684–1692.
14. Park S, Abdi T, Gentry M, et al. Histological disease activity as a predictor of clinical relapse among patients with ulcerative colitis: systematic review and meta-analysis. Am J Gastroenterol 2016; 111:1692–1701.
15. Kudo T, Matsumoto T, Esaki M, et al. Mucosal vascular pattern in ulcerative colitis: observations using narrow band imaging colonoscopy with special reference to histologic inflammation. Int J Colorectal Dis 2009;24:495–501.
16. Sasanuma S, Ohtsuka K, Kudo SE, et al. Narrow band imaging efficiency in evaluation of mucosal healing/relapse of ulcerative colitis. Endosc Int Open 2018;6:E518–E523.
17. Neumann H, Vieth M, Günther C, et al. Virtual chromoendoscopy for prediction of severity and disease extent in patients with inflammatory bowel disease: a randomized controlled study. Inflamm Bowel Dis 2013;19:1935–1942.
18. Iacucci M, Fort Gasia M, Hassan C, et al. Complete mucosal healing defined by endoscopic Mayo subscore still demonstrates abnormalities by novel high definition colonoscopy and refined histological gradings. Endoscopy 2015;47:726–734.
19. Iacucci M, Kiesslich R, Gui X, et al. Beyond white light: optical enhancement in conjunction with magnification colonoscopy for the assessment of mucosal healing in ulcerative colitis. Endoscopy 2017;49:553–559.
20. Iacucci M, Daperno M, Lazarev M, et al. Development and reliability of the new endoscopic virtual chromoendoscopy score: the PICaSSO (Paddington International Virtual ChromoendoScopy ScOre) in ulcerative colitis. Gastrointest Endosc 2017;86:1118–1127.
21. Trivedi PJ, Kiesslich R, Hodson J, et al. The Paddington International Virtual Chromoendoscopy Score in ulcerative colitis exhibits very good inter-rater agreement after computerized module training: a multicenter study across academic and community practice (with video). Gastrointest Endosc 2018;88:95–106.
22. Iacucci M, Smith SCL, Bazarova A, et al. An international multicenter real-life prospective study of electronic chromoendoscopy score PICaSSO in ulcerative colitis. Gastroenterology 2021;160:1558–1569.
23. Nardone OM, Bazarova A, Bhandari P, et al. PICaSSO virtual electronic chromendoscopy accurately reflects combined endoscopic and histological assessment for prediction of clinical outcomes in ulcerative colitis. United European Gastroenterol J 2022;10:147–159.
24. Cannatelli R, Bazarova A, Furfaro F, et al. Reproducibility of the electronic chromoendoscopy PICaSSO score (Paddington International Virtual ChromoendoScopy ScOre) in ulcerative colitis using multiple endoscopic platforms: a prospective multicenter international study (with video). Gastrointest Endosc 2022;96:73–83.
25. Iacucci M, Cannatelli R, Parigi TL, et al. A virtual chromoendoscopy artificial intelligence system to detect endoscopic and histologic activity/remission and predict clinical outcomes in ulcerative colitis. Endoscopy 2023;55:332–341.
26. Uchiyama K, Takagi T, Kashiwagi S, et al. Assessment of endoscopic mucosal healing of ulcerative colitis using linked colour imaging, a novel endoscopic enhancement system. J Crohns Colitis 2017;11:963–969.
27. Matsumoto K, Oka S, Tanaka S, et al. Clinical usefulness of linked color imaging for evaluation of endoscopic activity and prediction of relapse in ulcerative colitis. Int J Colorectal Dis 2021;36:1053–1061.
28. Nardone OM, Snir Y, Hodson J, et al. Advanced technology for assessment of endoscopic and histological activity in ulcerative colitis:

a systematic review and meta-analysis. Therap Adv Gastroenterol 2022;15:17562848221092594.
29. Laine L, Kaltenbach T, Barkun A, et al. SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease. Gastroenterology 2015;148:639–651.
30. Alexandersson B, Hamad Y, Andreasson A, et al. High-definition chromoendoscopy superior to high-definition white-light endoscopy in surveillance of inflammatory bowel diseases in a randomized trial. Clin Gastroenterol Hepatol 2020;18:2101–2107.
31. Wan J, Zhang Q, Liang SH, et al. Chromoendoscopy with targeted biopsies is superior to white-light endoscopy for the long-term follow-up detection of dysplasia in ulcerative colitis patients: a multicenter randomized-controlled trial. Gastroenterol Rep (Oxf) 2020;9:14–21.
32. Yang DH, Park SJ, Kim HS, et al. High-definition chromoendoscopy versus high-definition white light colonoscopy for neoplasia surveillance in ulcerative colitis: a randomized controlled trial. Am J Gastroenterol 2019;114:1642–1648.
33. Feuerstein JD, Rakowsky S, Sattler L, et al. Meta-analysis of dye-based chromoendoscopy compared with standard- and high-definition white-light endoscopy in patients with inflammatory bowel disease at increased risk of colon cancer. Gastrointest Endosc 2019;90:186–195.
34. Gondal B, Haider H, Komaki Y, et al. Efficacy of various endoscopic modalities in detecting dysplasia in ulcerative colitis: a systematic review and network meta-analysis. World J Gastrointest Endosc 2020;12:159–171.
35. 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;39:216–221.
36. 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;43:108–115.
37. 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;74:840–848.
38. Bisschops R, Bessissow T, Joseph JA, et al. Chromoendoscopy versus narrow band imaging in UC: a prospective randomised controlled trial. Gut 2018;67:1087–1094.
39. 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;113:225–234.
40. Kandiah K, Subramaniam S, Thayalasekaran S, et al. Multicentre randomized controlled trial on virtual chromoendoscopy in the detection of neoplasia during colitis surveillance high-definition colonoscopy (the VIRTUOSO trial). Gut 2021;70:1684–1690.
41. El-Dallal M, Chen Y, Lin Q, et al. Meta-analysis of virtual-based chromoendoscopy compared with dye-spraying chromoendoscopy standard and high-definition white light endoscopy in patients with inflammatory bowel disease at increased risk of colon cancer. Inflamm Bowel Dis 2020;26:1319–1329.
42. Resende RH, Ribeiro IB, de Moura DT, et al. Surveillance in inflammatory bowel disease: is chromoendoscopy the only way to go?: a systematic review and meta-analysis of randomized clinical trials. Endosc Int Open 2020;8:E578–E590.
43. Neumann H, Neurath MF, Mudter J. New endoscopic approaches in IBD. World J Gastroenterol 2011;17:63–68.
44. Rabinowitz LG, Kumta NA, Marion JF. Beyond the SCENIC route: updates in chromoendoscopy and dysplasia screening in patients with inflammatory bowel disease. Gastrointest Endosc 2022;95:30–37.
45. Bisschops R, East JE, Hassan C, et al. Advanced imaging for detection and differentiation of colorectal neoplasia: European Society of Gastrointestinal Endoscopy (ESGE) Guideline: update 2019. Endoscopy 2019;51:1155–1179.
46. Murthy SK, Feuerstein JD, Nguyen GC, et al. AGA clinical practice update on endoscopic surveillance and management of colorectal dysplasia in inflammatory bowel diseases: expert review. Gastroenterology 2021;161:1043–1051.
47. Carballal S, Maisterra S, López-Serrano A, et al. Real-life chromoendoscopy for neoplasia detection and characterisation in long-standing IBD. Gut 2018;67:70–78.
48. Sugimoto S, Naganuma M, Iwao Y, et al. Endoscopic morphologic features of ulcerative colitis-associated dysplasia classified according to the SCENIC consensus statement. Gastrointest Endosc 2017;85:639–646.
49. Aladrén BS, González-Lama Y, García-Alvarado M, et al. Even non-experts identify non-dysplastic lesions in inflammatory bowel disease via chromoendoscopy: results of a screening program in real-life. Endosc Int Open 2019;7:E743–E750.
50. Matsumoto T, Kudo T, Jo Y, et al. Magnifying colonoscopy with narrow band imaging system for the diagnosis of dysplasia in ulcerative colitis: a pilot study. Gastrointest Endosc 2007;66:957–965.
51. Bisschops R, Bessissow T, Dekker E, et al. Pit pattern analysis with high-definition chromoendoscopy and narrow-band imaging for optical diagnosis of dysplasia in patients with ulcerative colitis. Gas-

trointest Endosc 2017;86:1100–1106.
52. Iacucci M, McQuaid K, Gui XS, et al. A multimodal (FACILE) classification for optical diagnosis of inflammatory bowel disease associated neoplasia. Endoscopy 2019;51:133–141.
53. Cassinotti A, Buffoli F, Fociani P, et al. Virtual chromoendoscopy with FICE for the classification of polypoid and nonpolypoid raised lesions in ulcerative colitis. J Clin Gastroenterol 2019;53:269–276.
54. Cassinotti A, Fociani P, Duca P, et al. Modified Kudo classification can improve accuracy of virtual chromoendoscopy with FICE in endoscopic surveillance of ulcerative colitis. Endosc Int Open 2020;8:E1414–E1422.