Advanced Endoscopic Imaging for Dysplasia Characterization in Inflammatory Bowel Disease

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KEYWORDS

• Dysplasia • Inflammatory bowel disease • Malignancy surveillance
• Virtual chromoendoscopy

KEY POINTS

- The presence of active inflammation, mucosal scars, and (post-) inflammatory lesions complicate the accurate characterization of inflammatory bowel disease-related dysplasia.
- When characterizing possible dysplastic lesions, the classification used (eg, Kudo-IBD or Frankfurt Advanced Chromoendoscopic IBD LEsions [FACILE]) is of greater importance than the endoscopic imaging technique used.
- Artificial intelligence (AI) shows promising results in gastrointestinal endoscopy through computer-aided diagnostic (computer-aided detection and computer-aided characterisation [CADx]) models. However, its application in IBD dysplasia surveillance is nascent and limited by biases in current training datasets.
- The integration of ultra-high-definition endoscopy (CLE/EC) and AI-assisted technologies (eg, EndoBRAIN) holds potential to enhance dysplasia surveillance in IBD, offering clinicians powerful tools to improve outcomes and reduce colorectal cancer burden in high-risk populations.

INTRODUCTION

Patients with colonic inflammatory bowel disease (IBD) are known to be at an increased risk of developing colonic dysplastic lesions.[1–3] This risk is most elevated in patients with extensive Ulcerative Colitis (UC) and significantly increases 8 to 10 years after

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the initial diagnosis or when dysplasia is detected on colonic biopsies, especially in case of high-grade dysplasia.[4] A recent meta-analysis calculated that the relative risk (RR) for development of colon cancer and rectal cancer in patients with UC is 1.99 and 1.69, respectively.[5] Similarly, in patients with Crohn's disease (CD) there is an increase in RR for development of colon cancer (2.30) and rectal cancer (1.85).[5] This increased risk for colorectal cancer in IBD is based on inflammation-induced carcinogenesis. In this process, chronic inflammation induces oxidative stress-related DNA damage, which in turn may activate tumor promotor genes and/or silence tumor suppressor genes, leading to tissue genetic instability and eventually colorectal cancer.[6]

A recent systematic review showed that the incidence rate of patients with UC developing colorectal cancer has steadily decreased over the last 60 years from 4.29/1000 py in 1950 to 1.21/1000 in the period of 2010 to 2013.[7] On the one hand, this is probably due to the recent advances in therapeutic options, leading to better disease management. On the other hand, the establishment and broad application of surveillance recommendations (**Table 1**) advocating for more frequent surveillance colonoscopies have also led to an increased detection of early dysplastic lesions.[8]

Nevertheless, despite advancements in surveillance strategies and technologies, the effective detection and characterization of dysplastic lesions remain challenging. Currently, dye-based chromoendoscopy (DCE) has been established as the gold standard in IBD dysplasia surveillance and is incorporated in all international guidelines. This technique uses a topical dye, such as 0.1% methylene blue or 0.1% to 0.5% indigo carmine, to stain the entire colonic mucosa, enhancing the visualization of mucosal abnormalities. Many studies have demonstrated the superior dysplasia detection rate of DCE compared to standard white light endoscopy (SD-WLE).[9–11] However, in spite of its superior dysplasia detection rate, the adoption of dye-based chromoendoscopy in routine clinical practice has been very slow-going. This is partially because DCE is more laborious since the entire colonic mucosa has to be stained, which is a time-consuming process. Moreover, DCE is impractical in patients with suboptimal bowel preparation.

In more recent years, dye-less or virtual chromoendoscopy (VCE) has gained interest as a potential alternative technique for dysplasia detection and characterization. This technology aims to enhance the visualization of tissue characteristics without the use of dyes. There are 2 main classes of VCE, namely optical and digital VCE. In optical VCE, the endoscope's light source is equipped with special optical filters that selectively filter white light, resulting in a so-called "narrow-band" light being emitted from the scope. In contrast to this, digital VCE uses post-processing of the video-output to enhance the image displayed on the monitor. Both technologies aim to enhance the visualization and characterization of mucosal and vascular features, hereby facilitating the detection of dysplasia.[12]

The use of these advanced endoscopic imaging techniques have the potential to facilitate the detection of dysplastic lesions, allow for a better characterization of lesions, and reduce the number of unnecessary biopsies (**Fig. 1**A, B).[13] Moreover, they have the potential to improve lesions demarcation, potentially resulting in more frequent R0 resection, guiding organ-sparing endotherapy.[4]

RISK FACTORS FOR DYSPLASIA

Even though patients with CD or UC have an increased risk for development of colorectal cancer, the absolute risk remains rather low.[5] The cumulative incidence of colorectal cancer was calculated to be 2.5% after 20 years and 10.8% after 40 years by *Rutter* and colleagues[14] Numerous risk factors for colorectal cancer development,

Table 1
Summary of recent international recommendations for dysplasia surveillance

	Imaging Modality	Biopsies	Reference
European Society of Gastrointestinal Endoscopy (2019)	Dye-based pancolonic chromoendoscopy or Virtual chromoendoscopy	• Targeted biopsies in patients with quiescent disease, adequate bowel preparation and proper endoscopist training • Targeted biopsies plus 4-quadrant random biopsies every 10 cm in high-risk patients (personal history of colonic neoplasia, tubular appearing colon, strictures, or primary sclerosing cholangitis [PSC])	Bisschops et al,[13] 2019
European Crohn's and Colitis Organization(2023)	Dye-based chromoendoscopy or Virtual chromoendoscopy	• Targeted biopsies • Random biopsies in high-risk patients (PSC or history of dysplasia)	Gordon et al,[4] 2023
American Gastroenterology Association (2021)	Dye-based chromoendoscopy (preferably with high-definition endoscope) or alternatively virtual chromoendoscopy with a high-definition endoscope.	• Targeted biopsies when using dye-based or virtual chromoendoscopy • Random biopsies when using standard definition white light endoscopy • Random biopsies in patients with history of dysplasia or PSC.	Murthy et al,[17] 2021
British Society for Gastroenterology (2019)	• High-definition endoscope recommended over standard definition when using white light endoscopy • Chromoendoscopy is recommended over white light endoscopy when using standard definition endoscopes • Chromoendoscopy is suggested over white light endoscopy when using high-definition endoscopes • Narrow band imaging is not suggested	Targeted biopsies recommended	Lamb et al,[16] 2019

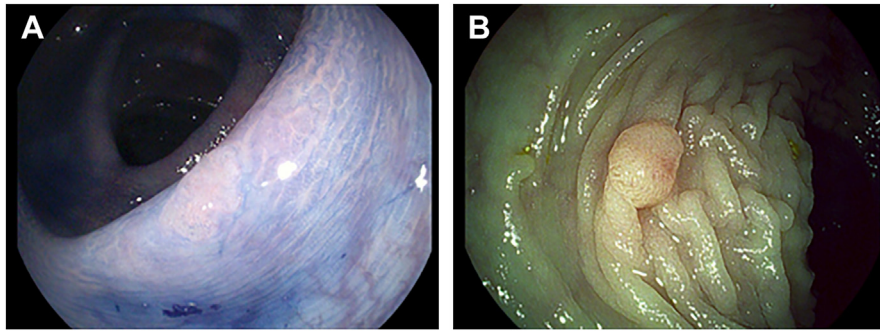

Fig. 1. Example of dye-based chromoendoscopy and i-scan virtual chromoendoscopy. (*A*) Detection of a small (4 mm), flat tubular adenoma with low-grade dysplasia in the colon ascendens using methylene-blue dye-based chromoendoscopy. (*B*) Improved visualization of a small (5 mm) tubular adenoma with low- grade dysplasia in the sigmoid using i-scan virtual chromoendoscopy.

such as male sex, young age at disease onset, disease duration greater than 8 years, extensive colonic disease, and presence of concomitant primary sclerosing cholangitis (PSC), have been identified over the years.[8,15]

Disease duration is one of the best-known risk factors. The incidence of dysplasia and colorectal cancer increases over time, rarely occurring within the first 6 to 8 years after disease onset. The same study calculated that the incidence of dysplasia is only 1.5% after 10 years and increases to 15.8% after 30 years of disease duration.[14] Therefore most surveillance guidelines advise to start screening colonoscopies 6 to 8 years after onset of symptoms (see **Table 1**).[4,13,16,17]

Disease location and/or disease extent represents another significant risk factor. There was a marked increase in standardized incidence rate (SIR) of colorectal cancer in patients with UC pancolitis (SIR 2.4–14.8) compared to patients with less extensive left-sided UC colitis (SIR 1.4–2.8). However, in patients with UC limited to the rectum, no increased colorectal cancer risk was observed.[4,18] In patients with CD, involvement of the colon was associated with an increased risk of colorectal cancer, usually in the distal colorectum.[4,19,20]

Many individual studies have shown that the concomitant presence of PSC significantly increases the risk of dysplasia. A recent systematic review reported that the presence of PSC was associated with an odds ratio (OR) of 4.14 (95% CI, 2.85–6.01).[8] Analogously, a high inflammatory burden, the presence of post-inflammatory polyps, and a stricturing phenotype have also been identified as significant risk factors for developing colorectal cancer.[4,8,21]

DYSPLASIA TERMINOLOGY

The accurate optical characterization of dysplasia in IBD presents significant challenges. Upon diagnosis of a dysplastic lesion, clear and consistent endoscopic terminology should be used to describe it. The European Crohn's and Colitis Organization guidelines have suggested a systemic approach ("Five S″) to describe dysplasia in IBD (**Table 2**).[4]

The first "S" refers to the localization of the lesion ("Site"). Using the biopsy forceps as reference, the size of the lesion can be grossly measured ("Size"). Next, classification of the lesion using the Modified Paris classification should be performed ("Shape"). Lesions are considered polypoid when they protrude $\geq$2.5 mm into the

Table 2
Standardized approach to visible dysplasia in inflammatory bowel disease (European Crohn's and Colitis Organization guidelines 2023)

Classification of Visible Dysplasia in Inflammatory Bowel Disease	
Site	Describe localization of the lesion
Size	Estimate lesion size using biopsy forceps as reference.
Shape	Polypoid lesion (Modified Paris Ip or Is) vs non-polypoid lesion (Modified Paris IIa, IIb, IIc) Distinct borders vs indistinct borders
Surface	Kudo classification Frankfurt Advanced Chromoendoscopic IBD LEsions classification
Surroundings	Mucosal activity, surrounding lesions or submucosal fibrosis

Adapted from Gordon, H., et al. (2023). ECCO Guidelines on Inflammatory Bowel Disease and Malignancies. Journal of Crohn's and Colitis, 17(6), 827–854. https://doi.org/10.1093/ecco-jcc/jjac187.

lumen (Modified Paris well-circumscribed pedunculated Ip and sessile Is). Non polypoid lesions consist of Modified Paris flat elevated IIa, flat IIb, and flat-depressed IIc lesions. The borders of the lesion can be described as distinct or indistinct.[4,22] Subsequently, the surface of the lesion should be described using standardized classifications such as the Kudo's pit pattern classification, the modified Kudo classification, or the Frankfurt Advanced Chromoendoscopic IBD Lesions (FACILE) classification ("Surface").[4,23,24] Lastly, relevant changes to the surroundings of the lesion, such as mucosal activity, surrounding lesions or tethering should be described ("Surroundings").[4]

SELECTION OF IMAGING MODALITY

All international guidelines currently recommend the routine use of 0.1% methylene blue or 0.1% to 0.5% indigo carmine pancolonic chromoendoscopy (DCE) with targeted biopsies for dysplasia surveillance. In patients with a high risk of dysplasia, random 4 quadrant biopsies every 10 cm are recommended in addition to the targeted biopsies of all visible lesions.[4,13,16,17] However, there are certain limitations associated with the use of DCE. Poor bowel preparation, presence of active inflammation at the time of investigation, and/or presence of pseudopolyps are most frequently associated with failure to accurately perform DCE.[25] Moreover, DCE should only be performed by trained endoscopists, although until the publication of the European Society of Gastrointestinal Endoscopy training curriculum for optical diagnosis in 2020, there was no definition of what this training should consist of or what competence standards endoscopists should reach.[26]

Following several new studies demonstrating that VCE, specifically i-scan (Pentax, Japan) and Narrow-band imaging (NBI, Olympus, Japan), has a non-inferior dysplasia detection rate compared to DCE in IBD dysplasia surveillance, international guidelines have started suggesting VCE as an alternative technique to DCE.[4,13,16,17,27–32] VCE has the additional advantage of being inherently more practical as well as less time-consuming than performing a pancolonic dye stain.[27–32]

ENDOSCOPIC MUCOSAL CLASSIFICATIONS FOR INFLAMMATORY BOWEL DISEASE-RELATED DYSPLASIA

Advanced endoscopic imaging techniques, such as DCE and VCE have been described to improve dysplasia detection in IBD, but the accuracy of characterization

of these advanced techniques remains controversial. Some guidelines, such as the SCENIC guidelines,[22] either do not mention these techniques or offer conclusions that are overly simplified and not easily applicable in everyday clinical practice. Beyond the challenge of correctly distinguishing non-dysplastic from dysplastic lesions, the presence of inflammatory and post-inflammatory changes further complicates the accurate characterization of IBD-related dysplasia.[33]

KUDO'S PIT PATTERN CLASSIFICATION

Even though the Kudo's pit pattern classification (**Fig. 2**) was originally developed for use in magnifying endoscopy in combination with Indigo Carmine and Cresyl Violet staining, it offers a structured approach to differentiate dysplastic and non-dysplastic colonic lesions based on their mucosal pit patterns.[34] For practical application in UC surveillance, a dichotomous approach to the Kudo classification has been proposed: Kudo's pit pattern type I (round pit pattern, typically indicative of normal colonic mucosa) and type II (stellar or papillary pattern, typically indicative of hyperplastic mucosa) are indicative of benign lesions, whereas type III and V are typically indicative of dysplastic changes.[9] Comprehensive training in the Kudo classification remains essential in enhancing its diagnostic reliability. In the absence of any prior experience in dysplasia characterization in IBD, it is advised to biopsy any visible lesion for histologic diagnosis and feedback. Additionally, it is important to recognize that optical diagnosis using the Kudo classification is not without its limitations. Therefore, the authors suggest taking biopsies from all visible lesions which are not typical type I pseudopolyps or hyperplastic polyps, in order to avoid missing dysplastic lesions. In case of large lesions and especially when the confidence is low, biopsies should be taken for histologic confirmation.[23]

The use of this dichotomous classification in non-magnified high definition chromoendoscopy (HD-CE) and NBI shows good diagnostic accuracy; however, a significant inter-observer variability was noted, largely due to differences in expertise.[23] This latter study also demonstrated that the assessment of pit pattern I or II with non-magnified HD-CE or NBI had a high negative predictive value (88%) to rule out dysplasia, with an acceptable sensitivity of 77%.[23] However, due to regenerative and inflammatory artifacts, which are very common in IBD, and because it was originally developed for magnification endoscopy, the use of the Kudo classification for

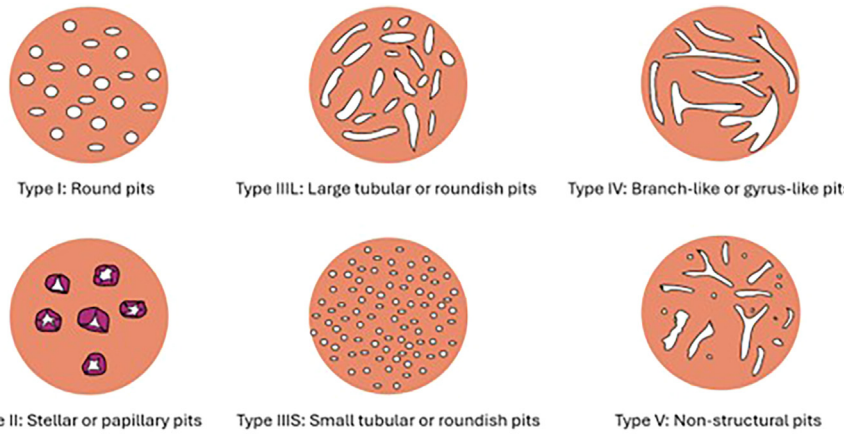

Fig. 2. Kudo's pit pattern classification.

IBD dysplasia characterization remains controversial. Therefore, it is important to remember that the absence of active inflammation remains a prerequisite for good-quality screening and to enable the optical diagnosis based on the pit pattern.

MODIFIED KUDO CLASSIFICATION (KUDO-INFLAMMATORY BOWEL DISEASE)

In a sub-analysis of a prospective study involving 205 lesions from UC patients undergoing surveillance endoscopy with Fujinon intelligent chromoendoscopy (FICE), Cassinotti and colleagues identified 4 endoscopic predictors—pit heterogeneity, micro-vessel positivity, presence of fibrin cap, and endoscopic inflammatory activity—to enhance the accuracy of the Kudo classification. Pit heterogeneity was significantly more frequently observed in dysplastic versus non-dysplastic lesions (91% vs 33%). Micro-vessel positivity (irregular, visible vessels) was also significantly associated with dysplastic lesions (48% vs 7%). The presence of a fibrin cap or inflammatory activity on the surface of the lesion was on the other hand negatively associated with dysplastic lesions.[35] The implementation of these endoscopic predictors resulted in the development of the Kudo-IBD classification (**Fig. 3**). The diagnostic performance of the Kudo-IBD classification versus standard WLE was significantly better (sensitivity

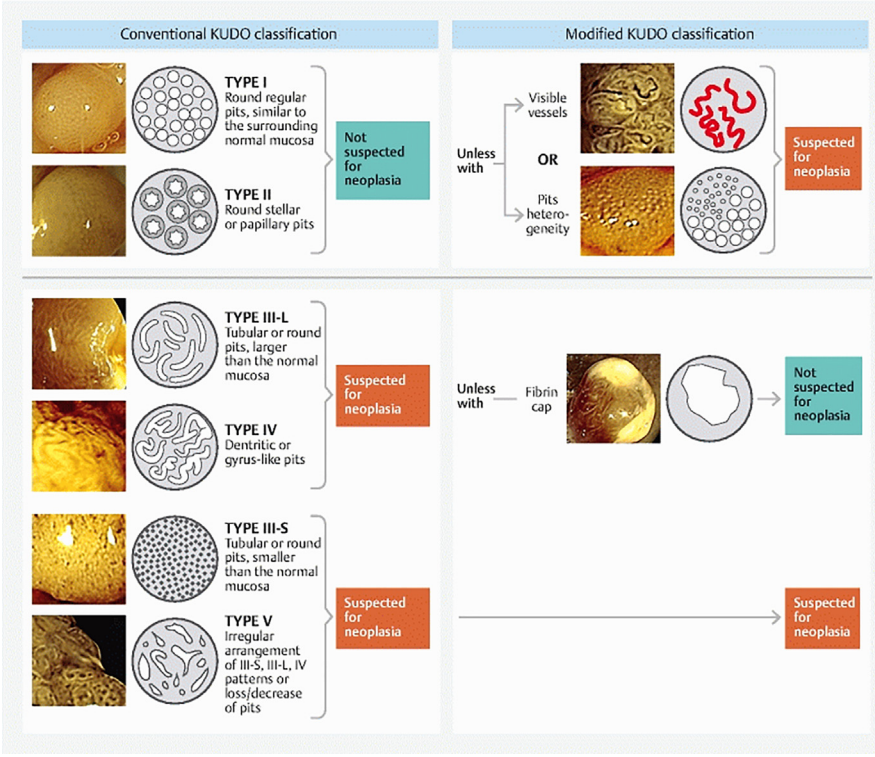

Fig. 3. Modified Kudo classification (Kudo-inflammatory bowel disease [IBD]). (*From* Cassinotti A, Fociani P, Duca P, Nebuloni M, Davies SEC, Sampietro G, Buffoli F, Corona A, Maconi G, Ardizzone S. Modified Kudo classification can improve accuracy of virtual chromoendoscopy with FICE in endoscopic surveillance of ulcerative colitis. Endosc Int Open. 2020 Oct;8(10):E1414-E1422. https://doi.org/10.1055/a-1165-0169. Epub 2020 Sep 22. PMID: 33015345; PMCID: PMC7508663.)

93% vs 64%, specificity 97% vs 86%).[36] Additionally 2 recent studies by the same research group support the use of the Kudo-IBD classification with other types of VCE, namely i-scan and NBI.[37,38]

FRANKFURT ADVANCED CHROMOENDOSCOPIC INFLAMMATORY BOWEL DISEASE LESIONS CLASSIFICATION

A more recent approach to the optical diagnosis of dysplastic lesions in IBD is the FACILE classification (**Fig. 4**). This multimodal classification system leverages advanced imaging techniques (DCE, i-scan and NBI), abandoning the traditional Kudo's pit pattern classification. The FACILE classification incorporates 4 key characteristics predictive of dysplastic histology: non-polypoid morphology, irregular surface and vascular patterns, and the presence of any inflammation within the lesion. Diagnostic accuracy using this classification reached 85% when high-confidence diagnoses were made by experienced endoscopists.[24] Moreover, the FACILE classification has shown potential for enhancing diagnostic capabilities among trainees. After undergoing training with the FACILE system, trainees without prior endoscopic expertise achieved a sensitivity of 80% and an accuracy of 77% in lesion characterization, demonstrating significant improvement in their diagnostic performance. This result highlights the FACILE classification's utility in both expert and novice settings, potentially standardizing and improving dysplasia detection in IBD patients.[24,39]

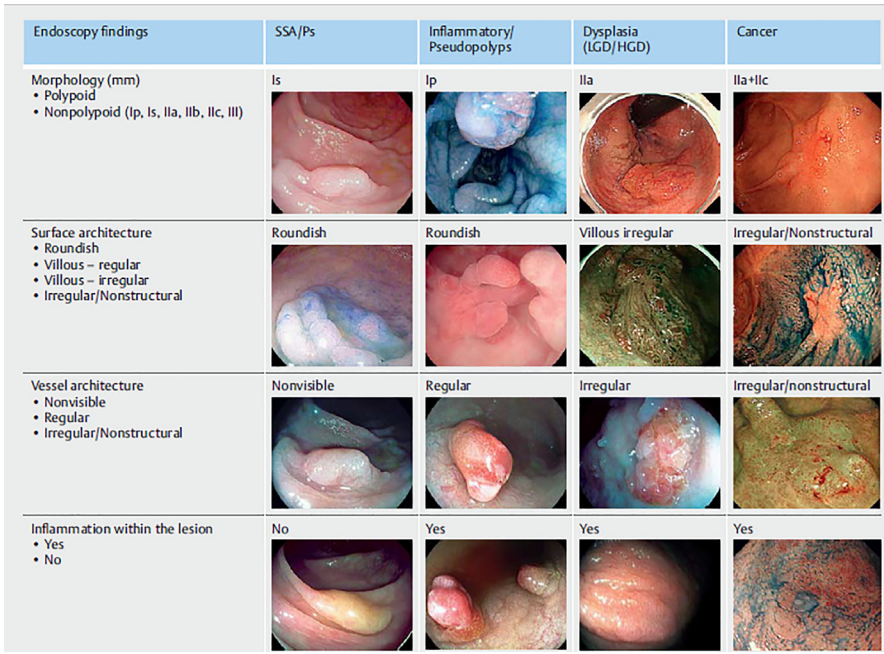

Fig. 4. Frankfurt Advanced Chromoendoscopic IBD LEsions classification. (*From* Iacucci M, McQuaid K, Gui XS, Iwao Y, Lethebe BC, Lowerison M, Matsumoto T, Shivaji UN, Smith SCL, Subramanian V, Uraoka T, Sanduleanu S, Ghosh S, Kiesslich R. A multimodal (FACILE) classification for optical diagnosis of inflammatory bowel disease associated neoplasia. Endoscopy. 2019 Feb;51(2):133-141. https://doi.org/10.1055/a-0757-7759. Epub 2018 Dec 12. PMID: 30541154.)

NEXT GENERATION ENDOSCOPY

Confocal Laser Endomicroscopy

Confocal Laser Endomicroscopy (CLE) is a relatively new endoscopic technique which was introduced approximately 15 years ago. Nowadays, classical CLE (using a proprietary CLE-capable endoscope) has mainly been replaced by Probe-based Confocal Laser Endomicroscopy (pCLE). pCLE is performed by administering intravenous or topical fluorescein, after which the colonic mucosa can be microscopically evaluated with the use of a special probe that is passed through the working channel of the endoscope. This probe emits a laser light which penetrates the mucosa to a depth up to 250 μm. Through this technique, the endoscopist can in vivo evaluate the crypt architecture, microvessels, inflammatory cell infiltration in the lamina propria, and increased vascular permeability as evidenced by intraluminal and intracryptic fluorescein leakage, enabling a comprehensive structural and functional assessment of the colonic mucosa.[40–42]

The role of pCLE in IBD endoscopy has been investigated over the last years and many studies have shown promising results in prediction of clinical response (eg, prediction of clinical response to anti-tumor necrosis factor [TNF] therapy in CD),[43] in differentiating CD from UC,[44] and assessment of disease activity.[45] However, pCLE can also play a role in the detection of dysplasia in patients with IBD. One randomized study found that chromoendoscopy with CLE was able to detect 4.75 × more dysplastic lesions compared to conventional endoscopy. Moreover, in this same study, 50% fewer biopsies were required when using chromoendoscopy with CLE.[45] Another study confirmed the high diagnostic accuracy of CLE for the detection of dysplasia compared to standard histology. In this study, CLE showed a sensitivity of 100% and a specificity of 90%, with a positive predictive value of 83% and a negative predictive value of 100%.[46] On the other hand, an RCT by Freire and colleagues showed no improvement in diagnostic yield when using CLE in the setting of dysplasia surveillance in longstanding IBD. This study confirmed, however, that the use of CLE was associated with a decreased number of biopsies and an increased per-biopsy yield for dysplasia, at the cost of a longer procedural time.[47] When investigating the incremental diagnostic yield and accuracy of CLE over CE, 3 prospective studies showed that the use of CLE showed no additional advantage over the use of chromoendoscopy (CE) in dysplasia surveillance in IBD.[48,49] Regarding the feasibility of pCLE, van den Broek and colleagues calculated that the use of pCLE leads to an increase of approximately 30 to 40 minutes in procedural time, with the possible addition of extra time when lesions are detected and need to be examined with pCLE.[50] This same study also examined the specificity of CLE, which was only 82%. The rather low specificity of CLE compared to standard histology can be explained because hyperplastic and inflamed patches of colon mucosa frequently display a reduction in goblet cells and an increase in striped/irregular epithelium, which is also seen in dysplasia.[50]

Despite the potential of (p)CLE, the high cost of equipment, increased procedural time, frequent equipment failure due to lens distortion, and uncertain incremental advantages of (p)CLE over chromoendoscopy (CE) are significant hindrances to the routine clinical adoption of (p)CLE for dysplasia screening in IBD.[42]

Endocytoscopy

Endocytoscopy (EC) is an endoscopic technique that allows ultra-high-magnification (450 ××–1400 ×) imaging of the gastrointestinal mucosa. This technique requires the use of an absorptive staining agent, such as methylene blue, and a mucolytic agent (ie,

N-acetylcysteine), which is sprayed upon the mucosa. Utilizing a proprietary EC system, this technique provides a real-time view of the superficial mucosal cells, including inflammatory cells, and allows for the observation of their cell morphology, mucosal surfaces, and nuclear details.[40,42]

EC has been shown to be useful in the assessment of inflammation using the EC scoring system "ECSS," to predict mucosal healing (increase in goblet cells and mucus production) or predict relapse using the ECSS. On the role of EC in dysplasia characterization in IBD, little evidence is currently available. One study found that irregularly formed nuclei (including fusiform nuclei and enlarged nuclei) was indicative of colorectal dysplasia.[51] A recent retrospective study by Kudo and colleagues compared the diagnostic accuracy of EC compared to classical pit pattern analysis for the diagnosis of UC-associated neoplasia (UCAN). This pilot study demonstrated that EC could effectively be used to predict UCAN based on nuclear irregularities.[52] While EC has the potential of becoming a powerful tool for dysplasia characterization in IBD, it also has certain limitations which may hinder its clinical adoption for dysplasia characterization. One significant challenge associated with the use of EC in IBD dysplasia surveillance is that neo-vascularization, which commonly occurs during inflammation, can mimic malignancy, leading to potential misclassifications.[42] Furthermore, there is a lack of studies investigating the additional advantage of EC over conventional endoscopy in IBD dysplasia surveillance, as well as EC has a high procedural cost and learning curve.

Artificial intelligence (AI) has the potential to improve the diagnostic accuracy and to reduce the interobserver variability, whilst reducing the learning curve for EC. Several studies have already shown that EC has good compatibility with AI.[53–55] The available evidence regarding AI-assisted EC for IBD dysplasia surveillance is currently limited to a case report of EndoBRAIN (Cybernet Systems Co, Tokyo, Japan) using NBI to identify UCAN.[56] It is self-evident that further studies on the application of AI-assisted EC/CLE for the characterization of dysplasia in IBD are necessary. Nevertheless, AI models such as EndoBRAIN hold the potential to overcome some of the inherent limitations of EC, such as accurately differentiating between inflammation-related neovascularization versus dysplasia-related neo-vascularization.

Artificial Intelligence-Enhanced Endoscopy

AI is revolutionizing the medical field at an unprecedented pace. In particular, AI is proving to be a valuable asset in digestive endoscopy, analyzing endoscopic footage in real-time parallel to the endoscopist. This has the potential of reducing the likelihood of errors and minimizing the inter-operator variability, ensuring a more consistent and accurate endoscopic assessment. In non-IBD endoscopy, AI tools have been developed and validated that are aimed to enhance the lesion detection and characterization. However, colorectal lesions of patients with IBD have traditionally been excluded from the training and testing datasets of these models. Instead, most of the AI research in IBD endoscopy has been focused on grading of disease activity, prediction of histologic remission, automatic video capsule endoscopy reading, and differentiation/diagnosis between the different types of IBD.[57–61] These models are mostly developed using still images rather than videos, potentially posing a hindrance for their application in everyday clinical practice. Only recently, has the first computer-aided detection (CADe) system been developed specifically for recognition of IBD-associated lesions. This IBD-CADe model was able to detect colorectal lesions in still endoscopic images of patients with IBD with high accuracy (AUC 0.85) in high definiteion White light endoscopy (HD-WLE). This specific model was less accurate when detecting colorectal lesions in DCE (AUC 0.65).[62] Again, this underlines the importance of the dataset that

is used during the training of computer aided detection (CADe)/computer aided characterisation (CADx) models, since the backbone CADe model was trained solely on HD-WLE images.

To the best of the authors' knowledge, no CADx models for differentiating between dysplastic and non-dysplastic lesions in IBD have been developed yet. However, a Japanese research team has recently published upon a deep convolutional neural network capable of differentiating lesions between "adenocarcinoma/high-grade dysplasia" and "low-grade dysplasia/sporadic adenoma/normal mucosa." This model achieved a sensitivity of 72.5%, specificity of 82.9%, and an accuracy of 79.0%, outcompeting the expert endoscopists (respectively 60.5%/88.0%/77.8%).[63]

SUMMARY

IBD poses a significant risk for the development of colorectal dysplasia and cancer, necessitating effective surveillance strategies. The presence of active inflammation, mucosal scars, and (post-)inflammatory lesions can complicate the accurate characterization of IBD-related dysplasia. Advanced endoscopic imaging techniques (ie, DCE and alternatively VCE) have been described to improve dysplasia detection in IBD. Nevertheless, it remains unclear which technique should be favored for dysplasia characterization after detection of a lesion. Recent research underscores that in the context of IBD surveillance, the classification used to characterize the lesion (eg, Kudo-IBD or FACILE) is of greater importance than the endoscopic imaging technique used.[33] Nevertheless, the use of the conventional Kudo classification has become increasingly more controversial for dysplasia characterization because of its low specificity, which is due to the frequent misclassification of regenerative and inflammatory artifacts. The modified Kudo classification (Kudo-IBD), taking into account 4 endoscopic predictors (pit heterogeneity, micro-vessel positivity, presence of fibrin cap, and endoscopic inflammatory activity), was shown to boast an improved accuracy compared to conventional endoscopy. However, it should be noted that the current recommendation for the use of Kudo-IBD is based on single-center results. Multicenter validation of this classification is warranted, though its results seem promising. The FACILE classification is another noteworthy recently developed classification. This multimodal classification is also based on VCE and incorporates 4 key characteristics predictive of dysplastic histology: non-polypoid morphology, irregular surface and vascular patterns, and the presence of any inflammation within the lesion. Preliminary results indicate promising potential for application in both expert and novice contexts.

While AI is rapidly advancing in gastrointestinal endoscopy, particularly through CADe and CADx models, its application in the context of IBD dysplasia surveillance remains in its infancy and is limited to a small number of studies and case reports. An important consideration in the development of AI algorithms is acknowledging the potential biases within the training dataset. Almost all developed CADe/CADx models have currently been trained on non-IBD associated lesions, which do not represent the diverse characteristics of IBD dysplasia. The development of a proprietary IBD-CADe system, which has been trained using IBD-related lesions, holds the potential to enhance dysplasia detection and characterization, guiding the targeted biopsy sampling thereby potentially reducing the need for random biopsies during surveillance colonoscopies. Addressing these challenges through focused research is crucial in realizing the full potential of AI in IBD dysplasia surveillance.

Ultra-high-definition endoscopy, such as (p)CLE and EC, is a promising tool in the field of IBD since it allows for real time in vivo histologic assessment of colonic lesions. Unfortunately, evidence supporting its role in IBD dysplasia surveillance is lacking.

Moreover, increased procedural time, learning curve, cost-effectiveness, the inability to assess all types of endoscopic lesions, and the uncertain incremental yield of EC/(p)CLE over conventional endoscopy are all hindrances in the routine clinical implementation of these technologies in IBD dysplasia surveillance. AI-assisted EC (EndoBRAIN) has the potential to overcome some of these inherent limitations, since it can help distinguish inflammation-related neo-vascularization from dysplasia-related neo-vascularization and can help in reducing the learning curve for EC.

Looking forward, the integration of advanced endoscopic techniques holds tremendous potential to further enhance dysplasia surveillance in IBD. Future research should focus on developing and validating proprietary AI models for IBD dysplasia characterization, since these technologies could redefine the landscape of dysplasia surveillance in IBD, offering clinicians powerful tools to improve patient outcomes and reduce the burden of colorectal cancer in this high-risk population.

CLINICS CARE POINTS

- When characterizing IBD-related lesions, consider the use of novel advanced classifications, such as Kudo-IBD or FACILE Frankfurt Advanced Chromoendoscopic IBD LEsions (FACILE); however, be aware of the need for further validation studies to establish their efficacy across different clinical settings (eg, active inflammation, suboptimal bowel preparation, mucosal scarring etc.).
- Ultra-High-definition endoscopy (ie, Confocal Laser Endomicroscopy and Endocytoscopy) shows a high potential for real-time in vivo histologic assessment of colonic lesions; however, be aware of their limitations such as increased procedural time and the learning curve associated with the use of these techniques.
- Recognize the potential of AI-assisted endoscopic technologies to distinguish between inflammation-related and dysplasia-related neo-vascularization, which can help reduce the learning curve and improve diagnostic accuracy.
- Be aware of the risks associated with the premature reliance on AI models trained on non-IBD-associated lesions, as they may not accurately represent the diverse characteristics of IBD dysplasia.

DISCLOSURE

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REFERENCES

1. Zhou Q, Shen ZF, Wu BS, et al. Risk of colorectal cancer in ulcerative colitis patients: a systematic review and meta-analysis. Gastroenterol Res Pract 2019;5363261.
2. Olén O, Erichsen R, Sachs MC, et al. Colorectal cancer in Crohn's disease: a Scandinavian population-based cohort study. Lancet Gastroenterol Hepatol 2020;5(5):475–84.
3. Abu-Freha N, Cohen B, Gordon M, et al. Colorectal cancer among inflammatory bowel disease patients: risk factors and prevalence compared to the general population. Front Med 2023;10. https://doi.org/10.3389/fmed.2023.1225616.

4. Gordon H, Biancone L, Fiorino G, et al. ECCO guidelines on inflammatory bowel disease and malignancies. J Crohns Colitis 2023;17(6):827–54.
5. Piovani D, Hassan C, Repici A, et al. Risk of cancer in inflammatory bowel diseases: umbrella review and reanalysis of meta-analyses. Gastroenterology 2022;163(3):671–84.
6. Shah SC, Itzkowitz SH. Colorectal cancer in inflammatory bowel disease: mechanisms and management. Gastroenterology 2022;162(3):715–30.e3.
7. Castaño-Milla C, Chaparro M, Gisbert JP. Systematic review with meta-analysis: the declining risk of colorectal cancer in ulcerative colitis. Aliment Pharmacol Ther 2014;39(7):645–59.
8. Wijnands AM, de Jong ME, Lutgens MWMD, et al. Prognostic factors for advanced colorectal neoplasia in inflammatory bowel disease: systematic review and meta-analysis. Gastroenterology 2021;160(5):1584–98.
9. 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(4):880–8.
10. 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. Available at: www.gutjnl.com.
11. 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(3):304–12.
12. Picot J, Rose M, Cooper K, et al. Virtual chromoendoscopy for the real-time assessment of colorectal polyps in vivo: a systematic review and economic evaluation. In: Health technology assessment (Winchester, England)21. NIHR Journals Library; 2017. p. 1–308.
13. 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(12):1155–79.
14. Rutter MD, Saunders BP, Wilkinson KH, et al. Thirty-year analysis of a colonoscopic surveillance program for neoplasia in ulcerative colitis. Gastroenterology 2006;130(4):1030–8.
15. Coelho-Prabhu N, Lewis JD. Update on endoscopic dysplasia surveillance in inflammatory bowel disease. Am J Gastroenterol 2023;118(10):1748–55.
16. Lamb CA, Kennedy NA, Raine T, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. Gut 2019;68:s1–106.
17. 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(3):1043–51.e4.
18. Fumery M, Singh S, Dulai PS, et al. Natural history of adult ulcerative colitis in population-based cohorts: a systematic review. Clin Gastroenterol Hepatol 2018;16(3):343–56.e3.
19. Freeman HJ. Colorectal cancer risk in Crohn's disease. World J Gastroenterol 2008;14(12):1810–1.
20. Duricova D, Pedersen N, Elkjaer M, et al. Overall and cause-specific mortality in Crohn's disease: A meta-analysis of population-based studies. Inflamm Bowel Dis 2010;16(2):347–53.
21. Rutter M, Saunders B, Wilkinson K, et al. Severity of inflammation is a risk factor for colorectal neoplasia in ulcerative colitis. Gastroenterology 2004;126(2):451–9.

22. 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(3):639–51.e28.
23. 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. Gastrointest Endosc 2017;86(6):1100–6.e1.
24. Iacucci M, McQuaid K, Gui XS, et al. A multimodal (FACILE) classification for optical diagnosis of inflammatory bowel disease associated neoplasia. Endoscopy 2019;51(2):133–41.
25. Megna B, Weiss J, Ley D, et al. Clear liquid diet before bowel preparation predicts successful chromoendoscopy in patients with inflammatory bowel disease. Gastrointest Endosc 2019;89(2):373–9.e2.
26. Dekker E, Houwen BBSL, Puig I, et al. Curriculum for optical diagnosis training in Europe: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. Endoscopy 2020;52(10):899–923.
27. Efthymiou M, Allen PB, Taylor ACF, et al. Chromoendoscopy versus narrow band imaging for colonic surveillance in inflammatory bowel disease. Inflamm Bowel Dis 2013;19(10):2132–8.
28. 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 longstanding inflammatory bowel disease: A prospective, randomized, crossover study. Gastrointest Endosc 2011;74(4):840–8.
29. Bisschops R, Bessissow T, Joseph JA, et al. Chromoendoscopy versus narrow band imaging in UC: A prospective randomised controlled trial. Gut 2018; 67(6):1087–94.
30. 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(2):225–34.
31. González-Bernardo O, Riestra S, Vivas S, et al. Chromoendoscopy with indigo carmine vs virtual chromoendoscopy (iSCAN 1) for neoplasia screening in patients with inflammatory bowel disease: a prospective randomized study. Inflamm Bowel Dis 2021;27(8):1256–62.
32. López-Serrano A, Suárez MJ, Besó P, et al. Virtual chromoendoscopy with iSCAN as an alternative method to dye-spray chromoendoscopy for dysplasia detection in long-standing colonic inflammatory bowel disease: a case–control study. Scand J Gastroenterol 2021;56(7):820–8.
33. Cassinotti A, Parravicini M, Chapman TP, et al. Endoscopic characterization of neoplastic and non-neoplastic lesions in inflammatory bowel disease: systematic review in the era of advanced endoscopic imaging. Therap Adv Gastroenterol 2023;16.
34. Kudo S ei, Tamura S, Nakajima T, et al. Diagnosis of colorectal tumorous lesions by magnifying endoscopy. Gastrointest Endosc 1996;44(1):8–14.
35. Cassinotti A, Buffoli F, Fociani P, et al. Virtual Chromoendoscopy with FICE for the Classification of Polypoid and Nonpolypoid Raised Lesions in Ulcerative Colitis. In: J Clin Gastroenterol53. Lippincott Williams and Wilkins; 2019. p. 269–76.
36. 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;08(10):E1414–22.
37. Cassinotti A, Duca P, Maconi G, et al. Accuracy of optical diagnosis with narrow band imaging in the surveillance of ulcerative colitis: a prospective study

comparing Kudo, Kudo-IBD and NICE classifications. Int J Colorectal Dis 2024;39(1).

38. Cassinotti A, Ardizzone S, Fociani P, et al. Differentiating neoplasic and non-neoplasic raised lesions (polyps and pseudopolyps) in long-standing ulcerative colitis: results from a prospective systematic study using virtual chromoendoscopy with i-SCAN and the Kudo classification. J Crohns Colitis 2016;10:S237. Available at: https://academic.oup.com/ecco-jcc/article/10/suppl_1/S237/2482032.
39. Dal Buono A, Gabbiadini R, Furfaro F, et al. Endoscopic surveillance in inflammatory bowel diseases: selecting a suitable technology. Front Med 2022;9. https://doi.org/10.3389/fmed.2022.855652.
40. 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(3):562–72.
41. Zammarchi I, Santacroce G, Iacucci M. Next-generation endoscopy in inflammatory bowel disease. Diagnostics 2023;13(15).
42. Pal P, Ramchandani M, Patel R, et al. Role of ultra-high definition endoscopy (endomicroscopy and endocytoscopy) and real-time histologic examination in inflammatory bowel disease: Scoping review. Dig Endosc 2024;36(3):274–89.
43. Atreya R, Neumann H, Neufert C, et al. In vivo imaging using fluorescent antibodies to tumor necrosis factor predicts therapeutic response in Crohn's disease. Nat Med 2014;20(3):313–8.
44. Yantiss RK, Das KM, Farraye FA, et al. Alterations in the immunohistochemical expression of das-1 and CG-3 in colonic mucosal biopsy specimens helps distinguish ulcerative colitis from Crohn Disease and from other forms of colitis. 2008. Available at: http://journals.lww.com/ajsp.
45. Kiesslich R, Goetz M, Lammersdorf K, et al. Chromoscopy-guided endomicroscopy increases the diagnostic yield of intraepithelial neoplasia in ulcerative colitis. Gastroenterology 2007;132(3):874–82.
46. Rispo A, Castiglione F, Staibano S, et al. Diagnostic accuracy of confocal laser endomicroscopy in diagnosing dysplasia in patients affected by long-standing ulcerative colitis. World J Gastrointest Endosc 2012;4(9):414.
47. Freire P, Figueiredo P, Cardoso R, et al. Surveillance in ulcerative colitis: Is chromoendoscopy-guided endomicroscopy always better than conventional colonoscopy? a randomized trial. Inflamm Bowel Dis 2014;20(11):2038–45.
48. Hlavaty T, Huorka M, Koller T, et al. Colorectal cancer screening in patients with ulcerative and crohn's colitis with use of colonoscopy, chromoendoscopy and confocal endomicroscopy. Eur J Gastroenterol Hepatol 2011;23(8):680–9.
49. Wanders LK, Kuiper T, Kiesslich R, et al. Limited applicability of chromoendoscopy-guided confocal laser endomicroscopy as daily-practice surveillance strategy in Crohn's disease. Gastrointest Endosc 2016;83(5):966–71.
50. Van Den Broek FJC, Van Es JA, Van Eeden S, et al. Pilot study of probe-based confocal laser endomicroscopy during colonoscopic surveillance of patients with longstanding ulcerative colitis. Endoscopy 2011;43(2):116–22.
51. Kudo SE, Wakamura K, Ikehara N, et al. Diagnosis of colorectal lesions with a novel endocytoscopic classification a pilot study. Endoscopy 2011;43(10):869–75.
52. Kudo S ei, Maeda Y, Ogata N, et al. Combined endocytoscopy with pit pattern diagnosis in ulcerative colitis-associated neoplasia: Pilot study. Dig Endosc 2022;34(1):133–43.

53. Misawa M, Kudo SE, Mori Y, et al. Characterization of colorectal lesions using a computer-aided diagnostic system for narrow-band imaging endocytoscopy. Gastroenterology 2016;150(7):1531–2.e3.
54. Mori Y, Kudo SE, Misawa M, et al. Real-time use of artificial intelligence in identification of diminutive polyps during colonoscopy a prospective study. Ann Intern Med 2018;169(6):357–66.
55. Kudo S-E, Misawa M, Mori Y, et al. Artificial intelligence-assisted system improves endoscopic identification of colorectal neoplasms. Clin Gastroenterol Hepatol 2020;18(8):1874–81.e2.
56. Fukunaga S, Kusaba Y, Ohuchi A, et al. Is artificial intelligence a superior diagnostician in ulcerative colitis? Endoscopy 2021;53(02):E75–6.
57. Bossuyt P, Nakase H, Vermeire S, et al. Automatic, computer-aided determination of endoscopic and histological inflammation in patients with mild to moderate ulcerative colitis based on red density. Gut 2020;69(10):1778–86.
58. Ribeiro T, Mascarenhas M, Afonso J, et al. Artificial intelligence and colon capsule endoscopy: Automatic detection of ulcers and erosions using a convolutional neural network. J Gastroenterol Hepatol 2022;37(12):2282–8.
59. Ruan G, Qi J, Cheng Y, et al. Development and validation of a deep neural network for accurate identification of endoscopic images from patients with ulcerative colitis and Crohn's disease. Front Med 2022;9.
60. Sutton RT, ZaiAne OR, Goebel R, et al. Artificial intelligence enabled automated diagnosis and grading of ulcerative colitis endoscopy images. Sci Rep 2022;12(1).
61. Pal P, Pooja K, Nabi Z, et al. Artificial intelligence in endoscopy related to inflammatory bowel disease: A systematic review. Indian J Gastroenterol 2024;43(1):172–87.
62. Guerrero Vinsard D, Fetzer JR, Agrawal U, et al. Development of an artificial intelligence tool for detecting colorectal lesions in inflammatory bowel disease. iGIE 2023;2(2):91–101.e6.
63. Yamamoto S, Kinugasa H, Hamada K, et al. The diagnostic ability to classify neoplasias occurring in inflammatory bowel disease by artificial intelligence and endoscopists: A pilot study. J Gastroenterol Hepatol 2022;37(8):1610–6.