



Role of image-enhanced endoscopy for the diagnosis of gastric intestinal metaplasia

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Gastric intestinal metaplasia (IM) is a key precursor lesion in gastric cancer progression, as described by the Correa model. Image-enhanced endoscopy (IEE) with magnifying endoscopy has significantly improved the visualization of the mucosal surfaces and microvascular structures, aiding in the accurate diagnosis of IM. While histological evaluation remains the gold standard, IEE might provide a practical and cost-effective alternative for the risk stratification of gastric IM.

Keywords: Endoscopy; *Helicobacter*; Metaplasia; Neoplasms

INTRODUCTION

Correa's theory is a multistep model of gastric carcinogenesis that describes the progressive changes that occur in the stomach lining. These changes start with chronic gastritis and progress to atrophic gastritis, gastric intestinal metaplasia (IM), dysplasia, and finally, gastric cancer. This has been widely accepted and has influenced the research on gastric cancer.¹⁻³

Based on previous studies' results, it is well known that gastric cancer can be predicted through histological and endoscopic evaluations of the IM.⁴⁻¹⁰ Histological evaluation can provide accurate and standardized information; however, since many biopsies are mandatory, convenience and cost-effectiveness

must be considered. Therefore, numerous studies have been conducted on the endoscopic evaluation of metaplastic gastritis; consequently, various image-enhanced endoscopy (IEE) techniques have been developed and investigated.¹¹

IEE aims to improve the visualization of the mucosal surface and microvascular structures, and consists of dye-based chromoendoscopy and electronic IEE.¹² IEE can overcome the limitations of conventional white light imaging (WLI) and aid in a more accurate diagnosis. In this review, the PubMed database was searched using the keywords "NBI, narrow band imaging," "LCI, linked color imaging," "BLI, blue light imaging," "i-scan," "IEE, image-enhanced endoscopy," "ME, magnifying endoscopy," "intestinal metaplasia," and "metaplastic gastritis" to identify relevant studies published until June 2025. Based on previous studies' results, the significance and diagnostic methods for gastric IM were reviewed, including the use of IEE for gastric IM diagnosis.

HISTOLOGICAL EVALUATION OF GASTRIC IM

Gastric IM is characterized by the replacement of the normal gastric mucosa with intestinal-type cells, including goblet, Paneth, and absorptive cells.^{13,14} Goblet cells can be identified

Received: August 6, 2025 **Revised:** October 28, 2025

Accepted: October 29, 2025

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histologically by their blue tinges to clear mucin vacuoles, which displace the nucleus to one side of the cell. Paneth cells are less common and are found in the deeper regions of the gastric gland. Absorptive cells, which are also present in the intestine, were observed.

IM is a precancerous change in stomach cells, typically diagnosed by histological evaluation. Pathology reports should include information specific to the location of the stomach (antrum, incisura, and corpus), the severity and extent of IM, the subtype of IM, and the presence or absence of *Helicobacter pylori* (*H. pylori*) organisms.¹³ IM is categorized as either complete (type I) or incomplete (types II and III), based on how closely they resemble intestinal cells.^{10,14} Complete metaplasia, which resembles small intestinal cells, is considered the initial stage. In contrast, incomplete metaplasia, which resembles large intestinal cells, is considered more advanced and associated with a higher risk of progression to dysplasia.

There are strong, consistent data that supports incomplete-type metaplasia is associated with greater cancer risk than complete-type metaplasia, especially in high-risk patients.^{1,3,9,10,15,16} A 2021 meta-analysis of 12 cohort studies comprising nearly 6,500 individuals reported a pooled risk ratio (RR) of 3.72 (95% confidence interval [CI], 1.42–9.72) and 5.16 (95% CI, 3.28–8.12) for dysplasia and gastric cancer, respectively, in patients with incomplete-type versus complete-type gastric IM.⁶ Another meta-analysis from 2021, which included a subgroup analysis according to geography, found that incomplete gastric IM was associated with a significantly higher risk of dysplasia/gastric cancer in Western European populations (pooled RR, 4.65; 95% CI, 2.30–9.92), but not in East Asian populations (pooled RR, 4.01; 95% CI, 0.82–19.61).¹⁷ Furthermore, a previous study suggests that the presence of complete-type gastric IM alone does not appear to increase the risk of gastric cancer compared to patients without IM (pooled odds ratio, 1.55; 95% CI, 0.91–2.65).¹⁸

IM in up to one-third and two-thirds of the glands can be regarded as mild or moderate, respectively, whereas greater than two-thirds are considered severe.^{19,20} Increased severity of IM is associated with a higher risk of neoplastic progression, regardless of the location and extent of the lesion.²¹

ENDOSCOPIC EVALUATION OF GASTRIC IM

ME and normal gastric mucosa

ME allows for detailed visualization of mucosal and vascular

structures in the stomach, enhancing the detection and characterization of lesions.²² ME can be used in conjunction with other IEE technologies, such as NBI, to enhance its effectiveness.²³ The appearance of the ME of normal gastric mucosa varies depending on the site. In the corpus, normal microvascular distribution can be seen as a subepithelial capillary network (SECN) consisting of numerous small honeycombs with collecting venules.²⁴ Microsurface structures are observed as dense pit patterns that are round to oval in shape. In contrast, in the antrum, microvessels are observed as spiral-shaped SECNs, and collecting venules are rarely observed because the antral mucosa is thicker than the corpus. The microsurface patterns were linear or mesh-like.

WLI and dye chromoendoscopy

Endoscopic evaluation of IM primarily assesses the extent of the lesion and confirms the presence or absence of neoplasia. On high-definition white light endoscopy, gastric IM appears as a tubule-villous mucosal pattern and are elevated with whitish patches. A recent study revealed that a dot pit pattern (regularly arranged, pinpoint small orifices of gastric glands) or regular vascular pattern (clearly visible, regularly arranged collecting venules with branches of uniform length and diameter resembling spider nevi) is highly unlikely to indicate metaplasia.²⁵ However, even with ME, endoscopic evaluation under white light is not highly accurate. In a previous study, detection of metaplasia through the pit pattern had a sensitivity and specificity of 98.0% and 31.3%, respectively, while detection of metaplasia through vessel evaluation had a sensitivity and specificity of 100% and 8.1%, respectively.²⁵ Additionally, methylene blue chromoendoscopy indicated IM with better accuracy than the pit pattern or vessel evaluation (71.7% vs. 60.5% and 49.6%, respectively).

Acetic acid (AA) chromoendoscopy is another good method for detecting and assessing the extent of gastric IM, and its effectiveness was further enhanced when AA was used in combination with electronic IEE.²⁶⁻²⁹ A previous study showed that AA-enhanced NBI (NBI; Olympus) significantly improved the detection sensitivity of gastric IM compared to conventional White light endoscopy (WLE) and standard NBI.²⁷

NBI

The characteristic findings of metaplasia under NBI are bluish-white areas with an irregular mucosal pattern, the presence of regular ridge/tubulovillous mucosa with regular vessels, and

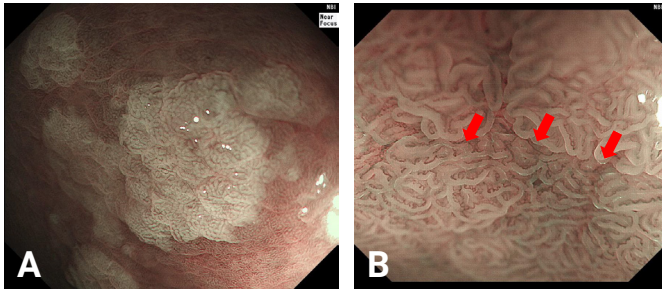


Fig. 1. Magnifying endoscopy with narrow-band imaging findings of white opaque substance (WOS) and light blue crest (LBC) in the gastric mucosa with intestinal metaplasia. (A) WOS visualized by the reflection and strong scattering of whole projected lights on the surface epithelium is observed sporadically throughout the image. WOS are microscopic droplets of lipids densely accumulated within the epithelium or subepithelial layer of the mucosa (near focus, GIF-HQ290; Olympus Medical Systems). (B) Fine light blue colored linear reflections are observed in the center of the image (LBC, red arrows) (magnifying endoscope, GIF290Z; Olympus Medical Systems). These signs are indicative of gastric intestinal metaplasia.

the presence of light blue crests (Fig. 1).^{24,30} Although NBI is the most widely studied electronic IEE, depending on the circumstances of each institution, flexible spectral imaging color enhancement (FICE; Fujifilm), blue laser imaging (BLI; Fujifilm), and i-Scan from Pentax may also be used.^{28,31,32}

The light blue crest is defined as a fine, blue-white line on the crest of the epithelial surface observed on magnified endoscopy with NBI.^{33,34} This is thought to be due to the reflection of short-wavelength visible light off the brush border of the metaplasia. A white, opaque substance is a white, grimy change on the mucosal surface that can be observed in IM, adenoma, and gastric cancer.³⁵ White opaque substances are thought to be lipid droplets that accumulate on the surface of gastric neoplasms of certain intestinal phenotypes. In a recent meta-analysis, NBI showed a pooled sensitivity of 80%, a specificity of 93%, and an area under the receiver operating characteristic curve (AUC) of 0.93 in detecting gastric IM. NBI with magnification performed better than NBI without magnification.³⁶

Persistent *H. pylori* infection can cause inflammation, atrophy, and IM of the gastric mucosa.² Inflammation of the fundic gland mucosa can result in an anomalous form of crypt opening.^{12,13} In such cases, capillaries may or may not be observed along the crypt opening. The vascular pattern of the atrophic mucosa is characterized by dilated and coiled subepithelial capillaries. Atrophic mucosa is often accompanied by IM, which exhibits a light blue crest.²²

LCI, texture, and color enhancement imaging

The signal processing in LCI (LCI; Fujifilm) is designed to increase color contrast by amplifying the intensity of reds and whites while maintaining the natural color of the real object.³⁷ The increased color contrast helps to detect lesions and inflammation, enabling more accurate delineation of lesions. LCI can be used to identify *H. pylori* infection status based on mucosal color and typical endoscopic findings. In patients with *H. pylori*, the mucosal color is red in WLI and crimson in LCI. In patients with a past infection and in uninfected patients, the mucosal color is orange on WLI and apricot on LCI.³⁸⁻⁴⁰ A meta-analysis showed that LCI is superior to WLI for diagnosing *H. pylori* infection.⁴¹ Under LCI, metaplasia appears purple, either deep or pale.^{39,42,43} A previous study found that the accuracy and sensitivity of LCI for diagnosing *H. pylori* infection were significantly higher than those of WLI. However, there were no significant differences in the accuracy, sensitivity, or specificity for diagnosing metaplastic gastritis between LCI and WLI.⁴⁴

Additionally, texture and color enhancement imaging, recently developed by Olympus, enhances color contrast, similar to LCI, to improve lesion visibility.¹² However, further research is needed to determine whether this technology can aid in the diagnosis or evaluation of gastric IM.

Optical enhancement and I-scan

Pentax et al. developed an i-scan to provide real-time image enhancement during endoscopic procedures. The subsequently developed optical enhancement (OE) can further improve high-contrast images generated by the i-scan. Whereas i-SCAN uses only white light for structural illumination, OE utilizes optical filters to generate a continuous wavelength spectrum by linking the peaks in the hemoglobin absorption spectrum.^{31,32} The use of i-scan alone may not significantly improve the diagnostic accuracy of gastric IM. In patients with IM or atrophic gastritis, targeted biopsies with i-scan were not significantly superior to either targeted or random biopsies with WLE.³¹ Conversely, ME-OE demonstrates excellent diagnostic accuracy and interobserver reliability for detecting gastric IM.^{29,32,45} A previous study has compared the diagnostic value of WLE, AA chromoendoscopy combined with ME (ME-AA), and ME-OE for the detection of gastric IM.⁴⁵ The overall diagnostic accuracy of ME-OE (91.7%) was higher than that of ME-AA (86.5%, $p=0.011$) and WLE (51.9%, $p<0.001$).

In conclusion, for the endoscopic evaluation of metaplasia, it is essential to use ME in conjunction with electronic IEE and/or

dye-based chromoendoscopy. Additional requirements include high-quality evaluation of the entire stomach, which involves adequate mucosal cleansing, sufficient endoscopy time, and trained endoscopists.¹³

CANCER RISK STRATIFICATION OF GASTRIC IM

Operative link for gastric IM

The (operative link for gastric IM) OLGIM, published in 2010, is a validated histological scoring system that considers the extent and severity of gastric IM and is strongly associated with the risk of progression.⁸ The OLGIM diagnosis requires at least five biopsies: one biopsy each from the lesser curvature (LC) and greater curvature (GC) sides of the antrum, one biopsy from the angle, and one biopsy each from the LC and GC sides of the body. In the OLGIM system, stages III and IV are high-risk factors for developing gastric cancer. A meta-analysis showed that the cumulative risk of gastric cancer among patients with stage III/IV OLGIM was 3.99.⁷

Kyoto classification of gastritis

The OLGIM helps predict gastric cancer risk; however, it has the disadvantage of requiring numerous biopsies. Therefore, in 2013, the Kyoto classification was developed to predict the risk of gastric cancer based on endoscopic findings without biopsy. The Kyoto classification defines 19 endoscopic findings of gastritis to classify the gastric mucosa into *H. pylori* uninfected, *H. pylori* infected, and post-eradication mucosa.⁴⁶ In addition, the Kyoto scoring system was used to predict the risk of gastric cancer.⁴ A high Kyoto classification score is believed to reflect a higher risk of current *H. pylori* infection and gastric cancer. A Kyoto classification score of 0 indicates the absence of *H. pylori* infection. A score of 2 or higher indicated a current *H. pylori* infection. A score of ≥ 4 suggests an increased risk of gastric cancer.⁴⁷

The most frequent endoscopic findings of *H. pylori* infection were atrophy (45%), red streak (22%), and absence of regular arrangement of collecting venules (59%), which had fair accuracy rates of 67%, 65%, and 73%, respectively.⁴⁸ Mucosal nodularity (89%) and swelling (77%) showed the highest diagnostic accuracy. However, this study showed that the mean accuracy rate of endoscopic diagnosis using WLI was only 67%, which was not sufficiently high.

Endoscopic grading of gastric IM

Recently, a new scoring system, the endoscopic grading of gastric IM (EGGIM), was developed. The EGGIM evaluates IM using endoscopic evaluation alone without biopsy. EGGIM requires evaluation of metaplasia in the above-mentioned five gastric areas, with a score of 1 for focal metaplasia and 2 for extensive metaplasia ($>30\%$ of the area) using NBI.⁵ For the presence of OLGIM 3 and 4, the AUC of EGGIM classification was 0.96. Thus, using EGGIM to assess gastric cancer risk can reduce the burden of requiring multiple biopsies while demonstrating a utility comparable to that of OLGIM.

Recently, artificial intelligence (AI)-related studies have been conducted in the field of IM; however, more evidence needs to be accumulated before this technology can be applied.⁴⁹⁻⁵¹ A recent study demonstrated the potential of applying AI tools in endoscopic image analyses by estimating EGGIM with high accuracy (balanced accuracy of 87%).⁴⁹

CONCLUSIONS

The use of high-definition ME with IEEs (or dye chromoendoscopy) is necessary for the proper endoscopic evaluation of gastric IM. EGGIM with NBI can be used to diagnose IM and determine the risk of gastric cancer without biopsy. LCI is a useful tool for diagnosing *H. pylori* infection; however, its usefulness for diagnosing metaplasia remains understudied.

Conflicts of Interest

The authors have no potential conflicts of interest.

Funding

None.

Author Contributions

Conceptualization: SPL; Data curation: SPL; Formal analysis: SPL; Investigation: SPL; Methodology: SPL; Project administration: SPL; Supervision: SPL; Validation: SPL; Visualization: all authors; Resources: all authors; Writing—original draft: all authors; Writing—review & editing: all authors.

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