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MINIREVIEWS

Clinical applicability of gastroscopy with narrow-band imaging for the diagnosis of *Helicobacter pylori* gastritis, precancerous gastric lesion, and neoplasia

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Abstract

Premalignant gastric lesions such as atrophic gastritis and intestinal metaplasia frequently occur in subjects with long-term *Helicobacter pylori* (*H. pylori*) infection. The regular arrangement of collecting venules (RAC) is seen in the normal gastric corpus, whereas mucosal swelling and redness without RAC are observed in *H. pylori*-infected mucosa. Despite successful *H. pylori* eradication, the presence of atrophic gastritis and/or gastric intestinal metaplasia (GIM) is a risk factor for gastric cancer. With the development of advanced imaging technologies, recent studies have reported the usefulness of narrow-band imaging (NBI) for endoscopic diagnosis of atrophic gastritis and GIM. Using NBI endoscopy with magnification (M-NBI), atrophic gastritis is presented as irregular coiled microvessels and loss of gastric pits. Typical M-NBI endoscopic findings of GIM are a light blue crest and a white opaque substance. Based on the microvascular patterns, fine network, core vascular, and unclear patterns are useful for predicting gastric dysplasia in polypoid lesions. For diagnosis of early gastric cancer (EGC), a systematic classification using M-NBI endoscopy has been proposed on the basis of the presence of a demarcation line and an irregular microvascular/microsurface pattern. Furthermore, M-NBI endoscopy has been found to be more accurate for determining the horizontal margin of EGC compared to conventional endoscopy. In this review, we present up-to-date results on the clinical usefulness of gastroscopy with NBI for the diagnosis of *H. pylori* gastritis, precancerous gastric lesion, and neoplasia.

Key words: Gastroscopy; Narrow-band imaging; Magnification; *Helicobacter pylori*; Atrophic gastritis; Intestinal metaplasia; Dysplasia; Cancer

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Core tip: Image-enhanced endoscopy techniques such as narrow-band imaging (NBI) improve the diagnosis of *Helicobacter pylori* infection, atrophic gastritis, and gastric intestinal metaplasia (GIM). When NBI is combined with magnifying endoscopy, typical endoscopic findings can clearly be observed. Thus, the extent and severity of GIM can be endoscopically evaluated by close mucosal observation. Based on the microvascular patterns, fine network, core vascular, and unclear patterns are useful for predicting gastric dysplasia in polypoid lesions. When the endoscopists find a small flat or depressed lesion, magnifying NBI endoscopy is helpful for differentiating between cancer and gastritis. The presence of a demarcation line and an irregular microvascular/microsurface pattern are highly suspicious for high grade dysplasia and cancer. For endoscopic treatment of early gastric cancer, the horizontal tumor margin can be assessed by magnifying NBI endoscopy.

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INTRODUCTION

Gastric cancer is the third most common cause of cancer-related mortality worldwide[1]. Long-term *Helicobacter pylori* (*H. pylori*) infection causes premalignant gastric conditions, such as atrophic gastritis and intestinal metaplasia[2]. In particular, gastric intestinal metaplasia (GIM) is a risk factor for gastric cancer development[3]. Although GIM is reportedly improved after *H. pylori* eradication, complete elimination of the gastric cancer risk cannot be guaranteed[4]. Thus, surveillance endoscopy is recommended in subjects with precancerous lesions at the time of eradication[5]. The diagnostic accuracy for precancerous lesions and gastric neoplasia of image-enhanced endoscopy has been increased by the advent of narrow-band imaging (NBI) endoscopy[6,7]. Before endoscopic submucosal dissection, NBI endoscopy can determine the margin of gastric dysplasia and cancer to promote complete removal[8]. Although pathologic diagnosis is the gold standard, accurate endoscopic prediction is important to minimize the number of biopsies and prevent post-biopsy bleeding. Herein, we present up-to-date results on the clinical usefulness of NBI endoscopy for the diagnosis of *H. pylori* gastritis, precancerous gastric lesion, and neoplasia. This review consists of the following: (1) *H. pylori* gastritis; (2) Atrophic gastritis and GIM; (3) Gastric dysplasia; and (4) Early gastric cancer (EGC).

PRINCIPLE OF NARROW-BAND IMAGING WITH MAGNIFICATION

In 2005, technological advances resulted in the advent of NBI. NBI is an innovative optical method that modifies the wavelengths and bandwidths of the light into narrow bands of 415 ± 30 nm and 540 ± 30 nm[9]. In this endoscopy system, which uses a red (R), green (G), and blue (B) sequential imaging system, the gastrointestinal mucosa is illuminated sequentially with R, G, and B light through a rotating RGB filter wheel[10]. When the endoscopist presses the button on the handle, a narrow-band filter is inserted between the lamp and the RGB filter. Red light (long wavelength) diffuses widely and deeply, whereas blue light (short wavelength) diffuses within a smaller range and less deeply. Because short-wavelength light strongly reflects from the epithelial surface, it is suitable for visualizing its morphology. Therefore, NBI improves upon the detailed visualization possible by magnifying endoscopy (Figure 1).

Magnifying endoscopy enables examination of the microanatomy of the gastric mucosa[11]. When a soft black cap is fixed to the tip of the endoscope, it is possible to maintain a distance of approximately 2 mm, at which up to 100-fold magnification is feasible. This system produces sharp images of microvascular architecture and

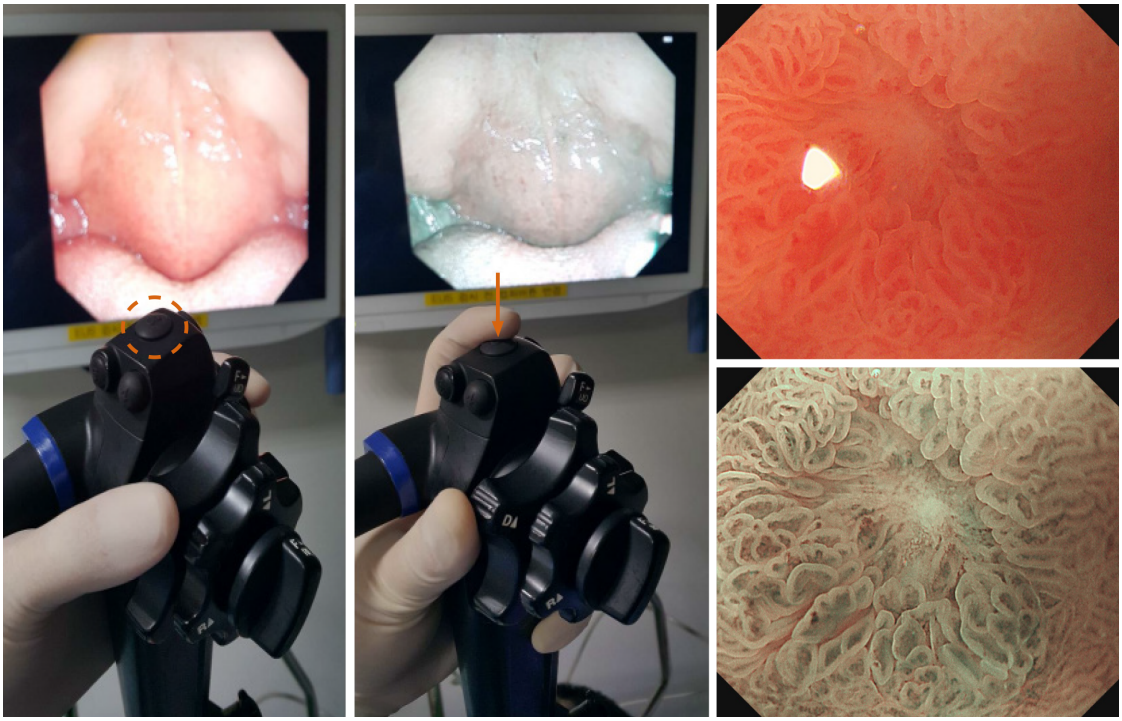

Figure 1 Narrow-band imaging system. When the button is pressed by the endoscopist, the endoscopy monitor changes from white-light imaging to narrow-band imaging (NBI) mode. Compared to the magnification mode without NBI (upper-right panel), NBI enables examination of the mucosal surface and microvessels around the erosion (lower-right panel).

microsurface structure. In the upper gastrointestinal tract, the line of sight may be disrupted by respiration movement and great vessel pulsation. To climb the learning curve of magnifying endoscopy, a proper training system under an experienced supervisor is required.

H. PYLORI GASTRITIS

Initially, the main tests for *H. pylori* infection were the rapid urease test and pathologic examination, both of which require a biopsy specimen[12]. The development of endoscopy techniques enabled detection in real time, earlier than possible using these biopsy-based tests. In 2005, a regular arrangement of collecting venules (RAC) was suggested as the normal pattern in gastric mucosa without *H. pylori* infection[13]. When the gastric corpus was examined by magnifying endoscopy, *H. pylori*-infected mucosa showed dilation of gastric pits and disappearance of RAC[14]. For predicting histological chronic gastritis, Tahara *et al*[15] observed the gastric corpus using magnifying NBI (M-NBI) endoscopy, which enabled visualization of the micromucosal pattern. The normal pattern was defined as a honeycomb-like subepithelial capillary network (SECN) and the presence of RAC (Figure 2A). The abnormal pattern of *H. pylori*-induced gastritis is typically polygonal swollen mucosa with enlarged crypt openings (Figure 2B). The sensitivities and specificities of magnifying endoscopy for *H. pylori* infection are 93.8% to 100% and 82.2% to 96.2%, respectively[13-15].

Recently, endoscopists have attempted to diagnose *H. pylori* infection by white-light imaging (WLI) or non-magnifying endoscopy with other image-enhanced techniques[16,17]. The typical endoscopic findings of *H. pylori*-induced gastritis are mucosal swelling and redness with disappearance of RAC at the gastric corpus[18]. Although M-NBI has good diagnostic accuracy, non-magnifying endoscopy is also useful for detecting *H. pylori* gastritis by close observation of the greater curvature side of the corpus[19]. Furthermore, the rapid urease test from the corpus mucosa had a faster positive reaction, compared to the antrum[20]. However, an endoscopic classification based on WLI has not yet been established. Furthermore, a comparison study between M-NBI and WLI endoscopy for *H. pylori* diagnosis is needed.

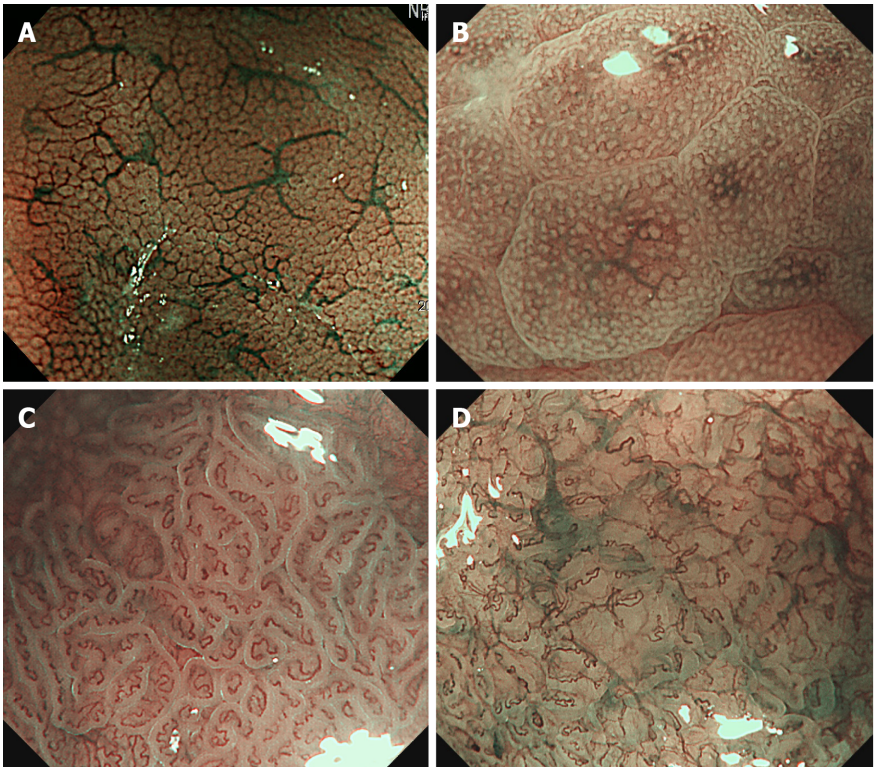

Figure 2 Magnifying narrow-band imaging endoscopy images of *Helicobacter pylori*-positive corpus mucosa and atrophic gastritis. A: Normal mucosal pattern showing a honeycomb-like subepithelial capillary network and regular arrangement of collecting venules; B: *Helicobacter pylori*-infected status presenting as polygonal swollen mucosa with dilated round crypt opening; C: Ridged surface structures encasing dilated coiled subepithelial capillaries indicate the presence of atrophic gastritis; D: Severe mucosal atrophy characterized by irregular coiled microvessels, loss of gastric pits, and greenish submucosal vessels.

ATROPHIC GASTRITIS

In the *H. pylori*-infected stomach, chronic active inflammation becomes persistent, leading to mucosal atrophy with destruction of gastric glands. In Japan, atrophic gastritis is often evaluated according to the endoscopic Kimura-Takemoto classification[21]. This classification has showed the good agreement with the histological assessment of atrophic gastritis[22,23]. Because of high risk for gastric cancer development, surveillance endoscopy is required in subjects with severe atrophic gastritis[24]. Compared to conventional WLI endoscopy, M-NBI enables a reliable diagnosis for the degree of atrophic gastritis.

Before the NBI system was introduced, Yagi *et al*[13] classified magnified endoscopic findings of the *H. pylori*-infected corpus mucosa into three types (Z-1 to Z-3). Of these, type Z-3 mucosal pattern corresponded to histological features of marked atrophy of the gastric glands. Recent studies have reported the typical endoscopic findings using M-NBI in diagnosing atrophic gastritis[25,26]. Ridged surface structures encasing dilated coiled subepithelial capillaries indicates the presence of atrophic gastritis (Figure 2C). With progression to severe mucosal atrophy, irregular coiled microvessels and loss of gastric pits are observed by M-NBI endoscopy (Figure 2D). The sensitivities and specificities of M-NBI endoscopy for atrophic gastritis are 50.0% to 90.0% and 96.0% to 96.3%, respectively[14,15].

GASTRIC INTESTINAL METAPLASIA

All subjects with intestinal metaplasia are at risk for gastric cancer development. Whether the gastric cancer risk is low or high depends on the extent and severity of intestinal metaplasia[27]. Since the advent of endoscopy, pathologic examination by forceps biopsy has been the gold standard for diagnosis of GIM. In the updated Sydney System, multiple mucosal biopsies from the gastric corpus and antrum are required to obtain the specimens[28]. The diagnostic criteria of the operative link for gastritis assessment (OLGA) and operative link for gastric intestinal metaplasia assessment (OLGIM) enable more reliable risk stratification of gastric cancer and

identification of patients at high risk who need endoscopic surveillance[29,30]. However, OLGA and OLGIM staging are based on pathologic analyses of gastric biopsies from five sites. In clinical practice, elderly patients taking antiplatelets or anticoagulants are at risk for post-biopsy bleeding. Furthermore, biopsy-based methods can considerably increase the medical costs and procedure time.

Based on WLI, the presence of light gray granular patches is the only endoscopic finding of GIM[31]. However, endoscopic diagnosis using only WLI is limited by its low sensitivity. Several investigators have proposed NBI endoscopic criteria for diagnosis of GIM (Table 1). In 2006, Uedo *et al*[32] suggested a light blue crest (LBC) as a new diagnostic criterion for GIM. In M-NBI endoscopy, LBC was observed as a fine, blue line on the crests of the epithelial surface (Figure 3). The presence of LBC was correlated with histological GIM (sensitivity 89% and specificity 93%). Savarino *et al*[33] reported that LBC was a good indicator of GIM (sensitivity 80%, specificity 96%, and accuracy 93%). For diagnosing GIM, An *et al*[34] suggested the marginal turbid band (MTB), which was defined as an enclosed, white turbid band on the epithelial surface. The presence of both MTB and LBC is more frequent in moderate to severe GIM. The presence of MTB without LBC is considered indicative of early-stage GIM. LBC may be present in subjects who progress to severe GIM. In Japan, Kanemitsu *et al*[35] reported that a white opaque substance (WOS) was a marker for M-NBI diagnosis of GIM. The sensitivity of LBC for histological GIM was 62.5%. When the presence of WOS was added to the criteria, the sensitivity increased to 87.5%. The specificity and accuracy of WOS and/or LBC were 93.8% and 90.0%, respectively. Saka *et al*[36] performed M-NBI endoscopic staging of gastritis using the diagnostic criteria of a tubular/granular mucosal pattern plus LBC or WOS. The accuracy for assessing OLGA and OLGIM was 69.1% for the antrum and 72.7% for the corpus. The degree of gastritis was classified as low or high risk by summing the scores of the corpus and antrum. The concordance of M-NBI endoscopy with histologic severity for differentiating the low- and high-risk groups was 89.1%.

In 2012, Pimentel-Nunes *et al*[37] performed a validation study for endoscopic classification of premalignant gastric lesions and dysplasia. Using NBI endoscopy without magnification, they defined a regular tubulovillous or ridge glandular pattern as intestinal metaplasia. This mucosal pattern showed 90% sensitivity, 81% specificity, and 84% accuracy for diagnosing GIM. They used a web-based video system to address the learning curve of this classification by endoscopists[38]. The sensitivity and specificity for GIM reached 73% and 81% by the trainees, respectively. An NBI classification seemed to be easily learned for the identification of precancerous gastric lesions. A multicenter prospective study evaluated endoscopic grading of GIM using the same NBI classification[39]. Five different areas (each of the lesser and greater curvature of the corpus and antrum, and the gastric angle) were closely observed by NBI endoscopy. The endoscopic grades of GIM were evaluated on a three-point scale [no = 0, focal (≤ 30%) = 1, and extensive (> 30%) = 2] according to the extent of metaplastic mucosa. Compared to WLI, NBI had a higher diagnostic accuracy for GIM (83% *vs* 94%). NBI increased the sensitivity for GIM from 53% to 87%. The endoscopic grading was concordant with an extensive degree of histological GIM (OLGIM III/IV). If the cutoff value was > 4 (total score = 5–10), the sensitivity and specificity for OLGIM III/IV were 94.2% and 95.2%, respectively. The area under the receiver operating characteristic curve was 0.98. Esposito *et al*[40] suggested that NBI endoscopy for diagnosing GIM is useful for evaluating the risk for OLGIM without performing mucosal biopsy. By contrast, another study reported that the diagnostic yield for GIM using NBI endoscopy was 53% to 65%[41]. NBI-targeted biopsy is still recommended for detection of GIM. A further largescale study is required to standardize the diagnosis of GIM using NBI endoscopy.

GASTRIC DYSPLASIA

Gastric dysplasia is the precursor lesion of gastric adenocarcinoma, particularly of the intestinal type[42]. The World Health Organization (WHO) defines dysplasia in the gastrointestinal tract as the presence of histologically unequivocal neoplastic epithelium without evidence of tissue invasion[43]. According to the revised Vienne classification, low and high grade dysplasia (category 3 and 4.1) is classified as non-invasive gastric neoplasia[44]. Endoscopic resection is recommended for the management of gastric dysplasia due to the possibility of malignant transformation[45]. Indefinite pathology for neoplasia on forceps biopsy specimens (category 2 of the revised Vienne classification) is often observed in clinical practice. Although

Table 1 Endoscopic criteria using narrow-band imaging for diagnosis of gastric intestinal metaplasia

Ref.	Year	Endoscopy mode	Diagnostic criteria	Concordance with histopathology		
				Sensitivity	Specificity	Accuracy
Pimentel-Nunes *et al*[37]	2012	NBI	Regular tubulovillous/ridge glandular pattern	90%	81%	84%
Saka *et al*[36]	2015	M-NBI	Tubular/granular mucosa with LBC or WOS	N/A	N/A	69.1-72.7%[1]
Pimentel-Nunes *et al*[39]	2016	NBI	Regular tubulovillous/ridge glandular pattern	87%	97%	94%
Buxbaum *et al*[41]	2017	NBI	Tubulovillous/ridge pattern and/or LBC	N/A	N/A	53-65%[2]
Esposito *et al*[40]	2019	NBI	Regular tubulovillous/ridge glandular pattern	89.4%	94.6%	N/A
An *et al*[34]	2012	M-NBI	MTB and/or LBC	72.1-100%[3]	66.0-96.0%[3]	81.7-84.9%[3]
Savarino *et al*[33]	2013	M-NBI	LBC	80%	96%	93%
Kanemitsu *et al*[35]	2017	M-NBI	WOS and/or LBC	87.5%	93.8%	90.0%

[1]Concordance rate between the M-NBI and histopathology was 69.1% for the antrum and 72.7% for the corpus.
[2]Diagnostic yield per-patient and per-site was 65% and 53%, respectively.
[3]MTB and LBC had sensitivities, specificities, and accuracy of 100/72.1%, 66.0/96.0%, and 81.7/84.9%, respectively. NBI: Narrow-band imaging; M-NBI: Magnifying narrow-band imaging; LBC: Light blue crest; WOS: White opaque substance; MTB: Marginal turbid band; N/A: Not applicable.

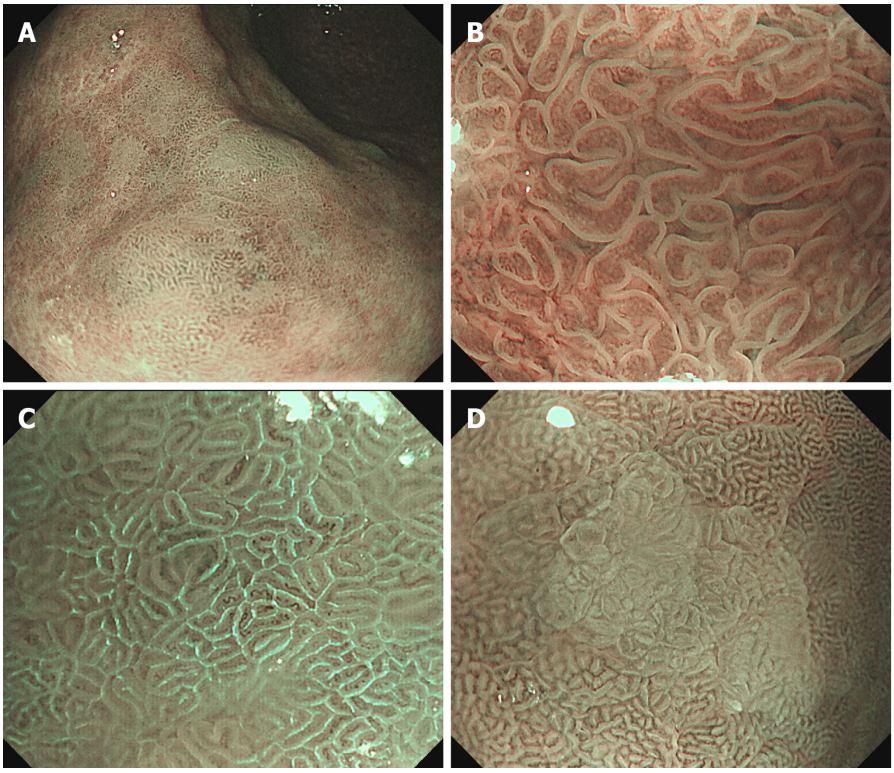

Figure 3 Narrow-band imaging endoscopy images of intestinal metaplastic mucosa. A: Gastric mucosa covered with multiple whitish green-colored patches; B: Thick borders enclosing a tubulovillous mucosal pattern, the so-called marginal turbid band (MTB); C: Thin fluorescent lines along the MTB, the so-called light blue crest; D: White opaque substance obscuring the mucosa surface.

endoscopic biopsy is essential before planning an endoscopic resection, there are reportedly histological discrepancies between forceps biopsy and post-resection specimen[46]. In a study by Lee *et al*[47], up to 64.5% of gastric lesions with indefinite pathology were upgraded to dysplasia and cancer after endoscopic submucosal dissection (ESD). Endoscopic biopsy may not be representative of the entire lesion due to its superficiality and sampling errors[48]. Repeated biopsy can make the subsequent

endoscopic treatment to be difficult due to submucosal fibrosis. Therefore, advanced endoscopic imaging such as M-NBI is required for the management of gastric dysplasia.

Using M-NBI endoscopy, Omori *et al*[49] suggested the characteristics of fine mucosal structures and microvascular pattern for diagnosing the gastric polypoid lesions. Most reliable microvascular patterns were honeycomb for fundic gland polyp (sensitivity 94.7%, specificity 97.4%) and dense vascular patterns for hyperplastic polyp (sensitivity 93.6%, specificity 91.6%). For predicting gastric neoplasia, fine network, core vascular, and unclear patterns showed the high specificity of 97%, 100%, and 100%, respectively (Figure 4). Hwang *et al*[50] reported the association between the M-NBI findings and upgraded histology in biopsy-proven low grade dysplasia. Positive M-NBI findings were defined as the irregularity of microvascular and/or microsurface patterns within the lesion (Figure 5). In cases with positive M-NBI findings, 76.6% (n = 59/77) was diagnosed as high grade dysplasia and cancer in post-resection pathology. If either an irregular microvascular or microsurface pattern is present, the gastric lesion can be diagnosed as high grade dysplasia or EGC[51]. In addition, M-NBI endoscopy is useful for determining the horizontal margin of gastric dysplasia before ESD (Figure 6).

EARLY GASTRIC CANCER

Differential diagnosis between focal gastritis and small depressed cancer

During endoscopy, EGCs are recognized based on a color or morphological change. Particularly in small (≤ 10 mm) gastric cancer, pathologic examination may be misdiagnosed due to targeted biopsy failure. If the opportunity for treatment by endoscopic resection is missed, false negativity based on the pathologic result alone is of great concern. Because conventional WLI endoscopy cannot be used to examine the gastric micromucosal pattern in detail, its utility for real-time endoscopic diagnosis is limited. To overcome this, the diagnostic efficacy of magnifying endoscopy has been investigated (Table 2).

In 2007, Yao *et al*[52] reported that cancerous lesions can be diagnosed by close observation using magnifying endoscopy. They defined the characteristics of EGC as a demarcation line (DL) between the lesion and the background mucosa, and an irregular microvascular pattern within the lesion. When these criteria were used, the sensitivity, specificity, and accuracy for distinguishing cancerous from benign lesions were 92.9%, 99.3%, and 98.7%, respectively. Ezoe *et al*[53] performed a prospective comparative study of magnifying NBI and magnifying WLI for diagnosing cancer in small depressed lesions. The NBI mode enabled the gastric micromucosal patterns around the lesion to be more clearly visualized, increasing the diagnostic performance (sensitivity of 70.0% *vs* 33.3%, specificity of 88.8% *vs* 66.6%, and accuracy of 78.9% *vs* 43.8%). Yamada *et al*[54] compared WLI alone and M-NBI after WLI for the diagnosis of small, depressed EGC. When WLI endoscopy alone was performed according to criteria including irregular margin and spiny depressed area, the sensitivity was 40%, specificity was 68%, and accuracy was 65%. Remarkably, M-NBI after WLI showed improved sensitivity of 95%, specificity of 97%, and accuracy of 97%.

Systematic classification using M-NBI endoscopy based on microvascular and microsurface pattern (the VS classification) has been proposed[55]. When a suspicious mucosal lesion with color or morphological change is detected, the first step is to identify the presence of DL, which separates the lesion from the background mucosa. A lesion without DL is unlikely to be cancer. If a DL is seen, the diagnosis of gastric cancer can be determined by the presence of an irregular microvascular and/or microsurface pattern within the DL (Figure 7). In a prospective multicenter study, the sensitivity, specificity, and accuracy of M-NBI for diagnosis of EGC were 85.7%, 99.4%, and 98.1%, respectively[56]. However, there were false-negative cases of signet ring cell carcinoma despite the diagnosis being performed by well-trained endoscopists. Pale-colored lesions suspicious of undifferentiated-type carcinoma are indications not for M-NBI endoscopy but rather for pathologic study by targeted biopsy. Fugiwara *et al*[57] evaluated M-NBI diagnosis of minute gastric cancer (≤ 5 mm) compared to chromoendoscopy using indigo carmine. The sensitivity and diagnostic accuracy were significantly higher for M-NBI endoscopy than chromoendoscopy (78.0% *vs* 43.7% and 88.3% *vs* 69.9%, respectively).

Kato *et al*[58] suggested a diagnostic triad for gastric cancer by M-NBI endoscopy: Disappearance of fine mucosal structure, microvascular dilation, and heterogeneous shape. The sensitivity and specificity were significantly higher than those of

Table 2 Diagnostic performance of narrow-band imaging with magnification for early gastric cancer

Ref.	Year	Endoscopic criteria of NBI with magnification	NBI with magnification (*vs* white light imaging)		
			Sensitivity	Specificity	Accuracy
Yao *et al*[52]	2007	Irregular microvascular pattern	92.9%	99.3%	98.7%
Ezoe *et al*[53]	2010	Demarcation line	70.0% (33.3%[1])	88.8% (66.6%[1])	78.9% (43.8%[1])
		Irregular microvascular pattern			
Kato *et al*[58]	2010	Disappearance of fine mucosal structure	92.9% (42.9%)	94.7% (61.0%)	N/A
		Microvascular dilation			
		Microvascular heterogeneity in shape			
Yamada *et al*[54]	2014	Demarcation line	95% (40%[2])	97% (68%[2])	97% (65%[2])
		Irregular microvascular pattern			
Yao *et al*[56]	2014	VS classification	85.7%	99.4%	98.1%
Fugiwara *et al*[57]	2015	VS classification	78.0% (43.7%[3])	92.9% (81.6%[3])	88.3% (69.9%[3])
Kanesaka *et al*[59]	2015	Microvascular dilation	25%	90%	83%
		Microvascular tortuosity	55%	24%	28%
		Difference in caliber	13%	99%	89%
		Variation in shape	70%	95%	92%

[1]Diagnostic sensitivity, specificity, and accuracy using white-light endoscopy with magnification.
[2]Endoscopic criteria of white-light endoscopy for gastric cancer were an irregular margin and a spiny depressed area.
[3]Diagnostic sensitivity, specificity, and accuracy using chromoendoscopy with indigo carmine. NBI: Narrow-band imaging; VS: Vessel plus surface; N/A: Not applicable.

conventional WLI endoscopy (92.9% *vs* 42.9% and 94.7% *vs* 61.0%, respectively). Kanesaka *et al*[59] categorized the microvascular patterns of small depressed lesions as microvascular dilation, microvascular tortuosity, difference in caliber, and variation in shape. Among these microvascular findings by M-NBI endoscopy, variation in shape was the most significant feature, with a diagnostic accuracy of 92%.

Determination of the horizontal extent of early gastric cancer before endoscopic submucosal dissection

ESD is curative in selected patients with EGC[60]. For a successful outcome of ESD, the tumor margin should be clearly examined. In M-NBI endoscopy, EGC margin delineation can be achieved by close-up observation of DL (Table 3). In 2010, Kiyotoki *et al*[61] evaluated the usefulness of M-NBI endoscopy for determining the gastric tumor margin compared to conventional chromoendoscopy using indigo carmine. Before ESD, marking dots were made at the tumor margin using M-NBI or chromoendoscopy. If the distance was less than 1 mm between the endoscopic marking dot and pathologically confirmed margin, the diagnosis was defined to be accurate. The diagnostic accuracy was significantly higher for M-NBI endoscopy than chromoendoscopy (97.4% *vs* 77.8%, $P = 0.009$). In another comparison study, there was a significant difference in delineating the margin of EGC between M-NBI endoscopy and chromoendoscopy (89.4% *vs* 75.9%, $P = 0.007$)[62]. Similarly, several studies have demonstrated that M-NBI endoscopy improves the determination of horizontal extent before ESD in patients with an unclear margin of EGC[63,64]. Horii *et al*[65] showed that diagnostic accuracy using M-NBI was 96.7% when the successful demarcation of EGC was evaluated on the basis of the biopsy-negative rate outside the tumor. Complete resection of EGC with a tumor-negative horizontal margin was achieved in 97.9% ($n = 323/330$). However, Nagahama *et al*[66] reported that the diagnostic accuracy for EGC margin delineation of M-NBI endoscopy was not superior to that of chromoendoscopy using indigo carmine. Indeed, M-NBI endoscopy does not need a dye solution and so is less time consuming.

Table 3 Determination of the horizontal extent of early gastric cancer by magnifying narrow-band imaging

Ref.	Study design	Lesion (*n*)	Pathology	Diagnostic accuracy	*P* value
Kiyotoki *et al*[61]	Comparative study between CE and M-NBI Marking dots were placed on the tumor margins	EGC (70), adenoma (13)	ESD	77.8% *vs* 97.4%	0.009
Nagahama *et al*[63]	M-NBI for unclear margins by CE	EGC (350)	ESD	81.1% → 94.8%	< 0.001
Uchita *et al*[64]	Combination of CE and M-NBI	EGC (161)	ESD	72.7% → 98.1%	< 0.001
Asada-Hirayama *et al*[62]	Comparative study between CE and M-NBI Oral and anal tumor margins of the same lesion	EGC (109)	ESD	75.9% *vs* 89.4%	0.007
Nagahama *et al*[66]	Comparative study between CE and M-NBI Biopsies outside and inside the tumor margins	EGC (343)	Biopsy	85.7% *vs* 88.0%	0.63
Horii *et al*[65]	Non-comparative study using M-NBI only	EGC (330)	Biopsy, ESD	96.7%-97.9%	N/A

CE: Chromoendoscopy; M-NBI: Magnifying narrow-band imaging; EGC: Early gastric cancer; ESD: Endoscopic submucosal dissection; N/A: Not applicable.

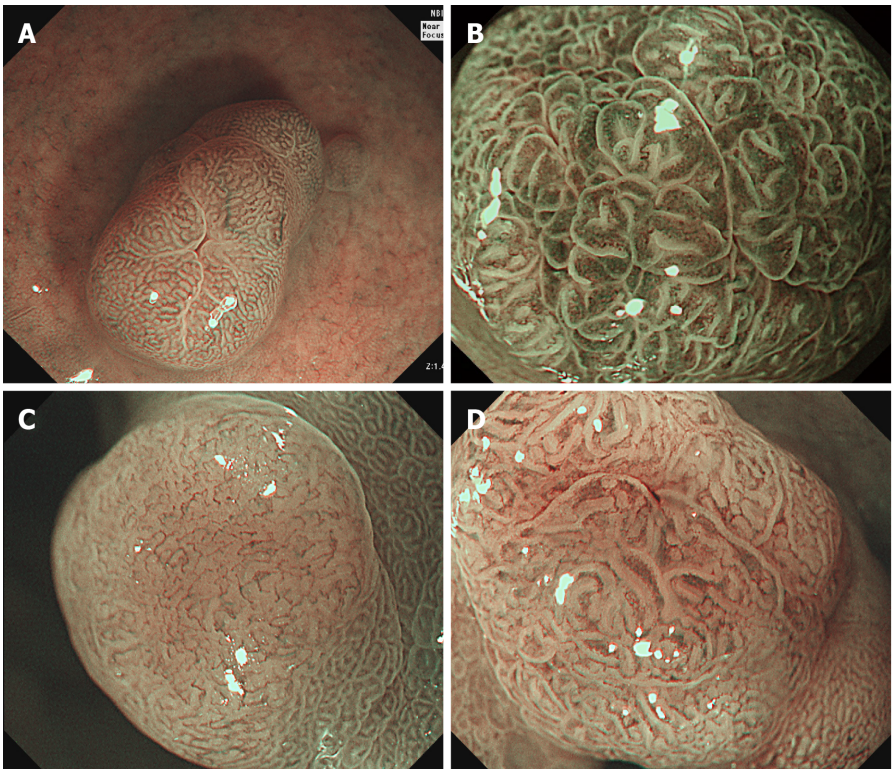

Figure 4 Magnifying narrow-band imaging findings of microvascular patterns for diagnosing the gastric polypoid lesions. A: Honeycomb-like pattern (fundic gland polyp); B: Dense vascular pattern (hyperplastic polyp); C: Fine network within a light brown area (low grade dysplasia); D: Core vascular pattern (low grade dysplasia).

CONCLUSION

In an era of high imaging quality in medical devices, magnifying endoscopy and NBI have enabled *H. pylori* diagnosis, endoscopic grading of GIM, and detailed characterization of small gastric cancer. Previously, the pathological report was the absolute authority for diagnosis of gastrointestinal tract diseases. Henceforth, image-enhanced endoscopy can make a big step to optical biopsy, which is a real-time diagnosis during gastrointestinal endoscopy. Furthermore, confocal laser endomicroscopy and endocytoscopy may become available in the future[67]. If endoscopists are well-trained in advanced endoscopic imaging, they may evolve into endo-pathologists[68].

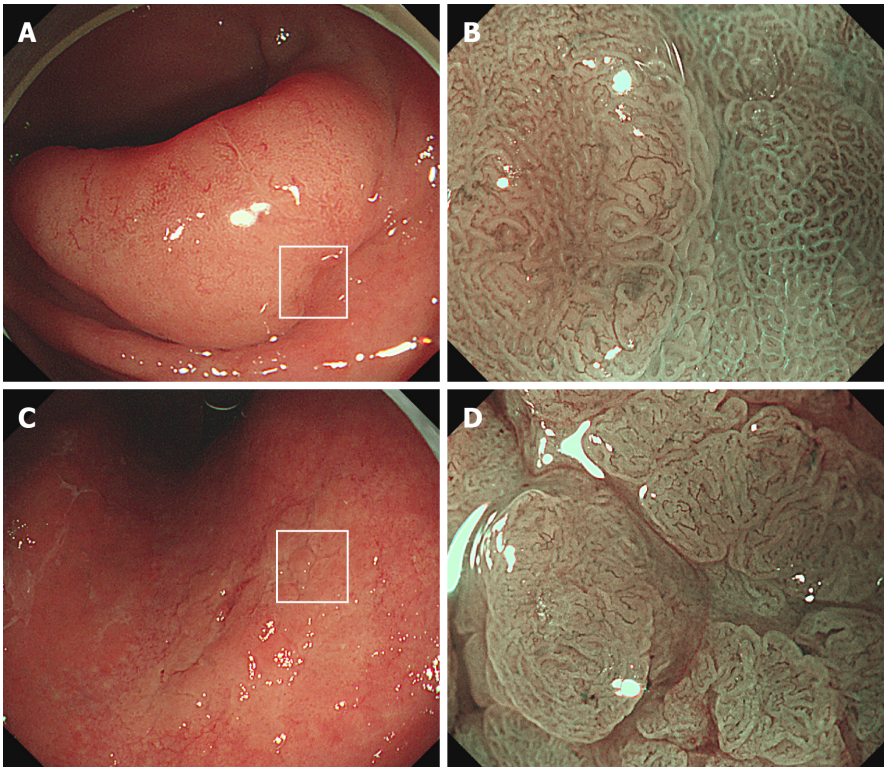

Figure 5 White-light endoscopy and magnifying narrow-band imaging images of high grade dysplasia. A: An elevated lesion (40 mm × 30 mm) at the gastric antrum; B: Brownish area showing an irregular mucosal surface and a microvascular pattern (left side), indicating a high grade dysplasia. The demarcation line is evident between the dysplasia and background mucosa with intestinal metaplasia (also see white box in A); C: A slightly elevated lesion (35 mm × 20 mm) at the lesser curvature of the gastric corpus; D: The microvessels within irregular, nodular lesion show tortuosity and variation in shape. This magnifying narrow-band imaging endoscopic finding indicates high grade dysplasia (also see white box in C).

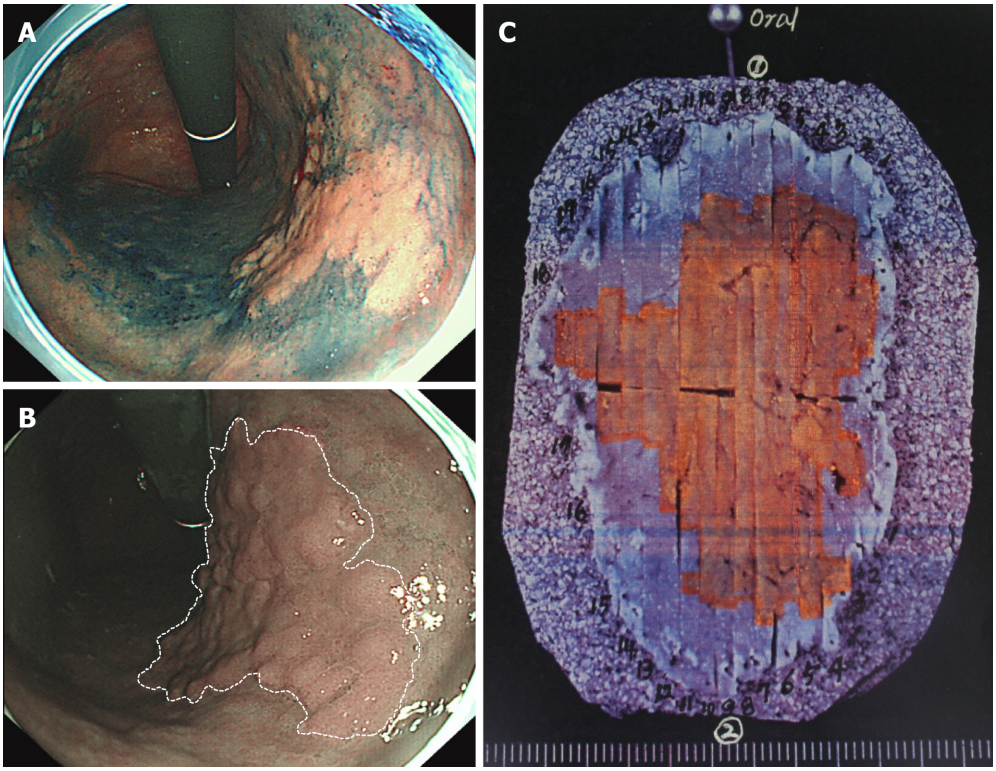

Figure 6 Narrow-band imaging endoscopy for determining the horizontal margin of gastric dysplasia before endoscopic submucosal dissection. A: Conventional chromoendoscopy using indigo carmine is useful for determining the horizontal margin of gastric neoplasia. However, this procedure requires a dye solution and is time-consuming; B: When the endoscopist presses the button, narrow-band imaging (NBI) endoscopy can be easily performed as a virtual chromoendoscopy. The tumor margin is evident between the large brownish lesion and greenish background mucosa (dotted white line); C: An *en bloc*-resected specimen by endoscopic submucosal dissection. The orange-colored area indicates a tubulovillous adenoma of 46 mm × 36 mm size, corresponding to the tumor extent determined by NBI endoscopy.

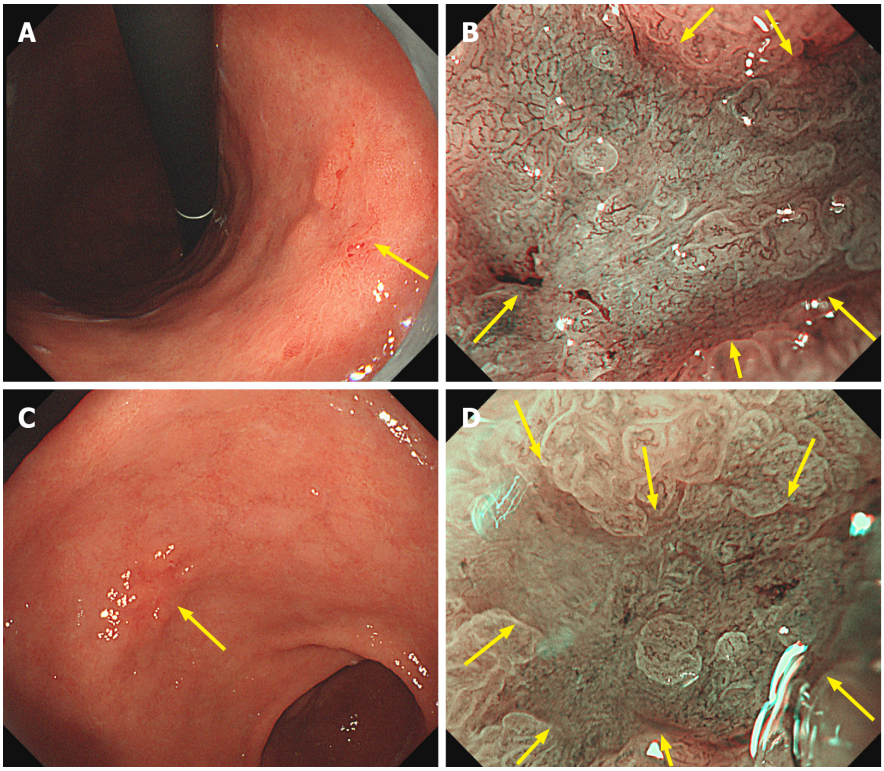

Figure 7 Magnifying narrow-band imaging endoscopic findings of early gastric cancers. A: Conventional white-light endoscopy shows a slightly elevated and depressed lesion at the gastric corpus; B: Magnifying narrow-band imaging (NBI) endoscopy demonstrates an irregular microvascular and microsurface pattern with a demarcation line (yellow arrows); C: Conventional white-light endoscopy shows a reddish depressed lesion at the gastric antrum; D: By magnifying NBI endoscopy, an irregular microsurface pattern is identified within the demarcation line (yellow arrows).

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