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ORIGINAL ARTICLE

Observational Study

Standard *vs* magnifying narrow-band imaging endoscopy for diagnosis of *Helicobacter pylori* infection and gastric precancerous conditions

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Abstract

BACKGROUND

Advances in endoscopic imaging enable the identification of patients at high risk of gastric cancer. However, there are no comparative data on the utility of standard and magnifying narrow-band imaging (M-NBI) endoscopy for diagnosing *Helicobacter pylori* (*H. pylori*) infection, gastric atrophy, and intestinal metaplasia.

AIM

To compare the diagnostic performance of standard and M-NBI endoscopy for *H. pylori* gastritis and precancerous conditions.

METHODS

In 254 patients, standard endoscopy findings were classified into mosaic-like appearance (type A), diffuse homogenous redness (type B), and irregular redness with groove (type C). Gastric mucosal patterns visualized by M-NBI were classified as regular round pits with polygonal sulci (type Z-1), more dilated and linear pits without sulci (type Z-2), and loss of gastric pits with coiled vessels (type Z-3).

RESULTS

The diagnostic accuracy of standard and M-NBI endoscopy for *H. pylori* gastritis was 93.3% and 96.1%, respectively. Regarding gastric precancerous conditions,

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the accuracy of standard and M-NBI endoscopy was 72.0% *vs* 72.6% for moderate to severe atrophy, and 61.7% *vs*. 61.1% for intestinal metaplasia in the corpus, respectively. Compared to type A and Z-1, types B+C and Z-2+Z-3 were significantly associated with moderate to severe atrophy [odds ratio (OR) = 5.56 and 8.67] and serum pepsinogen I/II ratio of ≤ 3 (OR = 4.48 and 5.69).

CONCLUSION
Close observation of the gastric mucosa by standard and M-NBI endoscopy is useful for the diagnosis of *H. pylori* gastritis and precancerous conditions.

Key Words: Endoscopy; Magnifying narrow-band imaging; *Helicobacter pylori*; Gastric atrophy; Intestinal metaplasia; Pepsinogen

Core Tip: In Correa's model of gastric carcinogenesis, *Helicobacter pylori* infection, gastric atrophy and intestinal metaplasia are linked to gastric cancer development. The low level of serum pepsinogens was known to be highly associated with extensive atrophic gastritis. High-resolution and magnifying narrow-band imaging (M-NBI) facilitate the detailed examination of gastrointestinal mucosa. However, there was no comparative data regarding the usefulness of standard and M-NBI endoscopy for H. pylori infection and gastric precancerous conditions. We found the significant relationship between endoscopic mucosal patterns and degree of gastric precancerous conditions (moderate to severe gastric atrophy and serum pepsinogen I/II ratio of ≤ 3). These results seem to be valuable for identifying a group at risk of gastric cancer using high quality endoscopy.

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INTRODUCTION

The global prevalence of *Helicobacter pylori* (*H. pylori*) infection is reportedly > 50%[1]. In the *H. pylori*–infected stomach, chronic active inflammation of the mucosa becomes persistent, leading to gastric atrophy and intestinal metaplasia (IM)[2]. According to Correa's model of gastric carcinogenesis, gastric atrophy and IM are linked to progression to gastric cancer[3]. Advanced gastric atrophy and IM are considered to be precancerous conditions because they correlate with gastric carcinogenesis[4-6]. Accurate diagnosis of gastric precancerous conditions is essential for identifying patients at risk of gastric cancer[7].

Narrow-band imaging (NBI) is an innovative optical method that facilitates detailed examination of the gastric mucosa[8]. Furthermore, magnifying NBI (M-NBI) endoscopy with 80-fold magnification can visualize the fine mucosal structure and microvessels[9]. M-NBI endoscopy can be used to diagnose *H. pylori* infection and classify gastritis by histological severity[10]. Recent improvements in the resolution (> 1 million pixels) of gastrointestinal endoscopy have enhanced image quality, facilitating characterization of the gastric mucosal pattern[11]. Close observation of the gastric corpus mucosa by standard endoscopy without magnification enables prediction of *H. pylori* gastritis[12]. Moreover, the severity of gastric atrophy and IM differ according to the endoscopic mucosal pattern. In a systematic review, standard endoscopy was effective as an alternative method for diagnosing *H. pylori* infection[13]. However, there are no comparative data on the utility of standard and M-NBI endoscopy for diagnosing *H. pylori* infection, gastric atrophy, and IM.

In this study, we evaluated the diagnostic performance of standard and M-NBI endoscopy for *H. pylori* infection and advanced gastritis, and investigated the association between the endoscopic mucosal pattern and gastric precancerous

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conditions.

MATERIALS AND METHODS

Patients and study design

From June 2016 to April 2020, we prospectively enrolled patients who underwent gastroscopy for epigastric symptoms, diagnostic work-up for gastric neoplasia, and gastric cancer screening. Before endoscopic examination, all patients had the informed consents about the evaluation of *H. pylori* infection status and gastric precancerous conditions. We performed a complete blood cell count, blood chemistry assays, coagulation test, chest X-ray, and electrocardiogram. The exclusion criteria were: Age < 20 or > 80 years, anemia, severe systemic disease, current use of proton pump inhibitors, history of *H. pylori* eradication, and history of gastric surgery. The study protocol was approved by the Institutional Review Board of our hospital (SCHUH 2016-05-001) and was registered at ClinicalTrials.gov (NCT04489030).

Endoscopic equipment and procedure

Endoscopic procedures were performed using a high-resolution endoscope (GIF-H260Z, H290Z; Olympus, Tokyo, Japan). The whole stomach was examined in a routine manner by a single experienced endoscopist (Cho JH). First, we performed close-up observation of the mucosal patterns at the greater curvature of the middle or lower corpus *via* non-magnified white-light imaging in structural enhancement mode A5. We captured endoscopic images while maintaining a distance of ≤ 10 mm between the endoscope tip and mucosal surface. We previously classified abnormal mucosal patterns using a simple standard endoscopy technique (Figure 1)[12]. When a regular arrangement of numerous minute red dots (normal pattern) was absent, abnormal patterns were categorized as mosaic-like appearance (type A), diffuse homogenous redness (type B), or irregular redness with groove (type C). After completing the mucosal examination by standard endoscopy, the greater curvature side of the gastric corpus was observed by M-NBI. Before the procedure, a soft black hood was attached to the endoscope tip to fix the distance between the endoscope tip and mucosal surface to about 2 mm. When white-light endoscopic image was magnified 80-fold (Supplementary Figure 1), we pressed the NBI button on the handle for the enhanced visualization of mucosal structures and microvessels[14]. NBI was set in enhancement mode A7 and color mode 2. Next, we classified the M-NBI still images as normal or one of three abnormal patterns according to Yagi's classification (Figure 2)[15]. A regular arrangement of collecting venules (RAC) and honeycomb-like subepithelial capillary network was considered a normal pattern. If RAC was not visualized by M-NBI endoscopy, abnormal mucosal patterns were classified as regular round pits with polygonal sulci (type Z-1), more dilated and linear pits without sulci (type Z-2), or loss of gastric pits with coiled vessels (type Z-3). In cases of mixed mucosal patterns, the most prominent was reported after discussion with another expert endoscopist (Jeon SR).

Evaluation of H. pylori infection and gastric precancerous conditions

To increase the *H. pylori* detection rate, a biopsy was taken from the greater curvature of the gastric corpus. *H. pylori* infection status was confirmed by rapid urease test (Pronto Dry; Gastrex Sarl, Gilly les Citeaux, France) or molecular test (Seeplex® *H. pylori*-ClaR ACE Detection; Seegene Inc., Seoul, South Korea). For the histological assessment of glandular atrophy and IM, biopsy specimens were obtained from the lesser curvature of the gastric antrum and corpus. The specimens were fixed in 10% formalin and embedded in paraffin wax, and 5-μm sections were stained with hematoxylin and eosin. The gastric atrophy was defined as loss of glandular tissue and scored on a four-point scale in accordance with the updated Sydney System[16]. The degree of atrophy was classified as mild (1-2), moderate (3-4), or severe (5-6) by summing the scores of the antrum (score 0-3) and corpus (score 0-3). IM was diagnosed by the presence of goblet cells in foveolar epithelium[17]. The pathological examination was performed by an expert pathologist (Jin SY), who was blinded to the patients' data and endoscopic findings.

Before endoscopy, blood samples were collected during a 12-h fasting period. Blood samples were immediately centrifuged at 4 °C and stored at -70 °C until required. Serum pepsinogen (PG) I and PG II levels were measured by latex turbidimetric immunoassay (HiSens; HBI, Anyang, South Korea), and the PG I/II ratio was calculated[18]. A serum PG I level of ≤ 70 ng/mL and PG I/II ratio of ≤ 3 are highly

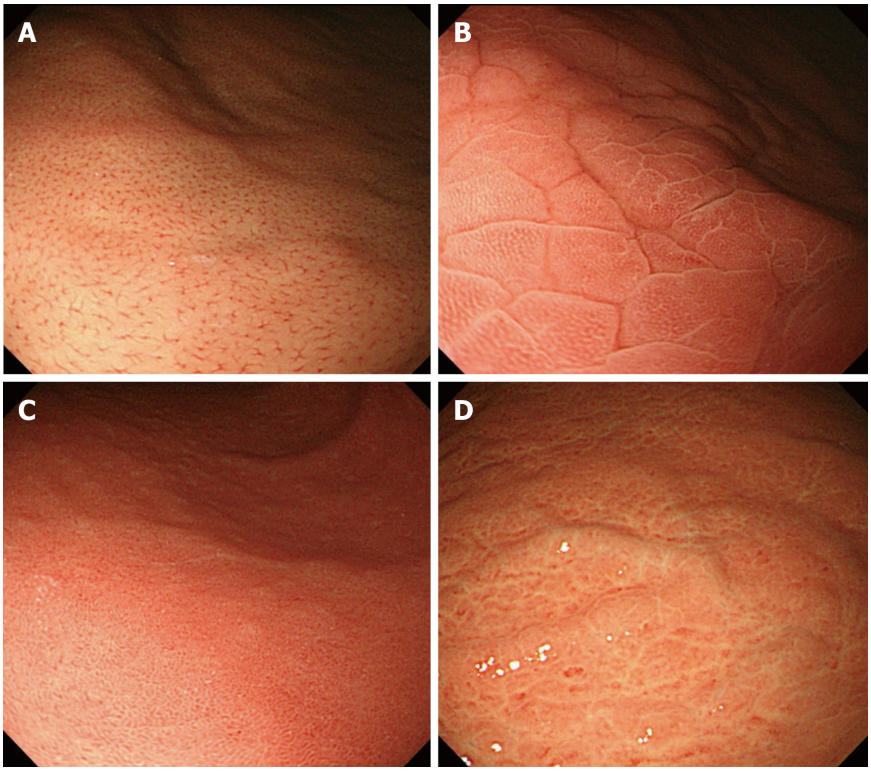

Figure 1 Normal and three abnormal mucosal patterns in the gastric corpus by standard endoscopy. A: Normal pattern, numerous minute red dots; B: Type A, mosaic-like appearance; C: Type B, diffuse homogenous redness; D: Type C, irregular redness with grooves.

associated with extensive atrophic gastritis[19]. A cutoff PG I/II ratio of ≤ 3 was used to assess the risk of gastric precancerous conditions.

Statistical analysis

Continuous data are presented as means and standard deviations and categorical data as numbers and percentages. The Pearson chi-squared test or linear-by-linear association was used to analyze categorical data. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of the two endoscopic classifications were compared by McNemar test. Diagnostic performance was assessed by computing area under the curve (AUC) values. The adjusted odds ratios (ORs) of endoscopic mucosal patterns for predicting gastric precancerous conditions were calculated by logistic regression analysis. Statistical analysis was conducted using SPSS software (version 19.0; IBM Corp., Armonk, NY, United States). A value of $P < 0.05$ was considered indicative of statistical significance.

RESULTS

Characteristics of the study population

A total of 254 patients was eligible for the study (Table 1). The mean age was 45.9 (± 14.6) years and the proportion of male patients was 46.9%. The most frequent endoscopic findings were chronic active gastritis (53.1%), peptic ulcer (4.3%), gastric neoplasia (9.8%), and non-neoplastic polyp (7.5%). Current *H. pylori* infection was confirmed in 64.2% of the patients. According to the degree of gastric atrophy, 117 patients (66.9%) were classified into the none/mild atrophy group, 37 (21.1%) into the moderate atrophy group, and 21 (12.0%) into the severe atrophy group. Regarding the extent of IM, 115 patients (65.7%) had no IM in the antrum or corpus, and 22 (12.6%) and 38 (21.7%) patients had IM in the antrum only and in both the antrum and the corpus, respectively. The mean serum PG I and PG II concentrations and PG I/II ratio were 64.4 ± 32.4 ng/mL, 20.5 ± 14.7 ng/mL, and 4.11 ± 2.2, respectively. The mean serum gastrin concentration was 123.1 ± 149.9 pg/mL.

Table 1 Baseline characteristics of the study population

Characteristic	*n* = 254
Age (yr, mean ± SD)	45.9 ± 14.6
Sex, male, *n* (%)	119 (46.9)
Indication for endoscopy, *n* (%)	
Screening	132 (52.0)
Dyspepsia	42 (16.5)
Abdominal pain	47 (18.5)
Other	33 (13.0)
Endoscopic diagnosis, *n* (%)	
Peptic ulcer	11 (4.3)
Gastric neoplasia	25 (9.8)
Non-neoplastic polyp	19 (7.5)
Chronic active gastritis	135 (53.1)
Helicobacter pylori infection, *n* (%)	163 (64.2)
Gastric atrophy, *n* (%)	
None/mild	117 (66.9)
Moderate	37 (21.1)
Severe	21 (12.0)
Intestinal metaplasia, *n* (%)	
None	115 (65.7)
Antrum only	22 (12.6)
Corpus	38 (21.7)
Serum PG (ng/mL, mean ± SD)	
PG I	64.4 ± 32.4
PG II	20.5 ± 14.7
PG I/II ratio	4.11 ± 2.2
Serum gastrin (pg/mL, mean ± SD)	123.1 ± 149.9

SD: Standard deviation; PG: Pepsinogen.

Diagnostic performance of standard and M-NBI endoscopy

By standard endoscopy, the *H. pylori* infection rate was 91.5% (n = 43/47) for type A, 100% (n = 84/84) for type B, and 100% (n = 23/23) for type C (Table 2). By M-NBI endoscopy, the proportion of *H. pylori* infection was 97.6% (n = 124/127) for type Z-1, 96.3% (n = 26/27) for type Z2, and 100% (n = 7/7) for type Z-3. The rate of advanced gastritis was calculated according to the endoscopic mucosal pattern among 175 patients whose samples were subjected to pathologic examination. Moderate to severe gastric atrophy and the presence of IM in the corpus were considered to be advanced gastritis with a high risk of gastric cancer. By standard endoscopy, the proportions of patients with moderate to severe atrophy were 27.3% (n = 9/33) for type A, 74.0% (n = 37/50) for type B, and 50.0% (n = 10/20) for type C. By M-NBI endoscopy, the proportions of patients with moderate to severe atrophy were 45.9% (n = 39/85) for type Z-1, 88.2% (n = 15/17) for type Z-2, and 100% (n = 4/4) for type Z-3. If the gastric mucosal pattern was normal, however, the rate of moderate to severe atrophy was 2.8% (n = 2/72) by standard endoscopy and 0% (n = 0/69) by M-NBI endoscopy. Similarly, the rate of IM in the corpus differed significantly between normal and abnormal mucosal patterns by both standard (types A+B+C, $P < 0.001$) and M-NBI endoscopy (types Z-1+Z-2 +Z-3, $P < 0.001$).

Table 2 *Helicobacter pylori* gastritis, gastric atrophy, and intestinal metaplasia observed by standard and magnifying narrow-band imaging endoscopy

Endoscopy	*H. pylori* gastritis		Gastric atrophy		Intestinal metaplasia	
	Negative	Positive	None/mild	Moderate/severe	None/antrum	Corpus
	(*n* = 91)	(*n* = 163)	(*n* = 117)	(*n* = 58)	(*n* = 137)	(*n* = 38)
Standard						
Normal	87/100 (87.0)	13/100 (13.0)	70/72 (97.2)	2/72 (2.8)	71/72 (98.6)	1/72 (1.4)
Type A	4/47 (8.5)	43/47 (91.5)	24/33 (72.7)	9/33 (27.3)	25/33 (75.8)	8/33 (24.2)
Type B	0/84 (0)	84/84 (100)	13/50 (26.0)	37/50 (74.0)	24/50 (48.0)	26/50 (52.0)
Type C	0/23 (0)	23/23 (100)	10/20 (50.0)	10/20 (50.0)	17/20 (85.0)	3/20 (15.0)
M-NBI						
Normal	87/93 (93.5)	6/93 (6.5)	69/69 (100)	0/69 (0)	69/69 (100)	0/69 (0)
Type Z-1	3/127 (2.4)	124/127 (97.6)	46/85 (54.1)	39/85 (45.9)	59/85 (69.4)	26/85 (30.6)
Type Z-2	1/27 (3.7)	26/27 (96.3)	2/17 (11.8)	15/17 (88.2)	7/17 (41.2)	10/17 (58.8)
Type Z-3	0/7 (0)	7/7 (100)	0/4 (0)	4/4 (100)	2/4 (50.0)	2/4 (50.0)

M-NBI: Magnifying narrow-band imaging; *H. pylori*: *Helicobacter pylori*.

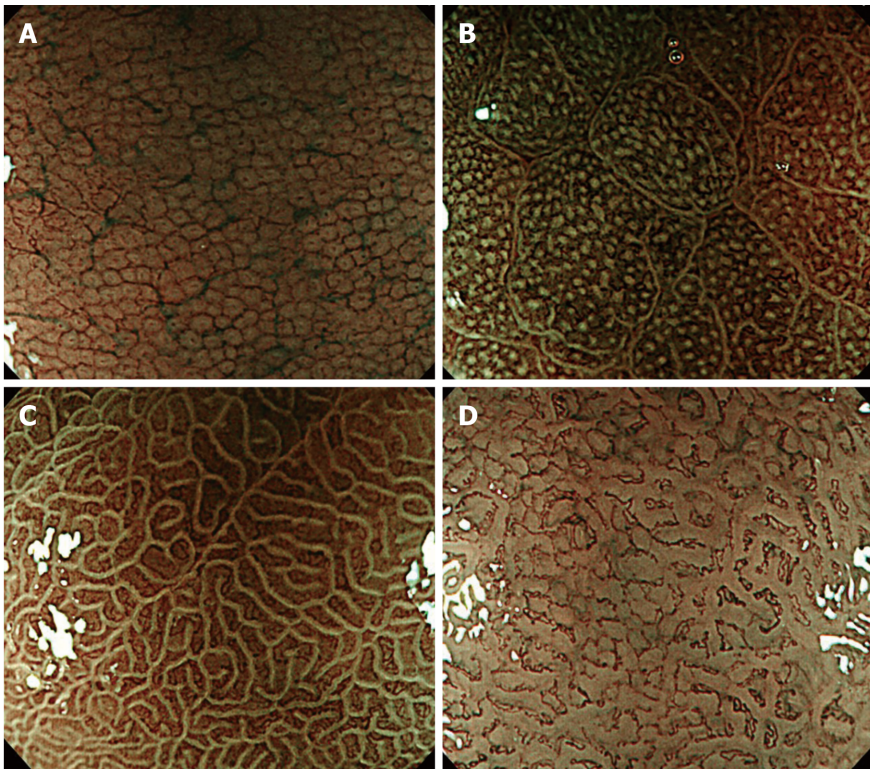

Figure 2 Micromucosal patterns in the gastric corpus observed by magnifying narrow-band imaging endoscopy. A: Normal pattern characterized by regular arrangement of collecting venules and honeycomb-like subepithelial capillary network; B: Type Z-1, regular round pits with polygonal sulci; C: Type Z-2, more dilated and linear pits without sulci; D: Type Z-3, loss of gastric pits with coiled microvessels.

For the diagnosis of *H. pylori* gastritis, the sensitivity of standard endoscopy was 92.0%, while the specificity was 95.6%, the PPV was 97.4%, the NPV was 87.0%, and the accuracy was 93.3%. The sensitivity of M-NBI endoscopy was 96.3%, while the specificity was 95.6%, the PPV was 97.5%, the NPV was 93.5%, and the accuracy was 96.1%. The sensitivity of M-NBI endoscopy was significantly greater than that of standard endoscopy (P = 0.016; Table 3). For the diagnosis of moderate to severe atrophy, the sensitivity of standard endoscopy was 96.6%, while the specificity was

Table 3 Diagnostic performance of standard and magnifying narrow-band imaging endoscopy for *Helicobacter pylori* gastritis, gastric atrophy, and intestinal metaplasia

Endoscopy	Diagnosis	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	AUC
Standard	*H. pylori* gastritis	92.0[a]	95.6	97.4	87.0	93.3	0.93
	Moderate to severe atrophy	96.6	59.8	54.4	97.2	72.0	0.78
	Intestinal metaplasia, corpus	97.4	51.8	35.9	98.6	61.7	0.74
M-NBI	*H. pylori* gastritis	96.3[a]	95.6	97.5	93.5	96.1	0.96
	Moderate to severe atrophy	100	59.0	54.7	100	72.6	0.79
	Intestinal metaplasia, corpus	100	50.4	35.8	100	61.1	0.75

[a]$P = 0.016$, McNemar test indicated a significant difference in sensitivity for diagnosis of *Helicobacter pylori* infection between standard and magnifying narrow-band imaging endoscopy. M-NBI: Magnifying narrow-band imaging; PPV: Positive predictive value; NPV: Negative predictive value; AUC: area under the curve; *H. pylori*: *Helicobacter pylori*.

59.8%, the PPV was 54.4%, the NPV was 97.2%, and the accuracy was 72.0%. The sensitivity of M-NBI endoscopy was 100%, while the specificity was 59.0%, the PPV was 54.7%, the NPV was 100%, and the accuracy was 72.6%. For diagnosis of IM in the corpus, the sensitivity of standard endoscopy was 97.4%, while the specificity was 51.8%, the PPV was 35.9%, the NPV was 98.6%, and the accuracy was 61.7%. The sensitivity of M-NBI endoscopy was 100%, while the specificity was 50.4%, the PPV was 35.8%, the NPV was 100%, and the accuracy was 61.1%. The diagnostic performance of standard and M-NBI endoscopy for moderate to severe atrophy and IM in the corpus was not significantly different. The AUC values of standard and M-NBI endoscopy were 0.93 and 0.96 for *H. pylori* gastritis, 0.78 and 0.79 for moderate to severe atrophy, and 0.74 and 0.75 for IM in the corpus, respectively.

Association of endoscopic patterns with gastric precancerous conditions

Table 4 shows the relationships between endoscopic mucosal patterns and a serum PG I/II ratio of ≤ 3. Among 127 patients who underwent measurement of serum PG concentration, 44.1% (n = 56) had a PG I/II ratio of ≤ 3. Of patients with a normal mucosal pattern, the rate of a PG I/II ratio of ≤ 3 was 2.6% (n = 1/39) by standard endoscopy and 0% (n = 0/36) by M-NBI endoscopy. By standard endoscopy, the rate of a PG I/II ratio of ≤ 3 was 36.0% (n = 9/25) for type A, 71.7% (n = 33/46) for type B, and 76.5% (n = 13/17) for type C. By M-NBI endoscopy, the rate of a PG I/II ratio of ≤ 3 was 54.2% (n = 39/72) for type Z-1, 86.7% (n = 13/15) for type Z-2, and 100% (n = 4/4) for type Z-3. The rate of a PG I/II ratio of ≤ 3 differed between normal and abnormal mucosal patterns according to two endoscopic classifications ($P < 0.001$).

The age- and sex-adjusted ORs of abnormal mucosal patterns for gastric precancerous conditions were calculated by logistic regression analyses (Table 5). Compared to type A, the OR for moderate to severe atrophy was 5.56 [95% confidence interval (CI): 2.07-14.92, $P = 0.001$] for types B+C. Compared to type Z-1, the OR for moderate to severe atrophy was 8.67 (95%CI: 1.82–41.30, $P = 0.007$) for types Z-2+Z-3. Compared to type A, the OR for a serum PG I/II ratio of ≤ 3 was 4.48 (95%CI: 1.60-12.54, $P = 0.004$) for types B+C. Compared to type Z-1, the OR for a serum PG I/II ratio of ≤ 3 was 5.69 (95%CI: 1.19-27.18, $P = 0.029$) for types Z-2+Z-3. For IM in the corpus, there was no significant difference in abnormal mucosal patterns according to two endoscopic classifications (type A *vs* types B+C, $P = 0.189$; and type Z-1 *vs* types Z2+Z-3, $P = 0.162$, respectively).

DISCUSSION

Pathological examination plays an important role in the diagnosis of gastrointestinal diseases by endoscopy[20]. Endoscopists tend to focus on detecting abnormal lesions, and macroscopic examination by conventional endoscopy has limitations for characterizing mucosal lesions. Therefore, the final diagnosis of detected lesions is dependent

Table 4 Serum pepsinogen I/II ratio according to gastric mucosal pattern observed by standard and magnifying narrow-band imaging endoscopy

PG I/II ratio	Standard (%)				M-NBI (%)			
	Normal	Type A	Type B	Type C	Normal	Type Z-1	Type Z-2	Type Z-3
> 3 (n = 71)	38/39 (97.4)	16/25 (64.0)	13/46 (28.3)	4/17 (23.5)	36/36 (100)	33/72 (45.8)	2/15 (13.3)	0/4 (0)
≤ 3 (n = 56)	1/39 (2.6)	9/25 (36.0)	33/46 (71.7)	13/17 (76.5)	0/36 (0)	39/72 (54.2)	13/15 (86.7)	4/4 (100)

PG: Pepsinogen; M-NBI: Magnifying narrow-band imaging.

Table 5 Logistic regression analysis of the associations of endoscopic mucosal patterns with gastric precancerous conditions

Mucosal pattern	Moderate to severe atrophy		Intestinal metaplasia, corpus		PG I/II ratio ≤ 3	
	OR (95%CI)	*P* value	OR (95%CI)	*P* value	OR (95%CI)	*P* value
Standard		0.001		0.189		0.004
Type A	1 (ref.)		1 (ref.)		1 (ref.)	
Type B + C	5.56 (2.07-14.92)		1.96 (0.72-5.33)		4.48 (1.60-12.54)	
M-NBI		0.007		0.162		0.029
Type Z-1	1 (ref.)		1 (ref.)		1 (ref.)	
Type Z-2 + Z-3	8.67 (1.82-41.30)		2.12 (0.74-6.07)		5.69 (1.19-27.18)	

M-NBI: Magnifying narrow-band imaging; PG: Pepsinogen; OR: Odds ratio; CI: Confidence interval.

on the pathological report. To identify those at risk of gastric cancer, the presence of precancerous conditions is evaluated by non-targeted protocol-guided biopsies in different areas[21]. However, multiple mucosal biopsies increase medical costs and the procedure time.

High-resolution and high-magnification endoscopy facilitate detailed examination of the gastrointestinal mucosa[22]. In 2002, Yagi *et al*[23] used magnifying endoscopy to show that RAC was a characteristic finding in the normal stomach without *H. pylori* infection. Abnormal mucosal patterns without RAC were classified as Z-1 to Z-3 in accordance with the degree of mucosal damage in the *H. pylori*–infected stomach[24]. Anagnostopoulos *et al*[25] demonstrated that magnifying endoscopic examination could identify normal gastric mucosa, *H. pylori*–related gastritis, and gastric atrophy in a Western population. The severity of chronic gastritis has been investigated based on the micro-mucosal patterns observed by M-NBI[26]. Kanzaki *et al*[27] reported that groove-type mucosa had a higher grade of atrophy and IM compared to foveolar-type mucosa. However, M-NBI endoscopy is not available in all endoscopy units and training program is required prior to its clinical application[28].

In a previous study, we determined *H. pylori* infection status by close observation of the gastric corpus mucosa by high-resolution endoscopy without magnification[12]. The sensitivity and specificity of all abnormal patterns for predicting *H. pylori* infection were 93.3% and 89.1%, respectively, and the overall diagnostic accuracy was 91.6%. The inter- and intra-observer agreement for the endoscopic mucosal patterns was 91.7% and 90.0%, respectively. This simplified endoscopic technique has enabled reliable prediction of gastric *H. pylori* infection in other countries[29,30]. Recent advances in endoscopic imaging technology have increased the diagnostic accuracy for *H. pylori* infection[13,31]. To our knowledge, this is the first study comparing diagnostic performance between standard and M-NBI endoscopy for *H. pylori* infection. We also analyzed the degree of gastric atrophy, IM, and serum PG levels according to two endoscopic classifications. A decrease in the serum PG I/II ratio is reportedly a non-invasive marker for advanced corpus gastritis and gastric cancer[32,33]. Wang *et al*[34] reported that the serum PG level was strongly correlated with the Operative Link for Gastritis Assessment (OLGA) and Operative Link for Gastric Intestinal Metaplasia (OLGIM) stage. Therefore, a serum PG I/II ratio of ≤ 3 is a serologic marker of gastric precancerous conditions.

Except for sensitivity, the diagnostic performance for *H. pylori* infection was similar between standard and M-NBI endoscopy. Seven patients with a normal pattern by standard endoscopy had *H. pylori* infection. In contrast, these patients were classified as type Z-1 (n = 4), type Z-2 (n = 2), and type Z-3 (n = 1) by M-NBI endoscopy. This is likely because of the ability of M-NBI to examine the superficial microanatomy of the areae gastricae and the pit pattern, which is not possible with standard endoscopy. Nevertheless, standard endoscopy may enable detection of *H. pylori* infection in routine clinical practice (diagnostic accuracy, 93.3%).

For diagnosis of gastric atrophy and IM, standard and M-NBI endoscopy had excellent sensitivity, NPV (> 95%), and AUC (> 0.7) values; however, the specificity and PPV values were not acceptable. According to the Kimura–Takemoto classification, gastric atrophy progresses more frequently along the lesser curvature than the greater curvature of the corpus[35]. When atrophic change extends into the anterior and posterior mucosa of the corpus, the topographic pattern of IM becomes more diffuse throughout the stomach[36]. In this study, we focused on the mucosal pattern in the greater curvature of the gastric corpus. Atrophy of the gastric mucosa and transformation to IM occur last at the greater curvature of the corpus, hampering evaluation of gastric precancerous conditions. A systematic screening protocol for the stomach has been developed to ensure high-quality endoscopic evaluation[37], and enables detection of gastric atrophy and IM in various areas of the stomach[38]. Using NBI without magnification, Pimentel-Nunes *et al*[39] created an endoscopic classification to grade gastric IM; a tubulovillous mucosal pattern was highly concordant with histological IM. However, image-enhanced endoscopic findings for diagnosing and grading gastric atrophy remain to be established[40].

The *H. pylori*–infected stomach exhibits redness and swelling of the corpus mucosa[41,42]. Histologically, *H. pylori* infection causes infiltration of neutrophils and mononuclear cells in the gastric mucosa[43]. In biopsy specimens, lymphoid hyperplasia is a specific immunological reaction to *H. pylori* infection[44]. During long-term *H. pylori*–induced inflammation, the presence of lymphoid hyperplasia decreased with increasing severity of gastric atrophy and IM. In young women, nodular gastritis is induced by *H. pylori* infection and lymphoid follicles in nodular lesions can be detected histologically[45]. Miyamoto *et al*[46] reported that nodular gastritis showed a lower atrophic score than other forms of *H. pylori*–related gastritis. Similarly, we postulated that a swollen areae gastricae would be present in early stage *H. pylori* infection. Therefore, type A was used as a reference for evaluating the risk of gastric cancer according to abnormal mucosal pattern by standard endoscopy. By M-NBI endoscopy, type Z-1 was reported to correlate with less severe gastric atrophy and IM compared to other types[27]. In this study, types A and B+C showed significantly different serum PG I/II ratios (3.82 *vs* 2.74, P = 0.007), as did types Z-1 and Z-2+Z-3 (3.24 *vs* 2.28, P = 0.005). However, there was no significant difference among abnormal mucosal patterns for IM in the corpus. Based on the multifocal patterns of IM, an endoscopic mucosal examination of the entire stomach is recommended[47]. Marcos *et al*[48] reported that NBI endoscopic grading of IM was useful for risk assessment of early gastric neoplasia.

This study had several limitations. First, we did not evaluate the severity of gastric atrophy and IM using the OLGA and OLGIM staging systems. Second, only *H. pylori* treatment-naïve patients were enrolled. Therefore, the results may be not be applicable to endoscopic surveillance after *H. pylori* eradication. Finally, this study was conducted in a single center. A multicenter trial involving endoscopists with varying levels of experience is required to confirm the reliability of the results.

CONCLUSION

In conclusion, close observation of the gastric corpus mucosa by standard and M-NBI endoscopy enables diagnosis of *H. pylori* infection and gastric precancerous conditions. Furthermore, our results suggest an association of endoscopic mucosal patterns with moderate to severe atrophy and a serum PG I/II ratio of ≤ 3.

ARTICLE HIGHLIGHTS

Research background

In Correa's model of gastric carcinogenesis, *Helicobacter pylori* (*H. pylori*) infection,

gastric atrophy and intestinal metaplasia (IM) are linked to gastric cancer development. The low level of serum pepsinogens (PG) was known to be highly associated with extensive atrophic gastritis.

Research motivation

High-resolution and magnifying narrow-band imaging (M-NBI) facilitate the detailed examination of gastrointestinal mucosa. M-NBI endoscopy can be used to diagnose *H. pylori* infection and classify gastritis by histological severity. Moreover, recent improvements in the resolution (> 1 million pixels) of gastrointestinal endoscopy have enhanced image quality, facilitating characterization of the gastric mucosal pattern. Close observation of the gastric corpus mucosa by standard endoscopy without magnification enables prediction of *H. pylori* gastritis and precancerous lesions.

Research objectives

To date, there was no comparative data regarding the usefulness of standard and M-NBI endoscopy for *H. pylori* infection and gastric precancerous conditions. We compared the diagnostic performance of standard and M-NBI endoscopy for *H. pylori* gastritis and precancerous conditions.

Research methods

In total, 254 patients who underwent gastroscopy were prospectively enrolled. Standard endoscopy findings of the gastric mucosal surface were classified into mosaic-like appearance (type A), diffuse homogenous redness (type B), and irregular redness with groove (type C). Gastric mucosal patterns visualized by M-NBI endoscopy were classified as regular round pits with polygonal sulci (type Z-1), more dilated and linear pits without sulci (type Z-2), and loss of gastric pits with coiled vessels (type Z-3). We evaluated the utility of the two endoscopic classifications for the diagnosis of *H. pylori* gastritis, gastric atrophy, IM, and a serum PG I/II ratio of ≤ 3.

Research results

The diagnostic accuracy of standard and M-NBI endoscopy for *H. pylori* gastritis was 93.3% and 96.1%, respectively. Regarding gastric precancerous conditions, the diagnostic accuracy of standard and M-NBI endoscopy was 72.0% *vs* 72.6% for moderate to severe atrophy, and 61.7% *vs* 61.1% for IM in the corpus, respectively. Compared to type A and Z1, types B+C and Z-2+Z-3 were significantly associated with moderate to severe atrophy [odds ratio (OR) = 5.56, P = 0.001; OR = 8.67, P = 0.007] and a serum PG I/II ratio of ≤ 3 (OR = 4.48, P = 0.004; OR = 5.69, P = 0.029).

Research conclusions

Close observation of the gastric corpus mucosa by standard and M-NBI endoscopy enables diagnosis of *H. pylori* infection and gastric precancerous conditions. Furthermore, our results suggest an association of endoscopic mucosal patterns with moderate to severe atrophy and a serum PG I/II ratio of ≤ 3.

Research perspectives

By gastric mucosal observation in detail, optical diagnosis of *H. pylori*–related gastritis may be achieved in real time. In the future, a multicenter trial is required to confirm the reliability of our results.

REFERENCES

1 **Hooi JKY**, Lai WY, Ng WK, Suen MMY, Underwood FE, Tanyingoh D, Malfertheiner P, Graham DY, Wong VWS, Wu JCY, Chan FKL, Sung JJY, Kaplan GG, Ng SC. Global Prevalence of Helicobacter pylori Infection: Systematic Review and Meta-Analysis. *Gastroenterology* 2017; **153**: 420-429 [PMID: 28456631 DOI: 10.1053/j.gastro.2017.04.022]

2 **Kuipers EJ**, Uyterlinde AM, Peña AS, Roosendaal R, Pals G, Nelis GF, Festen HP, Meuwissen SG. Long-term sequelae of Helicobacter pylori gastritis. *Lancet* 1995; **345**: 1525-1528 [PMID: 7791437 DOI: 10.1016/s0140-6736(95)91084-0]

3 **Correa P**, Piazuelo MB. The gastric precancerous cascade. *J Dig Dis* 2012; **13**: 2-9 [PMID: 22188910 DOI: 10.1111/j.1751-2980.2011.00550.x]

4 **Kaji K**, Hashiba A, Uotani C, Yamaguchi Y, Ueno T, Ohno K, Takabatake I, Wakabayashi T, Doyama H, Ninomiya I, Kiriyama M, Ohyama S, Yoneshima M, Koyama N, Takeda Y, Yasuda K. Grading of Atrophic Gastritis is Useful for Risk Stratification in Endoscopic Screening for Gastric Cancer. *Am J Gastroenterol* 2019; **114**: 71-79 [PMID: 30315306 DOI: 10.1038/s41395-018-0259-5]

5 **Shichijo S**, Hirata Y, Sakitani K, Yamamoto S, Serizawa T, Niikura R, Watabe H, Yoshida S, Yamada A, Yamaji Y, Ushiku T, Fukayama M, Koike K. Distribution of intestinal metaplasia as a predictor of gastric cancer development. *J Gastroenterol Hepatol* 2015; **30**: 1260-1264 [PMID: 25777777 DOI: 10.1111/jgh.12946]

6 **Uemura N**, Okamoto S, Yamamoto S, Matsumura N, Yamaguchi S, Yamakido M, Taniyama K, Sasaki N, Schlemper RJ. Helicobacter pylori infection and the development of gastric cancer. *N Engl J Med* 2001; **345**: 784-789 [PMID: 11556297 DOI: 10.1056/NEJMoa001999]

7 **Pimentel-Nunes P**, Libânio D, Marcos-Pinto R, Areia M, Leja M, Esposito G, Garrido M, Kikuste I, Megraud F, Matysiak-Budnik T, Annibale B, Dumonceau JM, Barros R, Fléjou JF, Carneiro F, van Hooft JE, Kuipers EJ, Dinis-Ribeiro M. Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019. *Endoscopy* 2019; **51**: 365-388 [PMID: 30841008 DOI: 10.1055/a-0859-1883]

8 **Gono K**, Obi T, Yamaguchi M, Ohyama N, Machida H, Sano Y, Yoshida S, Hamamoto Y, Endo T. Appearance of enhanced tissue features in narrow-band endoscopic imaging. *J Biomed Opt* 2004; **9**: 568-577 [PMID: 15189095 DOI: 10.1117/1.1695563]

9 **Muto M**, Horimatsu T, Ezoe Y, Morita S, Miyamoto S. Improving visualization techniques by narrow band imaging and magnification endoscopy. *J Gastroenterol Hepatol* 2009; **24**: 1333-1346 [PMID: 19702901 DOI: 10.1111/j.1440-1746.2009.05925.x]

10 **Tahara T**, Shibata T, Nakamura M, Yoshioka D, Okubo M, Arisawa T, Hirata I. Gastric mucosal pattern by using magnifying narrow-band imaging endoscopy clearly distinguishes histological and serological severity of chronic gastritis. *Gastrointest Endosc* 2009; **70**: 246-253 [PMID: 19386303 DOI: 10.1016/j.gie.2008.11.046]

11 **ASGE Technology Committee**. . High-definition and high-magnification endoscopes. *Gastrointest Endosc* 2014; **80**: 919-927 [PMID: 25442091 DOI: 10.1016/j.gie.2014.06.019]

12 **Cho JH**, Chang YW, Jang JY, Shim JJ, Lee CK, Dong SH, Kim HJ, Kim BH, Lee TH, Cho JY. Close observation of gastric mucosal pattern by standard endoscopy can predict Helicobacter pylori infection status. *J Gastroenterol Hepatol* 2013; **28**: 279-284 [PMID: 23189930 DOI: 10.1111/jgh.12046]

13 **Glover B**, Teare J, Patel N. A systematic review of the role of non-magnified endoscopy for the assessment of *H. pylori* infection. *Endosc Int Open* 2020; **8**: E105-E114 [PMID: 32010741 DOI: 10.1055/a-0999-5252]

14 **Cho JH**, Jeon SR, Jin SY. Clinical applicability of gastroscopy with narrow-band imaging for the diagnosis of *Helicobacter pylori* gastritis, precancerous gastric lesion, and neoplasia. *World J Clin Cases* 2020; **8**: 2902-2916 [PMID: 32775373 DOI: 10.12998/wjcc.v8.i14.2902]

15 **Yagi K**, Nakamura A, Sekine A. Comparison between magnifying endoscopy and histological, culture and urease test findings from the gastric mucosa of the corpus. *Endoscopy* 2002; **34**: 376-381 [PMID: 11972268 DOI: 10.1055/s-2002-25281]

16 **Dixon MF**, Genta RM, Yardley JH, Correa P. Classification and grading of gastritis. The updated Sydney System. International Workshop on the Histopathology of Gastritis, Houston 1994. *Am J Surg Pathol* 1996; **20**: 1161-1181 [PMID: 8827022 DOI: 10.1097/00000478-199610000-00001]

17 **Correa P**, Piazuelo MB, Wilson KT. Pathology of gastric intestinal metaplasia: clinical implications. *Am J Gastroenterol* 2010; **105**: 493-498 [PMID: 20203636 DOI: 10.1038/ajg.2009.728]

18 **Cho JH**, Jeon SR, Kim HG, Jin SY, Park S. The serum pepsinogen levels for risk assessment of gastric neoplasms: New proposal from a case-control study in Korea. *Medicine (Baltimore)* 2017; **96**: e7603 [PMID: 28723806 DOI: 10.1097/MD.0000000000007603]

19 **Kodoi A**, Yoshihara M, Sumii K, Haruma K, Kajiyama G. Serum pepsinogen in screening for gastric cancer. *J Gastroenterol* 1995; **30**: 452-460 [PMID: 7550854 DOI: 10.1007/BF02347560]

20 **Carpenter HA**, Talley NJ. Gastroscopy is incomplete without biopsy: clinical relevance of distinguishing gastropathy from gastritis. *Gastroenterology* 1995; **108**: 917-924 [PMID: 7875496 DOI: 10.1016/0016-5085(95)90468-9]

21 **El-Zimaity HM**, Graham DY. Evaluation of gastric mucosal biopsy site and number for identification of Helicobacter pylori or intestinal metaplasia: role of the Sydney System. *Hum Pathol* 1999; **30**: 72-77 [PMID: 9923930 DOI: 10.1016/s0046-8177(99)90303-9]

22 **Kiesslich R**, Goetz M, Hoffman A, Galle PR. New imaging techniques and opportunities in endoscopy. *Nat Rev Gastroenterol Hepatol* 2011; **8**: 547-553 [PMID: 21894196 DOI: 10.1038/nrgastro.2011.152]

23 **Yagi K**, Nakamura A, Sekine A. Characteristic endoscopic and magnified endoscopic findings in the normal stomach without Helicobacter pylori infection. *J Gastroenterol Hepatol* 2002; **17**: 39-45 [PMID: 11895551 DOI: 10.1046/j.1440-1746.2002.02665.x]

24 **Yagi K**, Honda H, Yang JM, Nakagawa S. Magnifying endoscopy in gastritis of the corpus. *Endoscopy* 2005; **37**: 660-666 [PMID: 16010611 DOI: 10.1055/s-2005-861423]

25 **Anagnostopoulos GK**, Yao K, Kaye P, Fogden E, Fortun P, Shonde A, Foley S, Sunil S, Atherton JJ, Hawkey C, Ragunath K. High-resolution magnification endoscopy can reliably identify normal gastric mucosa, Helicobacter pylori-associated gastritis, and gastric atrophy. *Endoscopy* 2007; **39**: 202-207 [PMID: 17273960 DOI: 10.1055/s-2006-945056]

26 **Kawamura M**, Abe S, Oikawa K, Terai S, Saito M, Shibuya D, Kato K, Shimada T, Uedo N, Masuda T. Topographic differences in gastric micromucosal patterns observed by magnifying endoscopy with

narrow band imaging. *J Gastroenterol Hepatol* 2011; **26**: 477-483 [PMID: 21155881 DOI: 10.1111/j.1440-1746.2010.06527.x]

27 **Kanzaki H**, Uedo N, Ishihara R, Nagai K, Matsui F, Ohta T, Hanafusa M, Hanaoka N, Takeuchi Y, Higashino K, Iishi H, Tomita Y, Tatsuta M, Yamamoto K. Comprehensive investigation of areae gastricae pattern in gastric corpus using magnifying narrow band imaging endoscopy in patients with chronic atrophic fundic gastritis. *Helicobacter* 2012; **17**: 224-231 [PMID: 22515361 DOI: 10.1111/j.1523-5378.2012.00938.x]

28 **Nakanishi H**, Doyama H, Ishikawa H, Uedo N, Gotoda T, Kato M, Nagao S, Nagami Y, Aoyagi H, Imagawa A, Kodaira J, Mitsui S, Kobayashi N, Muto M, Takatori H, Abe T, Tsujii M, Watari J, Ishiyama S, Oda I, Ono H, Kaneko K, Yokoi C, Ueo T, Uchita K, Matsumoto K, Kanesaka T, Morita Y, Katsuki S, Nishikawa J, Inamura K, Kinjo T, Yamamoto K, Yoshimura D, Araki H, Kashida H, Hosokawa A, Mori H, Yamashita H, Motohashi O, Kobayashi K, Hirayama M, Kobayashi H, Endo M, Yamano H, Murakami K, Koike T, Hirasawa K, Miyaoka Y, Hamamoto H, Hikichi T, Hanabata N, Shimoda R, Hori S, Sato T, Kodashima S, Okada H, Mannami T, Yamamoto S, Niwa Y, Yashima K, Tanabe S, Satoh H, Sasaki F, Yamazato T, Ikeda Y, Nishisaki H, Nakagawa M, Matsuda A, Tamura F, Nishiyama H, Arita K, Kawasaki K, Hoppo K, Oka M, Ishihara S, Mukasa M, Minamino H, Yao K. Evaluation of an e-learning system for diagnosis of gastric lesions using magnifying narrow-band imaging: a multicenter randomized controlled study. *Endoscopy* 2017; **49**: 957-967 [PMID: 28637065 DOI: 10.1055/s-0043-111888]

29 **Yumang ZL**, Pangilinan JA. Close observation endoscopy of gastric mucosal pattern in predicting Helicobacter pylori infection a single center cross-sectional study (a preliminary report). *Gut Liver* 2018; **12**: S26

30 **Garcés-Durán R**, García-Rodríguez A, Córdova H, Cuatrecasas M, Ginès À, González-Suárez B, Araujo I, Llach J, Fernández-Esparrach G. Association between a regular arrangement of collecting venules and absence of Helicobacter pylori infection in a European population. *Gastrointest Endosc* 2019; **90**: 461-466 [PMID: 31108089 DOI: 10.1016/j.gie.2019.05.027]

31 **Qi Q**, Guo C, Ji R, Li Z, Zuo X, Li Y. Diagnostic Performance of Magnifying Endoscopy for Helicobacter pylori Infection: A Meta-Analysis. *PLoS One* 2016; **11**: e0168201 [PMID: 27992489 DOI: 10.1371/journal.pone.0168201]

32 **Gantuya B**, Oyuntsetseg K, Bolor D, Erdene-Ochir Y, Sanduijav R, Davaadorj D, Tserentogtokh T, Uchida T, Yamaoka Y. Evaluation of serum markers for gastric cancer and its precursor diseases among high incidence and mortality rate of gastric cancer area. *Gastric Cancer* 2019; **22**: 104-112 [PMID: 29934751 DOI: 10.1007/s10120-018-0844-8]

33 **Kang JM**, Kim N, Yoo JY, Park YS, Lee DH, Kim HY, Lee HS, Choe G, Kim JS, Jung HC, Song IS. The role of serum pepsinogen and gastrin test for the detection of gastric cancer in Korea. *Helicobacter* 2008; **13**: 146-156 [PMID: 18321304 DOI: 10.1111/j.1523-5378.2008.00592.x]

34 **Wang X**, Lu B, Meng L, Fan Y, Zhang S, Li M. The correlation between histological gastritis staging- 'OLGA/OLGIM' and serum pepsinogen test in assessment of gastric atrophy/intestinal metaplasia in China. *Scand J Gastroenterol* 2017; **52**: 822-827 [PMID: 28436254 DOI: 10.1080/00365521.2017.1315739]

35 **Kimura K**. Chronological transition of the fundic-pyloric border determined by stepwise biopsy of the lesser and greater curvatures of the stomach. *Gastroenterology* 1972; **63**: 584-592 [PMID: 5077145 DOI: 10.1016/S0016-5085(19)33241-X]

36 **Cassaro M**, Rugge M, Gutierrez O, Leandro G, Graham DY, Genta RM. Topographic patterns of intestinal metaplasia and gastric cancer. *Am J Gastroenterol* 2000; **95**: 1431-1438 [PMID: 10894575 DOI: 10.1111/j.1572-0241.2000.02074.x]

37 **Yao K**. The endoscopic diagnosis of early gastric cancer. *Ann Gastroenterol* 2013; **26**: 11-22 [PMID: 24714327 DOI: 10.1016/S0016-5107(79)73384-0]

38 **Banks M**, Graham D, Jansen M, Gotoda T, Coda S, di Pietro M, Uedo N, Bhandari P, Pritchard DM, Kuipers EJ, Rodriguez-Justo M, Novelli MR, Ragunath K, Shepherd N, Dinis-Ribeiro M. British Society of Gastroenterology guidelines on the diagnosis and management of patients at risk of gastric adenocarcinoma. *Gut* 2019; **68**: 1545-1575 [PMID: 31278206 DOI: 10.1136/gutjnl-2018-318126]

39 **Pimentel-Nunes P**, Libânio D, Lage J, Abrantes D, Coimbra M, Esposito G, Hormozdi D, Pepper M, Drasovean S, White JR, Dobru D, Buxbaum J, Ragunath K, Annibale B, Dinis-Ribeiro M. A multicenter prospective study of the real-time use of narrow-band imaging in the diagnosis of premalignant gastric conditions and lesions. *Endoscopy* 2016; **48**: 723-730 [PMID: 27280384 DOI: 10.1055/s-0042-108435]

40 **Rodríguez-Carrasco M**, Esposito G, Libânio D, Pimentel-Nunes P, Dinis-Ribeiro M. Image-enhanced endoscopy for gastric preneoplastic conditions and neoplastic lesions: a systematic review and meta-analysis. *Endoscopy* 2020; **52**: 1048-1065 [PMID: 32663879 DOI: 10.1055/a-1205-0570]

41 **Uchiyama K**, Ida K, Okuda J, Asai Y, Ohyama Y, Kuroda M, Matsumoto N, Takami T, Ogawa T, Takaori K. Correlations of hemoglobin index (IHb) of gastric mucosa with Helicobacter pylori (H. pylori) infection and inflammation of gastric mucosa. *Scand J Gastroenterol* 2004; **39**: 1054-1060 [PMID: 15545161 DOI: 10.1080/00365520410009645]

42 **Kato T**, Yagi N, Kamada T, Shimbo T, Watanabe H, Ida K; Study Group for Establishing Endoscopic Diagnosis of Chronic Gastritis. Diagnosis of Helicobacter pylori infection in gastric mucosa by endoscopic features: a multicenter prospective study. *Dig Endosc* 2013; **25**: 508-518 [PMID: 23369058 DOI: 10.1111/den.12031]

43 **Wyatt JI**. Histopathology of gastroduodenal inflammation: the impact of Helicobacter pylori.

Histopathology 1995; **26**: 1-15 [PMID: 7713479 DOI: 10.1111/j.1365-2559.1995.tb00614.x]

44 **Chen XY**, Liu WZ, Shi Y, Zhang DZ, Xiao SD, Tytgat GN. Helicobacter pylori associated gastric diseases and lymphoid tissue hyperplasia in gastric antral mucosa. *J Clin Pathol* 2002; **55**: 133-137 [PMID: 11865009 DOI: 10.1136/jcp.55.2.133]

45 **Shiotani A**, Kamada T, Kumamoto M, Nakae Y, Nakamura Y, Kakudo K, Haruma K. Nodular gastritis in Japanese young adults: endoscopic and histological observations. *J Gastroenterol* 2007; **42**: 610-615 [PMID: 17701123 DOI: 10.1007/s00535-007-2073-5]

46 **Miyamoto M**, Haruma K, Yoshihara M, Hiyama T, Sumioka M, Nishisaka T, Tanaka S, Chayama K. Nodular gastritis in adults is caused by Helicobacter pylori infection. *Dig Dis Sci* 2003; **48**: 968-975 [PMID: 12772798 DOI: 10.1023/a:1023016000096]

47 **Correa P**, Haenszel W, Cuello C, Zavala D, Fontham E, Zarama G, Tannenbaum S, Collazos T, Ruiz B. Gastric precancerous process in a high risk population: cohort follow-up. *Cancer Res* 1990; **50**: 4737-4740 [PMID: 2369748 DOI: 10.1097/00002820-199008000-00007]

48 **Marcos P**, Brito-Gonçalves G, Libânio D, Pita I, Castro R, Sá I, Dinis-Ribeiro M, Pimentel-Nunes P. Endoscopic grading of gastric intestinal metaplasia on risk assessment for early gastric neoplasia: can we replace histology assessment also in the West? *Gut* 2020; **69**: 1762-1768 [PMID: 32051208 DOI: 10.1136/gutjnl-2019-320091]

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