Original Article

Validity of Magnify NBI for Gastric Intestinal Metaplasia Targeted Biopsy

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ABSTRACT

Background: Gastric intestinal metaplasia (GIM) is a premalignant condition of gastric cancer. The gold standard for GIM diagnosis is histology. GIM are scattered and focally located. Random biopsy is quite cumbersome and takes hours, thus targeted biopsy by endoscopic guidance is recommended. However, the diagnostic accuracy of conventional white light endoscopy is low due to sampling error and high inter-observer variability. Narrow band imaging with magnification endoscopy (NBI-ME) can be applied for more accurate targeted biopsy. However there is little data about the diagnostic accuracy of this technique.

Aim: To define the diagnostic accuracy of GIM detection by NBI-ME

Methods: Thirty eight patients with previously diagnosed as GIM by random biopsy were enrolled. NBI-ME (Olympus GIF Q160Z) with targeted biopsy for both positive and negative lesions from six areas (4 and 2 from antrum and incisura respectively) was done according to three endoscopic criteria including light blue crests (LBC), villous pattern (VP) and large long crests (LLC). All magnified images were interpreted by the other three gastroenterologists and the results were analyzed and compared to the pathological results. The specimens were read based on the updated Sydney classification by one pathologist.

Results: There were 85 of the 228 specimens with proven positive for GIM. The average accuracy, sensitivity, specificity, positive predictive value, and negative predictive value by using all three criteria were 73.10%, 66.67%, 76.92%, 63.38%, 79.50% respectively. The calculated Kappa score from all three interpreters was 0.83. When using each criterion, LBC provided the highest diagnostic accuracy. Importantly, early gastric cancers including one intestinal type and one signet ring cell adenocarcinoma were detected in two patients.

Conclusion: NBI-ME possesses a high accuracy with perfect agreement for GIM detection. LBC has the highest accuracy over VP and LLC. However, if all three criteria are used, the sensitivity and NPV improve. Thus NBI-ME might be useful for follow-up and early detection of early cancerous progression of patients with GIM.

Key words : Magnify NBI, intestinal metaplasia, endoscopy

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INTRODUCTION

Gastric cancer is the second leading cause of cancer-related death in the world. The diagnosis of gastric cancer is usually too late for the curable treatment due to no symptom in an early stage. Therefore identification of early gastric cancer or its pre-malignant stage is important and beneficial. It is well-established that gastric intestinal metaplasia is a pre-malignant condition for the development of intestinal-type gastric adenocarcinoma. According to Correa's cascade, chronic atrophic gastritis from *Helicobacter pylori* infection leads to the progressive development of gastric intestinal metaplasia, gastric dysplasia and eventually gastric adenocarcinoma[1]. The previously reported prevalence of GIM in Thai patients was about 15% and higher prevalence was associated with aging[2]. The incidence rate of gastric cancer from intestinal metaplasia range from 0.37% to 0.46 % per year[3,4]. Certainly the diagnosis of early gastric cancer during the surveillance of gastric intestinal metaplasia can improve survival[5]. Moreover it was proven that the follow-up of intestinal metaplasia by using the magnifying chromoendoscopy and serum pepsinogen level could be feasible and cost-effective[6]. Up to now there is no consensus for cancer surveillance in these patients. This might be no available diagnostic tools with good accuracy. The gold standard for diagnosis of gastric intestinal metaplasia is tissue pathology. According to updated Sydney classification, biopsy from 5 sites including 2 from antrum, 1 from incisura, 1 from greater curvature and 1 from lesser curvature is recommended to detect gastric intestinal metaplasia[7]. Unfortunately it was proven that this strategy seriously underestimated diagnosis in more than 50 percent[8]. Gastric intestinal metaplasia is generally scattered, small and focally located. Furthermore its typical endoscopic findings from the conventional white light endoscopy such as whitish plaques, patches or discoloration of gastric mucosa are quite variable and not sensitive[9].

Narrow-banded imaging with magnification (NBI-ME) has been used to evaluate the surface microstructure in the stomach mucosa which composes of the surface epithelium and the subepithelial capillaries network. The principle of NBI is based upon the depth of penetration into the gastrointestinal mucosa relying on the applied wave length. NBI contains three wave lengths including red, green and blue bands(R/G/B). The red band is the deepest penetration into subepithelial vessels, the green band is intermediate whereas the blue band is the most superficial. The normal antral gastric mucosa NBI findings reveal the epithelial crests separated with normal sulci and the coiled, elongated capillaries placed in the center of crests[10]. The data of gastric intestinal metaplasia findings from NBI-ME remain little. The three proposed findings in the literature include 1) depressed or elevated area of large, long epithelial crests with deep sulci 2) light blue crests[11] 3) villous pattern of epithelial crests. However only light blue crests had been evaluated for the correlation with histopathology in one study[11] which the results revealed an accuracy of 91%.

The objective of the present study is to validate the diagnostic performance of NBI-ME for gastric intestinal metaplasia targeted biopsy by applying all three proposed findings.

PATIENTS AND METHODS

The patients who were older than 18 year-old and previously diagnosed with gastric intestinal metaplasia by histopathology during 2001-2007 were invited to perform gastroduodenoscopy with NBI-ME and targeted biopsy. The exclusion criteria included previous gastric surgery such as gastrectomy and bypass surgery; bleeding tendency such as decompensated cirrhosis, chronic kidney disease, and treatment with antiplatelet agents or anticoagulants; and pregnancy.

The EVIS EXERA Gastrointestinal videoscope, Olympus GIF type Q160Z (Non-sequential NBI system), was applied in this study. A disposable plastic cap was attached to tip of the endoscope with a distance of approximately 3 millimeter between mucosa and scope tip. The power of magnification was about 100 times. Both 2.5-5 milligrams of intravenous midazolam and 10 milligrams of hyoscine were intravenously administrated to sedate and decrease bowel movement for easier and complete visualization. Simethicone solution was rinsed to reduce mucus and gas bubble in the stomach. Vedio recorder was used during routine white-light gastroduodenoscopy and then six non-magnifying snapshot images were recorded as four quadrants of antrum and two areas of incisura. The four quadrants of antrum were named as left anterior (AAL), left posterior (APL), right anterior (AAR) and right posterior (APR). The other two areas of incisura were right (ICR) and left (ICL) incisura. We selected antrum and incisura which were the

most frequent location of gastric intestinal metaplasia[12,13] and easier visualization. After that, NBI system was switched and then six non-magnifying together with six magnifying images were recorded. With three criteria mentioned above such as light blue crests (LBC), villous pattern of crests (VP) and depressed or elevated area of large, long crests with deep sulci (LLC), one magnifying image and targeted biopsy were done from each area. Therefore six magnifying images and their targeted biopsy were derived from each patient. The most prominent and lowest placed finding was selected in case of two findings in the same area. If there was no finding following three criteria, snapshot image and biopsy were done in the normal area. *Helicobacter pylori (H. pylori)* were examined by rapid urease test (Pronto Dry test®, Eisai, Bangkok, Thailand).

Tissues from targeted biopsy were sent to one GI pathologist blinded to clinical and endoscopic data. Hematoxylin and Eosin (H&E), Alcian Blue and Giemsa stain were used for the histological diagnosis of gastric intestinal metaplasia and the detection of *H. pylori*. All magnifying images were randomly sent to three other gastroenterologists in order to interpret whether there were the presence or absence of endoscopic criteria as described above.

Statistical analysis

Kappa score was used to evaluate agreement of interpretation of NBI findings by gastroenterologists. The diagnostic properties of the endoscopic criteria was evaluated in relation to pathological report as a gold standard and reported as sensitivity, specificity, positive predictive value, negative predictive value and accuracy.

RESULTS

There were 38 patients with prior history of GIM enrolled into the study. The baseline characteristics were shown in the Table 1. *H. pylori* was detected in 12/38 patients by rapid urease test. The histological diagnosis of gastric intestinal metaplasia persisted by NBI targeted biopsy in 31/38 patients. Median numbers of detected GIM site were two per each patient and the most common location was antrum. Among 228 specimens from targeted biopsy, GIM was histological diagnosed in 85 specimens which all of them were complete type. Conventional white light endoscopy revealed typical finding of GIM that was whitish color change with plaques, patches or homogeneous discoloration on gastric mucosa in only 5 patients (a sensitivity of 13.16%) but all five patients had biopsy proven GIM (a positive predictive value of 100%). The calculated Kappa score from all three interpreters was 0.83. Examples of NBI findings according to three criteria are shown as Figure 1. The average accuracy, sensitivity, specificity, positive predictive value, and negative predictive value by using all three criteria were 73.10%, 66.67%, 76.92%, 63.38%, 79.50% respectively. The total results of accuracy are shown in the Table 2. Early gastric cancer was detected in two patients in this study. One focal area of signet ring cell type gastric adenocarcinoma was identified in a 65 year-old male patient. In this case, white light endoscopy showed only mild antral gastritis without other abnormal findings. However one small ill-defined area of depressed lesion with diameter about 5 millimeters close to area with light blue crest was detected by NBI endoscopy. Targeted biopsy was done from both areas and the histological reports showed the focal infiltration of signet ring cell type adenocarcinoma. Endoscopic findings are shown as Figure 2. After repeated endoscopy with NBI-ME for targeting lesion and confirmation of histological diagnosis of early gastric cancer together with complete staging which revealed early signet ring cell type poorly differentiated adenocarcinoma, he underwent for subtotal gastrectomy. The final pathological report of gross specimen also showed only small focal area of early gastric cancer. Another patient was an 80 year-old man without dyspeptic symptom. At the first time of NBI endoscopy, GIM was found in all 6 areas together with high grade gastric dysplasia and 1 centimeter benign gastric ulcer at antrum. Three months after *H. pylori* eradication and acid suppression therapy, repeated NBI endoscopy revealed the elevated mucosal lesion with 3-centimeter

Table 1. Represents baseline characteristics of patients.

Characteristics	Results
Average age (years)	59.89 (27-80)
Gender - Male:Female	20:18
Mean duration after initial diagnosis (years)	2.2
Type of GIM	All complete GIM
Positive rapid urease test	12/38

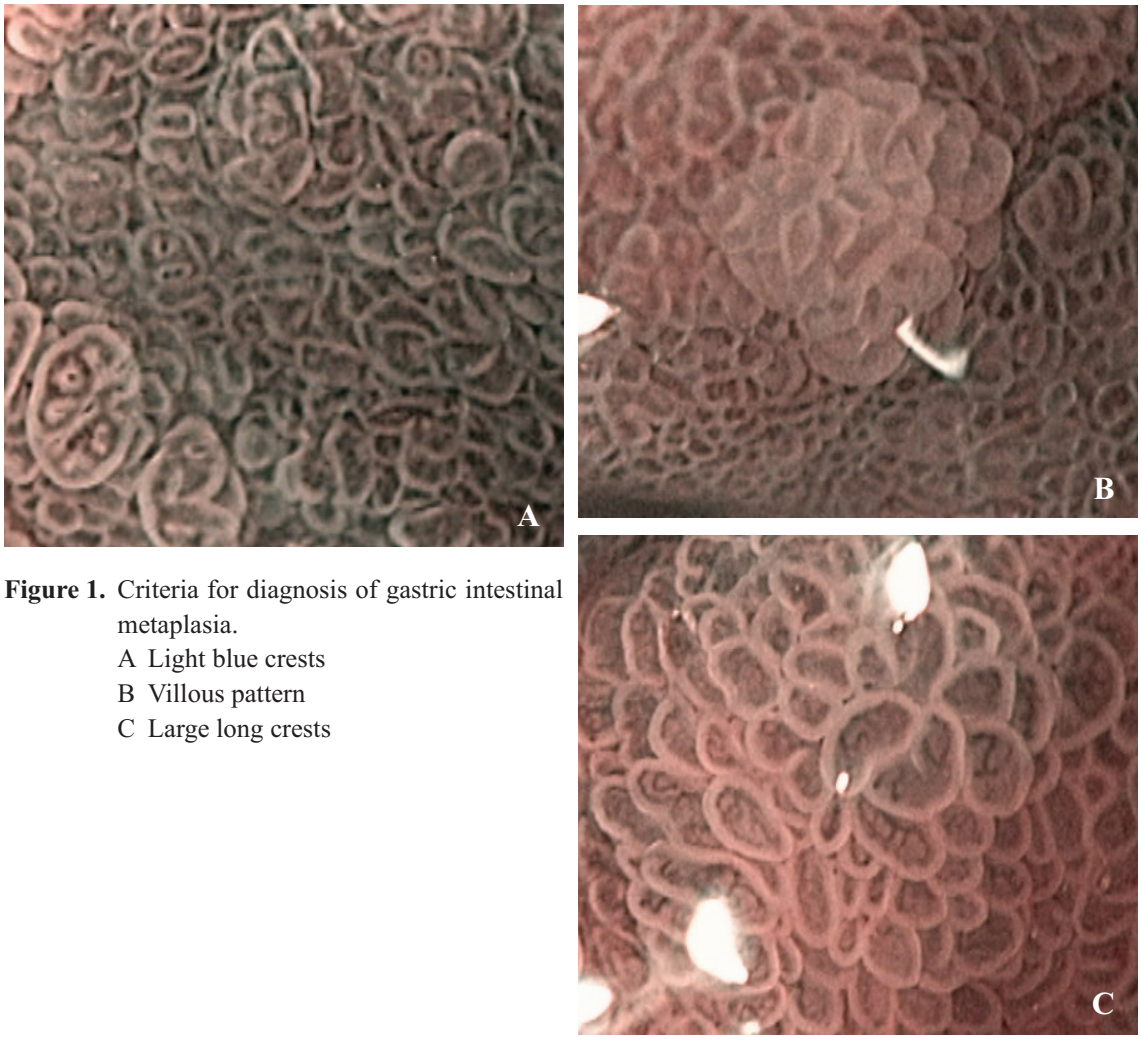

Figure 1. Criteria for diagnosis of gastric intestinal metaplasia.
A Light blue crests
B Villous pattern
C Large long crests

Table 2. Represents average accuracy of all three interpreters.

Findings	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
LBC	58.44	83.10	67.82	76.91	73.98
VP	18.83	94.64	69.22	66.55	66.37
LLC	13.40	92.69	52.56	63.42	62.28
All criteria	66.67	76.92	63.38	79.50	73.10

PPV = positive predictive value, NPV = negative predictive value, LBC = light blue crests, VP = villous pattern, LLC = large long crests

in size and irregular pit pattern and abnormal sub-epithelial capillaries network consistent with gastric cancer at lesser curvature of gastric body (Figure 3). The pathological results showed the intestinal type gastric cancer limited to the mucosa and submucosa layer. He was scheduled for further endoscopic submucosal resection.

DISCUSSION

Narrow band imaging with magnification endoscopy possessed significant benefit and feasibility to identify gastric intestinal metaplasia which was known as pre-malignant condition for gastric cancer. With all mentioned criteria involving light blue crests, villous

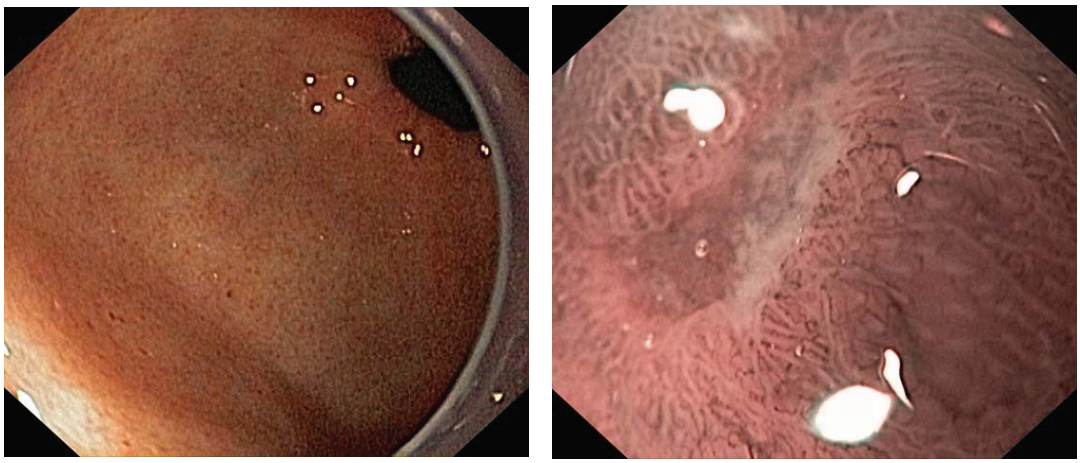

Figure 2. In the left picture, the conventional white light endoscopy revealed only mild antral gastritis. In the right picture, a small focal depressed area with the disappearance of both normal pit pattern and microvascular structure was identified by NBI-ME. The histopathology showed the focal infiltration of signet ring cell type adenocarcinoma.

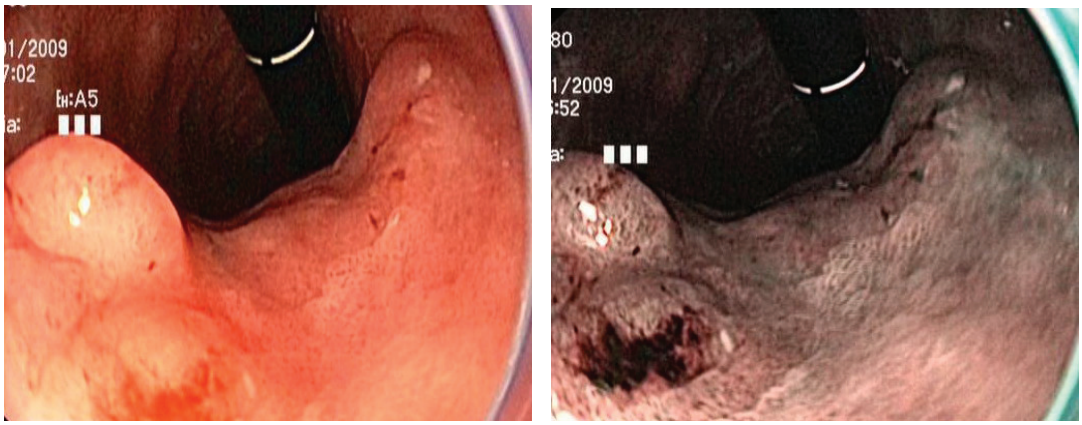

Figure 3. In the left picture, the elevated poorly demarcated mucosal lesion with 3-centimeter in size at lesser curvature of gastric body. NBI image was shown in the right picture as a well demarcated lesion with irregular pit pattern and abnormal sub-epithelial vessels. The histopathology showed the intestinal type gastric cancer.

pattern and large long crests which were used for targeted biopsy, it yielded a high diagnostic accuracy, whereas conventional white light endoscopy had very low sensitivity (13.16%) which was concordant with previous studies. Furthermore Kappa score represented almost perfect agreement for NBI interpretation. This represents the simple and easy advantage of our criteria for diagnosis. Nevertheless the accuracy of LBC was slightly lower when compared with previous study[11]. The reason was that the non-sequential NBI system was used in the present study which provided less prominent findings when compared with sequential system. In the present study, early gastric cancers including intestinal type and signet ring cell type were detected by NBI-ME in two patients with prior diagnosis of GIM. Therefore NBI might be useful for follow up of GIM and early detection of the cancerous progression.

Although a previous study using magnifying chromoendoscopy with methylene blue reported better sensitivity and specificity[14], but this prerequisite multi-step and time-consuming procedure together with potential oxidative damage should be considered[15-17]. This study evaluated only the areas in antrum and incisura but not fundus and body because of more predilection of GIM in distal part of stomach. In addition, the magnification was required for NBI to detect small lesions; it had limitation to extensively evaluate lesions throughout stomach such as body and fundus. In this study only patients with prior GIM was included, thus further studies were needed for more information about other high risk patients.

In conclusion, NBI-ME possesses a high accuracy with perfect agreement for GIM detection. LBC has the highest accuracy over VP and LLC. However, if all three criteria are used, the sensitivity and NPV improve. Furthermore NBI-ME might be useful for follow-up and early detection of early cancerous progression of patients with GIM.

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