RESEARCH ARTICLE

Improved Detection of *Helicobacter pylori* Infection and Premalignant Gastric Mucosa Using Conventional White Light Source Gastroscopy

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Abstract

Background: The gold standard diagnosis of *H. pylori* related gastritis is evidence of bacteria on histopathological examination of gastric mucosa. Our aim was to study the correlation between gastric mucosal morphology and histopathological severity of *H. pylori* related gastritis. Materials and Methods: Division was made on morphological features into:Type 1, showing regular arrangement of red dots; Type 2, showing cleft-like appearance; Type 3, with a mosaic appearance; and Type 4, having a mosaic appearance with focal or diffuse hyperemia. Results: Types 1 and 2 gastric mucosal morphologies were statistically significant in predicting an *H. pylori* negative status (137/145, p<0.01), while Types 3 and 4 were significant a positive status (139/155, p<0.01). The sensitivity, specificity, positive and negative predictive values of Type 3 and 4 morphologies for predicting *H. pylori* positive were 94.6%, 89.5%, 89.7% and 94.5%, respectively, with a good correlation with inflammation grading (p<0.01). Conclusions: Our study suggests that gastric mucosal morphology can be reliably identified using conventional white light source gastroscopy with good correlation between findings and inflammation grading.

Keywords: Gastric mucosa - premalignant gastric lesion - conventional white light source gastroscopy - *H pylori*

Asian Pac J Cancer Prev, **17 (4)**, 2099-2103

Introduction

Gastroscopy and biopsy for the rapid urease test and histopathological examination have been still standard diagnosis for *H. pylori* infection. Many studies have been attempted to classify the gastroscopic findings of *H. pylori* related gastritis. In 2002, Japanese endoscopist found that collecting venules, seen as numerous minute red dots in the gastric corpus, where a characteristic finding in the normal gastric mucosa morphology without *H. pylori* infection using both standard and magnifying endoscopy (Yagi et al., 2002). This finding was termed "regular arrangement of collecting venules" (RAC).

In 2005, Japanese endoscopists provided more precise information concerning the network of collecting venules (Yagi et al., 2005). The gastroscopic findings of *H. pylori* infected gastric mucosa were erythema, erosions, antral nodularity, thickened gastric folds, and visible submucosal vessels. However, these findings are not a reliable method of diagnosis because of their low sensitivity and specificity (Laine et al., 1995; Bah et al., 1995; Mihara et al., 1999; Redeen S et al., 2003). In 2010, Taiwanese endoscopist a study using close-up observation between the endoscope tip and the gastric mucosa and found the "mosaic pattern" in the corpus mucosa. This study can improve accuracy of *H. pylori* infection status (Yan et al., 2010). They classified gastric mucosal morphology into two categories (normal RAC and abnormal mosaic pattern). However, the classification was insufficient to predict all *H. pylori* infections.

In our study, we used 4 categories; Type1: showing regular arrangement of red dots (RAC), Type2: showing cleft-like appearance, Type 3: mosaic appearance, Type 4 mosaic appearance with focal or diffuse hyperemia. One recent study from the United States has indicated the usefulness of NBI for predicting *H. pylori* infection and the occurrence of intestinal metaplasia in the stomach (Anagnostopoulos et al., 2007). Many reports suggest that high resolution magnification endoscopy has been proved in the identification of normal gastric mucosa and *H. pylori*-related gastritis (Yagi et al., 2002). Our recent study, gastric mucosal morphological patterns in the *H. pylori* infected gastric mucosa can be reliably identified using C-NBI gastroscopy with good correlation

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with inflammation grading (Taweesak et al., 2015). The endoscopist can improve accuracy of gastric biopsy using the site specific biopsy technique (Taweesak et al., 2015). The Kyoto global consensus report on *H. pylori* gastritis suggested that atrophic mucosa and intestinal metaplasia can be accurately detected by image enhanced endoscopy, after appropriate training (Kentaro et al., 2015).

However, practicing high resolution magnification endoscopy in daily gastroscopic examination seems not to be feasible, because it takes more examination time and needs more experience of the endoscopist. If specific mucosal morphology of *H. pylori*-related gastritis can be identified using conventional white light source gastroscopy, they may be applicable to targeted biopsy of the suspected area of *H. pylori* infection in daily clinical practice. The aim of our study to classify the gastric mucosal morphology of *H. pylori* related gastritis using conventional white light source gastroscopy and correlation with severity grading of gastritis according to Sydney classification (Dixon et al., 1994; Tytgat et al., 1991).

Materials and Methods

Patients

A 200 patients underwent gastroscopy for the investigation of dyspeptic symptoms were enrolled in the our study from January 2014 to November 2014 in the Endoscopy unit, Suranaree Medical Center, Department of Surgery, Institute of Medicine, Suranaree University of Technology, Nakhon Ratchasima, Thailand. The following exclusion criteria were applied: age below 18 or above 70 years, *H. pylori* eradication treatment in the previous 2 months, suspected or confirmed malignancy on endoscopy, significant medical illnesses and history of previous gastric surgery, the use of antimicrobials or gastrointestinal medications like PPIs, H2blockers or bismuth compounds within the previous 2 months. All patients provided informed consent, and the study was approved by the institutional review board of Suranaree University of Technology, Nakhon Ratchasima, Thailand.

Diagnosis of H. pylori infection

A diagnosis of *H. pylori* infection was made if *H. pylori* bacteria were seen on histopathological examination and the rapid urease test was positive. Patients with negative results in one or both examinations were considered to be H.pylori negative, according to the European guidelines for the diagnosis of *H. pylori* infection (Malfertheiner P et al., 2002).

Biopsy specimens

Four biopsy samples were taken directly from the observation area as shown in Figure 1. Two samples were sent for histological analysis and two were used for rapid urease testing on site (ProntodyleR, GASTREX, France)

Histological analysis

Specimens for histological analysis were placed in 10% formalin solution and routinely processed. The hematoxylin and eosin stain and Giemsa stain were used for identification of *H. pylori*. All of the cases were evaluated by 5 pathologists of Bangkok Pathological Laboratory outside Suranaree University.

Endoscopic findings

The local anesthesia was the same as for conventional white light source gastroscopy. The gastroscopic procedures were performed using an upper GI videoendoscope (Olympus EVIS EXERA III, CV-190) in all cases. The whole stomach was examined with conventional white light source gastroscopy. The gastric mucosa was chosen for observation. The observed gastric mucosal morphology was classified into 4 morphologies. Type: 1 showing the regular arrangement of collecting venules, type 2: mucosal pattern showing cleft like appearance, Type 3: showing the mosaic appearance, Type 4 showing the mosaic appearance with focal or diffuse hyperemia.

Image evaluation

All gastroscopic examinations were digitally recorded and still images of the observation sites were captured for use in the reproducibility study. The selected images were transferred to a software program without distorting brightness, contrast or color balance. An endoscopist classified them as type 1 through type 4 gastric mucosal morphology as described above. All endoscopists were blinded to the results of the *H. pylori* status and histology before reviewing the slides.

Inter and intraobserver agreement study

During endoscopy, close-up still images were captured in the gastric antrum and the body of the stomach. Among the high quality images showing clear gastric mucosal morphology, a total of 200 pictures from 200 patients were selected for the intra and interobserver agreement study. All endoscopists were blinded to the results of the *H. pylori* status and histology before reviewing the pictures.

Statistical analysis

The sensitivity, specificity, and positive and negative predictive values of the various gastric mucosal morphologies were calculated. Clinicopathologic factors associated with the accuracy of predicting *H. pylori* positivity were assessed by logistic regression analysis. A p-value of <0.05 was considered significant. All statistical analyses were performed using the SPSS, version 16.0 (SPSS Inc., Chicago, IL, USA). The κ value was calculated for inter and intra observer variabilities. k values below 0.4 indicated poor agreement, values between 0.4 and 0.8 represent moderate agreement, values between 0.6 and 0.8 represented substantial agreement, and values greater than 0.8 corresponded to excellent agreement.

Results

A total of 200 consecutive patients (92 men, 118 women; mean age 49.0 years, range 19-69 years) were enrolled in our study from January 2014 to November 2014. The 200 patients included: 35 patients showing a type 1 pattern, 25 patients showing a type 2 pattern, 60 patients showing a type 3 pattern, 80 patients showing

a type 4 pattern (Table 1). *H. pylori* infection was demonstrated by both a positive result of the rapid urease test as well as bacteria seen on histological examination in 132 patients (66%). Type 1 and type 2 gastric mucosal morphology were statistically significant in predicting *H. pylori* negative status as compared with other mucosal morphologies (58/68, p<0.01). Type 3 and type 4 gastric mucosal morphology was statistically significant in predicting *H. pylori* positive status as compared with other mucosal morphologies (130/140, p<0.01). Furthermore, the sensitivity, specificity, positive and negative predictive values of type 3 and type 4 morphologies for predicting *H. pylori* positive were 98.48%, 92.85%, 98.48%, and 94.48% respectively with good correlation with inflammation grading according to the Sydney classification (p<0.01).

Gastric mucosal morphology and severity of gastric mucosal inflammation

Type 1 showing the regular arrangement of collecting venules, gastric mucosal morphology was associated with a regular arrangement of surface epithelium, with absent or minimal infiltration by inflammatory cells (Figure 1). Type 2 abnormal gastric mucosal morphology corresponded to mild gastritis with mild glandular atrophy, mild infiltration by inflammatory cells, irregular arrangement of surface epithelium, and irregular opening pits (Figure 2). Moderate gastritis was recognized in type 3, with moderate glandular atrophy, moderate infiltration by inflammatory cells, and irregular arrangement of surface epithelium (Figure 3).

Different conventional white light source gastroscopy of gastric mucosal morphologies and correlation with histopathological severity

Marked gastritis was found in type 4, with marked glandular atrophy, marked lymphocytic infiltration, lymphoid follicular hyperplasia, and intestinal metaplasia (Figure 4).

Interobserver and intraobserver agreement assessment

The k-values for inter and intra observer agreement for the gastroscopic mucosal morphologies were significant. The k-values for inter and intra observer agreement with regard to prediction of *H. pylori* infection status were also significant (Table 3).

Table 1. Correlation between Gastric Mucosal Morphology and *H. pylori* Infection Status

Mucosal morphology	H. pylori infection status		p-value
	Non-infected subjects (HP -)	infected subjects (HP +)	
Type 1	35 (35/35)	-	<0.01
Type2	23 (23/25)	2 (2/25)	<0.01
Type3	5 (5/60)	55 (55/60)	<0.01
Type4	5 (5/80)	75 (75/80)	<0.01

Table 2. Correlation between Gastric Mucosal Morphology and Inflammation Grading

Mucosal morphology	Inflammation grading			p-value
	mild	moderate	severe	
Type 1	35 (35/35)	-	-	<0.01
Type2	10 (10/25)	15 (15/25)	-	<0.01
Type3	5 (5/60)	55 (55/60)	-	<0.01
Type4	-	25 (25/80)	55 (55/80)	<0.01

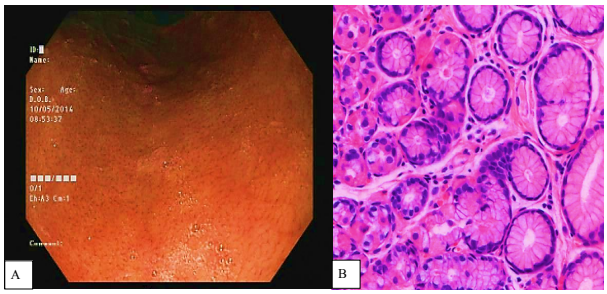

Figure 1. Type 1 Gastric Mucosal Morphology. Note regular arrangement of collecting venules (A) and associated with regular arrangement of surface epithelium, with absent or minimal infiltration by inflammatory cells (B)

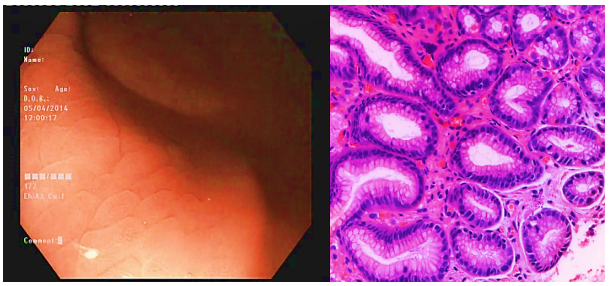

Figure 2. Type 2 Gastric Mucosal Morphology. Note cleft-like appearance (A) and associated mild infiltration by inflammatory cells, irregular arrangement of surface epithelium, and irregular opening pits (B)

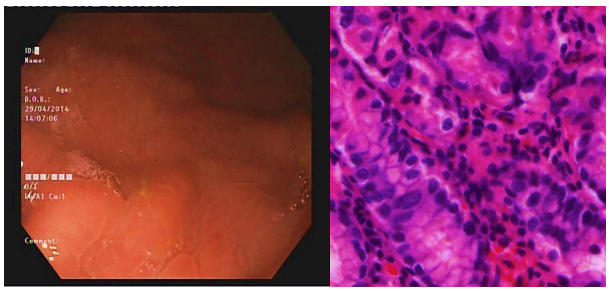

Figure 3. Type 3 Gastric Mucosal Morphology. Note mosaic appearance (A) and associated moderated infiltration by inflammatory cells (B)

Table 3. Inter- and Intra-Observer Agreement

	Interobserver agreement		Intraobserver agreement	
	% agreement	k value (95% CI)	% agreement	k value (95% CI)
Gastric mucosal morphology	91.8	0.91 (0.88–0.92)	89.9	0.88 (0.85–0.90)
H. pylori infection status	96.9	0.98 (0.96–0.97)	98.3	0.97 (0.97–0.98)

The k-values for inter- and intraobserver agreement for the various gastric mucosal morphologies were significant. CI, confidence interval

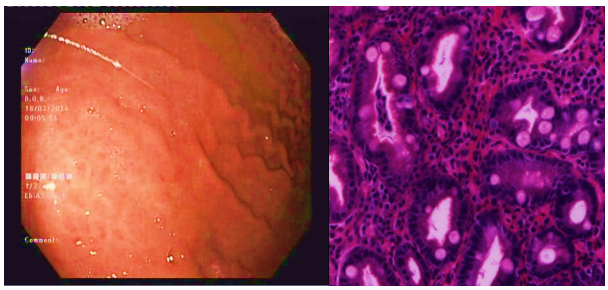

Figure 4. Type 4 Gastric Mucosal Morphology. Note mosaic appearance with focal area of hyperemia (A) and associated marked infiltration by inflammatory cell and present of intestinal metaplasia (B)

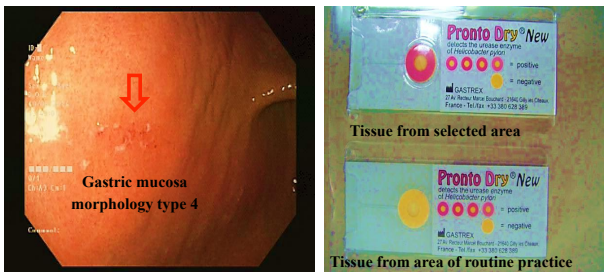

Figure 5. Gastric Mucosal Morphology Guided Biopsy

Discussion

Evident of bacteria on histopathological examination is therefore still considered to be the gold standard for diagnosis *H. pylori* related gastritis. The reliability of detecting H.pylori related gastritis and other conditions such as atrophy and intestinal metaplasia by "blind" biopsy sampling of gastric mucosa depend on the site, number, and size of biopsy specimens. This practice could result in sampling errors, missed pathology, and unnecessary work and costs for pathology departments.

Early diagnosis and eradication of *H. pylori* is a key step in eliminating gastric malignancy. Real time identification of the site of *H. pylori* related gastritis in the stomach during gastroscopy not only reduces the sampling error and excessive workload of pathologist, but also improves detection of early malignant lesions by indicating the need for more meticulous examination of the whole stomach. The development of high resolution magnified endoscopy markedly overcame these problems. Yet the use of magnified imaging for routine daily screening for *H. pylori* related gastritis is impossible in routine practice. It is not only costly, but also less widely available, and is also time consuming. In addition, it needs special patient preparation and a well-trained endoscopist. In our study, the gastric mucosal morphology was classified into 4 types using conventional white light source gastroscopy.

Gastric mucosal morphologies type 1 and type 2 were statistically significant in predicting *H. pylori* negative status as compared with other mucosal morphologies (58/68, $p<0.01$). Type 3, type 4 gastric mucosal morphology was statistically significant in predicting *H. pylori* positive status as compared with other mucosal morphologies (130/140, $p<0.01$). Furthermore, the sensitivity, specificity, positive and negative predictive values of type 3, type 4 morphologies for predicting *H. pylori* positive were 98.48%, 92.85%, 98.48%, and 94.48% respectively with good correlation with inflammation grading according to the Sydney classification ($p<0.01$).

In conclusion, considering the unsatisfactory sensitivity of conventional biopsy for diagnosing *H. pylori* and the limitations of the magnified image, our study suggests that gastric mucosal morphology in *H. pylori* infected gastric mucosa can be reliably identified using conventional white light source gastroscopy and can predict the histopathological severity of gastritis. In this study suggests that gastric mucosal morphology in the *H. pylori* infected gastric mucosa can be reliably identified using conventional white light source gastroscopy with good correlation with inflammation grading. Findings from our studies have shown a good correlation between gastric mucosal morphology and *H. pylori* status and severity of pathological inflammation grading especially premalignant gastric lesion. This benefit for target areas of the biopsy with suspected *H. pylori* infection in daily practice (Figure 5). Further studies to compare between gold standard biopsy and gastric mucosal morphology guided biopsy.

Acknowledgements

This study was supported by a grant for medical investigation from Suranaree University of Technology and was approved by the Ethics Committee for Research Involving Human Subjects Suranaree University of Technology (EC-57-34).

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