High Resolution Endoscopic Classification of Chronic Gastritis and Helicobacter Pylori Infection Through Microvascular Pattern

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Abstract

Background and Aims

The aim of this study was to validate the usefulness of high resolution (HR) endoscopy for predicting chronic gastritis and *H. pylori* (HP) infection status.

Method

Based on microvascular (MV) patterns, HR endoscopic findings were classified into three types; Class I: present with regular arrangement of collecting venule (RAC) and subepithelial capillary network (SECN), Class II: loss of RAC with uneven SECN, Class III: loss of RAC with loss of SECN. These findings were analyzed to determine how well it is correlated with histologic findings, serological analysis, and rapid urease test.

Result

Diagnostic accuracy compared with biopsy results were described. In the MV pattern, accuracy of class I in antrum and body were 56.3% and 100%, class II in antrum and body were 90% and 94.4%, and class III in antrum and body were 89.5% and 70%. In the PGI / PGII correlation with MV pattern classification, PGI / PGII was significantly higher in class I compared to class II or III ($p<0.001$). In the endoscopic prediction of HP infection, class I with negative HP infection rate 94.1%, however Class II and III showed positive HP infection in 100% and 90%.

Conclusion

Chronic gastritis classification algorithm through microvascular changes including RAC and SECN showed high accuracy in diagnosing chronic gastritis by HR endoscopy. In addition, the algorithm helps us to distinguish recent HP infections.

Introduction

Stomach cancer is the fifth most common cancer in the world, with the third mortality, being particularly prevalent in east Asia.[1] *Helicobacter pylori* (HP) infection is a representative cause of chronic inflammation of the stomach, which increases the risk of stomach cancer.[2] Most of gastric cancer develops through several stages of chronic inflammation. In south Korea, due to the high incidence of gastric cancer, as part of the National Cancer Early Screening Project (NCESP), adults over the age of 40 are recommended to undergo a gastroscopy every two years.

Regular gastroscopy is a major contributor to the early detection of precancerous lesions or gastric cancer, thus reducing mortality from gastric cancer.[3] However, in south Korea, the incidence of gastric cancer still ranks first in the world,[4] and gastric cancer prevention has emerged as an important task. The most direct way to prevent gastric cancer is to accurately identify the risk of stomach cancer through

gastroscopy, which is being implemented as a NCESP. Since most gastric cancers develop from chronic gastritis, it is important to correctly verify the degree of chronic gastritis and diagnose HP infection which is the most common cause of chronic gastritis.[2]

The degree of chronic gastritis can be verified by the Operative Link on Gastritis Assessment (OLGA) and the Operative link on gastric intestinal metaplasia assessment (OLGIM) algorithm.[5] However, this evaluation method has a limitation that it can be verified only through histologic result by biopsy. Since the diagnostic accuracy of chronic gastritis through Kimura-Takemoto classification,[6] which is clinically widely used, is only about 60%, a biopsy is still recommended as a gold standard to increase the accuracy.[7]

However, the high resolution (HR) scopes have allowed the gastric mucosa to be observed in detail, enabling more accurate prediction of the degree of chronic gastritis according to the gastric mucosal pattern, especially in changes of microvascular (MV) or microsurface pattern.[8] Also many studies have demonstrated by using magnifying endoscopy or narrow band imaging (NBI) endoscopy with showing higher diagnostic performance compared with OLGIM, so it is expected that now we can assess the risk of gastric cancer in chronic gastritis without biopsy.[9-12]

Therefore, this prospective pilot study was conducted to validate the diagnostic accuracy of endoscopic grading of chronic gastritis according to the MV pattern by observing with a HR scopes.

Methods

Study design and participants

From March 2016 to May 2018, the study was conducted in patients aged 20 to 80 who visited the CHA university hospital who underwent gastroscopy for gastric cancer screening. We exclude the patients who underwent gastroduodenal surgery and with a history of taking medications such as proton pump inhibitor, histamine-2 receptor antagonist, or non-steroidal anti-inflammatory drugs. We also excluded patients with severe systemic disease including chronic liver disease or uncontrolled coagulopathy.

Informed consent was obtained from all patients before the procedure and this study protocol was approved by institutional review board of CHA Medical Center, CHA university (approved number: 2015-114).

Endoscopic evaluation

Chronic gastritis was classified according to the MV pattern of gastric mucosa observed by gastroscopes. The study was performed by HR gastroscopes (GIF-HQ290; Olympus or IMAGE 1; Karl Storz). The MV of gastric mucosa is known that can be distinguished by regular arrangement of collecting venules (RAC) and subepithelial capillary network (SECN).

The three patterns of MVs were observed in the gastric mucosa, and classified chronic gastritis accordingly (Fig. 1); Class I: present with RAC and SECN which is normal gastric mucosa, Class II: loss of RAC with uneven SECN which is chronic superficial gastritis, Class III: loss of RAC with loss of SECN which is chronic atrophic gastritis.

Histopathological evaluation

Four biopsies were performed and compared with endoscopic findings. The biopsy was performed on the greater curvature (GC) and lesser curvature (LC) of antrum, GC and LC of body, respectively. Biopsy was classified according to updated Sydney classification.[7] Neutrophils, mononuclear cells, glandular atrophy, and intestinal metaplasia were recorded. Chronic superficial gastritis (CSG) was diagnosed with an increase in mononuclear cells (lymphocytes and plasma cells). Chronic atrophic gastritis (CAG) is defined as glandular atrophy or gastric mucosa replaced by metaplastic columnar absorptive cells and goblet cells. Steiner silver stain was used to assess the presence of HP. HP infection was also compared with the Campylobacter-like organism (CLO) test.

Serological evaluation

The three classifications for chronic gastritis were also compared with serum pepsinogen (PG), which indirectly assesses the secretory capacity of gastric cells. PG I / PG II of serum is collected and radioimmunoassay is performed and evaluated. According to a previous study, the serological degree of atrophic gastritis was also defined as follows: Normal, PG I > 70 ng/mL, PG I/II ratio > 3.0; Mild, PG I ≤ 70-51 ng/mL, PG I/II ratio ≤ 3.0; Severe, PG I ≤ 30 ng/mL, PG I/II ratio ≤ 2.0

Statistical analysis

Patients were performed on clinical characteristics and data were expressed as total number and/or percentage of total, median (interquartile range (IQR)). For comparison of PG I/II ratio, SPSS was used and $P < 0.05$ was regarded as significant. A subgroup analysis of diagnostic performance was performed with respect to the presence of HP infection.

Ethics

Written informed consent was obtained from all study subjects prior to study commencement. All methods were carried out in accordance with relevant guidelines and regulations that was approved by the Institutional Review Board of Inha University Hospital (2019-11-008).

Results

The total 45 patients had a median age of 57 (IQR 26–79) and 57.8% of them were women. Table 1 is comparing the endoscopic findings and histology according to the MV pattern at each observed site. First of all, 16 patients showed Class I in antrum. Of these, 9 patients showed normal findings on histologic evaluation, but 7 patients diagnosed the CSG. 10 patients had Class II, and biopsy showed 9 cases of the

CSG and the other one had the CAG. 19 patients showed Class III, of which 17 had the CAG findings and 2 had the CSG findings. In the Stomach body, 17 patients showed the Class I on endoscopic findings. All of them were also normal. One of 18 patients with Class II was diagnosed as a normal by biopsy. And 3 of 10 patients who were assessed Class III by endoscopy showed the CSG by biopsy.

Table 1
Comparison of endoscopic findings and histology according to the microvascular pattern at each observed site.

N (%)	MV patterns	Biopsy results		
		Normal	CSG	CAG
Antrum	I	9	7	0
	II	0	9	1
	III	0	2	17
Body	I	17	0	0
	II	1	17	0
	III		3	7
Numbers of biopsy results and MV pattern indicate I: Class I, II: Class II, III: Class III				
Abbreviation: MV: microvascular, CSG: chronic superficial gastritis, CAG: chronic atrophic gastritis				

Table 2 compares the accuracy of the two sites according to the degree of gastritis. For Class I pattern with normal findings, there were statistical differences, with antrum 56.3 (9/16)% and body with 100 (17/17)% accuracy. For Class II pattern showing CSG, there were no statistical differences, with 90 (9/10)% in antrum and 94.4 (17/18)% in body. For Class III pattern showing CAG, there were no statistical differences, with antrum 89.5 (17/19)% and body with 70 (7/10)% accuracy.

Table 2
Compares the accuracy of the body and antrum according to the degree of gastritis.

	N Accuracy (%)					
Location	I	P	II	P	III	P
ANTRUM	56.3 (9/16)	0.003	90.0 (9/10)	1.000	89.5 (17/19)	0.306
BODY	100 (17/17)		94.4 (17/18)		70.0 (7/10)	
Numers of N accuracy category indicate I: Class I, II: Class II, III: Class III						
Abbreviation: N: number, P: probability						

Table 3 divides the endoscopy findings into normal, CSG, and CAG, and compares this with serum pepsinogen, which indirectly evaluates the secretory capacity of gastric cells. The average PG I level in

normal was 160.64, but it decreased to 116.11 in CSG and 56.01 in CAG. Tended. PGI / PGII was also high in endoscopic normal mucosal findings to 27.1, but decreased to 8.98 in CSG and 4.06 in CAG.

Table 3
Difference in pepsinogen ratio according to the degree of chronic gastritis

	Total (n = 45)			
	I (n = 16)	**II (n = 10)**	**III (n = 19)**	***P*-value**
PG I (ng/mL)	160.64	116.11	56.01	0.005
PG II (ng/mL)	7.69	18.18	14.08	0.001
PG I : PG II	27.10	8.98	4.06	0.000
Numers of N accuracy category indicate I: Class I, II: Class II, III: Class III				
Abbreviation: CSG; chronic superficial gastritis, CAG; chronic atrophic gastritis, PG: pepsinogen, P: probability				

Finally, Table 4 shows how endoscopic findings can predict HP infection. In Class I pattern, 15 out of 16 showed HP negative, and in the Class III, 9 out of 10 showed HP negative and showed high accuracy. In Class II pattern showed HP positive in all 18 patients. Overall, HP infection prediction accuracy was high in 43 out of 45 patients (95.6%).

Table 4
Endoscopic accuracy in HP infection prediction

Diagnostic performance	**Endoscopic patterns**			
Criteria	I	II	III	**Total**
Accuracy (%)	94.1 (16/17)	100 (18/18)	90.0 (9/10)	95.6 (43/45)
Numbers of Endoscopic patterns indicate I: Class I, II: Class II, III: Class III				
Abbreviation: HP; *Helicobacter pylori*				

Discussions

It has long been known that gastric cancer mostly occurs through a gradual process of chronic inflammation of the stomach. Therefore, many studies have attempt to predict the risk of gastric cancer through the degree of chronic inflammation. Studies using special endoscopes such as an image-enhanced endoscopy or a magnifying endoscopy have been reported to be meaningful, but the classification of chronic gastritis using a general endoscope has been reported to have low diagnostic accuracy, thus a large number of biopsies were inevitable. Recently, as the quality of endoscopes has been improved rapidly, a HR endoscope can distinguish the change of gastric mucosa such as the effect of chronic inflammation on the changes in the shape of microvessels.

We classified the degree of chronic gastritis through the change of microvascular shape based on the change of RAC and SECN, and scored it and compared it with the biopsy results. The diagnostic accuracy of endoscopy imaging was the lowest at Class I, which is classified a normal. As a result of analyzing the accuracy in the antrum and body, the accuracy of the normal findings in the antrum was the lowest. It is thought that the accuracy of normal findings in antrum was lowered because the antrum had a thicker mucosa compared to the body, making it impossible to observe RAC. Except for the endoscopy findings at the antrum, the diagnostic accuracy improves from 73.3% (33/45) to 82.8% (24/29).

Also, when comparing the results of chronic gastritis with serum pepsinogen, it was observed that PG I and PGI / PGII ratio was decreased as chronic gastritis progresses. This shows that endoscopic findings can predict the extent of chronic gastritis.

Meanwhile, it is well known that gastric cancer is highly associated with HP infection. However, a recent study showed that endoscopic findings suggesting HP infection are too diverse and less accurate.[9,10] However, the results analyzed only through MV pattern showed surprising accuracy compared with the previous studies.

This study has several limitations. First of all, it was not a comparative study with another image-enhanced endoscopy or a magnifying endoscopy. But this pilot study was fiound out the algorithm for classifying chronic gastritis according to MV can be applied to HR endoscopy that can be easily used in clinical practice. Second, the number of patients examined in this study was small and single-arm study. Because of the results observed by a single endoscopic physician in a single institution, it was difficult to predict whether the results are due to endoscopic image quality or endoscopist experience. Third, pathologic findings may also challenge accuracy, as determined by a single pathologist at a single institution, although based on the commonly used Sydney classification. Fourth, the CLO test, which is the basis for HP infection, is not 100% accurate.

Despite these limitations, the significance of this study was to establish a scoring system that classifies chronic gastritis with a simple algorithm called MV shape change, rather than various conventional classification methods. It was more accurate than the Kimura classification known to diagnose chronic gastritis. This is easier and more broadly applicable to clinical practice than many known methods.

Conclusions

The chronic gastritis classification algorithm through microvascular changes classified by RAC and SECN showed high accuracy in diagnosing chronic gastritis with HR endoscopy, although the accuracy of antrum's normal differentiation was somewhat inferior. What's more, it helps to differentiate HP infections.

Declarations

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Author contributions statement

WJ Ko: Principal investigator, who contributed to the drafting and critical revision of the manuscript for important intellectual content. B Cha: study design, acquisition of data, analysis and interpretation of data. HK Shin, H Shin, YS Park: study conception and design and to the acquisition, analysis, and interpretation of data. All authors reviewed the manuscript.

Competing interests statement

The authors declare that they have no competing interests.

References

1. Bray, F. *et al.* Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* **68**, 394-424 (2018).
2. Uemura, N. *et al.* Helicobacter pylori Infection and the Development of Gastric Cancer. *New England Journal of Medicine* **345**, 784-789 (2001).
3. Lee, H. Y., Park, E. C., Jun, J. K., Choi, K. S. & Hahm, M. I. Comparing upper gastrointestinal X-ray and endoscopy for gastric cancer diagnosis in Korea. *World J Gastroenterol* **16**, 245-250 (2010).
4. Lee, H. J., Yang, H. K. & Ahn, Y. O. Gastric cancer in Korea. *Gastric Cancer* **5**, 177-182 (2002).
5. Cho, S. J. *et al.* Staging of intestinal- and diffuse-type gastric cancers with the OLGA and OLGIM staging systems. *Aliment Pharmacol Ther* **38**, 1292-1302 (2013).
6. Quach, D. T. & Hiyama, T. Assessment of Endoscopic Gastric Atrophy according to the Kimura-Takemoto Classification and Its Potential Application in Daily Practice. *Clin Endosc* **52**, 321-327 (2019).
7. Dixon, M. F., Genta, R. M., Yardley, J. H. & Correa, P. Classification and grading of gastritis. The updated Sydney System. International Workshop on the Histopathology of Gastritis, Houston 1994. *Am J Surg Pathol* **20**, 1161-1181 (1996).
8. Yao K, O. T. Microgastroscopic findings of mucosal microvascular architecture as visualized by magnifying endoscopy. *Digestive Endoscopy* **13**, 1161-1181 (2001).
9. Alaboudy, A. A., Elbahrawy, A., Matsumoto, S. & Yoshizawa, A. Conventional Narrow-Band Imaging Has Good Correlation with Histopathological Severity of Helicobacter pylori Gastritis. *Digestive Diseases and Sciences* **56**, 1127-1130 (2011).
10. Anagnostopoulos, G. K. *et al.* High-resolution magnification endoscopy can reliably identify normal gastric mucosa, Helicobacter pylori-associated gastritis, and gastric atrophy. *Endoscopy* **39**, 202-207 (2007).

11. Tahara, T. *et al.* Gastric mucosal pattern by using magnifying narrow-band imaging endoscopy clearly distinguishes histological and serological severity of chronic gastritis. *Gastrointest Endosc* **70**, 246-253 (2009).
12. Esposito, G. *et al.* Endoscopic grading of gastric intestinal metaplasia (EGGIM): a multicenter validation study. *Endoscopy* **51**, 515-521 (2019).

Figures

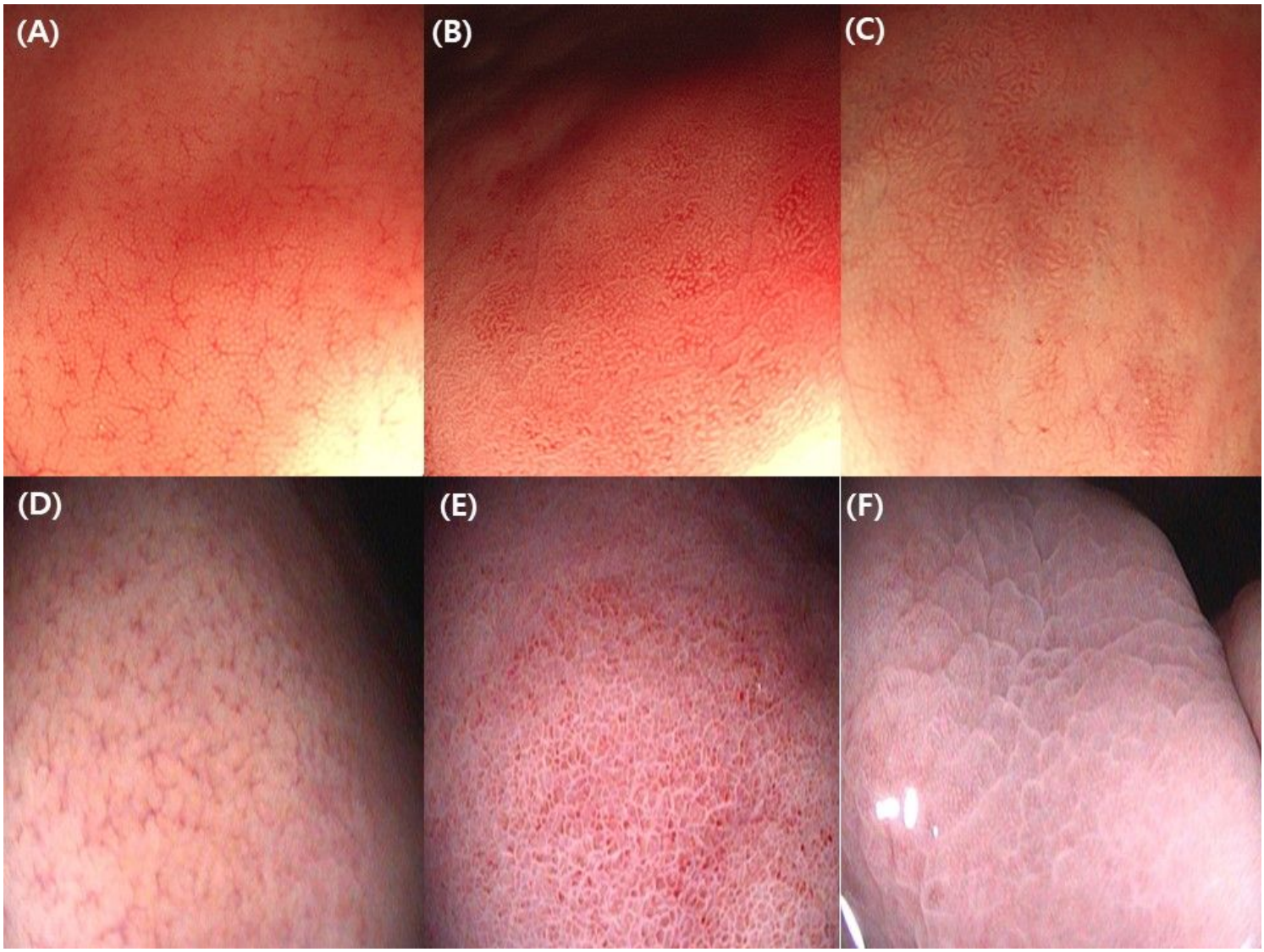

Figure 1

Chronic gastritis was classified according to microvascular patterns (A) Class I on Olympus system (B) Class II on Olympus system (C) Class III on Olympus system (D) Class I on Storz system (E) Class II on Storz system (F) Class III on Storz system