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• CLINICAL RESEARCH •

Endoscopic patterns of gastric mucosa and its clinicopathological significance

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Abstract

AIM: To explore the correlation of magnifying endoscopic patterns and histopathology, *Helicobacter pylori (H pylori)* infection of the gastric mucosa.

METHODS: Gastric mucosal patterns in 140 patients with chronic gastritis were studied using Olympus GIF-Q240Z magnifying endoscope. Histopathological examination, rapid urease test and Warrthin-Starry staining were taken with biopsy samples from the magnified sites of stomach. The magnifying endoscopic patterns were compared with histopathological results and *H pylori* detection.

RESULTS: The pit patterns of gastric mucosa were classified as types A (round spot), B (short rod), C (branched), D (reticular) and E (villus). The detection rate of chronic atrophic gastritis (CAG) by magnifying endoscopy was 94.3 % (33/35), which was significantly higher than that by routine endoscopy (22.9 %, 8/35) ($P<0.01$). The pit patterns of 31 cases of intestinal metaplasia (IM) appeared as type E in 18 cases (58.1 %), type D in 8 cases (25.8 %) and type C in 5 cases (16.1 %). Fourteen out of 18 patients (77.8 %) with complete type (type I) of IM appeared as type E of pit patterns, whereas only 4 of 13 (30.8 %) patients with incomplete type (types II and III) of IM appeared as type E ($P<0.05$). Collecting venules in the anterior of lower part of gastric corpus were subgrouped into types R (regular), I (irregular) and D (disappeared). *H pylori* infection was found in 12.2 %(9/74), 60 %(9/15) and 84.3 %(43/51) cases in these types respectively. *H pylori* infection rate in type R was significantly lower than that in other two types ($P<0.01$).

CONCLUSION: Magnifying endoscopy may have an obvious value in diagnosing chronic atrophic gastritis, intestinal metaplasia and *H pylori* infection.

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INTRODUCTION

Recently, magnifying endoscope has been used clinically for its developments in amplifying power, definition and operational capability. Lots of international studies on clinical application of magnifying endoscope especially from Japan have been reported, but most of them were focused on colon and esophagus, only a few of them on gastric mucosa have been published[1-28]. These studies implicate that classification of superficial mucosal appearances defined by magnifying endoscopy can reflect not only histological features but also mucin phenotypes. Magnifying endoscopy is helpful for more correctly distinguishing hyperplastic lesions from adenomatous and cancerous lesions, and for improving detection of early flat and depressed cancer. More interestingly, according to Japanese data, magnifying endoscopy could also be used to predict invasive depth and lymph node metastasis of cancer[6,16]. Up to now only a few studies on the field have been reported in China[29-33]. In this article, we reported our study on correlation of magnifying endoscopic patterns and histopathology, *Helicobacter pylori (H pylori)* infection of gastric mucosa in 140 patients with chronic gastritis to understand the value of magnifying endoscopy in diagnosing the minute lesions of gastric mucosa.

MATERIALS AND METHODS

Subjects

Subjects were 140 out-patients and in-patients (male: 68, female: 72, age range: 18-77 years old, average age: 50.6) with chronic superficial gastritis (CSG, $n=105$) and chronic atrophic gastritis (CAG, $n=35$) during June-August, 2002. All the patients had gastrointestinal symptoms such as abdominal distention, abdominalgia, belch and hyperhydrochloria.

Magnifying endoscope

New model of electronic magnifying endoscope GIF Q-240Z (Olympus Optical Co., Ltd., Tokyo, Japan) was used. It could be used to perform routine endoscopy (observation at standard magnification) as well as to magnify the image 80 times (in 14-inch monitor) as large as the original size through manual adjustment of the focal length.

Endoscopy

Magnifying endoscopy was performed by senior endoscopists and the real time static and successive images were recorded by computer image and text reporting system and video tape recorder. In order to inhibit gastrointestinal peristalsis, 10 mg of anisodaminum (654-2) and 5-10 mg of diazepamum were injected intramuscularly at 10 minutes pre-endoscopy. Routine endoscopy was performed first, and if necessary, dilution of dimethyl silicone oil was used to flush off the foam and mucus, then the appearance of gastric pits in the antrum, angel, corpus and fundus, and collecting venules in the anterior of lower part of gastric corpus were observed so that the patterns of gastric pits and collecting venules could be decided.

Histological examination

One piece of tissue in the greater curvature of gastric antrum was extracted for rapid urease test using RUT kit (Kedi Technology Co., LTD, Zhuhai, China). Two biopsies from the magnified sites in gastric antrum and corpus were performed for hematoxylin-eosin (HE) and Warrthin-Starry staining. Rapid urease test and Warrthin-Starry staining were used for

H pylori detection[34,35]. According to the national standard of China, *H pylori* infection was established after positive results were confirmed by both rapid urease test and Warrthin-Starry staining[35]. HE staining was performed for routine histopathological examination. Inflammatory levels were graded as mild, moderate and severe types according to the infiltration depth of <1/3, 1/3-2/3 and >2/3 of inflammatory cells in the mucous layer and CAG was graded as mild, moderate and severe types according to the decreased levels of <1/3, 1/3-2/3 and >2/3 of the intrinsic glands[35]. At the same time, mucus histochemical stainings of AB/PAS for distinguishing acid mucus from neutral mucus and AF/AB for distinguishing sulphomucins from sialomucins were performed on the samples with IM confirmed by histopathological examination. According to the histological structures and properties of mucus excreted by cells, IM was classified into type I (complete type), type II (incomplete small intestinal type) and type III (incomplete colonic type)[36].

Statistical analysis

Chi-square test was applied and *P* values less than 0.05 were considered significant.

RESULTS

Pit patterns and pathohistological findings

Classification of gastric pits Based on the analysis of recorded static and successive images and refered to Guelrud' s study on mucosal patterns of Barrett' s esophagus with enhanced magnification endoscopy[18], we classified gastric pits into the following five fundamental types: type A, round-spot-like, distributing only in the gastric corpus and fundus with basically normal histology; type B, short-rod-like, with deeper pits, branches and curvatures fewer than those in type C, mainly distributing in the gastric antrum without obvious lesions such as inflammation; type C, with elongated and tortuous pits with obviously increased branches and curvatures, connected to present branch-like form, seen in mucosa with pathological changes as inflammation, edema and IM; type D, with reticular pits, seen in areas with more severe inflammation, edema and IM, also found in mucosa around erosion and ulcers; and type E, with villus-like pits, or with finger-like tubers, similar to enteral villus-like changes, seen only in the areas with IM (Figure 1). Overlappings and crossings of gastric pits might be present except the above five fundamental patterns. For example, a combination of type A and type B of gastric pits was frequently presented in the gastric angle.

In types B, C, D and E, moderate and severe inflammations were seen in 18.6 %(26/140), 85.1 %(40/47), 100 %(13/13) and 88.9 %(16/18) cases respectively. The inflammatory levels in types C, D and E were significantly higher than those in type B ($P<0.01$).

Features of atrophic gastritis under magnifying endoscope Under routine endoscope, changes of rough mucosa, unflat granules, increased white areas, exposure of submucous vessels could be seen in CAG[35]. Generally, theses changes could be

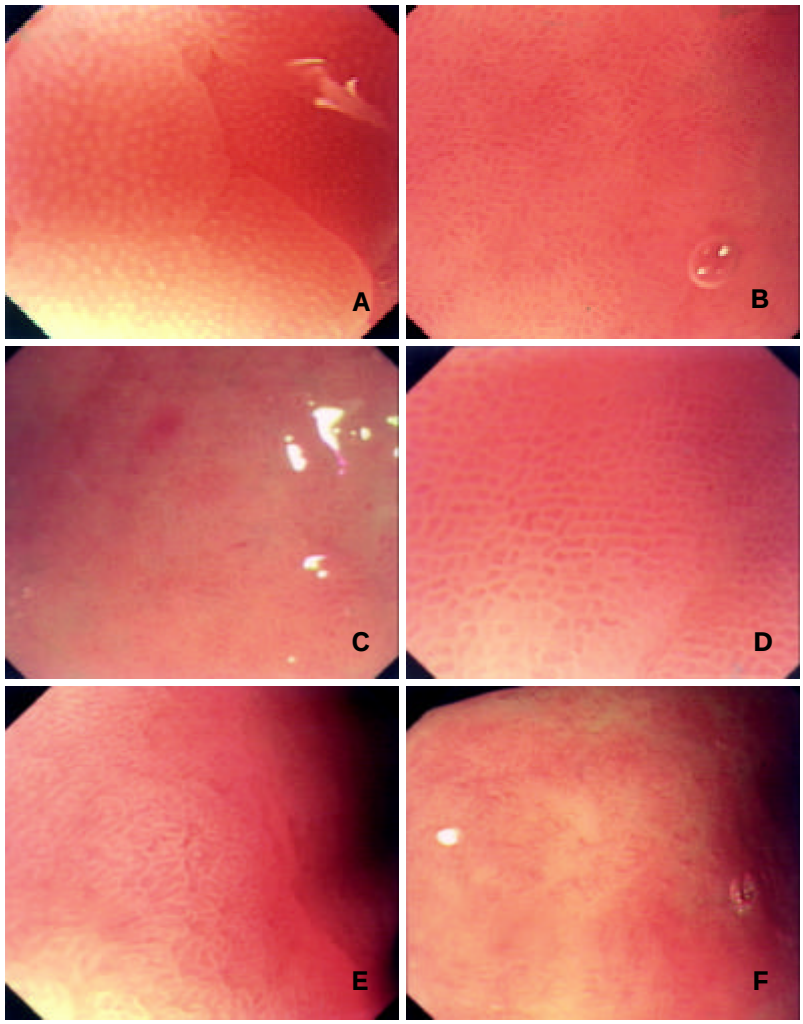

Figure 1 Pit patterns of gastric mucosa under magnifying endoscope. A: Type A: Gastric pits appeared as round spot, B: Type B: Gastric pits appeared as short rod, C: Type C: Gastric pits appeared as branched, D: Type D: Gastric pits appeared as reticular, E: Type E: Gastric pits appeared as villus, F: CAG: Decrease and disappearance of gastric pits.

more easily found in severe CAG, but it was hard to identify them in mild CAG. However, under magnifying endoscope, remarkably characteristic changes of CAG could be seen. With a comparatively low magnifying power, obvious red-white mucosa and increased white areas could be identified. When with enhanced magnifying power, disordered structures, decrease in quantity and even disappearance of pits as scar-like change could be observed in white areas (Figure 1-F).

Thirty-five patients with different grades of gastric mucous atrophy were confirmed by pathological examination in 140 patients, in which 27 in gastric antrum, 5 in gastric angle, 3 in gastric corpus, 16 with mild atrophy, 7 with moderate atrophy and 12 with severe atrophy. By routine endoscopy, only 8 patients (2 with moderate atrophy, 6 with severe atrophy), but by magnifying endoscopy, CAG-related changes were found in 33 patients (14 with mild atrophy, 7 with moderate atrophy, 12 with severe atrophy). The detection rates of atrophic gastritis by routine endoscopy and magnifying endoscopy were 22.9 %(8/35) and 94.3 %(33/35) respectively and significant difference was found by comparison of the two kinds of endoscopy (P<0.01).

Features of intestinal metaplasia under magnifying endoscope It was reported that characteristic changes such as light yellow or ivory-white nodosity-like, fishscale-like and diffusing granule-like appearances of IM in gastric mucosa could be found under routine endoscopy[37]. In this study, by analysis of magnifying endoscopy images of 31 patients with IM, we found that there were mainly three patterns of gastric pits in IM mucosal areas: type C (5 cases), type D (8cases) and type E (18cases). Particularly, very high specificity was found in type E. IM was confirmed pathologically in all the samples of 18 patients with type E. After classification of all the samples with IM by mucous histochemical staining, a certain relation was found between the patterns of gastric pits and classification of IM mucin phenotypes, as was shown in Table 1. Fourteen out of 18 patients (77.8 %) with complete type (type I) of IM appeared as type E of pit patterns, whereas only 4 of 13 (30.8 %) patients with incomplete type (types II and III) of IM appeared as the same type of pit patterns (P<0.05).

Table 1 Relation between IM pit patterns and IM mucin phenotypes

Pit patterns	Cases	Type I IM	Type II IM	Type III IM
Type C	5	2	3	0
Type D	8	2	5	1
Type E	18	14	3	1
Total	31	18	11	2

Architecture of collecting venules and H pylori infection

With reference to Yagi's literature[26], we classified the architecture of collecting venules into the following three types: type R (regular type) with diameter of minor venules being 0.4-0.5 mm and regular spider-like and jellyfish-like arrangement, type I (irregular type) in which decrease in quantity of collecting venules could be unclearly found with irregular arrangement, and type D (disappeared) in which collecting venules could not be found under magnifying endoscope (Figure 2).

When the patients in which positive *H pylori* was confirmed by both rapid urease test and Warrthin-Starry staining were regarded as being infected by *H pylori*, the *H pylori* infection rates in the patients with regular (R), irregular (I) and disappeared (D) types of collecting venules were 12.2 %, 60 % and 84.3 %, respectively. Statistical analysis revealed that *H pylori* infection rates in the patients with types D and I were markedly higher than those in patients with type R (P<0.01), but there was no significance between type I and type D (P>0.05). A comparison of different types of collecting venules by the corresponding rapid urease test and by Warrthin-Starry staining is shown in Table 2.

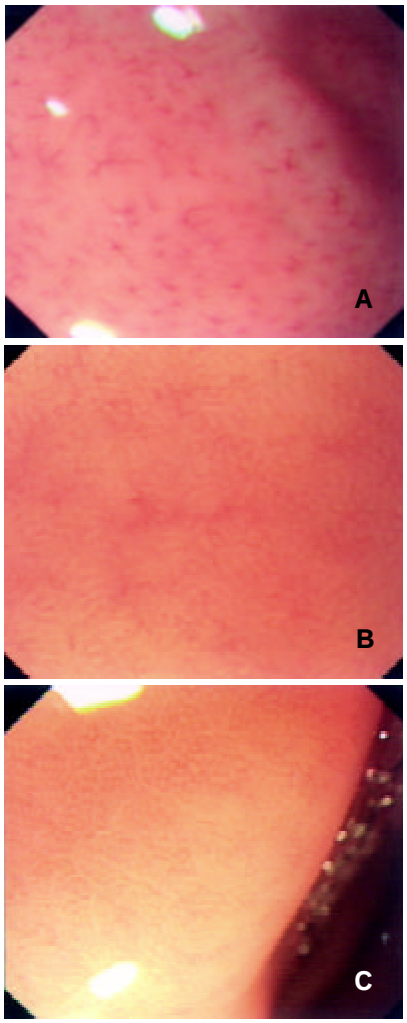

Figure 2 Architecture of collecting venules under magnifying endoscope. A: Type R: Regular spider-like arrangement of collecting venules, B: Type I: Unclear irregular arrangement of collecting venules, C: Type D: Disappearance of collecting venules.

Table 2 Relation of different architectures of collecting venules and *H pylori* infection

Collecting venules	Cases	Rapid urease test (+)	W-S staining (+)	Both methods(+)
Type R	74	9(12.2 %)	13(17.6 %)	9(12.2 %)
Type I	15	11(73.3 %)	9(60 %)	9 (60 %)
Type D	51	43(84.3 %)	45(86.3 %)	43(84.3 %)

DISCUSSION

The pit patterns observed on the mucosal surface are considered to reflect the arrangement and structure of surface epithelia, morphology, number, distribution, and function of glands, mucosal edema and inflammation, and vascular morphology, arrangement, number and distribution. The basic units of the microstructures on the surface of gastric mucosa are countless gastric pits that form gastric areas separated by minor gastric grooves (also called interval grooves). As the openings of glands, gastric pits are the first to have changes of the structures due to gastric mucosal lesions. Magnifying endoscope can be

used to observe the minute architecture of gastric pits because it has the similar magnifying power to that of stereomicroscope.

In this research, we studied the correlation of magnifying endoscopic patterns and histopathology, *Helicobacter pylori* infection of the gastric mucosa in 140 patients with chronic gastritis. There has been no widely accepted standard to the classification of gastric pits under magnifying endoscope, so the classification method, we used, was based on the analysis of our recorded static and successive images by magnifying endoscopy in the 140 patients and referred to Guelrud' s study on mucosal patterns of Barrett' s esophagus with enhanced magnification endoscopy[18]. Type A and type B represented the manifestation of normal gastric pits in gastric corpus and antrum, which concerned the distribution of gastric glands. Single tabular glands with short and fine neck were found in the gastric corpus and fundus, so gastric pits were presented with round spots as the openings of the gastric glands. Glands in frontal area of pyloric ostium and in gastric antrum were of multi-branches and curvatures and 3-5 glands often shared the same opening in one pit, thus the pits in frontal area of pyloric ostium and gastric antrum were short rod-like and deeper and longer than those of type A. Types C and D were formed by the enlargement, elongation, tortuosity of pits and connection of pits due to the pathological changes as inflammation and edema but type E might be the characteristic changes of intestinal metaplasia. Studies by Endo *et al.* of the mucosa with intestinal metaplasia in Barret esophagus in gastric cardia also revealed that villus-like pits were the characteristic change due to intestinal metaplasia[15].

Gastric mucosal atrophy could be identified by routine endoscopy usually when it was at more severe grade. Under magnifying endoscopy, disordered structures, deficiency and even disappearance of gastric pits were of high detection rate and accuracy for atrophic gastritis. As to mild and moderated grades of atrophy, the diagnostic sensitivity by magnifying endoscopy was higher than that by routine endoscopy. The decrease and disappearance of gastric pits due to atrophy were different from mucosal defect due to erosion in which there usually smooth-edged pits belonging to types C and D.

It was reported that characteristic changes such as light yellow or ivory-white nodosity-like, fishscale-like and diffusing granule-like appearances of intestinal metaplsia in gastric mucosa could be found under routine endoscopy[37]. The intestinal metaplasia could be classified into complete and incomplete types according to the histological structures and the properties of mucus excreted by cells[36]. In our study, the pit patterns of 31 patients with intestinal metaplasia appeared as type E in 18 (58.1 %), type D in 8 (25.8 %) and type C in 5 (16.1 %). Fourteen out of 18 patients (77.8 %) with complete type (type I) of intestinal metaplasia appeared as villus-like and finger-like changes (type E) of pit patterns, whereas only 4 out of 13 (30.8 %) patients with incomplete type (types II and III) of intestinal metaplasia appeared as the same type of pit patterns ($P<0.05$), suggesting type E of gastric pits was the result of characteristic change of complete intestinal metaplasia. In addition, our study also reveals that pits of incomplete intestinal metaplasia mainly belonged to types C and D (9/13, 69.2 %). Nevertheless, the above studies were still at preliminary stage with a small number of samples and further studies should be conducted to draw the final conclusion.

Collecting venules are tiny venules in gastric mucosa directly connected with capillary vessels. A few reports have been made on the architecture of collecting venules in gastric mucosa by magnifying endoscopy in which it was regarded as having certain specificity and feasibility to detect *Helicobacter pylori* infection[25,26]. It has also been verified by our study that *Helicobacter pylori* infection rate of patients with type R collecting venules was significantly lower than that with types I and D, suggesting that magnifying endoscopy was of high value in the diagnosis of *Helicobacter pylori* infection in gastric mucosa. As to the causes leading to the changes of collecting venules when *Helicobacter pylori* infection occurs, it has been reported that they were found in types I and D, in which remarkable increase of infiltration of neutrophils and monocytes was found and the architecture of collecting venules might be affected by edema of mucosa due to *Helicobacter pylori* infection[25,26]. However, further studies of the precise mechanism should be conducted because there are some other causes resulting in edema of mucosa.

In conclusion, it is a novel topic in the field of digestive endoscopy to diagnose minute lesions in gastric mucosa by magnifying endoscopy. Our preliminary study has shown that magnifying endoscopy is of high value in the diagnosis of gastric mucosal atrophy, intestinal metaplasia and *Helicobacter pylori* infection. However, the pit patterns of gastric mucosa, particularly those under magnifying chromoendoscopy are very complicated and there has been no widely accepted standard on the classification. Therefore, further studies are suggested on the clinicopathological significance of different patterns of gastric pits, particularly the characteristic changes of gastric pits and microvessels of intramucosal gastric carcinomas.

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