Endoscopic diagnosis of early gastric cancer and precancerous lesion

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ABSTRACT

BACKGROUND

Gastric carcinoma is one of the most common malignant tumors and is the second commonest reason of cancer deaths worldwide. It is very important to detect gastric cancer at the early stage or the precancerous lesion in stomach in order to improve the prognosis of gastric cancer. However, it is still a clinical challenge because of the lack of any tell-tale gross endoscopic signs. There has been great advancement about the technology of endoscopic imaging in recent years, and these new technologies may beneficial for diagnosis of early gastric cancer and precancerous lesions. This
retrospective study was designed to compare the accuracy and sensitivity of conventional endoscopy, magnifying chromoendoscopy and magnifying narrow-band imaging for diagnosis of precancerous lesions and early gastric cancer.

METHOD:
142 patients whom were diagnosed with early gastric cancer or precancerous gastric lesions by endoscopy were enrolled in a prospective study. (93 male and 49 female, age ranging from 16 to 94 years, average 63.5 years old). The patients were first given an examination with conventional endoscopy. After detecting a lesion, magnifying chromoendoscopy or magnifying NBI examination was followed on the same day or another day, biopsies were taken and were studied by a expert pathologist. Presence of gastric carcinoma and high grade intraepithelial neoplasia were considered as a positive result. The morphology, pit patterns and blood capillary forms of lesions were observed and recorded, Images resolution was evaluated.

RESULTS:
The images of magnifying NBI and magnifying chromoendoscopy were significantly superior to those of magnifying conventional endoscopy in respect of morphology, pit pattern and blood capillary form (P <0.01), and the images of magnifying NBI is significantly superior to magnifying chromoendoscopy in respect of blood capillary form (P <0.05). But there is no significant difference between magnifying NBI and magnifying chromoendoscopy with regard to morphology and pit pattern(P>0.05). In patients with high grade intraepithelial neoplasia, IV type of gastric pit pattern was detected in 14 cases, V_{1} type of gastric pit pattern was detected in 43 cases and VI type of gastric pit pattern was detected in 17 cases; while in patients with early gastric cancer, V_{1} type of gastric pit pattern was detected in 9 cases and VI type of gastric pit pattern was detected in 39 cases. Furthermore, the presence of irregular minute vessels and of variation in the caliber of vessels can be found in 109 cases.

CONCLUSION:
This study demonstrated that magnifying chromoendoscopy and magnifying NBI endoscopy are superior to conventional endoscopy for the detection of early gastric cancer or precancerous gastric lesions and they can be used for the screening of early malignancies of the stomach.

**Keywords:** magnifying chromoendoscopy, narrow-band imaging, conventional endoscopy, early gastric cancer, precancerous gastric lesion

**BACKGROUND**

Gastric carcinoma is one of the most common malignant tumor and is the second commonest reason of cancer deaths worldwide\(^1\). About 870000 new gastric cancer cases are diagnosed every year on a global scale. There is a geographical variation in its incidence\(^2\). It is reported that high incidence countries are located in eastern Asia, while Europe, North America and Africa are low incidence areas\(^1\). Chinese are in high-risk groups, about 30% new cases are found in China, just less than Korea and Japan\(^3\). The prognosis of gastric carcinoma is closely related to the stage of disease at diagnosis and treatment. For early gastric cancer, the survival rate is greater than 90% in 5 years\(^4\); while for advanced gastric cancer, the prognosis is very poor. It is very important for an excellent prognosis to diagnose gastric cancer in the early stage. However, most patients with early gastric carcinoma do not have specific symptoms, which made it difficult to distinguish early gastric carcinoma form benign peptic ulcer or gastritis, and only about 10-20% of gastric cancers are diagnosed as early cancers in many countries\(^3\). With the development of technology, some endoscopic imaging modalities, such as magnifying chromoendoscopy and narrow-band imaging (NBI) have been used recently for the diagnosis of early gastric cancer. Although many studies reported that these endoscopic imaging modalities can increase the rate of diagnosis of early cancers and pre-cancerous lesions by enhancing visualization\(^5\)\(^,\)\(^6\), there is less study about comparison between them. This retrospective study was designed to compare the accuracy and sensitivity of magnifying chromoendoscopy,
NBI with conventional endoscopy for diagnosis of precancerous lesions and early gastric cancer.

**MATERIALS AND METHODS**

**Patients**

This prospective study was performed in the Department of Gastroenterology, Dalian central hospital. During January 2008 to January 2011, a total of 122 patients whom were diagnosed with early gastric cancer or precancerous gastric lesions were enrolled in this prospective study. Among the 122 patients, 83 were males and 39 were females, ages ranging from 16 to 94 years, with a mean age of 63.5 ± 14.1 years. Early gastric cancer was defined as cancer confined to the mucosa or submucosa regardless of lymph node metastasis. In our study, Precancerous lesions refer to high grade intraepithelial neoplasia, with included intraepithelial carcinoma and severe dysplasia according to the Vienna classification of gastrointestinal epithelial neoplasms[7]. All the lesions were confirmed by pathologic diagnosis of endoscopic resection or post-surgery tissue. Exclusion criteria were pre-existing or advanced gastric cancer, recent upper gastrointestinal bleeding or coagulation disorders, and severe comorbidities that may affect tolerance to upper endoscopy. The presenting manifestations were abdominal pain in 88 cases (72.1%), distension in 52 cases (42.6%), heartburn in 60 cases (49.2%), belching in 28 cases (23.0%), acid regurgitation in 32 cases (26.2%), nausea in 29 cases (23.8%).

**Procedures**

The patients were first given careful observation in order to identify any abnormalities of the surface or the color with conventional endoscopy. After detecting lesions, magnifying chromoendoscopy or NBI magnifying endoscopy examination was followed on the same day or on another day. The morphology, pit pattern and blood capillary form of lesions were observed and recorded, biopsies were taken and studied by a same expert pathologist. This study was approved by the Medical Science’s ethics committee of Dalian central hospital, patients were informed of the possible risks and
benefits of participation in the study and written informed consent was obtained from all the patients or their relatives before their examination.

**Instruments**

The NBI main unit was an Olympus CV-260SL and the endoscope was an Olympus GIF-H260Z (80x) (Olympus Corporation, Japan); 1.2% iodine was used for staining (Micro-Tech, Nanjing, CO., LTD).

**Image evaluation**

The image quality of early gastric cancer and precancerous lesions were scored as follow: 1 point: obscure; 2 points: clouding; 3 points: more clear; and 4 points: clear\(^8\).

**Statistical analysis**

Data analysis was performed using SPSS 10.0 software (Chicago, IL, USA). Analysis of variance (ANOVA) or Wilcoxon statistical methods were used to determine statistical significance. All measurements in this study were expressed as mean ± SD. P < 0.05 was considered statistically significant.

**RESULTS**

A total of 122 cases were diagnosed as early gastric cancer or precancerous lesions by pathologic diagnosis of endoscopic resection or post-surgery tissue. The lesions were located in gastric antrum in 67 cases (54.9%), gastric angle in 29 cases (23.8%), gastric body in 22 cases (18.0%), cardia and gastric fundus in 4 cases (3.3%). The image quality of 3 modes were compared concerning the morphology, pit pattern and blood capillary form of early gastric cancer and precancerous lesions. We found that magnifying NBI and magnifying chromoendoscopy were significantly superior to magnifying conventional endoscopy in respect of morphology, pit pattern and blood capillary form (P <0.01), and magnifying NBI is significantly superior to magnifying chromoendoscopy in respect of blood capillary form (P <0.01). But there is no
significant difference between magnifying NBI and magnifying chromoendoscopy with regard to morphology and pit pattern (P >0.05) (Table 1).

The gastric pit pattern is classified into six types according to Sakaki\(^9\). In our studies, a total of 122 patients with early gastric cancer or precancerous gastric lesions were diagnosed, including 74 cases of high grade intraepithelial neoplasia and 48 cases of early gastric cancer. In patients with high grade intraepithelial neoplasia, IV type of gastric pit pattern was detected in 14 cases, V\(_1\) type of gastric pit pattern was detected in 43 cases and VI type of gastric pit pattern was detected in 17 cases; while in patients with early gastric cancer, V\(_1\) type of gastric pit pattern was detected in 9 cases and VI type of gastric pit pattern was detected in 39 cases.

We also observed blood capillary form of gastric lesions. The presence of irregular minute vessels and of variation in the caliber of vessels can be found in 109 cases.

**Discussion**

Gastric cancer is one of the main causes of cancer death in China. Most of these patients have poor prognosis because of late presentation and diagnosis. The best tactics for the dealing with gastric cancer is prevention, early detection and early treatment. It is generally believed that gastric cancer is a multi-step progression from chronic gastritis to gastric atrophy, intestinal metaplasia, dysplasia and cancer. EGC is defined as a cancer confined to the mucosa or submucosa regardless of lymph node metastasis\(^{10}\). If can be detected in early stage, the prognosis for gastric cancer is excellent, the survival rate is greater than 90% in 5 years, and curative endoscopic resection may be possible in some cases with early gastric cancer and precancerous gastric lesions, without the need for surgery. So it is necessary to mass screen for symptomatic groups in high-incidence areas, and endoscopy has been considered as one of the most useful tool for detecting ACG. However, at present, only about 4-10% of patients with gastric cancer are diagnosed as early cancer in our country, and the missed diagnosis of gastric cancer on endoscopy is a common occurrence. It is
reported that the false-negative rates are high up to 5-19%. There may be two reasons for this situation. One reason is that the symptoms of early gastric cancer are not specific and difficult to distinguish from those of gastritis and benign peptic ulcer disease. In our group, about 60-90% of patients with early gastric carcinoma have heartburn, abdominal pain and discomfort in the upper abdomen. Other reason is that some of the lesions are so subtle that they may be overlooked by inexperienced endoscopist. Lack of aware of EGC, they pay much attention to the detection of gross lesions, rather than tiny changes in colour, vascularity or texture, which are distinctive characteristics of early gastric cancer. There has been great advancement about the technology of endoscopic imaging in recent years, and these new technologies have improved the sensitivity in identifying EGC.

Dye spray chromoendoscopy can enhance the recognition of minute structure alteration caused by neoplastic changes, otherwise it is difficult to be perceived by conventional endoscopy. Magnifying endoscope (GIF-Q240Z) used in our study can provide magnified images up to x80. By this new magnifying endoscope, minute changes of gastric mucosal surface can be seen, such as color of lesions: same color as surrounding tissues, red or pale; the lesion is flat, elevated or depressed; presence of granules or nodules, with ulcer or without; with fold change or not; and so on. Irregular and destruction of the minute surface pattern and color change of mucosal surface were all considered as characteristics to precancerous gastric lesion or early gastric cancer. Magnifying chromoendoscopy is also useful in observing the surface mucosal pattern and capillary structure. By analyzing the surface structure pattern, histological changes of carcinoma, dysplasia, adenoma and hyperplasia might be suspected. Since histopathological examination of biopsy material is very important for the final diagnosis, accurate biopsy contributes to acquire the correct diagnosis of the lesion. Magnifying chromoendoscopy can improve the diagnosis of early gastric cancer and precancerous lesions in stomach by facilitating the identification and biopsy of abnormal areas. It is difficult in some cases to identify the margins of the lesions by conventional endoscopy, especially those of superficial or
flat-type lesions, magnifying chromoendoscopy has an advantage in coping with this difficulty \cite{16, 17}, we found in our group that magnifying chromoendoscopy were significantly superior to magnifying conventional endoscopy in respect of morphology, pit pattern and blood capillary form of abnormal areas.

Narrow-band imaging (NBI) is a new kind of endoscopic technology designed to increase enhance the contrast of the mucous membrane without staining. NBI uses special narrow-band filters which filters broad-band spectrum and only left a narrow-band spectrum for the diagnosis of digestive tract disease\cite{18-20}. NBI endoscopy significantly improves diagnostic accuracy in two ways. First, because the shorter wavelength light which was left by special narrow-band filter can not penetrate deeply into the mucosa, NBI improves visibility of mucosal pit pattern. Second, since the specific wavelength 415 nm left by special narrow-band filter is correspond to the peak absorption spectrum for hemoglobin\cite{21}. So magnifying the image with NBI can give important information about microvascular pattern\cite{22}.

In our study, we found that magnifying NBI is superior not only to magnifying conventional endoscopy, but also to magnifying chromoendoscopy concerning blood capillary form. Moreover, NBI has all the functions that conventional endoscopy has and the NBI and conventional endoscopy pattern can be easily switched just by pushing one button\cite{23, 24}.

Both NBI and chromoendoscopy can show the enhanced mucosal pattern and the microvascular structure of the mucosa by the amplificatory function\cite{25}, and mucosal pattern and microvascular structure have been regarded as distinctive characteristics of early gastric cancer and precancerous gastric lesions.

It has been known that angiogenesis is an important factor in gastrointestinal carcinogenesis\cite{26}, which means that the vascular of gastric cancer and precancerous gastric lesion is differ from that of normal mucosa\cite{27}, so observation of vascular pattern is contribute to diagnosis of such lesions\cite{28}. In our study, we found abnormal capillary patterns in 109 cases including tortuous minute vessels with irregular length and irregular arrangement, variation in the caliber of vessels or even
dilated microvessels with tortile tips.
Many studies have shown that gastric mucosa patterns of gastric cancer and precancerous gastric lesions are characteristic. Tanaka et al classified pit patterns of gastric mucosa into five types, and point out that differentiated tubular adenocarcinomas mainly showed the type IV, while poorly differentiated tubular adenocarcinomas mainly showed type V\[^{29}\]. Yoshida et al distinguished gastric cancer and precancerous gastric lesions from controls by analyzing the surface structure pattern\[^{30}\]. In our study, V\(_1\) and VI type of gastric pit pattern are the most common mucosa pattern of early gastric cancer and precancerous lesions. Therefore determination of pit pattern as well as microvascular architecture is very important for detecting early gastric cancer and precancerous lesion\[^{31}\].
In conclusion, magnifying chromoendoscopy and magnifying NBI have advantages in the detection of some lesions with minute changes of gastric mucosa pattern and capillary form and facilitate the diagnosis of early gastric cancer and precancerous gastric lesions by identification and biopsy of the lesions. Clearly, they can be used for the screening of early malignancies of the stomach.

**Competing interests**
The authors declare that they have no Competing interests.

**Author contributions**
Zhang J and Duan ZJ designed the experiment, Zhang J and Guo SB performed the experiments, analyzed the data and wrote the manuscript. Duan ZJ revised it.
Figure 1. Demonstration of gastric precancerous lesion with conventional endoscopy (A) and iodine staining pattern (B); Pit pattern of this precancerous lesion with magnifying chromoendoscopy (C) and Blood capillary form with magnifying NBI (D).
Table 1 Comparison of image quality among magnifying conventional endoscopy, magnifying NBI and magnifying chromoendoscopy

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a P magnifying NBI vs conventional endoscopy;
b P magnifying chromoendoscopy vs conventional endoscopy
c P magnifying NBI vs magnifying chromoendoscopy
Reference


compared with high-resolution magnification endoscopy in Barrett’s esophagus. Gastroenterology 2008; 134: 670-679. PMID: 18242603


