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ORIGINAL ARTICLE

Blue laser imaging with acetic acid enhancement improved the detection rate of gastric intestinal metaplasia

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Abstract
Our aim was to evaluate the ability of blue laser imaging (BLI) combined with acetic acid (BLI-AA) to detect gastric intestinal metaplasia (GIM). Participants undergoing gastroscopy from July 2017 to February 2018 in our hospital were enrolled prospectively. The abilities of white light imaging endoscopy, BLI endoscopy, and BLI-AA to detect GIM were compared. One hundred six patients undergoing gastroscopy met the inclusion criteria. GIM was diagnosed in 41 patients. For BLI-AA, the sensitivity, specificity, positive predictive, and negative predictive values were 85.4%, 84.6%, 77.8%, and 90.2% respectively. The diagnostic accuracy rate for BLI-AA was 84.9%, which was higher than that of white light imaging endoscopy and BLI endoscopy. For target biopsy, the GIM detection rate for the BLI-AA mode was significantly higher (77.8%, 105/135) than that for the BLI mode (58.3%, 84/144) or the white light endoscopy mode (40.4%, 57/141) ($p < 0.05$). BLI-AA is an efficient and simple method for the detection of GIM.

Keywords Acetic acid · Intestinal metaplasia · Blue laser imaging · Detection

Introduction

Gastric intestinal metaplasia (GIM) is considered to be associated with an increased risk for gastric cancer [1, 2]. The screening of populations with GIM may improve early detection of gastric cancer [3, 4]. The most common method to detect GIM is a biopsy-based method. In this method, the extent of GIM is assessed on the basis of five standardized biopsies, according to the updated Sydney System [5]. GIM is usually present as multiple flat lesions that are indistinguishable in color and is not easily detectable by white light endoscopy (WLE). Thus, several real-time methods were developed to increase the detection rate of GIM [6–8]. The diagnostic accuracy rates for those techniques, however, were variable. Moreover, these techniques are difficult to perform in clinical settings and systematic training for operators is required [9]. Therefore, there is a need for a simple technique with a high diagnostic accuracy rate in clinical practice.

Recently, a new IEE endoscope system was developed by FUJI FILM Corporation (Tokyo, Japan), namely the LASEREO endoscope system. This system, which enables high-definition endoscopy imaging contains two kinds of laser that allow narrow-band observation: a 450-nm wavelength laser for white light imaging and a 410-nm wavelength laser for blue laser imaging (BLI) [10]. Previous studies reported that the LASEREO endoscope system had a high detection rate of esophageal and gastric lesions and produced high-quality images [11, 12]. Our previous study showed that magnifying endoscopy with BLI can detect GIM easily through the light blue crest [13]. However, magnifying endoscopes, either with narrow-band imaging (NBI) or BLI, have not been used extensively.

Previous studies demonstrated that acetic acid-enhanced WLE and narrow-band imaging with magnifying endoscopes

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(NBI-ME) endoscopy increased the detection rate of GIM [14, 15]. Acetic acid reversibly denatures intracellular cytoplasmic proteins by destroying the disulfide bonds of glycoproteins [16]. Thus, acetic acid can enhance the mucosal architecture and pit-pattern of the columnar epithelium [17]. Currently, no studies have examined the effect of combined use of acetic acid and BLI on the detection of GIM. Therefore, in this study, we evaluated the efficacy of BLI combined with acetic acid (BLI-AA) in identifying GIM.

Methods

Subjects and ethics

Study subjects were between 40 and 75 years of age, without previous stomach surgeries, advanced gastric cancer, and digestive tract bleeding. We also excluded those who received anticoagulant, antiplatelet, or non-steroidal anti-inflammatory therapy. A total of 106 participants, who underwent gastroscopy at the Sixth Affiliated Hospital of Sun Yat-sen University from July 2017 to February 2018, were included in the study. Written informed consent was obtained from all participants. This study, which was approved by the Ethics Committee of the Sixth Affiliated Hospital of Sun Yat-sen University, was registered in the Chinese Clinical Trial Registry (ChiCTR-DDD-17011370) and conducted following the Declaration of Helsinki.

Study protocol and endoscopic procedure

In this study, characteristics of participants such as age, sex, and clinicopathological data were retrieved from the computerized database of our center. Midazolam was used for conscious sedation in all participants. All examinations were performed by experienced endoscopists, who have experience with over 500 procedures, using the LASEREO system and the EG-L590ZW endoscopes (FUJIFILM, Japan). LASEREO system have four types of light modes: white light imaging mode, link color imaging mode, blue laser imaging (BLI) mode, and blue laser imaging mode with bright enhancement (BLI-bri). White light is produced by an approximately 450-nm laser, exciting solids which then emit white light. On the other hand, the blue laser is at 410 nm. BLI-bri mode is designed for a brighter BLI image. These modes can be easily and instantly switched by pressing a button on the handle of the scope. Due to the effect of acetic acid on the gastric mucosa usually lasting from several seconds to several minutes, we chose to observe the gastric antrum. The gastric antrum was observed carefully by WLE, BLI, and BLI-AA endoscopy in turns by a single procedure and typical images were recorded. Firstly, the gastric antrum was carefully examined using WLE. Since no standard criteria have been established for the detection of GIM by WLE, any abnormal mucosal changes, such as rough mucosal surface and localized discoloration, were considered as a suspicious lesion (Fig. 1a). Then, the endoscopy was switched to BLI mode, where blue whitish patchy lesions, flat or depressed, with a regular mucosal pattern were defined as a suspicious lesion (Fig. 1b). The antrum was sprayed with 0.6% acetic acid through the scope after BLI observation. Several seconds later, the bright, almost-white patches appeared, and these patches were defined as a suspicious GIM lesion (Fig. 1d). Suspicious lesions were recorded by an assistant, and biopsies were taken from the suspicious lesions for the records. If no lesion was detected by WLE, BLI, or BLI-AA, three randomized biopsies were taken.

Histological analysis

The biopsy specimens were fixed in formalin and embedded in paraffin. Two experienced pathologists performed blind analysis of the histological sections and classified GIM into three grades (mild, moderate, and marked), following the modified Vienna criteria for neoplasia and the updated Sydney Classification for chronic gastritis. Each GIM was indicated by the percentage of metaplastic glands present in a given mucosal specimen (Fig. 1c). We also evaluated the *Helicobacter pylori* state based on immunohistochemistry staining.

Statistical analysis

The ability of different endoscopy modes to detect GIM was evaluated based on various parameters, including sensitivity values, specificity values, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy rate. If more than one lesion was present in a single participant, it was counted as a case. The detection accuracy of different endoscopy modes was evaluated per-biopsy, and the most precancerous lesion was considered for final statistics. The chi-squared test was used to compare the diagnostic accuracy between the groups, including WLE versus BLI-AA and BLI versus BLI-AA, using IBM SPSS software (version 22.0). A p value of < 0.05 was considered to be statistically significant.

Results

Subjects

Table 1 shows the characteristics of 106 patients who participated in the current study.

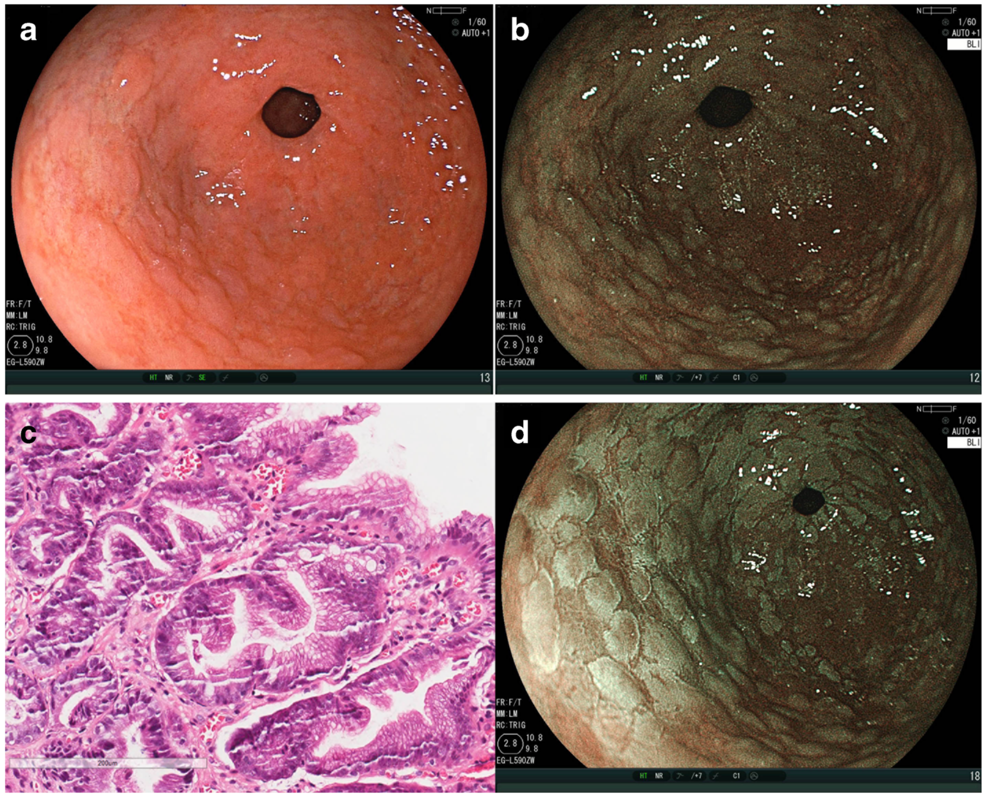

Fig. 1 Appearance of intestinal metaplasia lesions under three different endoscopic modes. **a** Lesions as ash-colored nodular changes under WLE mode. **b** Lesions exhibit as bluish-whitish areas under BLI mode. **c** Targeted biopsy shows intestinal metaplasia of the stomach (H&E, × 200). **d** Lesions as bright whitish patches under BLI-AA mode

Per-participant analysis

The prevalence of GIM in the study subjects was 38.7% (41/106). The WLE endoscopy identified lesions suspected as GIM in 57 participants, while only 17 participants were diagnosed to have GIM by histological analysis. The BLI endoscopy detected GIM in 48 participants, 28 of which were confirmed by histological analysis. Forty-five cases of GIM were diagnosed using BLI-AA, with 35 of those being histologically confirmed to have the condition. Three participants (2.8%) from which randomized biopsies were performed were suspected to have GIM based on histological examination. The sensitivity, specificity, PPV, NPV, and detection accuracy rate of WLE, BLI, and BLI-AA are summarized in Table 2.

Table 1 Characteristics of participants

Characteristic	Participants
Age, mean (SD)	50 (6.5)
Gender	
Male	56
Female	50
H. pylori infection	
Positive	33
Negative	73
Smoking	
Non-smoker	72
Current smoker	21
Former smoker	13
Alcohol	
Non-drinker	76
Current drinker	30
PPI users	
Yes	29
No	77

SD standard deviation

Per-lesion analysis

For WLE, a total of 141 targeted specimens were obtained and only 57 of those presented with GIM based on histological analysis. For BLI, a total of 144 targeted biopsies were taken, and histological analysis confirmed the presence of GIM in 84 specimens. For BLI-AA, we obtained 135 biopsies, and GIM was histologically observed in 105 specimens. Combined, the GIM detection rate for the BLI-AA mode was significantly higher (77.8%, 105/135) than that for the BLI mode (58.3%, 84/144) or the WLE mode (40.4%, 57/141) ($p < 0.05$).

Discussion

Gastric cancer is thought to arise in multiple steps, from chronic non-atrophic gastritis, atrophic gastritis, and GIM to

Table 2 Diagnostic accuracy of endoscopy in participants with GIM by WLE, BLI, and BLI-AA

GIM	Sensitivity	Specificity	PPV	NPV	Accuracy
WLE	41.5% (17/41)*	38.5 (25/65)*	29.8 (17/57)*	51.0 (25/49)*	39.6 (42/106)*
BLI	68.3% (28/41)	69.2% (45/65) **	58.3% (28/48) **	77.6% (45/58)	68.9% (73/106)**
BLI-AA	85.4% (35/41)	84.6% (55/65)	77.8% (35/45)	90.2% (55/61)	84.9% (90/106)

PPV positive predictive value, *NPV* negative predictive value

*WLE versus BLI-AA: $p < 0.05$; **BLI versus BLI-AA: $p < 0.05$

dysplasia and, finally, invasive carcinoma. GIM is commonly identified by endoscopy, and, usually, it initially appears in the antrum [18]. Because of the short-durational presence of bright white patches after treatment with acetic acid (usually several seconds to several minutes), we focused our examination on the gastric antrum.

Our results indicate that the ability of BLI-AA to detect GIM is the highest, with the sensitivity of 80.4%, the specificity of 90.9%, the PPV of 89.1%, the NPV of 83.3%, and the diagnostic accuracy rate of 85.8%. These values are higher than those for WLE and BLI (Table 2). The prevalence of GIM in the study subjects was 38.7%, which is consistent with that from previous studies conducted in China (16.79–38.56%) [19]. These results indicate that BLI-AA can detect GIM without a selection bias. Acetic acid is the major component of vinegar, which is available worldwide; it is inexpensive and can be easily applied in the endoscopy route. Therefore, BLI-AA can be used as a practical technique for the detection of GIM. In this study, we identified five cases of GIM using BLI-AA that were missed by BLI. This result indicates that BLI-AA has an improved ability to detect GIM compared to BLI alone.

Previously, Song et al. demonstrated that acetic acid could increase the diagnostic accuracy rate and determine the extent of GIM in white light endoscopy [14]. In addition, Sha et al. reported that acetic acid-enhanced NBI also improved GIM detection accuracy [15]. In our study, we found that acetic acid could improve the detection of GIM in endoscopy-targeted biopsies by BLI, which is consistent with the previous results obtained from WLE and NBI endoscopy.

Notably, there are some limitations to this study. Firstly, this study was conducted at a single center and only the gastric antrum was observed for analysis. Therefore, misdiagnosis of GIM may have taken place. Further studies from multiple centers and for other areas of the stomach are needed to verify the results of our study. Secondly, given that the subjects were examined using WLE, BLI, and BLI-AA by an identical endoscopist, the observations made may be biased. Thirdly, the relationship between the bright white patches and the GIM grade was unclear. Finally, we only included participants aged between 40 and 75 years in our study, and therefore, it may be necessary to expand our study to those younger than 40 years.

In summary, BLI-AA provides improvements in the ability of endoscopy to detect GIM. BLI-AA represents an easily operable and useful method for detection of GIM in routine clinical practice.

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Compliance with ethical standards

Written informed consent was obtained from all participants. This study, which was approved by the Ethics Committee of the Sixth Affiliated Hospital of Sun Yat-sen University, was registered in the Chinese Clinical Trial Registry (ChiCTR-DDD-17011370) and conducted following the Declaration of Helsinki.

Conflict of interest Honglei Chen has received funding from Guangdong province medical science and technology research fund project (grant number: A2017273). For the remaining authors, none were declared.

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