



Acetic acid chromoendoscopy for determining the extent of gastric intestinal metaplasia CME

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Background and Aims: The diagnosis of gastric intestinal metaplasia (IM) is currently performed by histologic assessment of multiple endoscopic biopsies, methylene blue chromoendoscopy, or narrow-band imaging with magnification. However, practical and readily available methods are lacking. We assessed the diagnostic accuracy and reproducibility of acetic acid chromoendoscopy (AAC) for determining the extent of gastric IM.

Methods: One hundred twenty-six participants were enrolled. The participants underwent screening EGD with 1.5% acetic acid instillation for the detection of acetowhite reaction. Subsequently, targeted biopsies were performed at the 5 standard intra-gastric locations of the updated Sydney system. The accuracy of AAC was calculated using the histology results as a reference. Two endoscopists, each of whom was blinded to the other's result, determined the presence or absence of acetowhite reaction.

Results: The overall diagnostic accuracy of AAC was 89.0%, and the sensitivity and specificity were 77.6% and 94.4%, respectively. The specificity for the gastric body was >94%. The proportion of extensive IM, a strong risk factor for gastric cancer, increased from 0.9% to 18.1% when AAC was used instead of conventional EGD alone ($P < .001$). Endoscopically determined atrophy had a negative effect on the diagnosis of AAC (odds ratio, 3.012; 95% confidence interval, 1.625-5.583). There was substantial inter- and intra-observer agreement.

Conclusions: AAC is a valid and reproducible tool for determining the extent of gastric IM and may serve as a practical method of identifying populations at high risk of gastric cancer. (Clinical trial registration number: NCT01499576.) (Gastrointest Endosc 2017;85:349-56.)

INTRODUCTION

Gastric intestinal metaplasia (IM) is considered a premalignant lesion for gastric cancer of either the intestinal or diffuse type.^{1,2} IM has been considered as the point of no return, even after *Helicobacter pylori* eradication therapy, and poses an important step in the precancerous cascade of gastric adenocarcinoma. Identification of individuals with gastric IM is important for the early detection

of candidates for regular screening or those at high risk of gastric cancer, and the development of a mass screening strategy.^{1,2} The relative risk of gastric cancer is about 10- to 20-fold higher if the patient has gastric IM.^{3,4} Although the presence of gastric IM has a somewhat significant clinical impact, the topological extent of the metaplastic area enables discrimination of patients at higher risk. In a cross-sectional study,⁵ IM progression was more frequent in patients with more extensive IM at baseline. Moreover,

Abbreviations: AAC, acetic acid chromoendoscopy; EGD, esophagogastroduodenoscopy; IM, intestinal metaplasia; NBI, narrow-band imaging.

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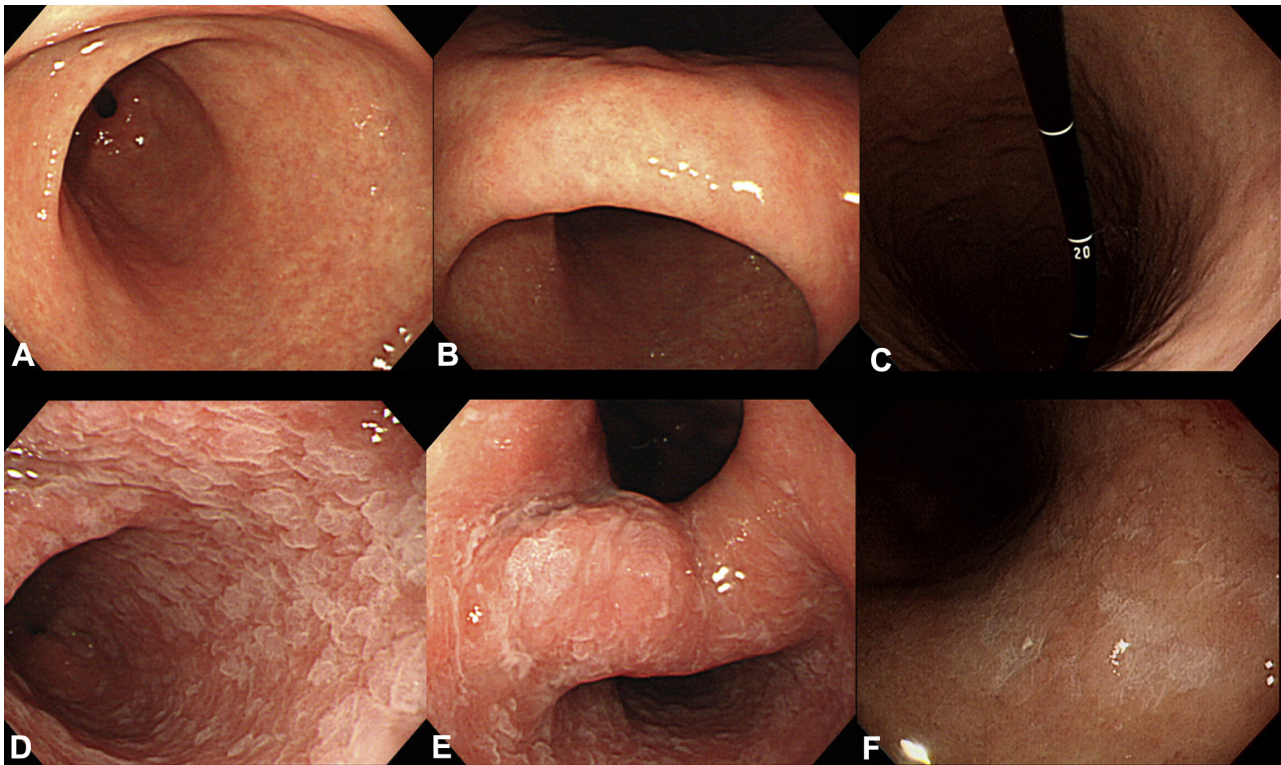


Figure 1. A representative acetowhite reaction for the diagnosis of intra-gastric IM after instillation of 1.5% acetic acid. **A, B, C,** Before acetic acid instillation, conventional EGD did not detect intragastric IM. Negative for IM by conventional EGD. **D, E, F,** After spraying acetic acid, the gastric mucosal surface shows multiple whitish patches, which is known as the acetowhite reaction. The patches are present in the antrum, angle, and lesser curvature of the gastric corpus. Therefore, the topological extent was rated as Magenstraße type. *IM*, intestinal metaplasia.

if the extent of IM involved the lesser curvature side of the gastric corpus over the antrum (Magenstraße type), the odds ratio (OR) of concomitant gastric cancer was 5.7 compared with topological patterns predominantly involving a focal area or the antrum, both of which are associated with an above-average risk. The risk was increased 12.2-fold if IM involved the greater curvature side of the gastric corpus (diffuse type). Therefore, when physicians encounter extensive IM involving the gastric corpus, regular surveillance is warranted. However, conventional endoscopy shows poor inter-observer agreement and very low sensitivity for detection of gastric IM.⁶ Thus, with the exception of a typical whitish patch, conventional white-light endoscopy is ineffective for its diagnosis, and conventional EGD alone also cannot be used to determine the topological extent of IM and efficiently discriminate extensive IM.

Currently, biopsy is the main modality used to assess intra-gastric IM.⁷ The updated Sydney system suggests 5 standard biopsy loci for assessing the extent of IM for screening purposes: A1, the lesser curvature of the antrum within 2 to 3 cm of the pylorus; A2, the greater curvature of the antrum within 2 to 3 cm of the pylorus; IA, the incisura angularis; B1, the lesser curvature of the corpus about 4 cm proximal to the angularis; and B2, the middle portion of the greater curvature of the corpus,

approximately 8 cm from the cardia.⁷ However, due to its workload, several real-time or minimally invasive alternative methods have been used to enhance the accuracy of gastric IM diagnosis and to determine its distribution such as methylene blue chromoendoscopy, index biopsy with pepsinogen I/II ratio,⁸ and narrow-band imaging (NBI) with magnifying endoscopy.⁶ Although these techniques are useful for identification of IM, they are not widely used in clinical practice because of lack of availability or high cost. Thus, practical and readily available methods are lacking.

Acetic acid chromoendoscopy (AAC) has not been investigated for this purpose. Acetic acid, the main component of vinegar, is a weak acid and can modify the optical properties of the epithelium by slightly altering the pH or by reversibly altering the structure of cellular proteins.⁹ After application of acetic acid, white light is reflected from the mucosal surface. This is known as the acetowhite reaction, which is prominent in the columnar epithelium, and is mainly used in screening for uterine cervical epithelial neoplasia. In gastroenterology, it is used to explore the esophagogastric junction to analyze columnar metaplasia in Barrett esophagus.¹⁰ We sought to validate the diagnostic accuracy of AAC for determining the extent of gastric IM using endoscopic biopsy as a reference. We also investigated the reproducibility of this new method by determining the intra- and inter-observer variability.

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