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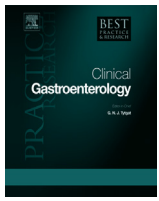

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Advanced endoscopic imaging for early gastric cancer

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A B S T R A C T

Considerable numbers of early gastric cancers can be missed or misdiagnosed with conventional white light imaging endoscopy (WLI), thus advanced endoscopic imaging modalities have been applied to overcome the issue. High definition endoscopy can improve diagnostic accuracy, but still misses 20–25% of early gastric cancer. Magnifying endoscopy combined with narrow band imaging (NBI) allows for very high accuracy, with sensitivity and specificity of over 95%. The algorithm for magnifying endoscopy diagnosis of gastric cancer is composed of 1) presence of demarcation line, and 2) presence of irregular microsurface and/or microvascular pattern. Ultra-high magnification of 400 times with endocytoscopy (ECS) can produce images reflecting structural and cellular atypia. Using high grade ECS atypia as the diagnostic criteria for gastric cancer, ECS achieves a high diagnostic accuracy (86% of sensitivity, 100% of specificity) although approximately 10% of target lesions are not assessable because of poor dye staining.

Introduction

Gastric cancer is the fifth most common malignancy in both sexes and is the third leading cause of cancer deaths in both sexes worldwide [1]. In 2012, approximately 723,000 people died of gastric cancer worldwide, accounting for 8.8% of the total cancer death. To decrease gastric cancer death rate, primary and secondary prevention are required to reduce *Helicobacter pylori (H. pylori)* infection, the

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main cause of gastric cancer. The other major strategy is early detection of curable gastric cancer in dyspeptic patients or in a high risk population selected by efficacious serological screening tests, such as *H. pylori* antibody, pepsinogen testing and serum trefoil factors [2–4]. Endoscopy is exclusively used for early diagnosis of gastric cancer because of a high detection rate [5]. Despite promising data, the technique depends heavily on observational skill and a considerable % of early gastric cancer may be missed by conventional white light imaging endoscopy (WLI) [6,7]. Therefore, various endoscopic modalities have been newly developed to enhance the value of endoscopy in effective gastric cancer diagnosis. High definition endoscopy and image-enhanced endoscopy [8] including narrow band imaging (NBI) [9] are the key modalities, which are commercially available for an advanced endoscopy imaging in early gastric cancer. The next stage is real-time endoscopic assessment of histology (optical biopsy) by endocytoscopy (ECS) [10,11] and confocal microendoscopy [12].

High definition endoscopy; it improves the detection and diagnosis of early gastric cancer

Although upper gastrointestinal endoscopy is more accurate than nonendoscopic modalities including integrated positron emission tomography [13] and barium meal examination, considerable numbers of superficial gastric cancers may be missed or misdiagnosed with conventional white light imaging endoscopy (WLI). High definition endoscopy (HDE) has been developed to improve the image quality and diagnostic accuracy of WLI.

To elucidate the potential of HDE, we prospectively compared ultrathin endoscopy (UTE) to HDE with respect to diagnostic accuracy of superficial gastric neoplasia [13]. A total of 57 patients were enrolled; 32 patients with early gastric neoplasia referred for endoscopic submucosal dissection (ESD), and 25 patients who underwent surveillance endoscopy after ESD. Patients with obvious advanced gastric carcinomas or cancerous lesions with deep invasion to the gastric submucosa were excluded. Each patient underwent UTE (GIF-XP260N; Olympus Medical Systems, Tokyo, Japan) and HDE (GIF-H260Z; Olympus Medical Systems, Tokyo, Japan) back-to-back in a randomized order. UTE and HDE were independently performed by two different endoscopists, who did not have access to any of the patient's clinical information. The endoscopists recorded the diagnosis of neoplastic lesions as well as nonneoplastic lesions including gastric ulcers or gastric polyps. All lesions recorded were biopsied by the second endoscopist under the supervision of the study coordinator, who attended all endoscopic examinations and was aware of the diagnosis given by the two endoscopists. The pathology results from the biopsy samples were used as a gold standard for the diagnosis of gastric cancer. In 57 enrolled patients, 41 lesions (16.5 ± 13.5 mm in diameter, mean ± SD) were pathologically diagnosed as neoplasias (27 carcinomas and 14 adenomas). Eleven of the 41 pathology-confirmed neoplasias were not detected by UTE, and three were diagnosed as nonneoplasias, indicating that the missing rate and misdiagnosis rate of UTE were 26.8%, and 14.6%, respectively. In contrast, five of the 41 pathology-confirmed neoplasias were not detected by HDE, and four were diagnosed as nonneoplasia by HDE, indicating that the miss rate and misdiagnosis rate of HDE were 12.2%, and 9.8%, respectively. Representative neoplastic lesions missed by UTE but correctly diagnosed by HDE are shown in Fig. 1.

Although UTE has emerged as an alternative to sedated endoscopy because it is well tolerated without sedation and costs less [14], our study demonstrates that the diagnostic accuracy of HDE is significantly higher than that of UTE for superficial gastric neoplasia, probably due to the differences in imaging quality. We need guidelines for selecting HDE or UTE in different clinical settings, recognizing the differences in the diagnostic accuracy and acknowledging the cost-effectiveness of unsedated screening endoscopy.

Autofluorescence endoscopy has limited clinical value in the diagnosis of early gastric cancer

Although HDE improves diagnostic accuracy of WLI, considerable rates over 20% of superficial gastric neoplasias are still missed or misdiagnosed. Image-enhanced endoscopy, including autofluorescence endoscopy (AFE) and narrow band imaging (NBI), has emerged in the effort to overcome the limits of WLI. There has been considerable interest in the use of AFE for the detection of early digestive neoplasias, and the diagnostic relevance of the modality has been demonstrated for the detection of early neoplasias in the esophagus [15] and colon [16,17].