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Review Article

Early detection of early gastric cancer using image-enhanced endoscopy: Current trends

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A B S T R A C T

Image-enhanced endoscopy refers to techniques of enhancing mucosa surface contrast with the ultimate aim of improving lesion detection and diagnosis. It is vital to detect early gastric cancer as it may be possible to perform curative endoscopic resection. In this topic review, we summarize the options available, such as the traditional dye-based chromoendoscopy, as well as the newer equipment-based techniques such as narrow-band imaging, flexible spectral imaging color enhancement, and i-scan. We further discuss in greater detail the technique of narrow-band imaging combined with magnifying endoscopy, and how this has facilitated lesion characterization and diagnosis based on characteristic abnormal microvascular and microsurface features. Other endoscopic imaging modalities such as autofluorescence imaging and endoscopic microscopy are also briefly discussed.

Keywords: Early gastric cancer, Gastroscopy, Narrow band imaging, Magnifying endoscopy

Introduction

Globally, gastric cancer is the fourth most common cancer in men, the fifth most common cancer in women, and the second leading cause of death due to cancer. About 10% of annual cancer deaths worldwide are attributed to gastric cancer, which means that gastric cancer has a high fatality to case ratio of about 70%.[1] The highest incidence rates for gastric cancer occur in East Asia (China, Mongolia, Korea, and Japan).[2,3] Gastric cancer is histologically divided into two types in the Lauren classification: intestinal (with intercellular junctions) and diffuse (without intercellular junctions).[4] More than 90% of gastric cancers are intestinal-type adenocarcinoma, which is believed to be preceded by a "precancerous cascade," progressing in a sequential manner from chronic gastritis, atrophic gastritis, intestinal metaplasia, and adenoma to early gastric cancer (EGC).[5]

The overall prognosis of gastric cancer is dismal; the average 5-year survival rate is less than 20% and EGC are often clinically silent. However, if the cancer is detected and endoscopically resected prior to invasion into the muscularis propria occurs, the 5-year survival rate can reach 90%.[6] EGC, a term defined by Japanese researchers in 1962, is meant to denote the curable phase of the disease when cancer cells are confined within the mucosal or submucosal layer (T1 cancer) regardless of the presence of lymph node metastasis.[7] Endoscopic resection using the endoscopic mucosal resection (EMR) technique or endoscopic submucosal dissection (ESD) is potentially curative for the patient if there is no nodal metastasis, and can avoid the morbidity associated with gastrectomy. Candidates for EMR are patients with EGC that is differentiated adenocarcinoma, is less than 2 cm, has no ulceration, and has no lymphovascular involvement.[8] Gotoda et al[9] reviewed surgical pathological data and found that differentiated cancers less than 3 cm in diameter and undifferentiated cancers less than 2 cm in diameter had negligible nodal metastasis. Submucosal cancers that were differentiated, were less than 3 cm in diameter, and invaded less than 500 μm into the submucosal were also free of nodal metastasis.[9] Another large study involving 5265 patients found similar results and proposed that endoscopic resection should be considered for undifferentiated intramucosal cancers, which are less than 2 cm in diameter and has no ulcerative findings or lymphovascular involvement, as the risk of lymph node metastasis was negligible.[10] This led to expanded criteria for endoscopic resection. *En bloc* resection is crucial for accurate histopathological assessment and, in the context of lesions larger than 2 cm or in the presence of fibrosis or ulceration, ESD rather than EMR would be the technique of choice.

Thus, the early detection of EGC is important. However, the sensitivity of conventional white light imaging (C-WLI) in detecting EGC had been reported to range only from 77% to 84%.[11] Image-enhanced endoscopy (IEE) involves the use of dyes, optical methods (by manipulation of the light source), and electronic methods (by manipulation of captured light), to increase the contrast of surface structure, and thus improve visualization and diagnostic accuracy. There are three different commercially available systems for equipment-based IEE: (1) narrow-band imaging (NBI; Olympus Corporation, Tokyo, Japan); (2) flexible spectral

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imaging color enhancement (FICE; Fujifilm, Tokyo, Japan); and (3) i-scan (Pentax, Tokyo, Japan). IEE can be combined with magnifying endoscopy to further characterize focal lesions. This review will focus on the utility of IEE techniques and briefly discuss other endoscopic imaging modalities such as autofluorescence imaging (AFI) and endoscopic microscopy.

Chromoendoscopy

Chromoendoscopy involves the spraying of a dye onto the gastric mucosa after a complete inspection with C-WLI to highlight any subtle mucosal irregularities that could have been missed. Absorptive dye such as methylene blue is actively absorbed by intestinal epithelium, therefore highlighting the area of intestinal metaplasia. Contrast dyes such as indigo carmine have no cellular staining; the dye pools in the crevices of the lesion and accentuates its border and surface topography (Fig. 1A and B). This significantly helps detect nonpolypoid EGC. In some centers in Japan, diluted indigo carmine is routinely sprayed throughout the stomach after a complete screening examination.[12]

NBI

NBI is an endoscopic technique that uses narrow bandwidth filters in the red–green–blue sequential illumination system. The filters are enabled or disabled during endoscopy by pushing a button to limit the wavelengths of light to that of blue (400–430 nm) and green (430–460 nm) via the mechanical insertion of a narrow band filter in front of the xenon arc lamp. Blue and green light penetrate less deeply into the gastric mucosa and are preferentially absorbed by hemoglobin so that vessels appear dark colored. On the endoscopy monitor, the signals obtained from the blue and green filters are combined to form an image that highlights the vasculature on the superficial mucosa.[13–15] However, owing to the weak light intensity and the large size of the gastric lumen, the images obtained by NBI alone tend to be very dark, which significantly limits its utility for endoscopic screening and surveillance of gastric lesions.[16] Newer generation NBI processors (290 and 190 series) with higher light intensities have been developed and may potentially improve detection rates.[17]

FICE and i-scan

FICE is a spectral estimation technique that enhances the contrast of mucosal surfaces. The white-light image captured by the endoscope is sent to a spectral estimation matrix processing circuit. FICE processes the image into spectral images composed from a single wavelength and then displays them in real time. Unlike NBI, FICE is software driven and does not use optical filters. The wavelengths used with FICE are associated with laminar structures and blood flow in the gastrointestinal mucosa altered by inflammation or neoplasm, which acts as a scattering element and interferes with the reflectance spectrum. Like NBI, the operator can switch between the white-light image and the FICE image by a simple push of a button on the endoscope, and this technology can be coupled with optical or digital magnification.[18] The better contrast between the malignant lesion and the surrounding normal mucosa significantly helps in accurately diagnosing the lateral extent of gastric cancer compared to C-WLI (Fig. 1C, Fig. 2A and B).[19] i-Scan is another digital contrast method applying postprocessing algorithms to white light images to enhance the image contrast.[17] There are three modes: surface enhancement mode, contrast enhancement mode, and tone enhancement mode. Similar to FICE, i-scan uses software to improve the contrast of gastric lesions against the normal mucosa (Fig. 3A and B). In contrast to NBI, for which there are abundant data concerning its utility in the diagnosis of EGC, the published data concerning the performance characteristics of FICE and i-scan in the diagnosis of EGC are limited.

Magnifying endoscopy

Standard high definition (HD) endoscopy can enlarge an image up to 30 times, whereas high-magnification endoscopy (ME) can enlarge an image up to 100 times. In terms of image resolution, optical zoom, in which a zoom lens is connected to the endoscope tip, is superior to digital zoom or electronic magnification.[20] Digital zoom relies on signal processing to enlarge images obtained from the charged-couple device (CCD), and this tends to decrease image quality. To optimize ME, adequate preparations are required. There must be optimal cleansing of the mucosal surface, such as with diluted 0.04% simethicone solution and mucolytics, to remove mucus and foam. HD white light endoscopy should be used. A soft black hood is essential; this should be mounted on the endoscopy tip to allow the endoscopist to consistently fix the mucosa at about 2–3 mm from the lens to allow maximal magnification and optimal image resolution. The entire mucosal surface should be carefully surveyed without magnification first; when a suspicious lesion is detected, the lesion should be inspected selectively by magnification in order to visualize the fine patterns and capillaries on the mucosa. ME, when combined with IEE, can clarify the microvascular and microsurface features and facilitate lesion characterization and diagnosis.

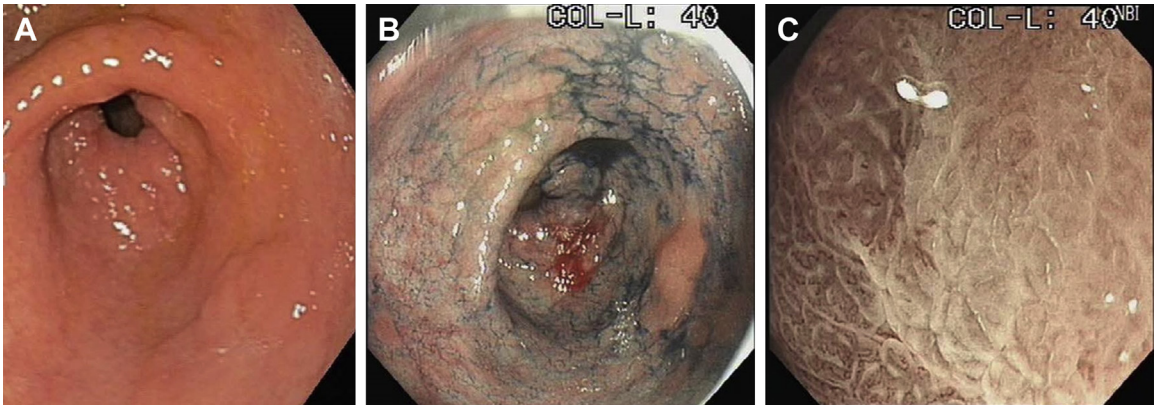

Fig. 1. Image enhanced endoscopy appearance of gastric adenoma. (A) White light endoscopy image of gastric adenoma with 0-IIa morphology. (B) Margins of gastric adenoma are accentuated by indigo carmine chromoendoscopy. (C) Narrow band magnifying image of gastric adenoma with regular microvascular and microsurface patterns.