“Advanced Imaging in Barrett's Esophagus”

By Prateek Sharma, M.D. VA Medical Center, Kansas City, USA.

Barrett’s Esophagus (BE) is a metaplastic change in the esophagus that results in replacement of the normal squamous lined epithelium with intestinal metaplasia. The incidence of esophageal adenocarcinoma has rapidly increased in recent years and BE has been found to be present as a precursor lesion in many of these cases. Patient’s with BE are thought to have an annual risk of developing esophageal cancer of 0.5% per year, substantially higher than the general population, but the absolute risk of developing cancer in BE patients is low.
Endoscopic screening of subjects with chronic reflux symptoms has been recommended as a method of detecting BE and early cancer and despite the lack of clinical evidence, BE patients are then routinely enrolled in surveillance programs.

Diagnosis of BE
Endoscopic assessment of the extent of Barrett’s esophagus (endoscopically visible esophageal columnar mucosa) is dependent on correctly locating esophageal landmarks such as the gastroesophageal junction (GEJ). Lack of simple, standardized criteria for identifying these landmarks and reliably measuring the extent of Barrett’s esophagus has hindered consistency in research and clinical practice. Accordingly, a variety of ad hoc and frequently inadequately specified and validated approaches have been used. For instance, grading of patients into those with variably defined ‘short’ and ‘long’ segments of BE is an unsatisfactorily crude approach. An international Barrett’s esophagus working group was convened to standardize the endoscopic measurement of Barrett’s esophagus. The working group developed criteria to assess the circumferential and the maximal extent of esophageal columnar tissue, the Prague C and M criteria. Using these criteria, circumferential Barrett’s esophagus extending to 3 cm above the GEJ with a tongue extending 5 cm above the GEJ would be described as C3M5, while a tongue extending 3 cm above the GEJ with no circumferential extent of Barrett’s esophagus would be designated C0M3.

New Techniques to Improve Detection of Metaplasia and Dysplasia
Detection of intestinal metaplasia and dysplasia in BE patients using standard endoscopy with 4-quadrant biopsies every 2 cms is a challenge. Current screening and surveillance methods have several limitations – they are time consuming and labor intensive; associated with sampling errors, and finally the reliability of histologic interpretation of dysplasia remains questionable. Finally, both metaplasia and dysplasia have a patchy distribution within the columnar lined segment. Given that these biopsies are random in nature and sample only a small surface area of the Barrett’s segment, a number of new techniques (i.e. magnification endoscopy, spectroscopy, narrow band imaging optical coherence tomography, confocal microscopy etc.) are being evaluated to increase the yield of esophageal neoplasia.

Chromoendoscopy, high-resolution and magnification endoscopy
Chromoendoscopy employs staining agents to identify specific types of epithelia or to highlight surface characteristics of the mucosal lining and is performed to allow targeting of biopsies to increase the accuracy of detecting both metaplasia and dysplasia. The currently available high resolution endoscopes are equipped with charge-coupled devices with up to a million pixels that allow clear visualization of fine mucosal details whereas magnification endoscopy simply enlarges the video image up to 150x using a movable lens. Methylene blue, a vital stain taken up by tissues such as small-intestinal cells, is used in the esophagus theoretically for selective staining of intestinal metaplasia. The sensitivity and specificity of methylene blue-directed biopsies for detecting intestinal metaplasia have been reported to be as high as 95% and 97%; specifically to increase the diagnosis of short segments of intestinal metaplasia in the distal esophagus. In contrast, other studies have not demonstrated a significant benefit of methylene blue staining in the identification of intestinal metaplasia and dysplasia. A number of studies have suggested that chromoendoscopy along with magnification endoscopy reveals the mucosal patterns in BE that correlates with specialized intestinal metaplasia and high-grade dysplasia (HGD). Problems associated with chromoendoscopy include difficulty in achieving complete and even coating of the mucosal surface with the dye, need for equipment for dye spraying, and inability to detect superficial vascular patterns.

Spectroscopy, Auto-Fluorescence Imaging and Optical coherence tomography

Spectroscopy refers to the study of interactions between light and tissues. Spectroscopic detection of the changes that occur during progression from Barrett's metaplasia to dysplasia and carcinoma may allow early detection of neoplasia at stages when lesions are not associated with any macroscopic abnormalities (not seen by conventional endoscopy). Light scattering spectroscopy (LSS) examines the variations in intensity of the singly backscattered light as a function of wavelength and uses reflected white light to provide morphologic information eg. nuclear size, crowding etc. Another technique, laser induced fluorescence spectroscopy uses native tissue fluorophores that fluoresce in the ultraviolet and visible spectral regions – changes in fluorescence spectra caused by neoplastic tissue are analyzed. AFI involves stimulation of a number of biological substances (fluorophores) with submucosal collagen as the most important contributor to tissue autofluorescence in the gastrointestinal tract. The fluorophores on excitation emit fluorescent light spread over a range of longer wavelengths from green to red spectrum. Non-dysplastic and dysplastic BE have different fluorophore contents that result in different autofluorescence spectra. A recent multicenter randomized cross-over trial that compared AFI-targeted biopsy combined with 4-quadrant biopsies to conventional endoscopy showed that AFI required fewer endoscopic examinations to diagnose additional cases of HGD/EAC. However, the sensitivity was only 42% and 4-quadrant biopsies were still found to be necessary.

Optical coherence tomography (OCT) is an emerging cross-sectional imaging technique that uses infrared light applied to a target tissue. It provides real-time tissue images at a resolution much higher than that of endosonography. It has been demonstrated that the highly detailed view of the esophageal wall obtained with this technique allows reliable identification of intestinal metaplasia and dysplasia.

Narrow-band imaging

Narrow-band imaging (NBI) has recently been developed to improve the quality of endoscopic images and enhance microvasculature visualization - a novel endoscopic technique that is based on the optical phenomenon that the depth of light penetration into tissues is dependent on the wavelength; the shorter the wavelength, the more superficial the penetration. Therefore, use of blue light alone with the help of a special filter, can enable imaging of the superficial tissue surface structures without the need for chromoendoscopy. Preliminary studies suggest that NBI may represent a significant improvement over standard endoscopy for detection of metaplastic and neoplastic areas within the BE segment. The Kansas City group recently assessed the potential of NBI for the prediction of histology during screening and surveillance endoscopy in BE patients. The mucosal (ridge/villous, circular, irregular/distorted) and vascular (normal, abnormal) patterns were correlated with histology in a prospective and blinded fashion. The ridge/villous and irregular/distorted patterns showed excellent sensitivity and specificity for intestinal metaplasia and HGD respectively. Similarly, another study showed that an irregular mucosal pattern, irregular vascular pattern and the presence of abnormal blood vessels were all important findings on NBI in differentiating non-dysplastic BE from HGD.

Conclusions

Several promising endoscopic imaging techniques are currently being developed for the detection of metaplasia (screening) and dysplasia/cancer (surveillance). These new technologies represent a significant improvement over standard endoscopy for diagnosing metaplasia and dysplasia and even early cancer and will eventually have a major impact on the screening and surveillance of patients with Barrett's esophagus

RECOMMENDED READING:

1. Sharma P. Magnification endoscopy. Gastrointest Endosc 2005;61(3):435-443.
2. Kara MA, Peters FP, Rosmolen WD, Krishnadath KK, ten Kate F, Fockens P, Bergman JJ. High-resolution endoscopy plus chromoendoscopy or narrow-band imaging in Barrett's esophagus: a prospective randomized crossover study. Endoscopy 2005;37:929-36.
3. Sharma P, Bansal A, Mathur S, Wani S, Cherian R, McGregor D, Higbee A, Hall S, Weston A. The utility of a narrow band imaging endoscopy system in patients with Barrett's esophagus. Gastrointest Endosc 2006;64(2):167-75.
4. Borovicka J, Fischer J, Neuweiler J, Netzer P, Gschossmann J, Ehmann T, Bauerfeind P, Dorta G, Zurcher U, Binek J, Meyenberger C. Autofluorescence endoscopy in surveillance of Barrett's esophagus: a multicenter randomized trial on diagnostic efficacy. Endoscopy 2006;38(9):867-72.

5. Kara MA, Peters FP, ten Kate FJW, Van Deventer SJ, Fockens P, Bergman JJ. Endoscopic video autofluorescence imaging may improve the detection of early neoplasia in patients with Barrett's esophagus. Gastrointest Endosc 2005;61:679-85.
6. Wolfsen HC, Crook JE, Krishna M, Achem SR, Devault KR, Bouras EP, Loeb DS, Stark ME, Woodward TA, Hemminger LL, Cayer FK, Wallace MB. Prospective, controlled tandem endoscopy study of narrow band imaging for dysplasia detection in Barrett's Esophagus.Gastroenterology. 2008 Jul;135(1):24-31.
7. Sharma P, Weston AP, Topalovski M, et al. Magnification chromoendoscopy for the detection of intestinal metaplasia and dysplasia in Barrett's oesophagus. Gut 2003; 52 (1): 24-27.
8. Canto MIF, Setrakian S, Willis J, Chak A, Petras R, Powe NR, Sivak MV, Methylene blue-directed biopsies improve detection of intestinal metaplasia and dysplasia in Barrett's esophagus. Gastrointest Endosc 2000;51:560-8.
9. Poneros JM, Brand S, Bouma BE, Tearney GJ, Compton CC, Nishioka NS. Diagnosis of specialized intestinal metaplasia by optical coherence tomography. Gastroenterology 2001;120:7-12.

Wallace MB, Perelman LT, Bachman V, Crawford JM, Fitzmaurice M, Seiler M, Badizadegan K, Shields SJ, Itzkan I, Desari RR, Van Dam J, Feld MS. Endoscopic detection of dysplasia in patients with Barrett's esophagus using light-scattering spectroscopy. Gastroenterology 2000;119:677-682.