REVIEW ARTICLE

Barrett's esophagus: diagnosis and management

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Barrett's esophagus (BE) is characterized by a change of the normal stratified squamous epithelium lining the esophagus to a metaplastic columnar epithelium with goblet cells. The prevalence of BE is estimated to be 1.5% in the general population[1,2] and as high as 15% in those with GERD.[3,4] Other risk factors associated with BE are older age, male sex, smoking, central obesity, and white ethnicity.[5-10] There also appears to be an increased genetic predisposition among those with first-degree relatives with BE.[11]

BE is a known precursor to esophageal adenocarcinoma (EAC), and oncogenesis is thought to occur through a sequential progression from metaplasia to dysplasia to carcinoma. The risk of developing EAC is as high as 7% per year in those with high-grade dysplasia (HGD)[12] and 0.7% per year in those with low-grade dysplasia (LGD). However, reports of EAC risk in LGD are highly disparate, ranging from risks approximating that of nondysplastic BE to risks of progression to HGD or EAC of 10% per year or more.[8,13-16] EAC is associated with high mortality and is increasing in incidence in the western world.[17-19] Risk factors for progression of BE to EAC include increasing degree of dysplasia, increasing age, increasing BE segment length, male sex, and smoking, among others.[20] Therefore, there is a need to optimize screening, surveillance, and treatment of high-risk BE, with the ultimate goal of decreasing the disease burden and mortality associated with EAC.

Abbreviations: ACG, American College of Gastroenterology; AGA, American Gastroenterological Association; ASGE, American Society for Gastrointestinal Endoscopy; BE, Barrett's esophagus; EAC, esophageal adenocarcinoma; ESD, endoscopic submucosal dissection; HD-WLE, high-resolution white-light endoscopy; HGD, high-grade dysplasia; IM, intestinal metaplasia; LGD, low-grade dysplasia; NBI, narrow-band imaging; NSAID, nonsteroidal anti-inflammatory drug; PDT, photodynamic therapy; PIVI, Imaging in the Barrett's Esophagus Preservation and Incorporation of Valuable Endoscopic Innovations; PPI, proton pump inhibitor; RFA, radiofrequency ablation.

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In this review article, we will briefly discuss the diagnostic criteria and endoscopic screening for BE. We will then review the indications and performance of endoscopic surveillance, with an emphasis on possible new directions to improve the performance of surveillance. We will conclude with a discussion of the management of BE, with an emphasis on the indications, technique, and outcomes of endoscopic therapy for BE.

DIAGNOSIS

Diagnostic criteria

Current guidelines recommend that the diagnosis of BE should be based on the presence of columnar epithelium ≥1 cm proximal to the gastroesophageal junction, with biopsy results consistent with those of intestinal metaplasia (IM).[8] This is in contrast to British diagnostic criteria, in which confirmation of IM is not required for diagnosis.[21] The relationship between the presence of IM and progression to EAC has been conflicting[2-24] and complicated by sampling errors[25] and interobserver variability among pathologists.[26] Studies have shown that there is a significant increase in the likelihood of finding IM with increasing number of biopsy samples taken during endoscopy.[27]

As a result, the recommended number of random biopsy samples is 4 for every 2 cm of BE segment length or 8 for segment length <2 cm in those with suspected BE.[28] In addition, a normal or mildly irregular Z-line should not call for routine biopsy, because IM of the cardia is common in patients with chronic GERD,[29] and chronic GERD has not been definitively demonstrated to imply an increased risk of EAC.[30,31] In terms of BE classification, a segment >3 cm is defined as long-segment BE, and a segment <3 cm is defined as short-segment BE. The Prague classification,[32] describing the circumferential and maximal extent of BE, is used for standardized reporting, in addition to endoscopic landmarks such as the diaphragmatic hiatus, gastroesophageal junction, and the squamocolumnar junction.[8]

Screening

The primary goal of screening is to identify patients with BE. However, the question of whom to screen is complex,

because >90% of patients whom develop EAC have no history of BE, and the traditional practice of screening patients with GERD misses a substantial group destined to develop EAC, because approximately 40% of EAC patients do not have a history of chronic GERD.[33-35] Despite these shortcomings, screening guidelines have traditionally focused on a subset of people who are at higher risk for BE and EAC, which includes men with chronic GERD symptoms and 2 additional risk factors including age >50, white race, central obesity, smoking history, and family history.[8] Although risk-stratification models[36-38] have been developed to aid in determining who to screen for BE, these models need further validation, and their role in clinical practice currently is limited.

The most commonly used screening modality for BE is conventional per-oral upper endoscopy with biopsy samples from any endoscopically visible columnar mucosa in the tubular esophagus. Limitations of endoscopy for screening are that it is an invasive procedure requiring a specialist and that it is costly.[39] Brush cytology sampling might reduce cost, increase the surface area that can be analyzed, and be used in combination with molecular markers to aid in risk stratification. Wide-area transepithelial sampling uses computer-assisted analysis of an abrasive transepithelial brush biopsy to sample a larger surface area to help overcome the issue of sampling error. When wide-area transepithelial sampling was used in conjunction with 4-quadrant biopsies, there was on average a 40% incremental yield of dysplasia and metaplasia detection in 2 prospective trials.[40,41] In addition, there is high interobserver agreement[42] for detection not only of BE ($\kappa = 0.88$), HGD, and/or EAC ($\kappa = 0.95$), but also for LGD ($\kappa = 0.74$), in contrast to the low interobserver agreement with traditional 4-quadrant biopsies.[43] However, this technology is currently used as an adjunct to per-oral endoscopy, meaning that costs associated with endoscopy are not avoided.

Alternative endoscopic techniques for screening include transnasal endoscopy and single-fiber endoscopy. Transnasal endoscopy uses a smaller-caliber endoscope, which is inserted into the esophagus orally or nasally without the need for sedation.[44] Transnasal endoscopy may be comparable to standard endoscopy for detection of BE and for the quality of biopsy specimens.[45-47] In addition, transnasal endoscopy is well-tolerated and has demonstrated efficacy in a community setting.[44,48,49] However, most gastroenterologists have limited experience with transnasal approaches, which require good nasopharyngeal anesthesia and knowledge of pertinent landmarks. Endoscopes with a disposable sheath (EndoSheath; Vision Sciences, Orangeburg, NY) and disposable esophagoscopes (EG scan; IntroMedic, Seoul, South Korea) may be limited by the quality of images generated, a problem likely to be addressed by continuing technological advances. Single-fiber endoscopes are smaller in diameter (1.6 mm) compared with transnasal endoscopy and allow for narrow-band imaging (NBI) but do not provide operator control or the ability to collect biopsy samples.[50]

There are nonendoscopic screening devices for BE that are designed to obtain tissue for histologic evaluation. The Cytosponge (Medtronic, New Haven, Conn) is a gelatin-coated sponge attached to a string, which collects cytology specimens from the esophageal mucosa when withdrawn and may have the potential to replace traditional endoscopic screening in a cost-effective manner.[51] Preliminary data showed a sensitivity of 73% to 90% for identifying BE when used in combination with immunohistochemistry staining for trefoil factor 3,[4] but the diagnostic accuracy is still being validated.

Esophageal capsule endoscopy, another noninvasive capsule device, has shown conflicting data as to effectiveness in BE diagnosis[52-54] without being more cost-effective[55] and, as a result, is not commonly used for screening. Tethered capsule endomicroscopy can provide additional information regarding the microscopic features and architecture of the esophageal wall, and it is being investigated.[50]

Surveillance

Surveillance in BE is aimed at early detection of dysplasia. Dysplasia is categorized as nondysplastic BE, indeterminate dysplasia, LGD, HGD, or carcinoma.[56] The presence of dysplasia should be confirmed by a second pathologist expert in GI histopathology, because of a high degree of interobserver variability.[56] The degree of dysplasia dictates recommended surveillance intervals. Patients with nondysplastic BE are recommended to have a repeat endoscopy in 3 to 5 years, and those with indeterminate dysplasia are recommended to undergo a repeat examination in 3 to 6 months after optimization of proton pump inhibitor therapy.[8] Patients with LGD can undergo eradication therapy, although ongoing endoscopic surveillance is an acceptable alternative for LGD. Those with a higher degree of dysplasia should be considered for endoscopic eradication therapy (Fig. 1).

Careful endoscopic examination of esophageal mucosa and obtaining an adequate number of biopsy samples is vital for effective surveillance.[57,58] Longer mucosal inspection time has been associated with increased detection of HGD and/or EAC.[59] In addition, highly dysplastic lesions in BE are more often found in the right side of the esophagus, so particular attention to this area maybe beneficial.[60-63] A standardized biopsy protocol for surveillance includes random 4-quadrant biopsies every 2 cm in nondysplastic BE and every 1 cm in dysplastic BE,[64] in addition to targeted sampling of focal mucosal abnormalities. Any mucosal abnormalities noted on surveillance should be sampled; among those with a history of dysplasia, EMR is recommended for optimal disease staging.[65] Empiric data demonstrate that in current practice, a majority of patients often do not undergo adequate biopsies when surveillance is performed, leading to decreased dysplasia detection.[66]