American Gastroenterological Association Technical Review on the Management of Barrett's Esophagus

Learning Objectives

This article has an accompanying continuing medical education activity on page e13. Learning Objective: At the end of this activity, the successful learner should:

1. Identify the risk factors associated with development of esophageal adenocarcinoma.
2. Determine who should undergo surveillance after being diagnosed with Barrett's esophagus.
3. Assess the role of endoscopic therapy for patients with Barrett's esophagus.

American Gastroenterological Association Institute Process for Development of Technical Reviews

The aim of evidence-based medicine is to improve the quality of health care by integrating the best research evidence with clinical expertise and patient values. Evidence-based clinical guidelines are sets of recommendations intended to assist health care providers and patients in selecting the best management for common clinical situations while accounting for patient-specific circumstances. In addition to providing optimal, patient-centered care and improved outcomes, guidelines can reduce practice variability, identify gaps in evidence, enhance efficiency of resource use, and facilitate development of outcome and performance measures.

The American Gastroenterological Association Institute (AGAI) Medical Position Statement Procedure Manual, released in 2007, endorses the 2003 version of the US Preventive Services Task Force system to grade strength of recommendations. Although an excellent standard for producing recommendations regarding preventive services, the US Preventive Services Task Force has limitations when used to assess interventions that are not based on prevention. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system (http://www.gradeworkinggroup.org/index.htm) has been adopted by several national and international societies and was constructed to address the shortcomings of existing grading systems, including the US Preventive Services Task Force system. GRADE separates quality of evidence from the strength of recommendation to ensure that the magnitude of benefits and harms is assessed as rigorously as the efficacy of interventions. With regard to strength of recommendations, GRADE has 2 categories: strong and weak (Table 1). Strong recommendations are meant to signify interventions that should be received by most individuals with a particular condition and can be adopted as policy in most circumstances. Weak recommendations require individualized scrutiny of the evidence and policy making would require substantial debate and involvement from multiple stakeholders. The classification requires consideration of 4 factors: quality of evidence, uncertainty about the balance between desirable and undesirable effects, variability in values and preferences, and uncertainty about whether the intervention represents a wise use of resources (Table 2). Of importance to our current health care debate is that interventions receiving a strong recommendation may be targets for development of performance measures.

Quality of evidence is assessed on a 4-point scale: high, moderate, low, and very low. Instead of being classified strictly on the basis of study design (ie, randomized, controlled clinical trials automatically receiving "high" quality marks), these levels reflect the likelihood that further research would change our confidence in the estimate of the beneficial effect of a particular intervention. Five factors that determine quality include study limitations, inconsistency of results between studies, indirectness (generalizability) of results, imprecision, and publication bias. For this reason, randomized, controlled clinical trials that have methodological flaws may be downgraded, whereas well-done observational studies that have large effect sizes (ie, relative risk [RR] >2–5 or <0.5–0.2) may be upgraded.

AGAI Procedure for Construction of Technical Reviews

The AGAI Clinical Practice and Quality Management Committee (CPQMC) chooses a topic by consensus discussion, votes after reviewing a list of potential topics derived from AGAI member recommendations, and develops the specific questions the guideline will answer. The CPQMC committee chair, with support of AGA staff, then contacts the AGAI clinical counsel chair and re-

Abbreviations used in this paper: AFI, autofluorescence imaging; AGAI, American Gastroenterological Association Institute; APC, argon plasma coagulation; CI, confidence interval; CPQMC, Clinical Practice and Quality Management Committee; EMR, endoscopic mucosal resection; EUS, endoscopic ultrasonography; GEJ, gastroesophageal junction; GERD, gastroesophageal reflux disease; GRADE, Grading of Recommendations Assessment, Development and Evaluation; LOH, loss of heterozygosity; MPEC, multi-polar electrocoagulation; NBI, narrow band imaging; PDT, photodynamic therapy; PPI, proton pump inhibitor; QOLRAD, Quality of Life in Reflux and Dyspepsia; RFA, radiofrequency ablation; RR, relative risk; SEER, Surveillance, Epidemiology and End Results; SF-36, 36-Item Short Form Health Survey; TR, technical review.

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Table 1. GRADE: Strength of Recommendation

Strength of recommendation	Clinical implication	Policy implication
Strong	"Do it" or "Don't do it"	Adherence to this recommendation could be used as a quality or performance measure
Weak	"Probably do it" or "Probably don't do it"	Recommendation not suitable for quality or performance measure

quests the input of the counsel for authorship and external reviewers.

Authors are selected and write a technical review (TR), which is an evidence-based document that provides the basis for clinical practice recommendations. For each of the specific questions raised by the CPQMC, authors conduct an independent systematic review of the literature using published guidelines (PRISMA). Articles selected for inclusion in the TR are based on a priori inclusion and exclusion criteria agreed on by all authors. Data extraction is shared among TR authors, and the individual study and summary results are reviewed and approved by all authors. The search terms for each topic included in the TR are included in the Appendix. It is not the function of the TR to provide a summary estimate for each variable included in the review. For this reason, results are summarized in the text of the TR and not subjected to a formal meta-analysis. The draft TR is compiled by the lead author and approved by all authors before submission for publication.

A medical position panel composed of the TR authors, additional content experts, practicing gastroenterologists, other specialists (eg, surgeon, pathologist), a patient representative, a payer representative, and American Gastroenterological Association staff meet through a series of face-to-face and telephone meetings to construct the medical position statement, which is based on the TR but also reflects these discussions by the medical position panel. The medical position panel approves the medical position statement, after which this document and the TR are reviewed by the CPQMC. Based on the vote of the committee, a recommendation is submitted to the AGAI Governing Board, which provides final approval. When approval is granted, the medical position statement is published in GASTROENTEROLOGY and is also posted on the American Gastroenterological Association web site.

The objectives of the AGAI TR on the management of patients with Barrett's esophagus were to evaluate diagnostic and management strategies for patients at risk for or diagnosed with Barrett's esophagus. Specifically, 10 broad questions were developed by interaction among the authors, the AGAI, the Clinical Practice and Quality Management Committee, and representatives from the AGAI Council. The questions were designed to encapsulate the major management issues leading to consultations for Barrett's esophagus and esophageal adenocarcinoma in clinical practice in 2010. For each question, a comprehensive literature search was conducted, pertinent evidence reviewed, and a summary of relevant data produced. The conclusions of this review were based on the best available evidence or, in the absence of quality evidence, the expert opinion of the authors of the TR.

What Landmark Identifies the Gastroesophageal Junction? What Epithelial Type Is Required for the Diagnosis of Barrett's Esophagus? What Is the Definition of Barrett's Esophagus? Should Endoscopists Measure the Extent of Barrett's Metaplasia?

Authorities generally have defined Barrett's esophagus conceptually as the condition in which metaplastic columnar epithelium replaces the stratified squamous epithelium that normally lines the distal esophagus.[1–4] Unfortunately, this deceptively simple conceptual definition does not translate readily into clinically useful diagnostic criteria for 2 major reasons. (1) There are no universally accepted, precise, and validated landmarks that delimit the distal extent of the esophagus (ie, that identify the gastroesophageal junction [GEJ]). If it cannot be determined precisely where the esophagus ends and the stomach begins, then it may not be possible to ascertain the type of epithelium that lines the most distal esophagus. (2) There is no way to verify that gastric-type columnar epithelia found in the distal esophagus are metaplastic. These 2 factors become major confounders when attempting to establish a diagnosis of Barrett's esophagus for patients with only short segments of esophageal columnar epithelium.

What Landmark Identifies the Gastroesophageal Junction?

The diagnosis of Barrett's esophagus can be suspected when, during endoscopic examination, columnar epithelium (which has a characteristic endoscopic appearance) is observed to extend above the GEJ into the esophagus. Of course, this diagnostic suspicion is based on

Table 2. GRADE: Quality of Evidence

Quality of evidence	Estimate of certainty of effect
High	Further research is very unlikely to change the estimate of effect
Moderate	Further research is likely to have an important impact and may change the estimate of effect
Low	Further research is very likely to have an important impact and is likely to change the estimate of effect
Very low	Any estimate of effect is uncertain