

American Gastroenterological Association Medical Position Statement on the Management of Barrett's Esophagus

The AGA Institute Medical Position Panel consisted of the authors of the technical review (Stuart J. Spechler, MD, AGAF, Prateek Sharma, MD, Rhonda F. Souza, MD, AGAF, John M. Inadomi, MD, AGAF, Nicholas J. Shabeen, MD, MPH, AGAF), the chair of the Medical Position Panel (John I. Allen, MD, MBA, AGAF), the chair of the AGA Institute Practice Management and Economics Committee and the AGA Institute CPT Advisor (Joel V. Brill, MD, AGAF), a community-based gastroenterologist (Ronald E. Pruitt, MD, FACP, AGAF, FACG), an author of the AGA Institute Technical Review on the Management of Gastroesophageal Reflux Disease (Peter J. Kabrilas, MD, AGAF), a general surgeon (Jeffrey H. Peters, MD), a primary care physician (Kenneth Nix, MD), a pathologist (Elizabeth A. Montgomery, MD), a patient advocate (B. Donald Mitchell), and an insurance provider representative (John Yao, MD, MBA, MPH, MPA, Senior Medical Director, Blue Shield of California).

Podcast interview: www.gastro.org/gastropodcast.

This medical position statement considers a series of broad questions on the diagnosis, key clinical features, and management of Barrett's esophagus. It is published in conjunction with a technical review¹ on the same subject, and interested readers are encouraged to refer to this publication for in-depth considerations of topics covered by these questions. Topics were developed during discussions among the authors of the technical review, representatives from the American Gastroenterological Association (AGA) Institute Council, and the AGA Institute Clinical Practice and Quality Management Committee (CPQMC). The medical position statement considers major clinical issues encountered by physicians who treat patients with Barrett's esophagus. General issues related to the management of gastroesophageal reflux disease (GERD), which often accompanies Barrett's esophagus, have been discussed in an earlier AGA medical position statement² and are not considered here.

For each question, the authors of the technical review conducted a comprehensive literature search, reviewed pertinent reports, and analyzed the rigor and quality of the evidence. Once the technical review was completed, the authors submitted it to a medical position panel (MPP), which then developed the medical position statement. The MPP was composed of the authors of the technical review, gastroenterologists from a variety of community practice settings, a pathologist, a gastrointestinal surgeon whose area of expertise includes Barrett's esophagus, an author of the AGA technical review on the management of GERD, a health plan representative, and a patient with Barrett's esophagus.

Developing recommendations for the management of Barrett's esophagus proved especially challenging given

the limited data available. The MPP ranked the strength of each recommendation based on the strength of evidence for each of its original recommendations after considering the quality of evidence for a specific question and the "net health benefit," that is, the difference between estimated benefits and the risks of the intervention. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) process was used to assess the strength of recommendations, as outlined in a previously published AGA document.³

Once the MPP approved the document, it was forwarded to the CPQMC for further review, comment, and modification. The CPQMC met on September 24, 2010, and reviewed the recommendations of the MPP. The final committee-approved medical position statement then was forwarded to the AGA Institute Governing Board, where endorsement was decided by majority vote of the board. The final document is published without further modification in *GASTROENTEROLOGY* and becomes the official position of the AGA Institute.

The medical position statement presents information by addressing clinically related questions and summarizing key points from the technical review. When specific recommendations about medical interventions or management strategies for patients with Barrett's esophagus are stated, a "strength of recommendation" and "quality

Abbreviations used in this paper: AGA, American Gastroenterological Association; CPQMC, Clinical Practice and Quality Management Committee; EMR, endoscopic mucosal resection; GEJ, gastroesophageal junction; GERD, gastroesophageal reflux disease; GRADE, Grading of Recommendations Assessment, Development and Evaluation; MPP, medical position panel; PDT, photodynamic therapy; PPI, proton pump inhibitor; RFA, radiofrequency ablation.

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of evidence” is stated. The strength of recommendation is scored either “weak” or “strong” and quality of evidence is ranked as high, moderate, low, or very low in accordance with GRADE criteria. Recommendations are highlighted by appearing within a text box.

A strong recommendation implies that benefits outweigh risks for most patients. A weak recommendation implies that benefits, risks, and the burden of intervention are balanced among several legitimate management options or that appreciable uncertainty existed.

Clinicians are aware of the importance of patient values and preferences in making clinical decisions. The MPP and CPQMC recognized that fully informed patients could make different choices about medical interventions. When a clear recommendation was not possible based on scientific evidence but rational clinicians and patients might opt for different management choices, a weak recommendation was assigned. Applying this approach, high-quality evidence does not always result in strong recommendations and, conversely, strong recommendations can emerge from lower-quality evidence.

Areas of Debate

There are several specific issues with regard to Barrett’s esophagus that generated significant debate and for which there was not uniform consensus. We acknowledge that some conclusions concerning strengths of recommendation do not represent full consensus of the MPP and/or the CPQMC and/or the authors of the technical review. Conclusions will impact management decisions for individual patients and may be used by a variety of entities to make decisions about cost-effectiveness and insurance coverage.

In the 5 decades since Norman Barrett first described the condition that bears his name, multiple definitions of Barrett’s esophagus have been used to establish study populations for research and by clinicians to manage patients. As a result, the true incidence of Barrett’s esophagus in the general population and the risk of progression to cancer both continue to be areas of uncertainty and debate. Current recommendations are based in large part on data derived from recent treatment trials, where clear endoscopic definitions of landmarks are recorded and expert pathologists performed biopsy analysis within a centralized pathology laboratory.

Given the continuing variability in diagnosis of Barrett’s esophagus and dysplasia, the MPP based their recommendations for patient management on the assumption that a patient’s diagnosis of Barrett’s esophagus and the presence or absence of low-grade and high-grade dysplasia would be accurate to the highest degree possible using best current standards of practice. Such standards would include an endoscopic definition of Barrett’s esophagus as defined in this medical position statement and confirmation of a diagnosis of dysplasia by at least one additional pathologist, preferably one who is an

expert in esophageal histopathology. We recognize that, at this time, additional qualifications that establish a pathologist as one with specialized expertise in gastrointestinal pathology and Barrett’s histology do not exist and furthermore that this recommendation will result in a financial impact on the health care system that we believe is justified given the clinical implications associated with making an accurate diagnosis.

A second area of debate concerned the clinical end point needed to recommend an intervention. On one hand, several experts advocated using reductions in cancer incidence or cancer deaths as the sole criteria upon which to recommend certain management strategies (such as endoscopic surveillance of Barrett’s esophagus or endoscopic ablation of Barrett’s mucosa). Others considered intermediate end points (for example, 5-year sustained elimination of Barrett’s mucosa in the case of endoscopic ablation) to be an acceptable clinical outcome. There is no consensus in the medical literature about this issue, and it remains an area of controversy influenced by various and legitimate but differing points of view.

The MPP recognized current limits of scientific knowledge and the importance of the relationship between a treating physician and an informed patient in which known risks and potential benefits of a proposed medical intervention are discussed. Ultimately, patients should share in decisions about what care they receive. Within areas of uncertainty, physicians and patients should have options of therapy available if the net health benefit is acceptable.

Definition of Barrett’s Esophagus

For the purposes of this statement, the definition of Barrett’s esophagus is the condition in which any extent of metaplastic columnar epithelium that predisposes to cancer development replaces the stratified squamous epithelium that normally lines the distal esophagus. Presently, intestinal metaplasia is required for the diagnosis of Barrett’s esophagus because intestinal metaplasia is the only type of esophageal columnar epithelium that clearly predisposes to malignancy.

Discussion

The diagnosis of Barrett’s esophagus can be suspected when, during endoscopic examination, columnar epithelium is observed to extend above the gastroesophageal junction (GEJ) into the tubular esophagus. Numerous authorities have defined Barrett’s esophagus variably for more than 5 decades, and any definition of the condition will continue to have an arbitrary component. If Barrett’s esophagus is to be considered a medical condition rather than merely an anatomic curiosity, then it should have clinical importance. The columnar-lined esophagus has clinical importance primarily because it predisposes to esophageal cancer. Therefore, Barrett’s esophagus can be defined conceptually as the condition

in which any extent of metaplastic columnar epithelium that predisposes to cancer development replaces the stratified squamous epithelium that normally lines the distal esophagus.

Intestinal-type epithelium in the esophagus is clearly abnormal and metaplastic and predisposes to cancer development. Therefore, an esophageal biopsy specimen that shows intestinal-type epithelium above the GEJ establishes the diagnosis of Barrett's esophagus. Recent data suggest that cardia-type epithelium in the esophagus is also abnormal and may predispose to malignancy. The key unanswered clinical question for patients who have cardia-type epithelium in the distal esophagus is this: What is the risk of developing esophageal cancer? A great majority of studies on the risk of cancer in Barrett's esophagus have included patients with esophageal intestinal metaplasia either primarily or exclusively. Although cardia-type epithelium might be a risk factor for malignancy, the magnitude of that risk remains unclear.

Presently, there are insufficient data to make meaningful recommendations regarding management of patients who have solely cardia-type epithelium in the esophagus, and we do not recommend use of the term "Barrett's esophagus" for those patients. Based on this lack of data, it is justified not to perform endoscopic surveillance for patients solely with cardia-type epithelium in the esophagus.

The issue of what endoscopic landmark best identifies the GEJ (ie, the level at which the esophagus ends and the stomach begins) is likely to remain controversial because currently available data do not support a universally accepted definition. A majority of published studies on Barrett's esophagus conducted over the past 20 years have used the proximal extent of the gastric folds as the landmark for the GEJ. In the absence of compelling data for the use of alternative markers, we advocate the continued use of this landmark.

There may be clinical value in measuring and recording the extent of Barrett's metaplasia visualized during endoscopic examination (ie, the distance between the GEJ and the squamocolumnar junction in the esophagus). The likelihood of finding intestinal metaplasia in the columnar-lined esophagus, the severity of underlying GERD, and the magnitude of the cancer risk appear to vary directly with the extent of the metaplastic lining. Therefore, we advocate systematic recording of the circumferential extent and maximum extent of metaplasia in endoscopic reports using a methodology such as the Prague C (circumferential extent in centimeters) and M (maximum extent in centimeters) system.

The Impact of Barrett's Esophagus on the Individual Patient

Although the risk of esophageal cancer or death from Barrett's esophagus is low for an individual, the impact of this diagnosis on patients is great because

mortality from esophageal cancer remains high and psychological and financial consequences have been documented.

- The annual incidence of esophageal cancer for the general population of patients with Barrett's esophagus is approximately 0.5% per year.
- Although deaths from esophageal adenocarcinoma clearly occur with increased frequency in patients with Barrett's esophagus, on an actuarial basis the impact on overall life expectancy for the individual patient is low.
- Mortality from cardiovascular disease may be increased in patients with Barrett's esophagus, perhaps because both are associated with obesity.
- Patients with Barrett's esophagus report a poorer quality of life than individuals in the general population. It is unclear whether this is due to anxiety about cancer, discomfort due to GERD symptoms, or other factors.
- A diagnosis of Barrett's esophagus causes psychological stress in many patients and may increase financial burdens due to increased life and health insurance premiums.

Discussion

Early studies of Barrett's esophagus tended to overestimate cancer risk due to the size of studies and selection bias. More recent studies and large meta-analyses have reported risks of 0.5% per year. Thus, 1 in 200 patients with Barrett's esophagus will develop esophageal cancer each year. It is not known if this risk varies (either increases or decreases) as time passes from the original diagnosis. Some reports suggest a higher risk for patients with long-segment Barrett's esophagus and a greater risk in men compared with women.

The impact of esophageal adenocarcinoma on an individual is devastating because current treatment options are limited and odds of survival remain low. Therefore, patients with Barrett's esophagus, especially those with dysplasia, justifiably experience an increased level of anxiety and emotional burden. From a population risk standpoint, however, a diagnosis of Barrett's esophagus has little impact on overall life expectancy because the lifetime risk of developing esophageal cancer, even within the Barrett's population, is low on an actuarial basis. Increased risk of death can come from cardiovascular causes because of the association of both cardiac disease and Barrett's esophagus with obesity.

Despite the fact that, on a population basis, the risk of cancer is not greatly increased for patients with Barrett's esophagus, there is published evidence of adverse insurance selection and increased premium rates after a diagnosis of Barrett's esophagus. It is imperative, therefore, that treating physicians realize the impact of this diag-

nosis and make every attempt to provide accurate evaluation and appropriate counseling concerning risks of cancer and expectations from surveillance or treatment strategies.

Barrett's Esophagus Risk and Screening

In patients with multiple risk factors associated with esophageal adenocarcinoma (age 50 years or older, male sex, white race, chronic GERD, hiatal hernia, elevated body mass index, and intra-abdominal distribution of body fat), we suggest screening for Barrett's esophagus (weak recommendation, moderate-quality evidence).

We recommend against screening the general population with GERD for Barrett's esophagus (strong recommendation, low-quality evidence).

- Well-established risk factors for Barrett's esophagus include age older than 50 years, male sex, white race, chronic GERD, hiatal hernia, elevated body mass index, and intra-abdominal distribution of body fat. **Quality of Evidence: High**
- Endoscopic screening for Barrett's esophagus may be warranted on an individual basis for patients who have multiple risk factors, as noted previously. There is inadequate evidence of benefit to recommend endoscopic screening for Barrett's esophagus in the general population of patients with GERD who do not have risk factors. **Quality of Evidence: Low**

Discussion

Despite the dearth of studies showing clinical benefit from endoscopic screening for Barrett's esophagus, the practice remains widespread among clinicians in the United States. Cost-effectiveness analyses suggest that endoscopic screening may be warranted if certain predefined clinical parameters are met, but several conceptual and logistical difficulties diminish the utility of screening endoscopy as it is currently practiced in the United States. First and foremost, approximately 40% of subjects who have adenocarcinoma of the esophagus report no history of chronic GERD symptoms, and the number of patients with GERD compared with the number with esophageal adenocarcinoma makes screening all patients with GERD cost-ineffective. A reasonable middle ground would be to select individuals with multiple risk factors for endoscopic examination once a discussion between physician and patient occurs concerning expectations, risks, benefits, and implications of the examination.

Risk of Progression in Barrett's Esophagus

The diagnosis of dysplasia in Barrett's esophagus should be confirmed by at least one additional pathologist, preferably one who is an expert in esophageal histopathology (strong recommendation, moderate-quality evidence).

- Published rates of progression from low-grade dysplasia to either high-grade dysplasia or esophageal adenocarcinoma range from 0.5% to 13.4% per patient per year, depending on the rigor of pathologic confirmation of dysplasia. **Quality of Evidence: Low**
- A recent meta-analysis of multiple historical studies reported an overall risk of progression from high-grade dysplasia to cancer of 6% per patient per year. **Quality of Evidence: Moderate**

Discussion

The risk of progression from low-grade dysplasia in Barrett's esophagus to either high-grade dysplasia or adenocarcinoma remains controversial, based in large part on the difficulty in distinguishing dysplasia from nondysplastic Barrett's esophagus and determining with reproducible accuracy the degree of dysplasia. Criteria used to distinguish low-grade dysplasia from nondysplastic Barrett's esophagus (especially in the presence of esophageal inflammation) and low-grade dysplasia from high-grade dysplasia are based primarily on the degree of architectural and cytologic aberrations, which are, to some degree, subjective in nature. Because dysplasia progresses to cancer in a manner that lacks definitive markers of progression, there are no well-defined cutoff points that separate low-grade from high-grade dysplasia at this time. There is active research focused on biomarkers of progression, and if such markers are defined, management recommendations will likely change.

Low-grade dysplasia tends to be overcalled among community pathologists, especially during an initial endoscopic examination where esophageal inflammation may be present. This situation has been documented during controlled trials in which pathologists with extensive experience in Barrett's histology reviewed biopsy specimens obtained from general community practice and the diagnosis of dysplasia was made only when consensus among the expert panel was reached.

Endoscopic Surveillance in Patients With Barrett's Esophagus

We suggest that endoscopic surveillance be performed in patients with Barrett's esophagus (weak recommendation, moderate-quality evidence).

We suggest the following surveillance intervals (weak recommendation, low-quality evidence):

- No dysplasia: 3–5 years
- Low-grade dysplasia: 6–12 months
- High-grade dysplasia in the absence of eradication therapy: 3 months.

- Biopsy specimens obtained as part of an endoscopic surveillance program can detect curable neoplasia in patients with Barrett's esophagus. Whether endoscopic surveillance reduces cancer incidence or mortality is not known because no long-term trial designed to answer this question has been performed.

Discussion

Endoscopic surveillance has become the standard of practice for patients with Barrett's esophagus based on the unproven assumption that the practice will reduce deaths from esophageal adenocarcinoma and thereby prolong survival. Societal guidelines generally have recommended endoscopic surveillance for patients with Barrett's esophagus at intervals that vary with grade of dysplasia found in the metaplastic epithelium. Intervals of 3 to 5 years have been suggested for patients who have no dysplasia, 6 to 12 months for those found to have low-grade dysplasia, and every 3 months for patients with high-grade dysplasia who receive no ablation therapy. Studies suggest that adherence to recommended surveillance biopsy protocols (for details, refer to the technical review) is associated with higher rates of dysplasia and cancer detection, but many practicing gastroenterologists do not adhere to those guidelines and adherence appears to be poorest for the population at highest risk for cancer development (ie, patients with extensive Barrett's metaplasia).

The preponderance of evidence, virtually all derived from retrospective or poorly controlled studies, suggests that endoscopic surveillance can reduce mortality from esophageal adenocarcinoma through the early detection of treatable cancers when attention is paid to recommended biopsy techniques (see the following text).

Biomarkers in the Management of Barrett's Esophagus

We suggest against the use of molecular biomarkers to confirm the histologic diagnosis of dysplasia or as a method of risk stratification for patients with Barrett's esophagus at this time (weak recommendation, low-quality evidence).

Although biomarkers show promise, they cannot be used to confirm the diagnosis of Barrett's dysplasia and have not been shown to predict which patients with Barrett's are at risk for progression. To date, neither individual biomarkers nor panels of markers can be recommended. **Quality of Evidence: Low**

Biopsy Protocol for Endoscopic Surveillance of Barrett's Esophagus

For patients with Barrett's esophagus who are undergoing surveillance:

We recommend endoscopic evaluation be performed using white light endoscopy (strong recommendation, moderate-quality evidence).

We recommend 4-quadrant biopsy specimens be taken every 2 cm (strong recommendation, moderate-quality evidence).

We recommend specific biopsy specimens of any mucosal irregularities be submitted separately to the pathologist (strong recommendation, moderate-quality evidence).

We recommend 4-quadrant biopsy specimens be obtained every 1 cm in patients with known or suspected dysplasia (strong recommendation, moderate-quality evidence).

We suggest against requiring chromoendoscopy or advanced imaging techniques for the routine surveillance of patients with Barrett's esophagus at this time (weak recommendation, low-quality evidence).

- During endoscopic surveillance of Barrett's esophagus, careful inspection of the entire area of metaplasia using white light endoscopy remains the standard of care. Specific biopsy sampling of any mucosal irregularities should be performed. In areas without mucosal irregularities, 4-quadrant biopsy sampling of the Barrett's epithelium at intervals of every other centimeter is recommended for patients who are not known to have dysplasia. For patients

who are known to have dysplasia, 4-quadrant biopsy sampling of the Barrett's epithelium at intervals of every centimeter is recommended. **Quality of Evidence: Moderate**

- For the routine endoscopic evaluation of Barrett's esophagus, the use of chromoendoscopy or electronic chromoendoscopy or advanced imaging techniques such as confocal laser endomicroscopy is not necessary. These technologies may be helpful in guiding the performance of biopsies in patients who are known to have dysplasia and in patients who have mucosal irregularities detected by white light endoscopy. **Quality of Evidence: Low**

Prevention of Cancer in Barrett's Esophagus

We recommend against attempts to eliminate esophageal acid exposure (proton pump inhibitors [PPIs] in doses greater than once daily, esophageal pH monitoring to titrate PPI dosing, or antireflux surgery) for the prevention of esophageal adenocarcinoma (strong recommendation, moderate-quality evidence).

We recommend screening patients to identify cardiovascular risk factors for which aspirin therapy is indicated (strong recommendation, high-quality evidence).

We suggest against the use of aspirin solely to prevent esophageal adenocarcinoma in the absence of other indications (weak recommendation, moderate-quality evidence).

- For patients with Barrett's esophagus, GERD therapy with medication effective to treat GERD symptoms and to heal reflux esophagitis is clearly indicated, as it is for patients without Barrett's esophagus. **Quality of Evidence: High**
- Evidence to support use of acid-reducing agents, specifically PPIs, in patients with Barrett's esophagus solely to reduce risk of progression to dysplasia or cancer is indirect and has not been proven in a long-term controlled trial. The risks and potential benefit of long-term PPI therapy should be discussed carefully with patients with Barrett's esophagus in the context of their overall health status and medication use. **Quality of Evidence: Low**
- Evidence does not support greater than standard doses of PPI therapy with an expectation of cancer risk reduction. **Quality of Evidence: Low**

- Antireflux surgery is not more effective than medical GERD therapy for the prevention of cancer in Barrett's esophagus. **Quality of Evidence: Moderate**
- Although available evidence suggests that nonsteroidal anti-inflammatory drugs (NSAIDs) may decrease the incidence of esophageal cancer, it is not clear that this potential benefit outweighs the risks of the medications. However, given that cardiovascular deaths are more common than deaths from esophageal adenocarcinoma among patients with Barrett's esophagus, screening for cardiovascular risk factors and interventions is warranted. **Quality of Evidence: Moderate**

The Role of Endoscopic Therapy in Patients With Barrett's Esophagus

We recommend endoscopic eradication therapy with radiofrequency ablation (RFA), photodynamic therapy (PDT), or endoscopic mucosal resection (EMR) rather than surveillance for treatment of patients with confirmed high-grade dysplasia within Barrett's esophagus (strong recommendation, moderate-quality evidence).

We recommend EMR for patients who have dysplasia in Barrett's esophagus associated with a visible mucosal irregularity to determine the T stage of the neoplasia (strong recommendation, moderate-quality evidence).

Discussion

The goal of endoscopic eradication therapy for patients with dysplasia in Barrett's esophagus is to permanently eliminate all intestinal metaplasia and achieve a complete reversion to squamous epithelium. Although endoscopic eradication therapy is not suggested for the general population of patients with Barrett's esophagus in the absence of dysplasia, we suggest that RFA, with or without EMR, should be a therapeutic option for select individuals with nondysplastic Barrett's esophagus who are judged to be at increased risk for progression to high-grade dysplasia or cancer. Specific criteria that identify this population have not been fully defined at this time. When such criteria are identified from controlled trials, then management recommendations should be updated.

Endoscopic eradication therapy with RFA should also be a therapeutic option for treatment of patients with confirmed low-grade dysplasia in Barrett's esophagus. We recognize the controversies surrounding both definition and management of dysplasia in Barrett's esophagus and that the risk of progression to cancer in this population of patients can vary greatly among individuals. The AGA

Institute strongly supports the concept of shared decision making where the treating physician and patient together consider whether endoscopic surveillance or eradication therapy is the preferred management option for each individual.

The current literature is inadequate to recommend endoscopic eradication therapy with cryotherapy for patients with confirmed low-grade or high-grade dysplasia within Barrett's esophagus or patients judged to be at high risk for progression to high-grade dysplasia or esophageal carcinoma. Further studies are needed to assess whether reversion to squamous epithelium can persist long-term after cryotherapy.

As stated in the introduction, recommendations for clinical management are based on the assumption that a patient's diagnosis of Barrett's esophagus and the presence or absence of low-grade and high-grade dysplasia is accurate to the highest degree possible using best current standards of practice. The statement regarding "confirmed" low-grade or high-grade dysplasia refers to patients in whom the diagnosis is confirmed by at least 2 pathologists, preferably one of whom is an expert in esophageal histopathology. We recommend that the diagnosis of dysplasia be confirmed in this manner before initiating endoscopic eradication therapy for any stage of dysplasia.

- Current endoscopic techniques used to eradicate Barrett's esophagus include RFA, PDT, cryotherapy, thermal energy application, and EMR. Details of each technology are found in the technical review. The most commonly used technologies currently are RFA and EMR used alone or in combination. Evidence for their efficacy has emerged rapidly over the past decade. **Quality of Evidence: Moderate**
- The goal of endoscopic eradication therapy is the elimination of all Barrett's epithelium to prevent neoplastic progression. Complete eradication appears to be more effective than therapy that removes only a localized area of dysplasia in Barrett's epithelium. **Quality of Evidence: Low**
- Although RFA and PDT have not been compared head-to-head in controlled trials, RFA appears to have at least comparable efficacy and fewer serious adverse effects compared with PDT. **Quality of Evidence: Moderate**
- The second goal of eradication therapy is to achieve reversion to normal-appearing squamous epithelium within the entire length of the esophagus without islands of buried intestinal metaplasia. RFA can lead to reversion of the metaplastic mucosa to normal-appearing squamous epithelium in a high proportion of subjects at any stage of Barrett's esophagus. The data to date show that reversion to squamous epithelium can persist for up to 5 years. **Quality of Evidence: High**

- There are no data from controlled trials showing that endoscopic eradication therapy, including RFA and cryotherapy, is more effective at reducing cancer risk or more cost-effective than long-term endoscopic surveillance in patients with Barrett's esophagus in the absence of dysplasia (nondysplastic Barrett's metaplasia). **Quality of Evidence: Very Low**
- RFA therapy for patients with low-grade dysplasia leads to reversion to normal-appearing squamous epithelium in >90% of cases. **Quality of Evidence: High**
- RFA therapy for patients with high-grade dysplasia reduces progression to esophageal cancer, as shown in a randomized sham-controlled trial. Several additional uncontrolled trials have shown a similar reduction in cancer development and sustained reversion to squamous mucosa in a large percentage of patients. **Quality of Evidence: High**
- The current literature is inadequate to assess the ability of cryotherapy to achieve sustained reversion of the metaplastic mucosa to normal-appearing squamous epithelium in subjects at any stage of Barrett's esophagus. Further longitudinal studies are needed. **Quality of Evidence: Very Low**
- EMR is both a valuable diagnostic/staging procedure and a potentially therapeutic procedure that should be performed in patients who have dysplasia associated with visible mucosal irregularities in Barrett's esophagus. **Quality of Evidence: High**

The Role of Esophagectomy

- Most patients with high-grade dysplasia (70%–80%) can be successfully treated with endoscopic eradication therapy. Esophagectomy in patients with high-grade dysplasia is an alternative; however, current evidence suggests that there is less morbidity with ablative therapy. **Quality of Evidence: Moderate**
- Before proceeding with esophagectomy, patients with high-grade dysplasia or intramucosal carcinoma with Barrett's esophagus should be referred for evaluation by surgical centers that specialize in the treatment of foregut cancers and high-grade dysplasia. **Quality of Evidence: High**

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Reprint requests

Address requests for reprints to: Chair, Clinical Practice and Quality Management Committee, AGA National Office, 4930 Del Ray Avenue, Bethesda, Maryland 20814. e-mail: drobin@gastro.org; telephone: (301) 272-1189.

Conflicts of interest

The authors disclose the following: Dr Souza is a consultant for Takeda Pharmaceuticals and is a consultant for and receives grant support from AstraZeneca. Dr Inadomi receives grant/research support from NIH and BARRX; and is a consultant for Takeda Pharmaceuticals, AstraZeneca, and Ethicon Endo-Surgery, Inc. Dr Peters receives grant/research support from Torax Medical Inc, Medigus Ltd, and Takeda Pharmaceuticals. Dr Shaheen is a consultant to NeoGenomics Labs; AstraZeneca; CSA Medical; Oncoscope, Inc; and Takeda. He has also received research funding

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