



The role of endoscopy in the management of GERD

This is one of a series of statements discussing the use of GI endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy prepared this text. In preparing this guideline, a search of the medical literature from January 1990 to August 2014 was performed by using PubMed. Additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. When limited or no data exist from well-designed prospective trials, emphasis is given to results from large series and reports from recognized experts. Guidelines for appropriate use of endoscopy are based on a critical review of the available data and expert consensus at the time the guidelines are drafted. Further controlled clinical studies may be needed to clarify aspects of this guideline. This guideline may be revised as necessary to account for changes in technology, new data, or other aspects of clinical practice. The recommendations were based on reviewed studies and were graded on the strength of the supporting evidence (Table 1).<sup>1</sup>

This guideline is intended to be an educational device to provide information that may assist endoscopists in providing care to patients. This guideline is not a rule and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment. Clinical decisions in any particular case involve a complex analysis of the patient's condition and available courses of action. Therefore, clinical considerations may lead an endoscopist to take a course of action that varies from these guidelines. This guideline replaces our previous document on the role of endoscopy in GERD.<sup>2</sup>

GERD is a condition that develops when reflux of stomach contents causes troublesome symptoms (eg, heartburn and regurgitation) or adverse events (eg, erosive esophagitis).<sup>3-5</sup> In a recent systematic review, the prevalence of GERD in the United States was estimated to be 18% to 28%, when GERD was defined as at least weekly heartburn and/or acid regurgitation.<sup>6</sup> Outpatient visits for the evaluation of GERD have increased significantly over time.<sup>7</sup> It is also the most common indication for EGD in the United States.<sup>8</sup> In addition to its impact on quality of life,<sup>9</sup> the numerous adverse events of chronic GERD, such as esophageal stricture formation, Barrett's metaplasia, and esophageal adenocarcinoma, necessitate adequate diagnosis and treatment of this common entity.

## INDICATIONS FOR ENDOSCOPIC EVALUATION

A diagnosis of GERD can be made based on symptoms<sup>3</sup> and confirmed by a favorable response to antisecretory medical therapy.<sup>3,10,11</sup> It is important to note that epigastric pain can be the major symptom of GERD.<sup>3</sup> If the patient's history is consistent with typical or uncomplicated GERD, an initial trial of empiric medical therapy is appropriate before consideration of endoscopy in most patients.<sup>12</sup> Endoscopy at presentation should be considered in patients who have symptoms suggestive of complicated disease (eg, dysphagia, unintentional weight loss, hematemesis) or those with multiple risk factors for Barrett's esophagus (BE).<sup>13-17</sup> Risk factors for BE include older than 50 years of age, male sex, white race, a family history of BE or esophageal adenocarcinoma, prolonged reflux symptoms, smoking, and obesity.<sup>17</sup> In addition, failure to respond to appropriate antisecretory medical therapy should prompt evaluation with EGD and consideration of other diagnostic modalities, including ambulatory pH monitoring, esophageal manometry, and/ or multichannel impedance testing.<sup>18</sup>

The indications for EGD in patients with GERD are listed in Table 2. EGD may be necessary to detect erosive esophagitis, peptic strictures, esophageal cancer, gastric outlet obstruction, and other potentially significant upper GI tract findings. Additionally, EGD is often performed as part of the preoperative evaluation of patients being considered for antireflux surgery or for the placement of wireless esophageal pH monitoring devices<sup>19</sup> and is an inherent part of various endoscopic antireflux procedures. Endoscopy is often performed in the evaluation of patients with suspected extraesophageal manifestations of GERD who present with symptoms such as choking, coughing, hoarseness, asthma, laryngitis, chronic sore throat, or dental erosions.<sup>20</sup> Given that the majority of these patients will not have endoscopic evidence of erosive esophagitis, especially when taking empiric medical therapy for GERD, the routine use of EGD to evaluate extraesophageal symptoms of GERD is not recommended.<sup>21-26</sup> Evidence is also lacking to support the routine use of EGD in patients with uncomplicated GERD who are responsive

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TABLE 1. GRADE system for rating the quality of evidence for guidelines

Quality of evidence	Definition	Symbol
High quality	Further research is very unlikely to change our confidence in the estimate of effect.	⊕⊕⊕⊕
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.	⊕⊕⊕⊖
Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.	<b>\$\$</b> 00
Very low quality	Any estimate of effect is very uncertain.	000

Adapted from Guyatt et al.1

to medical therapy. There is a paucity of outcomes research to suggest that early or even once-in-a-lifetime EGD has a favorable effect on the management, course, or health-related quality of life of patients with typical symptoms of GERD without alarm features (dysphagia, odynophagia, weight loss, bleeding, or anemia).<sup>10</sup>

#### DIAGNOSIS AND CLASSIFICATION OF GERD INDUCED ESOPHAGEAL INFLAMMATION

Patients with reflux esophagitis have endoscopic and/or histopathologic changes of esophageal mucosal injury and inflammation. The presence of typical findings of reflux esophagitis on EGD such as erythema, erosions, ulceration, peptic strictures, and BE is diagnostic of GERD with a specificity as high as 95%.<sup>27,28</sup> However, at least 50% of patients with reflux symptoms have normal esophageal endoscopic findings (nonerosive reflux disease) or uncomplicated GERD.<sup>3,26</sup> In addition, dyspepsia is a diagnosis often confused with GERD. Furthermore, the severity of GERD symptoms does not correlate with the degree of underlying esophageal damage, supporting current recommendations to initiate empiric antisecretory therapy in patients with typical GERD symptoms in the absence of alarm features.<sup>10,29</sup>

There are several classification systems for grading the endoscopic severity of erosive reflux esophagitis and associated adverse events.<sup>30</sup> These classification systems have been primarily used in clinical trials to study the efficacy of medical therapy of reflux esophagitis. However, these systems are useful in clinical practice for documenting disease severity. Currently, the most commonly used systems are the Los Angeles classification and the Savary-Miller classification (Table 3). The Los Angeles classification has been shown to be reliable, with good intra- and interobserver agreement when tested among

expert and inexperienced endoscopists.<sup>13,30</sup> When using this system, the severity of esophagitis has been demonstrated to correlate with the extent of esophageal acid exposure determined by 24-hour pH monitoring.<sup>31</sup>

When esophagitis is encountered endoscopically, tissue samples of the esophageal mucosa should be obtained under the following circumstances: underlying immunocompromised state, the presence of irregular or deep ulceration, proximal distribution of esophagitis, the presence of an esophageal mass lesion or nodularity, bullous changes suggestive of esophageal pemphigus vulgaris, visible changes of eosinophilic esophagitis (rings, linear furrows, white plaques, fragile mucosa), changes of esophageal dessicans superficialis, or an irregular or malignantappearing esophageal stricture. In these situations, forceps tissue samples and/or brush cytology specimens are necessary to exclude other diagnoses, including infectious etiologies and malignancy. Tissue sampling has also been recommended in patients with dysphagia without evidence of erosive esophagitis to evaluate for eosinophilic esophagitis.<sup>29</sup> However, routine sampling of the esophagus or gastroesophageal junction in patients with heartburn and a normal findings on endoscopy are not recommended.<sup>32</sup>

Historically, follow-up EGD for patients with GERD and esophagitis has been reserved for patients whose symptoms fail to respond to medical therapy, those who had severe esophagitis or an esophageal ulcer, or those who needed additional biopsies to clarify a diagnosis such as BE or BE-associated dysplasia because the presence of erosive esophagitis may impair the accurate histopathologic detection of BE and dysplasia.<sup>32,33</sup> Multiple trials have demonstrated that 8 weeks of proton pump inhibitor (PPI) treatment is adequate to achieve mucosal healing in most patients with erosive esophagitis due to GERD.<sup>34-36</sup> Upon healing of erosive esophagitis, BE can be identified in as many as 12% of these patients.<sup>32,37,38</sup>

#### Adverse events of GERD

**Peptic strictures.** The endoscopic evaluation and management of peptic strictures is discussed in another ASGE guideline.<sup>39</sup>

**Barrett's esophagus.** BE is a premalignant condition in which the squamous epithelium of the distal esophagus is replaced by an abnormal columnar epithelium known as specialized intestinal metaplasia.<sup>40,41</sup> BE is found in as many as 15% of patients undergoing EGD for GERD.<sup>42,43</sup> Recommendations regarding the role of EGD for screening and surveillance for BE were recently published.<sup>17</sup>

The value and optimal method of screening for BE remains unclear.<sup>17</sup> Widespread screening of the entire population with GERD would not be feasible given both the high prevalence of GERD in the Western world and the presence of many asymptomatic individuals harboring BE.<sup>44,45</sup> However, several factors associated with BE may facilitate the selection of at-risk individuals for screening EGD. These include white race, male sex, older age (older than 50 years of age), prolonged GERD symptoms (>5 years), a family history of BE and/or adenocarcinoma of the esophagus, nocturnal reflux symptoms, hiatal hernia, increased body mass index (BMI  $\geq$  25 kg/m<sup>2</sup>), tobacco use, and intra-abdominal distribution of fat.<sup>10,16,17,46,47</sup> The ASGE suggests that endoscopic screening for BE be considered in select patients with multiple risk factors for BE and esophageal adenocarcinoma, but patients should be informed that there is insufficient evidence to affirm that this practice prevents cancer or prolongs life.<sup>17</sup> Given the high costs of endoscopy and limitations of using GERD symptoms to screen for BE, alternative screening methods have been sought.

Endoscopy with tissue sampling is the most accurate tool for the detection and diagnosis of BE. To determine the presence of BE endoscopically, the squamocolumnar and gastroesophageal junctions must be clearly identified. Although proximal displacement of the squamocolumnar junction relative to the gastroesophageal junction is suggestive of BE, the endoscopic appearance of salmoncolored mucosa or an irregular Z line, either alone or in combination, is not sufficient to establish the diagnosis.<sup>40</sup> Esophageal tissue specimens should always be obtained for histopathologic confirmation of columnar epithelium when BE is suspected. The optimal number of tissue samples necessary to identify intestinal metaplasia is not known, but it is generally accepted that multiple biopsy specimens should be obtained in all areas of suspected BE.<sup>48,49</sup> Care should be taken to avoid obtaining specimens from a normal-appearing squamocolumnar junction or from the proximal cardia because tissue samples from these areas may demonstrate intestinal metaplasia and provide a false diagnosis of BE.49-51 Patients with a negative screening EGD for BE do not need follow-up endoscopy because only 1.8% of such patients were found to have BE on repeat EGD performed within 5 years.<sup>37</sup>

## ENDOLUMINAL ANTIREFLUX PROCEDURES

Endoluminal therapies for GERD have been used for more than a decade. The techniques used have included delivery of thermal energy intended to constrict the lower esophageal sphincter, intramural injection of bulking agents to augment lower esophageal sphincter pressures, and mechanical alterations of the gastroesophageal junction to mimic results achieved with surgical fundoplication.<sup>52-55</sup> Several devices and/or techniques have been abandoned due to a lack of efficacy or durability or for safety reasons. Currently, there are 2 endoluminal GERD therapies used in the United States: the Stretta procedure (Mederi Therapeutics, Greenwich, Conn) and transoral incisionless fundoplication (TIF) (Endogastric Solutions, Redmond, Wash).<sup>54</sup>

The Stretta procedure received initial U.S. Food and Drug Administration approval in 2000. This technique uses radiofrequency energy delivery to the distal

TABLE 2. Indications for endoscopy in patients with GERD		
	D symptoms that are persistent or progressive despite appropriate nedical therapy	
Dys	phagia or odynophagia	
Invo	bluntary weight loss $>5\%$	
Evic	dence of GI bleeding or anemia	
Find	ding of a mass, stricture, or ulcer on imaging studies	
	eening for Barrett's esophagus in selected patients (as clinically ndicated)	
Pers	sistent vomiting (7-10 days)	
	luation of patients before or with recurrent symptoms after ndoscopic or surgical antireflux procedures	
Placement of wireless pH monitoring		

esophagus and appears to reduce GERD by decreasing tissue compliance and reducing transient lower esophageal relaxations.<sup>54</sup> A recent meta-analysis of 18 studies involving 1441 patients found significant improvement in heartburn and GERD quality of life scores after the Stretta procedure.<sup>56</sup> However, although the esophageal acid exposure, as measured by the DeMeester score, was significantly reduced after treatment (44.4 vs 28.5, P = .007), it did not normalize. In addition, no significant increase in lower esophageal sphincter pressure was observed. Adverse events were infrequent and typically minor. The technique appears to durably relieve GERD symptoms for up to 10 years in the majority of patients.<sup>57,58</sup>

The TIF procedure received U.S. Food and Drug Administration approval in 2007 and has undergone several device and technique modifications since the initial approval.<sup>54</sup> Most studies involving TIF have been small with short-term follow-up. The results have been variable, with poorer results observed with earlier versions of the device/technique. A systematic review of TIF that included 15 studies and 550 procedures found improved GERD health-related quality of life scores (21.9 vs 5.9, P <.0001) after the procedure.<sup>59</sup> PPI use was discontinued in 67% of patients. Limitations of the analysis of these studies include a lack of routine reporting of pH data and a mean follow-up period of only 8.3 months. Major adverse events were reported in 3.2% of patients. Most recently, 3 randomized trials with at least 6-month followup found that TIF was more effective than high-dose PPI therapy in eliminating troublesome regurgitation or extraesophageal symptoms of GERD.<sup>60-62</sup>

Endoluminal antireflux techniques represent potentially new therapeutic indications for GI endoscopy. Prospective trials comparing these therapies with existing medical and surgical options by using objective measures of GERD as the primary endpoint could be useful in further defining the clinical role of these procedures. Appropriate patient selection and endoscopist experience and training should be carefully considered before pursuing these therapies.

TABLE 3. The Los Angeles and Savary-Miller classifications of esophagitis				
Classification	Grade	Description		
Los Angeles	А	One (or more) mucosal break no longer than 5 mm that does not extend between the tops of 2 mucosal folds		
	В	One (or more) mucosal break $>$ 5 mm that does not extend between the tops of 2 mucosal folds		
	C	One (or more) mucosal break that is continuous between the tops of $\geq$ 2 mucosal folds but that involves <75% of the circumference		
	D	One (or more) mucosal break that involves at least 75% of the esophageal circumference		
Savary-Miller	1	Single erosion above the gastroesophageal mucosal junction		
	2	Multiple, noncircumferential erosions above the gastroesophageal mucosal junction		
	3	Circumferential erosion above the mucosal junction		
	4	Chronic change with esophageal ulceration and associated stricture		
	5	Barrett's esophagus with histologically confirmed intestinal differentiation within the columnar epithelium.		

## ROLE OF ENDOSCOPY IN PEDIATRIC GERD

Although most infant reflux is physiologic, there are sparse data regarding the prevalence of GERD in the pediatric population.<sup>6</sup> Guidelines from the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition state that endoscopy is indicated in infants and children with GERD who fail to respond to pharmacologic therapy or as part of the initial management if symptoms of poor weight gain, unexplained anemia or fecal occult blood, recurrent pneumonia, or hematemesis exist.<sup>63</sup> Erosive esophagitis is reported less often in infants and children with GERD than in adults with GERD, but approximately 25% of infants younger than 1 year of age undergoing upper endoscopy will have histologic evidence of esophageal inflammation.<sup>64</sup> When EGD is performed in children with suspected GERD, tissue sampling of both normal and inflamed mucosa should be performed to exclude other conditions such as eosinophilic esophagitis, gastritis, and celiac disease.<sup>65,66</sup>

## SUMMARY

- We recommend that uncomplicated GERD be diagnosed on the basis of typical symptoms without the use of diagnostic testing, including EGD. ⊕⊕⊕⊕
- We recommend EGD for patients who have symptoms suggesting complicated GERD or alarm symptoms.
  ⊕⊕⊕○
- We recommend that EGD not be routinely performed solely for the assessment of extraesophageal GERD symptoms. ⊕⊕⊕○
- We recommend that endoscopic findings of reflux esophagitis be classified according to an accepted grading scale or described in detail. ⊕⊕⊕○
- We suggest that repeat EGD be performed in patients with severe erosive esophagitis after at least an 8-week course of PPI therapy to exclude underlying BE or dysplasia. ⊕⊕OO

- We recommend against obtaining tissue samples from endoscopically normal tissue to diagnose GERD or exclude BE in adults. ⊕⊕⊕○
- We suggest that endoscopy be considered in patients with multiple risk factors for Barrett's esophagus.
  ⊕○○○
- We recommend that tissue samples be obtained to confirm endoscopically suspected Barrett's esophagus.
  ⊕⊕⊕⊕
- We suggest that endoscopic antireflux therapy be considered for selected patients with uncomplicated GERD after careful discussion with the patient regarding potential adverse effects, benefits, and other available therapeutic options. ⊕⊕○○

# DISCLOSURE

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Abbreviations: BE, Barrett's esophagus; PPI, proton pump inbibitor; TIF, transoral incisionless fundoplication.

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