

# CLINICAL PRACTICE UPDATES

## AGA Clinical Practice Update on High-Quality Upper Endoscopy: Expert Review



Satish Nagula,<sup>1</sup> Sravanthi Parasa,<sup>2</sup> Loren Laine,<sup>3,4</sup> and Shailja C. Shah<sup>5,6</sup>

<sup>1</sup>Dr. Henry D. Janowitz Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, New York; <sup>2</sup>Swedish Medical Center, Seattle, Washington; <sup>3</sup>Section of Digestive Diseases, Yale School of Medicine, New Haven, Connecticut; <sup>4</sup>Veterans Affairs Connecticut Healthcare System, West Haven, Connecticut; <sup>5</sup>Gastroenterology Section, Jennifer Moreno Department of Veterans Affairs Medical Center, San Diego, California; and <sup>6</sup>Division of Gastroenterology, University of California, San Diego, San Diego, California

**DESCRIPTION:** The purpose of this Clinical Practice Update (CPU) Expert Review is to provide clinicians with guidance on best practices for performing a high-quality upper endoscopic exam.

**METHODS:** The best practice advice statements presented herein were developed from a combination of available evidence from published literature, guidelines, and consensus-based expert opinion. No formal rating of the strength or quality of the evidence was carried out, which aligns with standard processes for American Gastroenterological Association (AGA) Institute CPUs. These statements are meant to provide practical, timely advice to clinicians practicing in the United States. This Expert Review was commissioned and approved by the American Gastroenterological Association (AGA) Institute Clinical Practice Updates (CPU) Committee and the AGA Governing Board to provide timely guidance on a topic of high clinical importance to the AGA membership, and underwent internal peer review by the CPU Committee and external peer review through standard procedures of *Clinical Gastroenterology & Hepatology*.

**BEST PRACTICE ADVICE 1:** Endoscopists should ensure that upper endoscopy is being performed for an appropriate indication and that informed consent clearly explaining the risks, benefits, alternatives, sedation plan, and potential diagnostic and therapeutic interventions is obtained. These elements should be documented by the endoscopist before the procedure.

**BEST PRACTICE ADVICE 2:** Endoscopists should ensure that adequate visualization of the upper gastrointestinal mucosa, using mucosal cleansing and insufflation as necessary, is achieved and documented.

**BEST PRACTICE ADVICE 3:** A high-definition white-light endoscopy system should be used for upper endoscopy instead of a standard-definition white-light endoscopy system whenever possible. The endoscope used for the procedure should be documented in the procedure note.

**BEST PRACTICE ADVICE 4:** Image enhancement technologies should be used during the upper endoscopic examination to improve the diagnostic yield for preneoplasia and neoplasia. Suspicious areas should be clearly described, photodocumented, and biopsied separately.

**BEST PRACTICE ADVICE 5:** Endoscopists should spend sufficient time carefully inspecting the foregut mucosa in an anterograde and retroflexed view to improve the detection and characterization of abnormalities.

**BEST PRACTICE ADVICE 6:** Endoscopists should document any abnormalities noted on upper endoscopy using established classifications and standard terminology whenever possible.

**BEST PRACTICE ADVICE 7:** Endoscopists should perform biopsies for the evaluation and management of foregut conditions using standardized biopsy protocols.

**BEST PRACTICE  
ADVICE 8:**

Endoscopists should provide patients with management recommendations based on the specific endoscopic findings (eg, peptic ulcer disease, erosive esophagitis), and this should be documented in the medical record. If recommendations are contingent upon histopathology results (eg, *H pylori* infection, Barrett's esophagus), then endoscopists should document that appropriate guidance will be provided after results are available.

**BEST PRACTICE  
ADVICE 9:**

Endoscopists should document whether subsequent surveillance endoscopy is indicated and, if so, provide appropriate surveillance intervals. If the determination of surveillance is contingent on histopathology results, then endoscopists should document that surveillance intervals will be suggested after results are available.

*Keywords:* stomach; esophagus; duodenum; gastrointestinal; endoscopy.

Esophagogastroduodenoscopy (EGD) is a common and generally very safe procedure for the diagnosis and management of upper gastrointestinal (GI) symptoms and conditions involving the esophagus, stomach, and duodenum. Defining what constitutes a high-quality EGD poses somewhat of a challenge because the spectrum of indications and the breadth of benign and (pre)malignant disease pathology in the upper GI tract is very broad. This is in contrast to colonoscopy, for example, in which the predominant indication in the ambulatory setting is colorectal cancer screening and polyp detection and removal. Standardizing the measures defining a high-quality upper endoscopic examination is one of the first steps for assessing quality. The benchmarks for what defines high quality are somewhat arbitrary, but ultimately are driven by studies evaluating threshold measures and the associations with clinical, economic, and patient-reported outcomes at the individual and population levels. Numerous barriers to the widespread implementation of quality benchmarks in upper endoscopy were identified recently, and there are ongoing efforts by national and international gastroenterology societies to address these challenges.<sup>1</sup>

The scope of this Clinical Practice Update includes best practice advice on how to perform a high-quality upper endoscopic examination and encompasses the following: (1) optimization of endoscopic detection of upper GI pathology (eg, mucosal cleansing, visualization time); (2) evaluation of suspected esophageal and gastric premalignancy (eg, the role of image-enhanced endoscopy, use and documentation of standardized biopsy protocols); and (3) postprocedure follow-up evaluation (eg, *Helicobacter pylori* testing/treatment, need and interval for subsequent endoscopic surveillance, and medication management including the timing of resumption of antithrombotics).

## Preprocedure

### *Endoscopy Indication and Informed Consent: Best Practice Advice 1*

The benefits of performing an endoscopic procedure regardless of indication—screening, surveillance, diagnostic,

or therapeutic—must be balanced against the potential harms. Inappropriate use of upper endoscopy exposes patients to unnecessary procedural risks, in addition to excessive financial burdens placed on payors and patients. Before performing the procedure, informed consent outlining the risks, benefits, alternatives, and potential complications associated with the procedure should be obtained and documented. A large meta-analysis of 53,392 patients identified a high frequency of inappropriate indications for upper endoscopy (21.7%; 95% CI, 21.4–22.1). Notably, there was a higher diagnostic yield in patients who had an appropriate indication for the examination (odds ratio [OR], 1.42; 95% CI, 1.36–1.49).<sup>2</sup> Although the indications for upper endoscopy can be optimized to improve diagnostic sensitivity, inappropriate use of endoscopy wastes limited resources and may negatively impact environmental sustainability. Accordingly, it is important to follow society guidelines for upper endoscopy indications and to provide clear documentation in the endoscopy report.<sup>3</sup>

Endoscopists also should provide guidance to patients regarding recommended periprocedural management of antithrombotic drugs. Recent retrospective studies have shown poor compliance with GI society recommendations among endoscopists for the periprocedural management of antithrombotic agents, which has been associated with an increased risk of cardiovascular events.<sup>4,5</sup> Endoscopists should refer to published guidelines regarding the temporary interruption, reversal, and resumption of antithrombotic treatment.<sup>6,7</sup> Specific guidance regarding interruption of other medication classes before upper endoscopy is outside of the scope of this Clinical Practice Update. However, given the increasing use of glucagon-like peptide-1–receptor agonists for obesity and diabetes, it is important for endoscopists to recognize their potential association with delayed gastric emptying based on limited data. The American Society of Anesthesiologists has advocated holding 1 dose of medication before endoscopy to reduce aspiration risk.<sup>8–10</sup> As clinical data become more readily available, endoscopists should watch for additional guidance from professional societies.

## Intraprocedure

### *Achieving and Documenting Adequate Mucosal Visualization: Best Practice Advice 2*

The goal of the upper endoscopic examination is to detect and treat abnormalities in the upper GI tract. Careful mucosal inspection is key to adequately identifying and characterizing abnormalities (Figure 1). This is particularly important because recent studies have reported high rates of missed upper GI cancers. A systematic review and meta-analysis of 81,184 patients with upper GI cancers showed that 10.7% (95% CI, 8.0%–13.7%) of these cancers were diagnosed within 3 years of a previous EGD marked as negative for malignancy.<sup>11</sup> Another systematic review found that 23.9% (15.3%–35.4%) of all cases of esophageal adenocarcinoma in patients with baseline nondysplastic Barrett’s esophagus were diagnosed within 1 year of an EGD marked as negative for malignancy.<sup>12</sup> These reviews suggest that clinically significant neoplasia was missed on the recent endoscopy, underscoring the importance of adequate visualization and inspection of the entire upper GI tract mucosa.

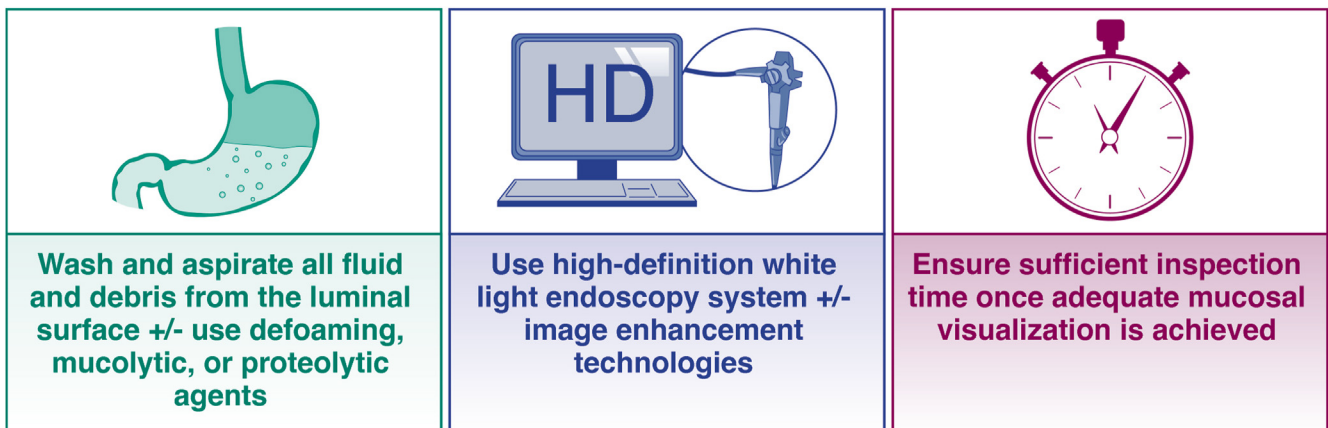
Adequate mucosal visualization is achieved only after aspiration of luminal contents, full insufflation, and use of mucosal cleansing agents as necessary. Adequate insufflation fully distends the GI tract lumen as well as expands the mucosal folds, thereby greatly increasing the visible surface area and ability to detect abnormalities. This is particularly relevant in the stomach where even large lesions can hide between folds or be covered by fluid or debris. All fluid and debris should be aspirated and the mucosal surface cleansed by flushing water through the accessory channel of the endoscope. Pre-medication with oral defoaming agents (simethicone), mucolytics (N-acetylcysteine), and proteolytic enzymes (pronase) has been studied in numerous clinical trials.<sup>13–16</sup> Simethicone and pronase each show an improvement in mucosal visualization in most studies, and the addition of N-acetylcysteine or pronase to

simethicone further increases visualization based on some, but not all, studies.<sup>14,17–20</sup> In these trials, oral administration of these agents 15 to 30 minutes before endoscopy appears safe and efficacious. However, theoretical concerns from anesthesia providers about intraprocedural aspiration may limit the generalizability of this practice. Mucosal irrigation with dilute simethicone is a commonly used practice to improve visualization, although this has not been studied in clinical trials. A concern has been raised regarding the potential for bio-film development and infectious risk resulting from the retention of simethicone droplets within the endoscope waterjet channel or working channel despite high-level disinfection. This concern has led multiple professional societies to suggest that if simethicone use is believed to be necessary, the lowest concentration ( $\leq 0.5\%$ ) and the smallest volume of simethicone should be used, with delivery via the working channel rather than the waterjet channel.<sup>21</sup>

### *Improving Lesion Detection by Using High-Definition White-Light Endoscopy and Image-Enhancing Technologies: Best Practice Advice 3 and 4*

High-definition white-light endoscopy (HD-WLE) systems are superior to standard-definition WLE systems for neoplasia detection<sup>22</sup> (Figure 1). Although HD imaging is a standard feature of newer-generation endoscopes, legacy standard-definition scopes remain in use. Moreover, to provide true HD image resolution, each component of the system (eg, the endoscope video chip, the processor, the monitor, and transmission cables) must be HD compatible. HD processors and monitors can up-convert input image signals from standard-definition endoscopes through pixel interpolation, although this ultimately may limit image quality.<sup>23</sup>

The use of image enhancement technologies (IET) further improves the detection of preneoplasia and neoplasia. IETs use endoscope and processor-based



**Figure 1.** Best practice elements of endoscopy to ensure adequate visualization of the upper gastrointestinal tract mucosa. HD, high-definition.

technology to provide contrast enhancement of the mucosal surface and blood vessels. Narrow band imaging (NBI; Olympus Medical Systems, Tokyo, Japan), i-Scan (PENTAX Endoscopy, Tokyo, Japan), and linked color imaging (LCI)/blue laser imaging (FUJIFILM, Tokyo, Japan) are the most readily available IETs in the United States. In patients with Barrett's esophagus, multiple studies have shown a 10% to 20% increased rate of detection and visual characterization of dysplastic lesions using NBI, LCI/blue laser imaging, or i-Scan, which ultimately may improve the yield of targeted biopsies.<sup>24–26</sup> Similarly increased detection of neoplasia in the stomach is reported with the use of IETs compared with HD-WLE alone. In a large multicenter trial of patients undergoing screening upper endoscopy, NBI detected more focal gastric lesions compared with HD-WLE (40.6% vs 29%;  $P = .003$ ), with an associated increased detection of gastric intestinal metaplasia (17.7% vs 7.7%;  $P = .001$ ).<sup>26</sup> A recent tandem trial with LCI showed a significantly lower rate of missed upper GI neoplasia compared with HD-WLE (0.67% vs 3.5%; relative risk, 0.19; 95% CI, 0.07–0.50).<sup>27</sup>

There is a paucity of comparative studies between the different IETs, as well as only limited data comparing each of the IETs with HD-WLE. The available data certainly show the augmented potential for detecting neoplastic lesions with IETs. Developing familiarity with any IET will be important in reducing the rate of missed lesions during endoscopic examinations. At a minimum, IETs should be used to further characterize abnormalities seen on HD-WLE and in patients for whom there is concern for upper GI preneoplasia or neoplasia. Recent advances in artificial intelligence have heralded the development of computer-aided detection and computer-aided diagnosis systems that appear to improve the detection and visual characterization of colon polyps. Computer-aided detection and computer-aided diagnosis systems for upper endoscopy are still in the early phases of development but do show similar promise for improving the detection and characterization of upper GI tract neoplasia.<sup>28</sup>

#### *Ensure Adequate Duration of Inspection: Best Practice Advice 5*

Ensuring sufficient inspection time of the upper GI tract mucosa once adequate mucosal visualization is achieved is another key aspect of the high-quality endoscopic examination (Figure 1). A longer examination time is associated with higher detection rates of preneoplastic and neoplastic lesions. Studies evaluating upper endoscopy in patients with obscure bleeding suggest a 3% to 25% miss rate for putative bleeding lesions in the upper GI tract. Although this miss rate is not related exclusively to examination time, it does underscore the importance of a careful endoscopic examination regardless of indication.<sup>29</sup> The optimal amount of

time spent inspecting each of the esophageal, gastric, and duodenal compartments separately for improved diagnostic yield remains to be determined. However, a total EGD duration of longer than 7 minutes has been associated with increased detection of Barrett's esophagus, gastric intestinal metaplasia, and upper GI cancer.<sup>30</sup> Based on 1 post hoc analysis of a multicenter prospective clinical trial (1 German, 1 French, and 3 US sites) that included patients with either suspected or established Barrett's esophagus, the duration of inspection time per centimeter of Barrett's esophagus was correlated directly with the detection rate of high-grade dysplasia and adenocarcinoma.<sup>31</sup> In this study, endoscopists with an average inspection time of longer than 1 minute per centimeter of Barrett's esophagus detected a higher percentage of patients with endoscopically suspicious lesions (54.2% vs 13.3%;  $P = .04$ ), and showed a suggestive trend toward a higher detection rate of advanced neoplasia including adenocarcinoma (40.2% vs 6.7%;  $P = .06$ ) compared with endoscopists who spent less time inspecting the Barrett's segment.<sup>31</sup> Data regarding optimal endoscopy times for maximal gastric neoplasia detection specifically in US populations are limited. A retrospective analysis of a Singaporean population determined that endoscopists who spent longer than 7 minutes to perform the entire EGD had 2.5-fold higher odds of detecting high-risk gastric lesions (OR, 2.50; 95% CI, 1.52–4.12) and 3.4-fold higher odds of detecting neoplasia (OR, 3.42; 95% CI, 1.25–10.38) compared with endoscopists who conducted shorter examinations.<sup>30</sup> Consistent with these findings, another retrospective study of 55,786 consecutive patients from Japan who underwent EGD showed that endoscopists who spent at least 5 to 7 minutes of inspection time during the EGD had higher odds of detecting gastric neoplasia (OR, 1.90; 95% CI, 1.06–3.40) as compared with endoscopists with inspection times slower than 5 minutes.<sup>32</sup> Data are limited, but these findings generally have been consistent irrespective of training level.<sup>30</sup> Although the specific duration of an EGD to maximize diagnostic yield has yet to be determined, it is clear that increased inspection time is associated with higher odds of detecting significant pathology.

#### *Photodocumentation Protocol: Best Practice Advice 6*

A high-quality upper endoscopic examination includes a standardized photodocumentation protocol of anatomic stations, which should be performed in tandem with careful inspection after adequate mucosal visualization is achieved. The objective of image documentation is to show that a thorough and complete examination was performed (including adequate insufflation and mucosal cleansing), to document any abnormal findings, show pertinent negative features (eg, normal esophagus in a patient with dysphagia), as well as to provide a

comparison for future examinations. Photodocumentation should strike a balance between conveying valuable information while also minimizing unnecessary additional procedural and postprocedural time. At a minimum, photodocumentation with at least 1 representative photograph of the following anatomic landmarks should be considered: lower esophagus/cardia with visualization of the squamocolumnar junction and the gastroesophageal junction, gastroesophageal junction/fundus in retroflexed view, body and antrum in antegrade view, incisura in retroflexed view, and distal extent of examination in the duodenum.<sup>33</sup> Other organizations have recommended photodocumentation of a greater number of landmarks (eg, 10 by the European Society of Gastrointestinal Endoscopy,<sup>34</sup> 28 by the World Endoscopy Organization).<sup>35</sup> However, in the absence of data clearly showing that more photographs are associated with improved outcomes, and in weighing the practical implications of onerous photodocumentation requirements, we posit that photodocumenting the anatomic stations listed earlier should be considered the minimum requirement for a high-quality EGD in average-risk patients. There are some scenarios in which more rigorous photodocumentation standards during upper endoscopy should be considered, such as patients with risk factors for neoplasia (eg, Barrett's esophagus, gastric intestinal metaplasia), or patients who are likely to be referred for endoscopic treatments.<sup>36</sup> Photodocumentation of any suspicious abnormalities, ideally with annotations, is strongly advised.

### *Standardized Terminology and Biopsy Protocols: Best Practice Advice 7*

Standard terminology and classification systems should be used when documenting endoscopic findings. Examples of these classification systems include the following: Los Angeles classification for erosive esophagitis,<sup>37,38</sup> Prague classification for Barrett's esophagus,<sup>38</sup> Forrest classification for bleeding peptic ulcers,<sup>39,40</sup> Paris classification for superficial neoplastic lesions,<sup>34,41,42</sup> Hill grade classification for gastroesophageal flap valve,<sup>43</sup> and the Eosinophilic Esophagitis Endoscopic Reference System<sup>44</sup> (Figure 2). The Index for Severity of Eosinophilic Esophagitis score is a recently developed novel clinicopathologic severity scale that incorporates many of the endoscopic features identified in the Eosinophilic Esophagitis Endoscopic Reference System and is anticipated to be the new standard for assessing disease activity in individuals with eosinophilic esophagitis.<sup>49</sup>

Biopsy protocols for some of the common upper GI tract conditions are provided in Table 1 and Figure 3. The endoscopist should clearly document the number of biopsy specimens and the location of the biopsy specimens in the procedure report.

Herein, we specifically highlight the best practice biopsy protocol for the evaluation of iron-deficiency

anemia given some divergence of recent international guidelines. In patients undergoing endoscopy for the evaluation of unexplained iron-deficiency anemia, some societies recommend duodenal biopsy specimens to evaluate for celiac disease.<sup>59,60</sup> However, the recent American Gastroenterological Association guideline suggested that the initial evaluation for celiac disease in patients with iron-deficiency anemia should be via serologic testing, with duodenal biopsy specimens reserved only for those who have positive serologies; the rationale is that this practice is cost saving compared with obtaining biopsy specimens at the time of endoscopy.<sup>61,62</sup> That said, sometimes it is not feasible to obtain celiac serologies before the endoscopy (eg, open-access referral). Nevertheless, if endoscopy shows findings suggestive of celiac disease (eg, scalloping) (Table 1), biopsy specimens should be taken. Based on the most recent iterations of some international guidelines, gastric biopsy specimens for *H pylori* and atrophic gastritis in patients with iron-deficiency anemia are no longer routinely recommended in the absence of endoscopic findings<sup>60,61</sup>; however, in the appropriate clinical scenario, such as a family history of gastric cancer, gastric biopsy specimens still may have a role. The American Gastroenterological Association suggests noninvasive nonserologic *H pylori* testing (eg, stool antigen) because this is more cost effective compared with performing routine gastric biopsies at endoscopy without compromising sensitivity and specificity.<sup>60,62</sup> Currently, there are no noninvasive tests with acceptable test performance for the diagnosis of gastric preneoplasia or neoplasia that are routinely available in the United States for clinical use.

## **Postprocedure**

### *Communication of Results and Follow-Up Recommendations: Best Practice Advice 8 and 9*

Ensuring that patients receive clear instructions regarding postprocedure expectations and anticipated follow-up evaluation is a critical but sometimes underappreciated and overlooked component of a high-quality upper endoscopic examination. Endoscopists should provide patients with management recommendations based on the specific endoscopic findings (eg, peptic ulcer disease, erosive esophagitis), and this should be documented in the medical record. When applicable, follow-up instructions should encompass any changes to diet, the timing of resumption or avoidance of antithrombotics or other medications (eg, nonsteroidal anti-inflammatory drugs), new medication prescriptions (eg, gastric acid-suppression therapy), smoking or alcohol cessation, anticipated time frame for communication of results from any collected specimens, and the need/timing of follow-up endoscopy. If specific follow-up recommendations can be provided based only on

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<p><b>Forrest classification of peptic ulcers</b></p>	<table border="1"> <thead> <tr> <th>Ia</th> <th>Ib</th> <th>IIa</th> <th>IIb</th> <th>IIc</th> <th>III</th> </tr> </thead> <tbody> <tr> <td>Spurting bleed</td> <td>Oozing bleed</td> <td>Non-bleeding visible vessel</td> <td>Adherent clot</td> <td>Flat spot in ulcer</td> <td>Clean based ulcer</td> </tr> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> </tbody> </table>	Ia	Ib	IIa	IIb	IIc	III	Spurting bleed	Oozing bleed	Non-bleeding visible vessel	Adherent clot	Flat spot in ulcer	Clean based ulcer																												
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<p><b>Paris classification of superficial lesions in the gastrointestinal tract</b></p>	<table border="1"> <thead> <tr> <th colspan="6">Type 0</th> </tr> <tr> <th colspan="2">Polypoid lesions 0-I</th> <th colspan="3">Non-polypoid 0-II</th> <th>Excavated 0-III</th> </tr> </thead> <tbody> <tr> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> </tr> <tr> <td>Pedunculated (0-Ip)</td> <td>Sessile (0-Is)</td> <td>Min. elevated (0-IIa)</td> <td>Truly flat (0-IIb)</td> <td>Min. depressed (0-IIc)</td> <td>Ulcerated (0-III)</td> </tr> </tbody> </table>	Type 0						Polypoid lesions 0-I		Non-polypoid 0-II			Excavated 0-III							Pedunculated (0-Ip)	Sessile (0-Is)	Min. elevated (0-IIa)	Truly flat (0-IIb)	Min. depressed (0-IIc)	Ulcerated (0-III)																
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**Figure 2.** Endoscopic classification systems for selected upper gastrointestinal pathology. GE, gastroesophageal; GEJ, gastroesophageal junction; Min., minimally. Figure reprinted with permission from Nayar and Vaezi,<sup>45</sup> Yen et al,<sup>46</sup> Kaltenbach et al,<sup>47</sup> and Kavitt and Hirano I.<sup>48</sup>

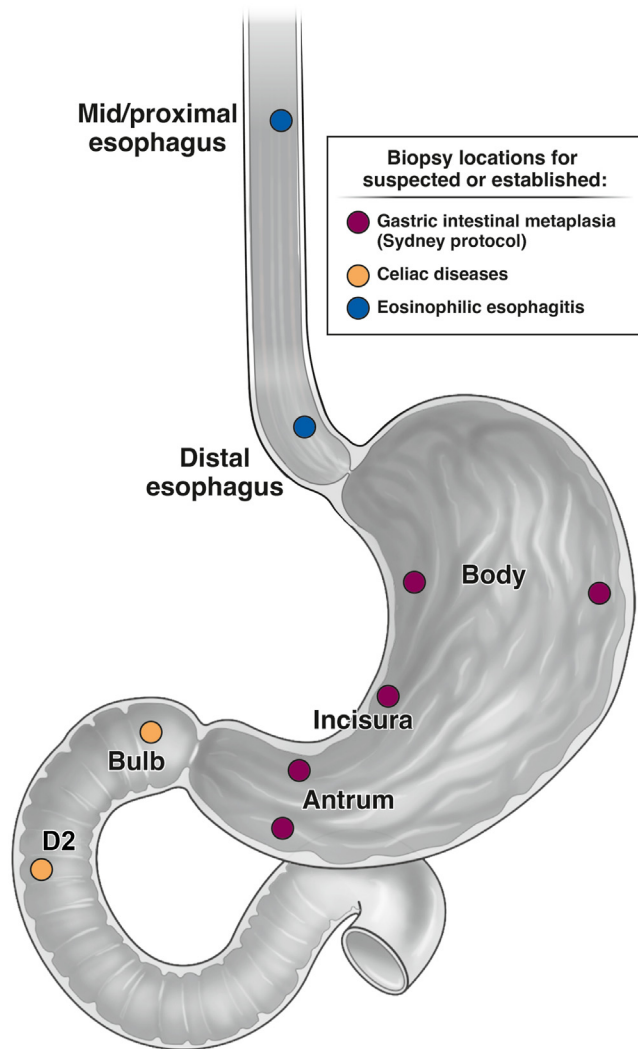
**Table 1.** Biopsy Protocols for the Evaluation of Selected Upper Gastrointestinal Conditions

	Biopsy protocol	Endoscopic appearance	Comments
Esophagus			
Eosinophilic esophagitis <sup>50</sup>	At least 6 biopsy specimens total, distal and mid/proximal esophagus	Edema, rings, exudates, furrows, stenosis Approximately 5%-10% of patients have an endoscopically normal-appearing esophagus	Improved yield with targeted and/or multilevel biopsy specimens Unclear benefit to separating midproximal and distal biopsy specimens into separate bottles
Barrett's esophagus <sup>51</sup>	Four-quadrant biopsy specimens for every 1-2 cm of Barrett's esophagus (Seattle protocol), along with targeted biopsy specimens of mucosal abnormalities	Diagnosis requires salmon-colored mucosa that extends a minimum of 1 cm above the proximal extent of the gastric folds—best examined after gastric decompression Avoid routine biopsy specimens of a normal or irregular Z-line	Diagnostic yield is improved significantly if at least 8 biopsy specimens are taken, even if patients have only 1-2 cm of Barrett's esophagus
Stomach			
Dyspepsia/ <i>H pylori</i> <sup>52</sup>	Obtaining 5 biopsy specimens from the following locations increases the sensitivity of <i>H pylori</i> detection: greater and lesser curve of gastric body, incisura, and greater and lesser curve of the antrum These ideally should be placed in 2 separately labeled jars (body; antrum/incisura) Obtaining gastric body biopsy specimens is especially important in patients using potent gastric acid-suppressing medications (eg, proton pump inhibitors, potassium-competitive acid blockers) owing to the proximal migration of <i>H pylori</i> organisms from the antrum to body	<i>H pylori</i> may be present despite normal-appearing stomach	No role for routine biopsy specimens of the esophagus or duodenum in the evaluation of dyspepsia symptoms
High risk for gastric preneoplasia (eg, gastric intestinal metaplasia) and neoplasia <sup>53,54</sup>	At least 5 biopsy specimens from the following locations should be obtained (updated Sydney System biopsy protocol): 2 from the antrum (within 2-3 cm from the pylorus, and from lesser and greater curvature), 1 from the incisura angularis, and 2 from the body (1 from lesser curvature, ~4 cm proximal from the angle, and 1 from greater curvature, ~8 cm distal to cardia) These should be separated in a minimum of 2 pathology jars (body and antrum/incisura) Targeted biopsy specimens of focal abnormalities should be placed in a separate jar	Atrophic mucosa has a pale appearance with increased visibility of submucosal vessels and loss of gastric folds Gastric intestinal metaplasia can be nodular with irregular mucosal pattern and narrow-band imaging may show bluish-white areas (light blue crest sign)	Separate antrum and gastric body biopsy specimens allows for assessment of extent, severity, and etiology of gastric atrophy and intestinal metaplasia Histologic subtyping of gastric intestinal metaplasia should be requested because this improves the prognostic value of biopsy specimens

Table 1. Continued

	Biopsy protocol	Endoscopic appearance	Comments
Peptic ulcer disease <sup>55</sup>	<p>If gastric ulcer biopsies are performed, then biopsy specimens should be taken from base and edges of the ulcer</p> <p>Routine biopsies of duodenal ulcers are not necessary</p> <p>Biopsy the remainder of the stomach for <i>H pylori</i> as previously described</p>		<p>Decision on biopsy of gastric ulcers may be individualized</p> <p>If very low risk of gastric cancer based on patient history and demographics (eg, young non-Hispanic white patient taking nonsteroidal anti-inflammatory drugs) and ulcer appearance (eg, shallow, flat ulcer with associated erosions), biopsy may not be necessary</p>
Gastric polyps <sup>56</sup>	<p>Polyps should be biopsied or preferably resected to definitively establish a histologic diagnosis, particularly if there is only a solitary polyp</p> <p>If multiple polyps, then the largest polyp(s) should be resected, and representative samples taken from the remaining polyps</p>		<p>Biopsy specimens of intervening mucosa for gastric atrophy, intestinal metaplasia, and <i>H pylori</i> should be considered if clinical suspicion for hyperplastic or adenomatous polyps</p> <p>Polypectomy of larger polyps can provide more accurate histology because histologic features may be patchy within a lesion</p>
Duodenum			
Celiac disease, suspected or established	<p>May have patchy distribution of histologic abnormalities</p> <p>As such, guidelines generally recommend at least 4 biopsy specimens from the postbulbar duodenum and an additional 1-2 biopsy specimens from the bulb<sup>57</sup></p>	<p>Reduced or scalloped duodenal folds, nodular mucosa, mucosal fissuring</p> <p>Approximately one-third have normal endoscopic appearance<sup>35</sup></p>	<p>Consider placing bulbar biopsy specimens in separate container</p> <p>Bulbar biopsy specimens may increase sensitivity but also may reduce specificity for celiac disease diagnosis given the histologic changes that can occur normally in the duodenal bulb<sup>57,58</sup></p>





**Figure 3.** Standardized biopsy protocols for selected upper gastrointestinal pathology (established or suspected).

histopathology results (eg, *H pylori* infection, gastric intestinal metaplasia, Barrett’s esophagus), then endoscopists should document that guidance will be provided after results are available. Endoscopists should ensure all patients and referring physicians receive final results and recommendations. There should be a recall system to notify patients when they are due for surveillance examinations.

### Conclusions

Upper endoscopy has a diverse array of indications and a wide variety of potential GI pathology that can be diagnosed during the examination. Irrespective of indication and examination findings, the advice presented herein represents a series of common best practices needed to perform a high-quality examination. These best practice advice statements are intended to improve measurable clinical, patient-reported, and economic health care outcomes and are not meant to put an additional burden on endoscopists. Ideally, future

research will set threshold indicators of adherence to these best practices that optimally are associated with these aforementioned objective outcomes.

### References

1. Bazerbachi F, Chahal P, Shaukat A. Improving upper gastrointestinal endoscopy quality. *Clin Gastroenterol Hepatol* 2023; 21:2457–2461.
2. Zullo A, Manta R, De Francesco V, et al. Diagnostic yield of upper endoscopy according to appropriateness: a systematic review. *Dig Liver Dis* 2019;51:335–339.
3. Park WG, Shaheen NJ, Cohen J, et al. Quality indicators for EGD. *Gastrointest Endosc* 2015;81:17–30.
4. Bruno M, Marengo A, Elia C, et al. Antiplatelet and anticoagulant drugs management before gastrointestinal endoscopy: do clinicians adhere to current guidelines? *Dig Liver Dis* 2015; 47:45–49.
5. Jiang W, Suen BY, Ho HT, et al. Impact of physicians’ and patients’ compliance on outcomes of colonoscopic polypectomy with anti-thrombotic therapy. *Clin Gastroenterol Hepatol* 2021; 19:2559–2566.e1.
6. Barkun AN, Douketis J, Noseworthy PA, et al. Management of patients on anticoagulants and antiplatelets during acute gastrointestinal bleeding and the peri-endoscopic period: a clinical practice guideline dissemination tool. *Am J Gastroenterol* 2022;117:513–519.
7. Abraham NS, Barkun AN, Sauer BG, et al. American College of Gastroenterology-Canadian Association of Gastroenterology Clinical Practice Guideline: management of anticoagulants and antiplatelets during acute gastrointestinal bleeding and the periendoscopic period. *Am J Gastroenterol* 2022;117:542–558.
8. Hjerpsted JB, Flint A, Brooks A, et al. Semaglutide improves postprandial glucose and lipid metabolism, and delays first-hour gastric emptying in subjects with obesity. *Diabetes Obes Metab* 2018;20:610–619.
9. Friedrichsen M, Breitschaft A, Tadayon S, et al. The effect of semaglutide 2.4 mg once weekly on energy intake, appetite, control of eating, and gastric emptying in adults with obesity. *Diabetes Obes Metab* 2021;23:754–762.
10. American Society of Anesthesiologists consensus-based guidance on preoperative management of patients (adults and children) on glucagon-like peptide-1 (GLP-1) receptor agonists 2023. Updated June 29, 2023. <https://www.asahq.org/about-asa/newsroom/news-releases/2023/06/american-society-of-anesthesiologists-consensus-based-guidance-on-preoperative>. Accessed September 2, 2023.
11. Alexandre L, Tsilegeridis-Legeris T, Lam S. Clinical and endoscopic characteristics associated with post-endoscopy upper gastrointestinal cancers: a systematic review and meta-analysis. *Gastroenterology* 2022;162:1123–1135.
12. Desai M, Lieberman D, Srinivasan S, et al. Post-endoscopy Barrett’s neoplasia after a negative index endoscopy: a systematic review and proposal for definitions and performance measures in endoscopy. *Endoscopy* 2022;54:881–889.
13. Elvas L, Areia M, Brito D, et al. Premedication with simethicone and N-acetylcysteine in improving visibility during upper endoscopy: a double-blind randomized trial. *Endoscopy* 2017; 49:139–145.
14. Monroy H, Vargas JI, Glasinovic E, et al. Use of N-acetylcysteine plus simethicone to improve mucosal visibility during upper GI endoscopy: a double-blind, randomized controlled trial. *Gastrointest Endosc* 2018;87:986–993.

15. Zhang LY, Li WY, Ji M, et al. Efficacy and safety of using premedication with simethicone/pronase during upper gastrointestinal endoscopy examination with sedation: a single center, prospective, single blinded, randomized controlled trial. *Dig Endosc* 2018;30:57–64.
16. Liu X, Guan CT, Xue LY, et al. Effect of premedication on lesion detection rate and visualization of the mucosa during upper gastrointestinal endoscopy: a multicenter large sample randomized controlled double-blind study. *Surg Endosc* 2018;32:3548–3556.
17. Asl SM, Sivandzadeh GR. Efficacy of premedication with activated dimethicone or N-acetylcysteine in improving visibility during upper endoscopy. *World J Gastroenterol* 2011;17:4213–4217.
18. Chang WK, Yeh MK, Hsu HC, et al. Efficacy of simethicone and N-acetylcysteine as premedication in improving visibility during upper endoscopy. *J Gastroenterol Hepatol* 2014;29:769–774.
19. Chang CC, Chen SH, Lin CP, et al. Premedication with pronase or N-acetylcysteine improves visibility during gastroendoscopy: an endoscopist-blinded, prospective, randomized study. *World J Gastroenterol* 2007;13:444–447.
20. Kuo CH, Sheu BS, Kao AW, et al. A defoaming agent should be used with pronase premedication to improve visibility in upper gastrointestinal endoscopy. *Endoscopy* 2002;34:531–534.
21. Day LW, Muthusamy VR, Collins J, et al. Multisociety guideline on reprocessing flexible GI endoscopes and accessories. *Gastrointest Endosc* 2021;93:11–33.e6.
22. Sami SS, Subramanian V, Butt WM, et al. High definition versus standard definition white light endoscopy for detecting dysplasia in patients with Barrett's esophagus. *Dis Esophagus* 2015;28:742–749.
23. Kwon RS, Adler DG, Chand B, et al. High-resolution and high-magnification endoscopes. *Gastrointest Endosc* 2009;69:399–407.
24. de Groof AJ, Fockens KN, Struyvenberg MR, et al. Blue-light imaging and linked-color imaging improve visualization of Barrett's neoplasia by nonexpert endoscopists. *Gastrointest Endosc* 2020;91:1050–1057.
25. Tokunaga M, Matsumura T, Ishikawa K, et al. The efficacy of linked color imaging in the endoscopic diagnosis of Barrett's esophagus and esophageal adenocarcinoma. *Gastroenterol Res Pract* 2020;2020:9604345.
26. Ang TL, Pittayanon R, Lau JY, et al. A multicenter randomized comparison between high-definition white light endoscopy and narrow band imaging for detection of gastric lesions. *Eur J Gastroenterol Hepatol* 2015;27:1473–1478.
27. Ono S, Kawada K, Dohi O, et al. Linked color imaging focused on neoplasm detection in the upper gastrointestinal tract. *Ann Intern Med* 2021;174:18–24.
28. Sharma P, Hassan C. Artificial intelligence and deep learning for upper gastrointestinal neoplasia. *Gastroenterology* 2022;162:1056–1066.
29. Fisher L, Lee Krinsky M, Anderson MA, et al. The role of endoscopy in the management of obscure GI bleeding. *Gastrointest Endosc* 2010;72:471–479.
30. Teh JL, Tan JR, Lau LJ, et al. Longer examination time improves detection of gastric cancer during diagnostic upper gastrointestinal endoscopy. *Clin Gastroenterol Hepatol* 2015;13:480–487.e2.
31. Gupta N, Gaddam S, Wani SB, et al. Longer inspection time is associated with increased detection of high-grade dysplasia and esophageal adenocarcinoma in Barrett's esophagus. *Gastrointest Endosc* 2012;76:531–538.
32. Kawamura T, Wada H, Sakiyama N, et al. Examination time as a quality indicator of screening upper gastrointestinal endoscopy for asymptomatic examinees. *Dig Endosc* 2017;29:569–575.
33. Aabakken L, Barkun AN, Cotton PB, et al. Standardized endoscopic reporting. *J Gastroenterol Hepatol* 2014;29:234–240.
34. Bisschops R, Areia M, Coron E, et al. Performance measures for upper gastrointestinal endoscopy: a European Society of Gastrointestinal Endoscopy (ESGE) Quality Improvement Initiative. *Endoscopy* 2016;48:843–864.
35. Emura F, Sharma P, Arantes V, et al. Principles and practice to facilitate complete photodocumentation of the upper gastrointestinal tract: World Endoscopy Organization position statement. *Dig Endosc* 2020;32:168–179.
36. Yao K. The endoscopic diagnosis of early gastric cancer. *Ann Gastroenterol* 2013;26:11–22.
37. Armstrong D, Bennett JR, Blum AL. The endoscopic assessment of esophagitis: a progress report on observer agreement. *Gastroenterology* 1996;111:85–92.
38. Sharma P, Dent J, Armstrong D. The development and validation of an endoscopic grading system for Barrett's esophagus: the Prague C & M criteria. *Gastroenterology* 2006;131:1392–1399.
39. Forrest JA, Finlayson ND, Shearman DJ. Endoscopy in gastrointestinal bleeding. *Lancet* 1974;2:394–397.
40. De Groot NL, Van Oijen MG, Kessels K. Reassessment of the predictive value of the Forrest classification for peptic ulcer rebleeding and mortality: can classification be simplified? *Endoscopy* 2014;46:46–52.
41. Lambert R, Lightdale CJ. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon – November 30 to December 1, 2002. *Gastrointest Endosc* 2003;58:S3–S4.
42. Axon A, Diebold MD, Fujino M. Update on the Paris classification of superficial neoplastic lesions in the digestive tract. *Endoscopy* 2005;37:570–578.
43. Hill LD, Kozarek RA, Kraemer SJ, et al. The gastroesophageal flap valve: in vitro and in vivo observations. *Gastrointest Endosc* 1996;44:541–547.
44. Hirano I, Moy N, Heckman MG, et al. Endoscopic assessment of the oesophageal features of eosinophilic oesophagitis: validation of a novel classification and grading system. *Gut* 2013;62:489–495.
45. Nayar DS, Vaezi MF. Classifications of esophagitis: who needs them? *Gastrointest Endosc* 2004;60:253–257.
46. Yen HH, Wu PY, Chen MF, et al. Current status and future perspective of artificial intelligence in the management of peptic ulcer bleeding: a review of recent literature. *J Clin Med* 2021;10:3527.
47. Kaltenbach T, Anderson JC, Burke CA, et al. Endoscopic removal of colorectal lesions-recommendations by the US Multi-Society Task Force on Colorectal Cancer. *Gastrointest Endosc* 2020;91:486–519.
48. Kavitt RT, Hirano I. Endoscopic assessment of eosinophilic esophagitis. *Tech Gastrointest Endosc* 2014;16:20–25.
49. Dellon ES, Khoury P, Muir AB, et al. A clinical severity index for eosinophilic esophagitis: development, consensus, and future directions. *Gastroenterology* 2022;163:59–76.
50. Aceves SS, Alexander JA, Baron TH, et al. Endoscopic approach to eosinophilic esophagitis: American Society for Gastrointestinal Endoscopy Consensus Conference. *Gastrointest Endosc* 2022;96:576–592.e1.

51. Shaheen NJ, Falk GW, Iyer PG, et al. Diagnosis and management of Barrett's esophagus: an updated ACG guideline. *Am J Gastroenterol* 2022;117:559–587.
52. Yang YX, Brill J, Krishnan P, et al. American Gastroenterological Association Institute guideline on the role of upper gastrointestinal biopsy to evaluate dyspepsia in the adult patient in the absence of visible mucosal lesions. *Gastroenterology* 2015;149:1082–1087.
53. Shah SC, Piazuelo MB, Kuipers EJ, et al. AGA Clinical Practice Update on the diagnosis and management of atrophic gastritis: expert review. *Gastroenterology* 2021;161:1325–1332.e7.
54. Shah SC, Gawron AJ, Li D. Surveillance of gastric intestinal metaplasia. *Am J Gastroenterol* 2020;115:641–644.
55. Banerjee S, Cash BD, Dominitz JA, et al. The role of endoscopy in the management of patients with peptic ulcer disease. *Gastrointest Endosc* 2010;71:663–668.
56. Evans JA, Chandrasekhara V, Chathadi KV, et al. The role of endoscopy in the management of premalignant and malignant conditions of the stomach. *Gastrointest Endosc* 2015;82:1–8.
57. Rubio-Tapia A, Hill ID, Kelly CP, et al. ACG clinical guidelines: diagnosis and management of celiac disease. *Am J Gastroenterol* 2013;108:656–676, quiz 77.
58. Husby S, Koletzko S, Korponay-Szabó I, et al. European Society Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for Diagnosing Coeliac Disease 2020. *J Pediatr Gastroenterol Nutr* 2020;70:141–156.
59. Al-Toma A, Volta U, Auricchio R, et al. European Society for the Study of Coeliac Disease (ESsCD) guideline for coeliac disease and other gluten-related disorders. *United European Gastroenterol J* 2019;7:583–613.
60. Snook J, Bhala N, Beales ILP, et al. British Society of Gastroenterology guidelines for the management of iron deficiency anaemia in adults. *Gut* 2021;70:2030–2051.
61. Bai JC, Ciacci C. World Gastroenterology Organisation Global Guidelines: celiac disease February 2017. *J Clin Gastroenterol* 2017;51:755–768.
62. Ko CW, Siddique SM, Patel A, et al. AGA Clinical Practice Guidelines on the gastrointestinal evaluation of iron deficiency anemia. *Gastroenterology* 2020;159:1085–1094.

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**Correspondence**

Address correspondence to: Shailja C. Shah, MD, MPH, 3350 La Jolla Village Drive, Gastrointestinal Section, 3rd Floor - South Wing, Mail Code 111D, San Diego, California 92161. e-mail: s6shah@health.ucsd.edu.

**Conflicts of interest**

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