

## The role of endoscopy in the management of patients with peptic ulcer disease

*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 (ASGE) prepared this text. In preparing this guideline, a search of the medical literature was performed by using PubMed. Additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. When few or no data exist from well-designed prospective trials, emphasis is placed on 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 are based on reviewed studies and are graded on the quality of the supporting evidence (Table 1).<sup>1</sup> The strength of individual recommendations is based on both the aggregate evidence quality and an assessment of the anticipated benefits and harms. Weaker recommendations are indicated by phrases such as “we suggest,” whereas stronger recommendations are typically stated as “we recommend.”*

*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 this guideline.*

Upper GI endoscopy has largely replaced upper GI barium x-ray series for the evaluation of upper GI tract disease or symptoms because it allows direct visualization, tissue acquisition, and therapeutic interventions. This guideline is an update of a previous ASGE document<sup>2</sup> and defines the role of upper GI endoscopy in the diagno-

sis and management of patients with known or suspected peptic ulcer disease (PUD).

### THE PATIENT WITH SUSPECTED PUD

A peptic ulcer is a defect in the gastric or duodenal wall that extends through the muscularis mucosa (the lowermost limit of the mucosa) into the deeper layers of the wall (submucosa or the muscularis propria).<sup>3</sup> Signs and symptoms of PUD include dyspepsia, GI bleeding, anemia, and gastric outlet obstruction. Dyspepsia is a nonspecific term denoting upper abdominal discomfort that is thought to arise from the upper GI tract. Dyspepsia is a common symptom, affecting 10% to 40% of the general population.<sup>4,5</sup> Although the majority of patients with dyspeptic symptoms have functional dyspepsia for which no organic etiology can be identified, PUD is found in 5% to 15% of dyspeptic patients.<sup>6-8</sup> Guidelines regarding the role of endoscopy in dyspeptic patients were recently updated by the ASGE.<sup>9</sup> These guidelines advise esophagogastroduodenoscopy (EGD) in patients older than age 50 with new-onset dyspepsia and in patients of any age with alarm features that suggest significant structural disease or malignancy. Alarm features include a family history of upper GI malignancy, unintended weight loss, overt GI bleeding, iron deficiency anemia, progressive dysphagia or odynophagia, persistent vomiting, a palpable mass, or lymphadenopathy. Dyspeptic patients younger than 50 years of age without alarm features may be tested for *Helicobacter pylori* and treated for the infection if they test positive. If they are taking nonsteroidal anti-inflammatory drugs (NSAIDs), these should be stopped, if possible. Patients who test negative for *H Pylori* can be offered either a short trial (4-8 weeks) of acid suppression or EGD. It should also be noted that the alarm features mentioned previously have limited predictive value for the identification of underlying PUD and/or upper GI malignancy.<sup>8</sup> Therefore, EGD is advisable for any patient with persistent dyspeptic symptoms.

### THE PATIENT WITH A CONFIRMED PUD

#### Uncomplicated PUD

PUD is a common condition with a yearly incidence of more than 5 cases per 1000 persons.<sup>10</sup> Most PUD is

**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	⊕⊕○○
Very low quality	Any estimate of effect is very uncertain	⊕○○○

Adapted from Guyatt et al.<sup>1</sup>

uncomplicated, implying the absence of GI bleeding, obstruction, and perforation. The main role of endoscopy in patients with uncomplicated PUD is to confirm the diagnosis and to rule out malignancy.

Duodenal ulcers are extremely unlikely to be malignant, and routine biopsy of these ulcers is not recommended. Likewise, endoscopy is not recommended to evaluate benign-appearing, uncomplicated duodenal ulcers identified on radiologic imaging. Biopsy of all gastric ulcers was recommended in the past because older data suggested that 5% to 11% of gastric ulcers represented malignancy,<sup>11</sup> most commonly gastric adenocarcinoma and less commonly lymphoma and occasionally metastatic cancer. However, the incidence of gastric cancer in the United States is declining.<sup>12</sup> There are no recent data to guide recommendations concerning the need for biopsy of all gastric ulcers. In situations in which the patient history and demographics suggest a very low risk of gastric cancer, such as a young patient taking NSAIDs for whom the endoscopic appearance of the PUD is suggestive of typical NSAID-associated lesions (eg, shallow flat antral ulcer with associated erosions), routine biopsy of visualized ulcers may not be necessary.

When the endoscopic appearance of a gastric ulcer is suggestive of malignancy because of specific features such as an associated mass lesion, elevated irregular ulcer borders, and abnormal adjacent mucosal folds, endoscopic biopsies should be performed. Although endoscopic appearance is a good predictor of the absence of malignancy,<sup>13,14</sup> some malignant ulcers may initially appear endoscopically benign. Therefore, in a substantial proportion of clinical circumstances, the endoscopist may choose to perform a biopsy of gastric ulcers, and such decisions should be individualized. When biopsy specimens of gastric ulcers are obtained, multiple specimens should be obtained from the base and edges of the gastric ulcer,<sup>15</sup> if clinically feasible. Routine cytologic brushings add little to the sensitivity and are not recommended as an alternative or adjunct to endoscopic biopsy.<sup>16</sup> Testing for the presence of *H Pylori* should be performed in all patients with PUD because it is a common

cause of PUD.<sup>17</sup> Endoscopic tests for *H Pylori* include endoscopic biopsies for histologic examination, culture, or for rapid urease testing.

### Role of endoscopic surveillance

**Duodenal ulcers:** When a duodenal ulcer is detected either on endoscopy or a radiologic study, surveillance endoscopy has a low yield if symptoms resolve after a course of acid suppression together with eradication therapy for *H Pylori* (when present) and discontinuation of NSAIDs. More than 90% of duodenal ulcers heal with 4 weeks of proton pump inhibitor therapy.<sup>18,19</sup> Surveillance endoscopy should be considered in patients with duodenal ulceration who experience persistent symptoms despite an appropriate course of therapy, specifically to rule out refractory peptic ulcers and ulcers with nonpeptic etiologies.

**Gastric ulcers:** The rationale for surveillance endoscopy in patients with gastric ulceration is based on the fact that some gastric ulcers that initially appear endoscopically and histologically benign may eventually prove to be malignant.<sup>20,21</sup> Additionally, it has been hoped that endoscopic surveillance may lead to early detection of gastric cancer, thereby improving survival. However, the efficacy of surveillance in meeting these goals and also the cost-effectiveness of this approach is unclear.<sup>14</sup> Although no U.S. or Canadian gastroenterologic society has recommended routine surveillance for gastric ulcers, it is a common practice.<sup>22</sup> A recent analysis of the Clinical Outcomes Research Initiative database found that approximately 25% of patients diagnosed with gastric ulceration undergo repeat upper endoscopy within 3 months despite the fact that multiple studies have found limited yield in identifying malignancy with surveillance endoscopy.<sup>23</sup>

The decision to perform surveillance endoscopy in patients with a gastric ulcer should be individualized. When the patient history and demographics suggest a low risk of gastric cancer (eg, a young patient taking NSAIDs with endoscopic appearance suggestive of typical NSAID-associated lesions), surveillance endoscopy may be unnecessary. Similarly, when the patient has a benign-appearing

gastric ulcer on endoscopy, confirmed on biopsy, with a defined etiology of PUD (eg, NSAID or *H Pylori* related) and is asymptomatic after a course of appropriate therapy, surveillance endoscopy has a low yield.

Surveillance endoscopy should be considered in patients whose gastric ulcer appears endoscopically suspicious for malignancy, even if biopsy samples from the index endoscopy are benign. False-negative biopsy specimen results have been reported to occur in 2% to 5% of malignant ulcers, and any unhealed ulcers at follow-up examination after 8 to 12 weeks of medical therapy should undergo repeat biopsy.<sup>11,24-26</sup> Surveillance endoscopy is also suggested for patients who remain symptomatic despite an appropriate course of antisecretory therapy and previous benign biopsy specimens to rule out refractory peptic ulceration, nonpeptic benign etiologies, and occult malignancy. It should also be considered in patients with gastric ulcers without a clear etiology and in those who did not undergo biopsy at the index endoscopy for any reason (eg, actively bleeding ulcer, coagulopathy, patient instability).

Patients diagnosed with gastric ulceration via radiologic imaging should undergo endoscopy. Although the presence of concurrent duodenal ulceration or deformity on the contrast study supports the diagnosis of a benign gastric ulcer, these radiologic criteria are not reliable. When a patient with a benign-appearing gastric ulcer identified via radiologic imaging appears to be responding satisfactorily to medical therapy and has no alarm features, it is reasonable to treat him with a course of appropriate medical therapy for a duration that would be expected to result in endoscopic healing (typically 8-12 weeks) before performing an endoscopy. If the ulcer has not healed within that period, biopsy specimens should be obtained.

## ATYPICAL PUD

### Giant ulcers

Older literature suggests that giant gastric ulcers (>3 cm) accounted for as many as 10% to 24% of all gastric ulcers.<sup>27-29</sup> With the current widespread use of antisecretory therapy, giant ulcers are rarely encountered, and no series were reported in the past decade. Patients with giant ulcers tend to be older and may present with atypical symptoms including anorexia and weight loss.<sup>28</sup> These patients often have more aggressive disease, with a higher incidence of bleeding, higher mortality rates (10% vs 3%), and greater need for urgent surgery (65% vs 12%) compared with patients with smaller ulcers.<sup>29</sup> Giant duodenal ulcers (>2 cm) also have a higher incidence of complications including bleeding, penetration, and perforation.<sup>30,31</sup>

Upper endoscopy is important for the diagnosis of giant gastric ulcers because barium contrast studies may occasionally miss these ulcers due to their large, shallow craters. Similarly, barium contrast studies may miss giant

duodenal ulcers, which, because of their large size, may be mistaken for the entire duodenal bulb, a pseudodiverticulum, or a true diverticulum of the duodenal bulb.<sup>32</sup> Endoscopy is also important in ruling out malignancy and rare causes of giant ulcers such as Crohn's disease,<sup>33</sup> eosinophilic gastroenteritis,<sup>34</sup> and ischemia<sup>35</sup> and may be required for the management of complications associated with giant ulcers. There are no data that clearly demonstrate improved clinical outcomes from surveillance endoscopy of giant peptic ulcers, although surveillance and documentation of healing could be justified, based on the increased rates of adverse outcomes associated with these lesions.

### Refractory ulcers

Refractory ulcers have been defined as those that fail to heal despite 8 to 12 weeks of antisecretory therapy.<sup>36</sup> In patients with refractory PUD, surveillance endoscopy should be considered until healing is documented or until the etiology is defined (eg, surreptitious NSAID use, high gastrin states, ischemia). Surgical consultation may be considered for persistent nonhealing PUD.

## COMPLICATED PUD

### Bleeding ulcers

The role of endoscopy in bleeding PUD has been discussed in detail in a previous ASGE guideline.<sup>37</sup> Endoscopy is an effective tool in the diagnosis, prognostication, and therapy of bleeding PUD and has been shown in randomized studies to lead to a reduction in blood transfusion requirements, to shortened intensive care unit and hospital stays, to a decreased need for surgery, and a lower mortality rate.<sup>38,39</sup> Early endoscopy (within 24 hours of admission) has been shown to reduce blood transfusion requirements and length of hospital stay.<sup>40</sup> Patients who are hemodynamically stable with endoscopy revealing ulcers without high-risk stigmata may be safely discharged home after endoscopy.<sup>41</sup> Patients with endoscopic stigmata indicating a high risk of rebleeding, including adherent clots, visible vessels, and active arterial bleeding should all undergo endoscopic therapy to achieve hemostasis and reduce the risk of rebleeding.<sup>37,42,43</sup> Recurrent bleeding may occur in as many as 10% of patients despite endotherapy and the use of high-dose proton pump inhibitors.<sup>44,45</sup> In patients who rebleed after initial endoscopic therapy, repeat endoscopic therapy is suggested before considering surgical<sup>46</sup> or radiologic intervention.

### Perforated peptic ulcer

Patients with clinical evidence of acute perforation generally should not undergo endoscopy. Endoscopic therapy (eg, mechanical clips) are not currently recommended for the management of acute perforation in the setting of PUD, for which surgical closure is the usual approach.

Closure of acute iatrogenic perforations with endoscopically placed clips has been described.<sup>47-49</sup> Because of the decreased tissue compliance of a perforated peptic ulcer compared with acute iatrogenic perforations, mechanical clips may be ineffective in the former case. Combined laparoscopic-endoscopic approaches to closure of perforated peptic ulcers have been described.<sup>50-52</sup> In some series, the role of endoscopy has been limited to the identification of the site of perforation and the guidance of subsequent laparoscopic intracorporeal suture repair with an omental patch.<sup>53,54</sup>

### Penetrating ulcer

Endoscopically obtained biopsy specimens have occasionally allowed diagnosis of ulcer penetration into organs adjacent to the stomach and duodenum, including the liver<sup>53</sup> and spleen.<sup>54</sup> Endoscopy has no therapeutic role in the management of penetrating ulcers.

### Gastric outlet obstruction

Gastric outlet obstruction may occur as a result of PUD with inflammation and scarring of the pylorus and/or duodenum. Patients typically present with loss of appetite, epigastric pain, bloating, nausea, vomiting, and weight loss. Endoscopy is important in confirming the diagnosis and in differentiating benign from malignant obstruction. Active ulcers may be noted in association with gastric outlet obstruction in as many as one third of patients undergoing endoscopy for this condition.<sup>55</sup> Biopsies to exclude malignancy should be considered. Management includes acid suppression with a proton pump inhibitor to heal any active ulcers and avoidance of NSAIDs. Eradication of *H Pylori* infection, when present, minimizes subsequent ulcer-related complications.<sup>56</sup>

Endoscopic balloon dilation has been used to manage benign gastric outlet obstruction. Limited case series suggest that 67% to 83% of patients will respond to treatment with endoscopic balloon dilation, with good to excellent short-term relief of symptoms.<sup>55-61</sup> In these series, dilation has been performed by using hydrostatic or pneumatic balloons for durations varying from 30 seconds to 3 minutes. Incremental, sequential dilation has been performed in most series, typically to a diameter of at least 15 mm and to as large as 20 mm in some series. Perforation rates associated with pyloric dilation are high (4%-7%).<sup>57,62,63</sup> In one series, dilation to 20 mm resulted in perforations in 2 of 3 patients.<sup>56</sup> Long-term results are poor, with restenosis developing in as many as 84% patients and 51% of patients requiring surgery.<sup>61,62</sup> Patients requiring more than 2 endoscopic dilations are at high risk of failure of endoscopic therapy and often require surgical intervention.<sup>59,63</sup>

In one study of 21 patients, however, symptomatic remission was maintained in all patients managed by balloon dilation (median 2 dilations) over a median follow-up of 43 months.<sup>57</sup> The authors attribute their excellent results to their careful management of potential etiologies for

PUD, including eradication of *H Pylori* in patients testing positive, stopping NSAID use when possible, and maintaining patients on antisecretory therapy when aspirin therapy was necessary or when the PUD was deemed idiopathic. Isolated case reports describe electrocautery with a sphincterotome<sup>64</sup> and temporary placement of self-expanding metal stents<sup>65</sup> in patients with pyloric stenosis failing to respond to balloon dilation.

### RECOMMENDATIONS

1. We recommend that testing for the presence of *H Pylori* be performed in all patients with PUD because it is a common etiology. ⊕ ⊕ ⊕ ○
2. Duodenal ulcers are extremely unlikely to be malignant, and routine biopsy of these ulcers is not recommended. ⊕ ⊕ ⊕ ○
3. Endoscopy is not recommended to evaluate benign-appearing, uncomplicated duodenal ulcers identified on radiologic imaging. ⊕ ⊕ ⊕ ○
4. We suggest that surveillance endoscopy be considered in patients with duodenal ulceration who experience persistent symptoms despite an appropriate course of therapy, specifically to rule out refractory peptic ulcers and ulcers with nonpeptic etiologies. ⊕ ⊕ ○ ○
5. We suggest that most gastric ulcers undergo biopsy because malignant gastric ulcers may appear endoscopically benign. However, in some clinical situations (eg, young patients taking NSAIDs with multiple benign-appearing ulcers), the risk of malignancy is very low. Therefore, the decision to perform biopsy and/or surveillance endoscopy should be individualized. ⊕ ⊕ ○ ○
6. We suggest that the decision to perform surveillance endoscopy in patients with a gastric ulcer be individualized. Surveillance endoscopy is suggested for those gastric ulcer patients who remain symptomatic despite an appropriate course of medical therapy. It should also be considered in patients with gastric ulcers without a clear etiology and in those who did not undergo biopsy at the index EGD. ⊕ ○ ○ ○
7. In patients with refractory PUD, we suggest surveillance endoscopy be performed until the ulcer has healed or the etiology has been defined. ⊕ ⊕ ○ ○
8. Because endoscopy is an effective tool in the diagnosis, prognostication, and therapy of bleeding peptic ulcers, we recommend that it be performed early in the course of hospitalization. ⊕ ⊕ ⊕ ⊕
9. In patients who rebleed after initial endoscopic hemostasis, repeat endoscopic therapy is recommended before considering surgical or radiologic intervention. ⊕ ⊕ ⊕ ○
10. We recommend against endoscopy in patients with clinical evidence of acute perforation. ⊕ ⊕ ⊕ ○
11. We recommend endoscopy for the evaluation of gastric outlet obstruction. ⊕ ⊕ ⊕ ⊕

12. We suggest endoscopic balloon dilation be considered for the management of benign gastric outlet obstruction. ⊕ ⊕ ○ ○

Abbreviations: EGD, esophagogastroduodenoscopy; NSAID, nonsteroidal anti-inflammatory drug; PUD, peptic ulcer disease.

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