

The role of endoscopy in the management of acute non-variceal upper GI bleeding

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 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 that 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 strength of the supporting evidence¹ (Table 1). 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 these guidelines.

INTRODUCTION

Upper GI bleeding (UGIB) results in over 300,000 hospital admissions annually in the United States, with a mortality of 3.5% to 10%.²⁻³ Appropriate management of

patients with non-variceal UGIB has been demonstrated to improve patient outcomes.⁴ This updated ASGE guideline focuses on the role of GI endoscopy in patients with acute non-variceal UGIB. This guideline will not address obscure GI bleeding or the role of endoscopy in the management of variceal bleeding, both of which are addressed in existing ASGE practice guidelines.⁵⁻⁶ UGIB refers to GI blood loss having an origin proximal to the ligament of Treitz. Acute UGIB can manifest as hematemesis, “coffee ground” emesis, the return of red blood via a nasogastric tube, and/or melena with or without hemodynamic compromise. Hematochezia may occur in patients with extremely brisk UGIB.⁷⁻⁸

INITIAL ASSESSMENT AND MANAGEMENT

Initial assessment

A primary goal of the initial assessment is to determine whether the patient requires urgent intervention (eg, endoscopic, surgical, transfusion) or can undergo delayed endoscopy or even be discharged to outpatient management. Although numerous factors from the patient history, physical examination, and initial tests have been examined for an association with a need for intervention, no single factor is sufficiently predictive of UGIB severity to be used for triage. The most predictive individual factors are a history of malignancy or cirrhosis,⁹ presentation with hematemesis,⁹⁻¹⁰ and signs of hypovolemia including hypotension,^{9,11} tachycardia and shock, and a hemoglobin <8 g/dL.⁹⁻¹⁰ Some factors, such as a history of aspirin or nonsteroidal anti-inflammatory drug (NSAID) use, may not be useful for immediate disposition but are still important to assess for future management (eg, if peptic ulcer disease [PUD] were the etiology of UGIB, then NSAID use should be discontinued).¹¹ Patients who have significant comorbidities may require admission regardless of the severity of the UGIB.

Because individual clinical factors are generally not diagnostic of UGIB severity, there have been attempts to create prediction rules. In 3 studies comparing clinical prediction rule scores in the same study population, the Blatchford score performed better than the Clinical Rockall score for predicting patients at high risk for clinical intervention.¹²⁻¹⁴ The Blatchford score¹⁵ and the Clinical Rockall score¹⁶ have been examined in several studies and may determine the need for urgent endoscopy. The

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

Quality of evidence	Definition	Symbol
High	Further research is very unlikely to change our confidence in the estimate of the effect	⊕⊕⊕⊕
Moderate	Further research is likely to have an important impact on our confidence in the estimate of the effect and may change the estimate	⊕⊕⊕○
Low	Further research is very likely to have an important impact on our confidence in the estimate of the effect and is likely to change the estimate	⊕⊕○○
Very low	Any estimate of effect is very uncertain	⊕○○○

Adapted from Guyatt GH, Oxman AD, Vist GE, et al; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336:924-6.¹

TABLE 2. Blatchford scoring: Admission risk markers and associated score component values

Admission risk marker	Score component value
Blood urea, mmol/L	
6.5-<8.0	2
8.0-<10.0	3
10.0-<25.0	4
≥25	6
Hemoglobin for men, g/dL	
12.0-<13.0	1
10.0-<12.0	3
<10.0	6
Hemoglobin for women, g/dL	
10.0-<12.0	1
10.0	6
Systolic blood pressure, mm Hg	
100-109	1
90-99	2
<90	3
Other markers	
Pulse ≥100/min	1
Presentation with melena	1
Presentation with syncope	2
Hepatic disease	2
Cardiac failure	2

Adapted with permission from Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. *Lancet* 2000;356:1318-21.¹⁵

Blatchford score uses data on blood urea and hemoglobin levels, systolic blood pressure, pulse, presentation with melena, presentation with syncope, history of hepatic disease, and history of heart failure (Table 2).¹⁵ A Blatchford score >0 was 99% to 100% sensitive for identifying a severe bleed in 5 studies.^{12-15,17} The specificity of the Blatchford scoring system is low (4%-44%), but clinically it is more important to be comfortable identifying all severe UGIB at the expense of admitting some patients with minor bleeding episodes. Patients found to have minor bleeding episodes typically may be discharged soon after endoscopy. Use of the Blatchford score may allow early discharge of 16% to 25% of all patients presenting with UGIB.¹²⁻¹⁵

Resuscitation

Initially, crystalloid fluids should be infused to maintain adequate blood pressure. Patients with evidence of severe hypovolemia, shock, or evidence of ongoing blood loss should be admitted to an intensive care setting. Blood products, such as packed red blood cells, should be transfused in patients with evidence of ongoing active blood loss or in patients who have experienced significant blood loss or cardiac ischemia. Other blood products, such as coagulation factors and platelets, also may be necessary to help control bleeding in the appropriate clinical setting.¹⁸

Nasogastric tube

The placement of a nasogastric tube should be considered in select patients who have suspected active UGIB. The presence of bright red blood in a gastric aspirate can

be useful in identifying patients with high-risk lesions, but is not as useful if coffee ground material or other findings are present without red blood.^{9-10,19} It should be noted that the absence of blood in a gastric aspirate does not exclude the presence of active UGIB, because approximately 15% of patients with active bleeding can have a negative result for nasogastric lavage.¹⁹ Because of these limitations, and the potential patient discomfort, use of a nasogastric tube remains controversial.²⁰⁻²¹

Before-procedure proton pump inhibitor therapy

The role of proton pump inhibitor (PPI) therapy in patients with suspected acute UGIB was systematically reviewed in a Cochrane meta-analysis that included 6 randomized controlled trials (RCT) published between 1992 and

2007.²² The analysis found that patients with nonvariceal UGIB administered intravenous PPI therapy prior to endoscopy did not experience any statistically significant differences in the outcomes of mortality, rebleeding, or progression to surgery compared with patients in the control group. However, the analysis did show that before-procedure PPI therapy resulted in significantly reduced rates of high-risk stigmata identified on endoscopy (odds ratio [OR] 0.67; 95% confidence interval [CI], 0.54-0.84) and need for endoscopic therapy (OR 0.68; 95% CI, 0.50-0.93). Therefore, intravenous PPI therapy is recommended for patients who are suspected of having acute UGIB.

Prokinetic agents

A recent meta-analysis of randomized trials evaluated the effectiveness of using prokinetic agents before endoscopy in acute UGIB.²³ The analysis demonstrated that intravenous erythromycin or metoclopramide administered 20 to 120 minutes before endoscopy in patients with acute UGIB decreased the need for a repeat endoscopy to determine the site and cause of bleeding (OR 0.55; 95% CI, 0.32-0.94). However, there was no improvement in other clinical outcomes, such as duration of hospitalization, transfusion requirements, or surgery. Although the routine use of prokinetic agents is not recommended, use in patients with a high probability of having fresh blood or a clot in the stomach when undergoing endoscopy may result in a higher diagnostic yield.²⁴⁻²⁷

ENDOSCOPY IN THE MANAGEMENT OF UGIB

Endoscopy in patients with UGIB is effective in diagnosing and treating most causes of UGIB and is associated with a reduction in blood transfusion requirements and length of intensive care unit/total hospital stay.²⁸ Early endoscopy (within 24 hours of hospital admission) has a greater impact than delayed endoscopy on length of hospital stay and requirements for blood transfusion.²⁹ In appropriate settings, endoscopy can be used to assess the need for inpatient admission. Several studies have demonstrated that hemodynamically stable patients who are evaluated for UGIB with upper endoscopy and subsequently found to have low-risk stigmata for recurrent bleeding can be safely discharged and followed as outpatients.³⁰⁻³³

ENDOSCOPIC TREATMENT MODALITIES FOR UGIB

There are a variety of endoscopic treatment modalities available for the management of UGIB, including injection methods, cautery, and mechanical therapy.³⁴ These are reviewed briefly here. A full discussion of these techniques and their risks can be found in other ASGE documents.³⁴⁻³⁵

Injection

The primary mechanism of action of injection therapy is tamponade resulting from volume effect.³⁴ Some agents also have a secondary pharmacologic effect. Agents available for injection to produce tamponade include normal saline solution and dilute epinephrine. Sclerosants such as ethanol, ethanolamine, and polidocanol are not used to produce tamponade, but instead cause direct tissue injury and thrombosis. Agents also can be used in combination, such as epinephrine followed by ethanolamine. Limited data suggest that higher volumes of epinephrine injected at endoscopy are superior to saline solution for achieving hemostasis.³⁶ A separate class of injectable agents includes thrombin, fibrin, and cyanoacrylate glues, which are used to create a primary tissue seal at a bleeding site.³⁷ With the exception of dilute epinephrine, injectable agents are not commonly used in the treatment of non-variceal UGIB.

Cautery

Cautery devices include heater probes, neodymium-yttrium aluminum garnet lasers, argon plasma coagulation, and electrocautery probes. Laser therapy is not widely used in many centers because of cost, training, and support issues. Electrocautery refers to the use of monopolar electrocautery or bipolar/multipolar electrocautery. Heater probes and electrocautery probes also use local tamponade (mechanical pressure of the probe tip on the bleeding site) combined with heat or electrical current to coagulate blood vessels, a process known as coaptation. Argon plasma coagulation uses a stream of ionized gas to conduct electricity, without mechanical contact, resulting in coagulation of superficial tissues. Argon plasma coagulation is primarily used for the treatment of superficial lesions, such as vascular abnormalities.³⁸

Mechanical therapy

Mechanical therapy refers to the use of a device that causes physical tamponade of a bleeding site. Currently, the only endoscopic mechanical therapies widely available are clips and band ligation devices. Endoscopic clips are deployed over a bleeding site (eg, visible vessel) and typically slough off within days to weeks after placement.³⁹ Endoscopic band ligation devices, commonly used in variceal bleeding, also have been used to treat non-variceal UGIB and involve the placement of elastic bands over tissue to produce mechanical compression and tamponade.⁴⁰

OVERVIEW OF ENDOSCOPIC APPROACHES TO COMMON CAUSES OF ACUTE UGIB

In patients with UGIB, the most common etiologies are: PUD (20%-50%), gastroduodenal erosions (8%-15%), esophagitis (5%-15%), varices (5%-20%), Mallory-Weiss tears (8%-15%), and vascular malformations (about 5%),

TABLE 3. Stigmata of ulcer hemorrhage and risk of recurrent bleeding without endoscopic therapy⁴⁷⁻⁵¹

Stigmata	Risk of recurrent bleeding without therapy
Active arterial bleeding (spurting)	Approaches 100%
Non-bleeding visible vessel	Up to 50%
Non-bleeding adherent clot	8%-35%
Ulcer oozing (without other stigmata)	10%-27%
Flat spots	<8%
Clean-based ulcers	<3%

with other conditions (eg, malignancy) making up the remaining cases.⁴¹⁻⁴²

Peptic ulcer bleeding

The most common causes of PUD are NSAID therapy and *Helicobacter pylori* infection, although a variety of other clinical scenarios can predispose patients to PUD. A 2009 meta-analysis of 75 studies evaluating endoscopic therapy for bleeding peptic ulcers demonstrated that thermal devices, injectable agents other than epinephrine (ie, sclerosants and thrombin/fibrin glue), and clips were all effective methods for achieving hemostasis in PUD, with no single modality being superior.⁴³ Multiple meta-analyses have demonstrated that combination therapy with epinephrine injection in conjunction with a second endoscopic treatment modality, such as cautery or clips, is superior to epinephrine alone for treating lesions with high-risk stigmata, significantly reducing the risk of rebleeding, surgery, and mortality.⁴³⁻⁴⁶ Therefore, it is recommended that if epinephrine is used to treat peptic ulcer bleeding with high-risk stigmata, a second endoscopic treatment modality (ie, coaptive thermal device, sclerosants, thrombin/fibrin glue, or clips) should also be used.

Endoscopic prognostic features in PUD

Several endoscopic findings portend a higher risk for recurrent bleeding and thus, potential benefit from endoscopic therapy (Table 3).⁴⁷⁻⁵¹ Endoscopic therapy is indicated for patients found to have actively bleeding or spurting arterial vessels and for those with a non-bleeding visible vessel (ie, pigmented protuberance) in an ulcer.⁴⁷ Ulcers with an overlying clot should be irrigated to evaluate and potentially treat the underlying lesion.²⁴ However, the management of peptic ulcers with overlying adherent clots that are resistant to removal by irrigation is controversial. A meta-analysis of 6 RCT including 240 patients with adherent clots suggested that endoscopic therapy is superior to medical therapy for preventing recurrent bleeding (pooled relative risk, 0.43; 95% CI, 0.19-0.98).

This analysis, however, failed to demonstrate any significant differences in the need for surgery, length of hospital stay, transfusion requirements, or mortality between endoscopic approaches. Another meta-analysis of 5 RCT that included 189 patients with adherent clots showed no significant differences in the risks of rebleeding, need for surgery, or mortality with endoscopic therapy versus no endoscopic therapy.⁴³ Therefore, in the absence of convincing evidence, the practice of clot removal followed by endoscopic therapy should be individualized. Similarly, flat, pigmented spots or lesions with slow oozing of blood without other stigmata have not been definitively shown to benefit from endoscopic therapy. Clean-based ulcers have an extremely low recurrent bleeding rate and do not require endoscopic treatment.⁴⁷⁻⁴⁸ Additional information regarding the management of patients with PUD is detailed in a 2009 ASGE guideline.⁵²

After-procedure PPI therapy

The administration of a continuous infusion, high-dose, intravenous PPI for a period of 72 hours has been demonstrated to be effective in reducing rebleeding rates and mortality after endoscopic therapy of ulcers with high-risk stigmata.⁵³⁻⁵⁶

Esophageal lesions

Esophagitis, a common cause of UGIB, can be caused by gastroesophageal reflux, infection, medications, caustic ingestion, or radiation.⁵⁷ In the majority of patients, no endoscopic therapy is required. A Mallory-Weiss tear is a laceration of the mucosa at the gastroesophageal junction, gastric cardia, or distal esophagus. Bleeding is usually self-limited.⁵⁸ Patients with ongoing or severe bleeding require endoscopic therapy. Multipolar electrocautery appears to be the most effective therapy, but epinephrine injection, clips, or band ligation also appear to be effective.⁵⁹⁻⁶³ There are no prospective trials comparing treatment methods for Mallory-Weiss tears. Uncontrolled bleeding may require angiographic therapy or surgery.

Vascular abnormalities

Vascular malformations typically cause chronic occult blood loss and occasionally acute GI hemorrhage. These lesions can occur sporadically or in association with other disorders, such as cirrhosis, renal failure, radiation injury, various collagen vascular diseases, and hereditary hemorrhagic telangiectasia. Endoscopic ligation, laser, argon plasma coagulation, coaptive cautery methods, and sclerotherapy can be effective therapies for UGIB due to vascular abnormalities.⁶⁴⁻⁶⁵ There are no prospective trials comparing treatment methods for acute UGIB caused by vascular malformations.

Dieulafoy lesions typically present with intermittent, recurrent, hemodynamically significant UGIB. The lesion occurs when an abnormally large-caliber submucosal artery becomes exposed at the surface of the mucosa and

then ruptures. These lesions are usually in the stomach but may occur throughout the GI tract.⁶⁶ Endoscopic methods to treat Dieulafoy lesions include banding, clipping, electrocautery, cyanoacrylate glue, sclerosant injection, epinephrine injection, heater probe, and laser therapy. Large, single-center experiences have not identified one modality as being superior to others; however, epinephrine injection monotherapy is associated with a higher rate of recurrent bleeding.⁶⁷⁻⁶⁹ Given the difficulty in identifying these lesions absent active hemorrhage, tattooing of the lesion should be considered to facilitate identification and treatment in the event of recurrent bleeding. If endoscopic therapy fails, interventional radiology or surgical approaches may be required. Placement of a clip can help identify the lesion should recurrent bleeding cease before these non-endoscopic interventions.

Aortoenteric fistulas

Aortoenteric fistulas may be primary (caused by atherosclerosis, aortic aneurysms, aortic infections),⁶⁸ or secondary (aortic repair with a synthetic graft).⁶⁹ This condition is a medical emergency that may present with what appears to be self-limited bleeding ("herald" bleed). The clinical suspicion of an aortoenteric fistula should prompt emergency CT imaging. CT scans and angiography can demonstrate the fistula if contrast extravasation into the bowel is visualized.⁷⁰⁻⁷² There is no endoscopic therapy for a bleeding aortoenteric fistula, although endoscopy may be required to confirm the diagnosis or exclude other causes of UGIB. Most aortoenteric fistulas occur at the level of the distal duodenum or the jejunum and may be beyond the reach of a standard upper endoscope. In some cases, aortic graft material may be seen protruding into the bowel lumen. Emergency surgical consultation should be obtained.

GI tumors

Benign or malignant GI tumors, whether primary or metastatic, cause approximately 5% of cases of UGIB.⁷³ Case series of endoscopic therapy have reported initial hemostasis rates similar to, or lower than, those seen in PUD and high recurrent bleeding rates, between 16% and 80%.⁷⁴⁻⁷⁶ Procedure-related complications also appear to be more common.⁷⁵⁻⁷⁶ The optimal treatment modality has not been defined and depends on the goals of therapy. Surgery or angiography may be better approaches to ensuring long-term hemostasis. Any lesion appearing malignant when seen in the context of an episode of UGIB should be biopsied.

RECURRENT BLEEDING AFTER ENDOSCOPIC THERAPY

Despite adequate initial endoscopic therapy, recurrent UGIB can occur in up to 24% of high-risk patients. The use of PPI therapy in addition to combination endoscopic

therapy reduces the rate of recurrent bleeding to approximately 10%.^{54,56} Patients with recurrent bleeding generally respond favorably to repeat endoscopic therapy.⁷⁷⁻⁷⁸ Routine second-look endoscopy, defined as a planned endoscopy performed within 24 hours of the initial endoscopy, is not recommended.⁷⁹ In cases where the initial endoscopy failed to identify the source (eg, because of a large clot in the stomach) or if there are concerns that inadequate therapy was delivered, repeat endoscopy may be appropriate.

RECOMMENDATIONS

- We recommend that patients with UGIB be adequately resuscitated before endoscopy. ⊕○○○
- We recommend antisecretory therapy with PPIs for patients with bleeding caused by peptic ulcers or in those with suspected peptic ulcer bleeding awaiting endoscopy. ⊕⊕⊕⊕
- We suggest prokinetic agents in patients with a high probability of having fresh blood or a clot in the stomach when undergoing endoscopy. ⊕⊕○○
- We recommend endoscopy to diagnose the etiology of acute UGIB. ⊕⊕⊕○

The timing of endoscopy should depend on clinical factors. Urgent endoscopy (within 24 hours of presentation) is recommended for patients with a history of malignancy or cirrhosis, presentation with hematemesis, and signs of hypovolemia including hypotension, tachycardia and shock, and a hemoglobin <8 g/dL.

- We recommend endoscopic therapy for peptic ulcers with high-risk stigmata (active spurting, visible vessel). ⊕⊕⊕⊕

The management of PUD with an adherent clot is controversial. Recommended endoscopic treatment modalities include injection (sclerosants, thrombin, fibrin, or cyanoacrylate glue), cautery, and mechanical therapies.

- We recommend against epinephrine injection alone for peptic ulcer bleeding. If epinephrine injection is performed, it should be combined with a second endoscopic treatment modality (eg, cautery or clips). ⊕⊕⊕⊕
- We recommend that patients with low-risk lesions be considered for outpatient management. ⊕⊕⊕○
- We recommend against routine second-look endoscopy in patients who have received adequate endoscopic therapy. ⊕○○○
- We recommend repeat endoscopy for patients with evidence of recurrent bleeding. ⊕⊕⊕○

DISCLOSURES

T. Ben-Menachem is a consultant for Boston Scientific. D. Fisher is a consultant for Epigenomics, Inc. K. Chathadi is a speaker for Boston Scientific. Rajeev Jain is a consultant for Boston Scientific and does research for Barxx. J. Saltzman is a consultant for Hemoclip Development and

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Abbreviations: NSAID, nonsteroidal anti-inflammatory drug; PPI, proton pump inhibitor; PUD, peptic ulcer disease; UGIB, upper GI bleeding.

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