Complete Summary

GUIDELINE TITLE

ASGE guideline: the role of endoscopy in acute non-variceal upper-GI hemorrhage.

BIBLIOGRAPHIC SOURCE(S)

Adler DG, Leighton JA, Davila RE, Hirota WK, Jacobson BC, Quereshi WA, Rajan E, Zuckerman MJ, Fanelli RD, Hambrick RD, Baron T, Faigel DO. ASGE guideline: the role of endoscopy in acute non-variceal upper-GI hemorrhage. Gastrointest Endosc 2004 Oct;60(4):497-504. [99 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Acute non-variceal upper-gastrointestinal (GI) hemorrhage caused by:

- Peptic ulcer disease (PUD)
- Gastroduodenal lesions
- Esophagitis
- Varices
- Mallory-Weiss tear
- Vascular malformations including aortoenteric fistula
- Gastrointestinal tumors

Note: This guideline will not address chronic gastrointestinal blood loss or bleeding secondary to portal hypertension.

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Gastroenterology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To describe the role of gastrointestinal (GI) endoscopy in patients with acute non-variceal upper-gastrointestinal hemorrhage

TARGET POPULATION

Patients with suspected acute non-variceal upper-gastrointestinal (GI) hemorrhage

INTERVENTIONS AND PRACTICES CONSIDERED

Initial Assessment

1. Vital signs
2. Patient history
3. Review of medications, with special attention to the use of anticoagulants, antiplatelet agents, or medications associated with gastrointestinal hemorrhage (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs])
4. Signs and symptoms of hypovolemia and/or shock

Diagnosis/Evaluation

1. Upper endoscopy
    - Esophagogastroduodenoscopy (EGD)
2. *Helicobacter pylori* testing
    - Rapid urease testing
3. Computed tomography (CT) scan
4. Angiography
5. Biopsy

Initial Treatment

1. Crystalloid fluids
2. Packed red blood cells
3. Proton pump inhibitors (PPIs)
    - Omeprazole (oral or intravenous [IV])
    - Pantoprazole (IV)
4. Somatostatin
5. Octreotide
6. Pre-procedure erythromycin

Endoscopic Treatment Modalities

1. Injection therapy:
    - Normal saline solution
    - Epinephrine (adrenaline)
    - Sclerosants (ethanol, ethanolamine, and polidocanol)
    - Thrombin
    - Fibrin
    - Cyanoacrylate glues
2. Cautery devices
    - Heat probes
    - Neodymium-yttrium aluminum garnet lasers
    - Argon plasma coagulation (APC)
    - Electrocautery probes
3. Mechanical therapy
    - Endoscopic clips
    - Endoscopic band ligation devices

Other Treatment Strategies

1. Angiographic therapy
2. Surgery

MAJOR OUTCOMES CONSIDERED

- Blood transfusion requirement
- Length of intensive care unit stay
- Length of total hospital stay
- Recurrence
- Need for surgery
- Mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

In preparing this guideline, a MEDLINE search was performed; additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review
Review of Published Meta-Analyses

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Guidelines for appropriate utilization of endoscopy are based on a critical review of the available data and expert consensus.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Not stated

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not applicable

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendations are followed by evidence grades (A-C) identifying the type of supporting evidence. Definitions of the evidence grades are presented at the end of the "Major Recommendations" field.

Definition

Upper-gastrointestinal (GI) bleeding refers to GI blood loss whose origin is proximal to the ligament of Treitz. Acute upper-GI bleeding (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 (bright red blood per rectum) may occur in patients with extremely brisk UGIB.

Initial Assessment and Treatment

Patients with UGIB should undergo stabilization and resuscitation before the initiation of endoscopic therapy. The initial assessment should focus on the patient's vital signs, the presence or absence of hypovolemia and/or shock, and other medical comorbidities. A thorough review of any medications the patient may be taking, with special attention to the use of anticoagulants, antiplatelet agents, or medications associated with GI hemorrhage (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs]) should be performed.

Initially, crystalloid fluids should be infused to maintain adequate blood pressure. Patients with evidence of severe hypovolemia, shock, or ongoing blood loss manifesting as hematemesis or frequent melena 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 patients who have experienced significant blood loss or cardiac ischemia. Antisecretory therapy with a proton pump inhibitor (PPI) is warranted, and this can be done intravenously or orally. Patients with ongoing, significant hematemesis or those who may not be able to protect their airway for any reason and are at risk for aspiration should be considered for endotracheal intubation before undergoing endoscopy.

The role of PPI use in patients with acute UGIB has been extensively studied. These studies are largely from outside of the United States and focused on the use of intravenous (IV) omeprazole. A recent review of these studies found that PPI therapy was warranted in all patients with UGIB severe enough to require endoscopic therapy and recommended considering PPI therapy in patients with suspected peptic ulcer bleeding associated with hemodynamic instability, patients in whom endoscopic evaluation is delayed or unavailable, and/or those who require blood transfusion. Furthermore, a recent study comparing IV omeprazole to IV omeprazole plus endoscopic therapy in patients with UGIB and non-bleeding visible vessel or adherent clot showed that patients in the combination therapy group experience fewer episodes of recurrent bleeding and had lower blood

transfusion requirements. In the United States, the only PPI approved for IV dosing is pantoprazole, but the optimal dosing regimen for UGIB has yet to be defined. Oral omeprazole, 40 mg administered every 12 hours for 5 days, was effective in reducing bleeding and the need for surgery in a randomized, placebo-controlled study of patients with peptic ulcer disease (PUD). There are no studies comparing oral with IV PPI administration.

Somatostatin and its analogue octreotide reduce portal venous blood flow and arterial flow to the stomach and the duodenum, while preserving renal arterial flow. Fourteen studies in 1,829 patients with non-variceal UGIB were summarized by a meta-analysis that concluded that somatostatin or octreotide reduced the risk of continued bleeding and the need for surgery, and that these agents are more effective in peptic ulcer bleeding than for non-peptic ulcer bleeding (i.e., hemorrhagic gastritis). These agents may be considered as an adjunct treatment before endoscopy or when upper endoscopy is unsuccessful, contraindicated, or unavailable.

Clinical features associated with a high risk of recurrent bleeding, need for surgery, and increased mortality are listed in the table below.

Table: Clinical risk factors for poor outcomes*
• Older age (>60 years) • Severe comorbidity • Active bleeding (witnessed hematemesis, red blood per nasogastric tube, hematochezia) • Hypotension or shock • Red blood cell transfusion ≥6 units • Inpatient status at time of bleed • Severe coagulopathy

*Recurrent bleeding, need for endoscopic hemostasis or surgery, or mortality.

Role and Effectiveness of 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 and total hospital stay. Early endoscopy (within 24 hours of hospital admission) has a greater impact than later endoscopy on length of hospital stay and requirements for blood transfusion. In appropriate settings, endoscopy can be used to assess the need for inpatient admission. When evaluated in emergency room settings, up to 46% of hemodynamically stable patients who are evaluated for UGIB with upper endoscopy and subsequently are found to have low-risk stigmata for recurrent bleeding can be safely discharged and followed as outpatients.

Intravenous erythromycin (250 mg IV bolus or 3 mg/kg over 30 minutes) 30 to 90 minutes before esophagogastroduodenoscopy (EGD) promotes gastric motility and emptying of gastric contents and can significantly improve the quality of the examination with regard to mucosal visibility.

Endoscopic Prognostic Features

Several endoscopic findings most closely associated with PUD but sometimes seen with other causes of UGIB (e.g., severe esophagitis with ulceration), have been associated with specific recurrent bleeding rates and, thus, the need for endoscopic therapy (see the table below titled "Stigmata of ulcer hemorrhage and risk of recurrent bleeding without endoscopic therapy").

Endoscopic therapy is indicated for patients found to have actively bleeding or spurting arterial vessels and for those with a non-bleeding visible vessel (i.e., pigmented protuberances) in an ulcer. Adherent clot seen in an ulcer has been a source of controversy with regard to the need for endoscopic treatment, but recent data has shown benefit to endoscopic clot removal and treatment of an underlying lesion instead of observation alone. 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.

Table: Stigmata of ulcer hemorrhage and risk of recurrent bleeding without endoscopic therapy

Stigmata	Risk of recurrent bleeding without therapy
Active arterial (spurting) bleeding	Approaches 100%
Non-bleeding visible vessel ("pigmented protuberance")	Up to 50%
Non-bleeding adherent clot	30-35%
Ulcer oozing (without other stigmata)	10-27%
Flat spots	<8%
Clean-based ulcers	<3%

Endoscopic Treatment Modalities of GI Hemorrhage

Injection methods. The method of action of injection therapy is primary tamponade because of volume effect, with some agents having a secondary pharmacologic effect. Agents available for injection to produce tamponade include normal saline solution and epinephrine (adrenaline). 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 have a superior effect in achieving hemostasis. 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. Thrombin has been used in several studies in conjunction with heat probe therapy and epinephrine injection, but only one of these studies (by using thrombin combined with epinephrine) showed any additional benefit conferred by the addition of thrombin. No prospective randomized trials of thrombin monotherapy have been performed.

Cautery. Cautery devices include heat probes, neodymium-yttrium aluminum garnet lasers, argon plasma coagulation (APC), 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. Heat probes and electrocautery probes also use local tamponade (mechanical pressure of the probe tip at/on the bleeding site) combined with heat or electrical current to coagulate (and thus close) the vessel in question, a process known as coaptation. Argon plasma coagulation uses a stream of ionized gas to conduct electricity resulting in coagulation of superficial tissues. Argon plasma coagulation is primarily used for the treatment of superficial lesions, such as vascular abnormalities, but may have a role in some patients with bleeding from other causes.

Mechanical therapy. Mechanical therapy refers to the implantation of a device that causes physical tamponade of a bleeding site. Currently, the only mechanical therapies widely available are endoscopically placed clips and band ligation devices. Endoscopic clips usually are placed over a bleeding site (e.g., visible vessel) and left in place. Clips currently are available in two or three pronged configurations, can be affixed to bleeding sites, and typically slough off days to weeks after placement. Endoscopic band ligation devices, commonly used in variceal bleeding, also have been used to treat non-variceal causes of bleeding and involve the placement of elastic bands over tissue to produce mechanical compression and tamponade.

Overview of Endoscopic Approaches to Common Causes of Acute UGIB

In patients with UGIB, the most common etiologies are as follows: PUD (35-50%), gastroduodenal erosions (8-15%), esophagitis (5-15%), varices (5-10%), Mallory-Weiss tear (15%), vascular malformations (5%), with other conditions (e.g., malignancy) making up the remaining cases.

PUD

Peptic ulcer disease represents the most common cause of UGIB, accounting for a third to a half of all episodes. The most frequent causes of PUD are nonsteroidal anti-inflammatory drugs (NSAIDs) and *Helicobacter pylori* infection, although a variety of other clinical settings can predispose patients to PUD.

Endoscopic therapy for patients with UGIB caused by PUD has been studied in randomized, controlled trials. Laser therapy; monopolar electrocautery; bipolar electrocautery; heat probe; epinephrine injection; and epinephrine injection with additives, such as the sclerosants ethanolamine and polidocanol, are all effective when compared with no therapy or sham therapy.

Numerous prospective randomized studies of endoscopic treatment methods have been performed. No single modality has been shown to be superior for treating UGIB caused by PUD. For epinephrine injection, the addition of a second modality (combination therapy) reduces further bleeding, the need for surgery, and mortality. Operator experience plays a significant role in modality choice and in achieving hemostasis.

All patients with PUD should undergo diagnostic testing *for H pylori* infection. In the setting of active bleeding, rapid urease tests have reduced sensitivity and cannot be relied upon to rule out infection. All patients with positive test results should be treated to eradicate infection. Patients with PUD and *H pylori* infection

who undergo treatment for infection have a significantly lower risk of recurrent bleeding than those who only receive antisecretory therapy.

Esophageal Lesions

Esophagitis, a common cause of UGIB, can be caused by gastroesophageal reflux, infection, medications, caustic ingestion, or radiation. 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 most commonly self-limited. 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. Uncontrolled bleeding may require angiographic therapy or surgery.

Vascular Abnormalities

Vascular abnormalities typically cause microscopic chronic blood loss and, occasionally, acute GI hemorrhage. These lesions can occur sporadically or in association with other disorders: cirrhosis, renal failure, radiation injury, various collagen vascular diseases, and hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu disease). Endoscopic ligation, laser, argon plasma coagulation, contact cautery, and sclerotherapy have been reported to be effective. There are no prospective trials comparing treatment methods for acute UGIB caused by vascular malformations.

Dieulafoy's lesion typically presents with intermittent, recurrent UGIB. The lesion occurs when an abnormally large-caliber submucosal artery becomes exposed at the surface of the mucosa and then ruptures, usually in the stomach, but also in the small bowel. Endoscopic methods to treat Dieulafoy's lesion include banding, clipping, electrocautery, cyanoacrylate glue, sclerosant injection, epinephrine injection, heat probe, banding, and laser therapy. Large single-center experiences have not identified one modality as being superior to others, and no prospective randomized trials have been published. Epinephrine injection monotherapy is associated with a higher rate of recurrent bleeding. Tattooing of the lesion should be considered to facilitate future treatment should recurrent bleeding occur. If endoscopic treatment is successful, recurrence of bleeding at the same site is rare. If endoscopic therapy fails, interventional radiology or surgical approaches may be required.

Aortoenteric Fistulas

Aortoenteric fistulas may be primary (caused by arteriosclerosis, aortic aneurysms, aortic infections), or secondary (aortic repair with implantation of a synthetic graft). Most aortoenteric fistulas occur at the level of the distal duodenum or the jejunum, which may be beyond the reach of a standard upper endoscope. Aortic graft material may be seen protruding into the bowel lumen. Computed tomography (CT) scans and angiography sometimes demonstrate the fistula if contrast can be seen extravasating into the bowel. There is no endoscopic therapy for aortoenteric fistula. Surgery is the only definitive treatment.

GI tumors

Benign or malignant GI tumors, whether primary or metastatic, cause approximately 5% of cases of UGIB. Case series of endoscopic therapy have reported initial hemostasis rates similar to or lower than that seen in PUD, but recurrent bleeding rates were high, between 16% and 80%. Procedure-related complications also were more frequent. The optimal treatment modality has not been defined. 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 Treatment

Despite adequate initial endoscopic therapy, recurrent bleeding in patients with UGIB can occur in up to 24% of high-risk patients, although more recent studies that emphasize the use of PPI therapy in addition to combination endoscopic therapy show recurrent bleeding rates of approximately 10%. Patients with recurrent bleeding respond favorably to repeat endoscopic therapy. Scheduled repeat endoscopy (e.g., at 24 hours) has been advocated for patients with high-risk stigmata that were treated at the time of the initial bleed. Retrospective and prospective studies have suggested that scheduled repeat endoscopy reduces recurrent bleeding rates and may be cost effective in these patients. The precise role of scheduled repeat endoscopy has yet to be defined.

Summary

- The initial management of UGIB is patient assessment and stabilization with volume resuscitation. **(C)**
- High-risk patients are those with hematemesis, hemodynamic instability, coagulopathy, renal failure, older age, and multiple comorbidities; these patients require more intensive monitoring. **(B)**
- Antisecretory therapy with PPIs is recommended for patients with bleeding caused by peptic ulcers or in those with suspected peptic ulcer bleeding in whom endoscopy is delayed or unavailable. **(A)**
- Preprocedure erythromycin improves mucosal visibility. **(A)**
- While not part of the routine management of non-variceal UGIB, somatostatin or octreotide can reduce the risk of continued bleeding and the need for surgery but should be viewed as an adjunct to endoscopic and PPI therapy. **(A)**
- Endoscopy is effective in the diagnosis and the treatment of UGIB. **(A)**
- Endoscopic stigmata that predict a high risk of recurrent bleeding in PUD are active spurting, a visible vessel, and an adherent clot; these lesions should be treated. **(A)**
- Patients with low-risk lesions can be considered for outpatient treatment. **(A)**
- Available endoscopic treatment modalities include injection, cautery, and mechanical therapies. **(A)**
- Studies have not demonstrated clear superiority of any one endoscopic treatment modality, although epinephrine injection alone is inferior to combination therapy for peptic ulcer bleeding. **(A)**
- Scheduled repeat endoscopy in patients at high-risk for recurrent bleeding may be beneficial but its role has yet to be defined. **(A)**
- Patients with PUD should be tested and treated for *Helicobacter pylori*. **(A)**

Definitions:

A. Prospective controlled trials
B. Observational studies
C. Expert opinion

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and classified for the recommendations using the following scheme:

A. Prospective controlled trials
B. Observational studies
C. Expert opinion

When little 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 utilization of endoscopy are based on a critical review of the available data and expert consensus.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of endoscopy in the diagnosis and management of patients with acute non-variceal upper-gastrointestinal (GI) hemorrhage

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Further controlled clinical studies are needed to clarify aspects of this statement, and revision may be necessary as new data appear. Clinical consideration may justify a course of action at variance to these recommendations.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Adler DG, Leighton JA, Davila RE, Hirota WK, Jacobson BC, Quereshi WA, Rajan E, Zuckerman MJ, Fanelli RD, Hambrick RD, Baron T, Faigel DO. ASGE guideline: the role of endoscopy in acute non-variceal upper-GI hemorrhage. Gastrointest Endosc 2004 Oct;60(4):497-504. [99 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Oct

GUIDELINE DEVELOPER(S)

American Society for Gastrointestinal Endoscopy - Medical Specialty Society

SOURCE(S) OF FUNDING

American Society for Gastrointestinal Endoscopy

GUIDELINE COMMITTEE

Standards of Practice Committee

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American Society for Gastrointestinal Endoscopy (ASGE) Web site.

Print copies: Available from the American Society for Gastrointestinal Endoscopy, 1520 Kensington Road, Suite 202, Oak Brook, IL 60523

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on March 23, 2005. The information was verified by the guideline developer on March 31, 2005.

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