Chapter 48: Gastrointestinal Bleeding

Loren Laine

INTRODUCTION

Gastrointestinal bleeding (GIB) presents as either overt or occult bleeding. *Overt GIB* is manifested by *hematemesis*, vomitus of red blood or "coffee-grounds" material; *melena*, black, tarry stool; and/or *hematochezia*, passage of red or maroon blood from the rectum. In the absence of overt bleeding, *occult GIB* may present with *symptoms of blood loss or anemia* such as lightheadedness, syncope, angina, or dyspnea; with iron-deficiency anemia; or a positive fecal occult blood test on colorectal cancer screening. GIB is also categorized by the site of bleeding as upper, from the esophagus, stomach, or duodenum; lower, from the colon; small intestinal; or obscure GIB if the source is unclear.

GIB is the most common gastrointestinal condition leading to hospitalization in the United States, accounting for ~513,000 admissions and $5 billion in direct costs annually. The case fatality of patients hospitalized with GIB is ~2% in the United States. Patients generally die from decompensation of other underlying illnesses rather than exsanguination.

SOURCES OF GASTROINTESTINAL BLEEDING

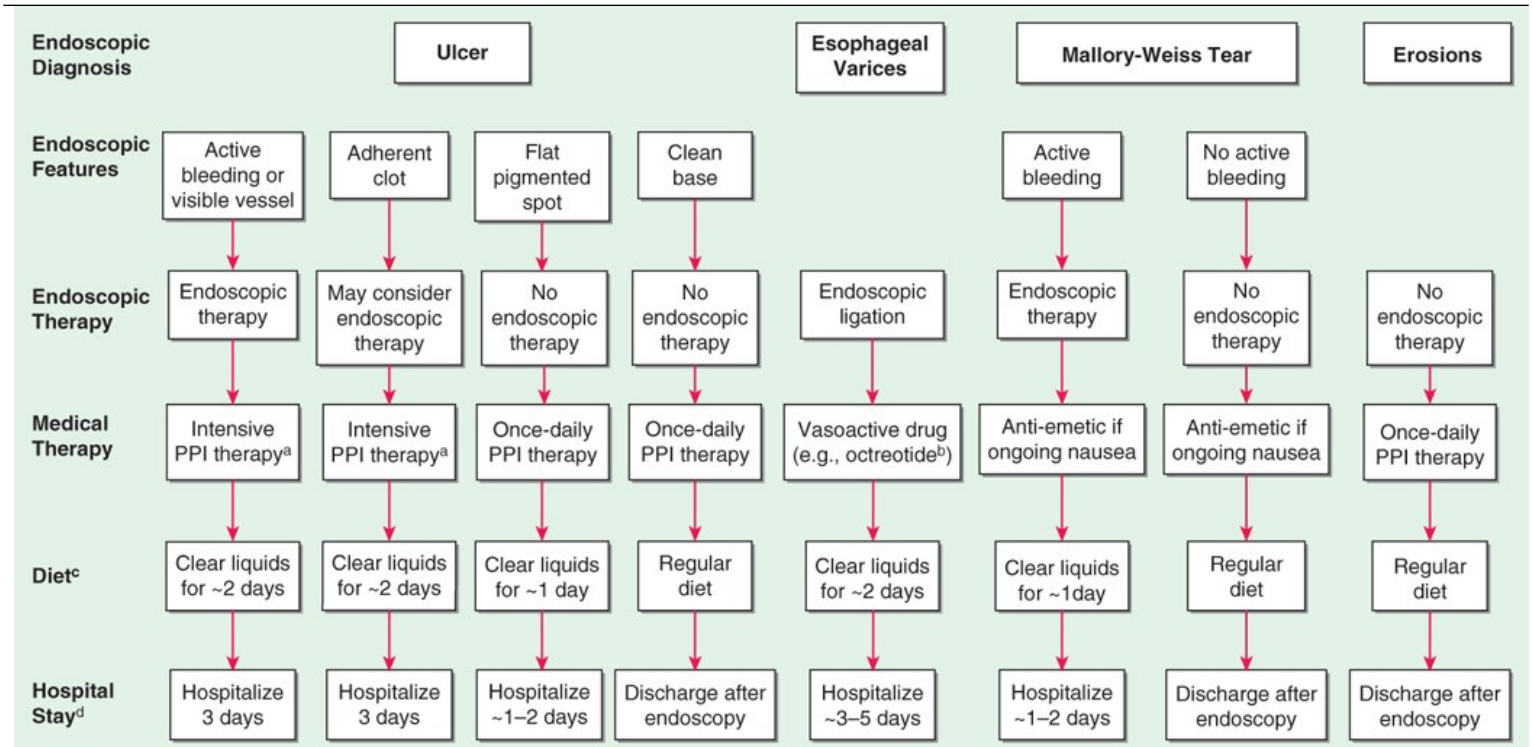
Upper Gastrointestinal Sources of Bleeding

PEPTIC ULCERS

Peptic ulcers are the most common cause of upper GIB (UGIB), accounting for ~50% of UGIB hospitalizations. Features of an ulcer at endoscopy provide important prognostic information that guides subsequent management decisions **(Fig. 48-1)**. Approximately 20% of patients with bleeding ulcers have the highest-risk findings of active bleeding or a nonbleeding visible vessel; one-third of such patients have further bleeding that requires urgent surgery if they are treated conservatively. These patients benefit from endoscopic therapy such as bipolar electrocoagulation, heater probe, injection therapy (e.g., absolute alcohol, 1:10,000 epinephrine), and/or clips with reductions in bleeding, hospital stay, mortality, and costs. In contrast, patients with clean-based ulcers have rates of serious recurrent bleeding approaching zero. If stable with no other reason for hospitalization, such patients may be discharged home after endoscopy.

FIGURE 48-1

Suggested algorithm for patients with acute upper gastrointestinal bleeding based on endoscopic findings.



[a]Intravenous bolus (80 mg) followed by infusion (8 mg/h) for 3 days; or oral or intravenous bolus (e.g., 80 mg) followed by intermittent high doses (e.g., 40–80 mg bid or 40 mg tid) for 3 days.Then twice-daily PPI on days 4–14 followed by once-daily PPI.
[b]Intravenous 50 µg bolus followed by 50 µg/h infusion for 2–5 days.
[c]Diet after endoscopy, assuming no nausea or vomiting.
[d]Duration after endoscopy assuming patient stable without further bleeding or concurrent medical conditions requiring hospitalization; PPI, proton pump inhibitor.

Randomized controlled trials document that high-dose, constant-infusion IV proton pump inhibitor (PPI) (80-mg bolus and 8-mg/h infusion), designed to sustain intragastric pH >6 and enhance clot stability, decreases further bleeding and mortality in patients with high-risk ulcers (active bleeding, nonbleeding visible vessel, adherent clot) when given after endoscopic therapy. Meta-analysis of randomized trials indicates that high-dose intermittent PPIs are noninferior to constant-infusion PPI therapy and thus may be substituted. Patients with lower-risk findings (flat pigmented spot or clean base) do not require endoscopic therapy and receive standard doses of oral PPI.

Approximately 10–50% of patients with bleeding ulcers rebleed within the next year if no preventive strategies are employed. Prevention of recurrent bleeding focuses on the three main factors in ulcer pathogenesis, *Helicobacter pylori*, nonsteroidal anti-inflammatory drugs (NSAIDs), and acid. Eradication of *H. pylori* in patients with bleeding ulcers decreases rebleeding rates to <5%. If a bleeding ulcer develops in a patient taking NSAIDs, the NSAIDs should be discontinued. If NSAIDs must be given, a cyclooxygenase (COX)-2 selective NSAID plus a PPI is recommended, based on results of a randomized trial. Patients with established cardiovascular disease who develop bleeding ulcers while taking low-dose aspirin for secondary prevention should restart aspirin as soon as possible after their bleeding episode (1–7 days). A randomized trial showed that immediate reinstitution of aspirin was associated with a lower 8-week mortality compared to not restarting aspirin (1% vs 13%; hazard ratio, 0.2; 95% CI, 0.1–0.6). In contrast, aspirin probably should be discontinued in most patients taking aspirin for primary prevention of cardiovascular events who develop UGIB. Patients with bleeding ulcers unrelated to *H. pylori* or NSAIDs should remain on PPI therapy indefinitely given a 42% incidence of rebleeding at 7 years without protective therapy.
Peptic ulcers are discussed in Chap. 324.

MALLORY-WEISS TEARS

Mallory-Weiss tears account for ~2–10% of UGIB hospitalizations. The classic history is vomiting, retching, or coughing preceding hematemesis, especially in an alcoholic patient. Bleeding from these tears, which are usually on the gastric side of the gastroesophageal junction, stops spontaneously in ~80–90% of patients and recurs in only 0–10%. Endoscopic therapy is indicated for actively bleeding Mallory-Weiss tears. **Mallory-Weiss tears are discussed in Chap. 323.**

ESOPHAGEAL VARICES

The proportion of UGIB hospitalizations due to varices varies widely, from ~2–40%, depending on the population. Patients with variceal hemorrhage have poorer outcomes than patients with other sources of UGIB. Esophageal varices are treated with endoscopic ligation and an IV vasoactive medication (octreotide, somatostatin, vapreotide, terlipressin) for 2–5 days. Combination of endoscopic and medical therapy is superior to either therapy alone in decreasing rebleeding. Over the long term, treatment with nonselective beta blockers plus endoscopic ligation is recommended because the combination is more effective than either alone in reduction of recurrent esophageal variceal bleeding. Transjugular intrahepatic portosystemic shunt (TIPS) is recommended in patients who have persistent or recurrent bleeding despite endoscopic and medical therapy. TIPS also should be considered in the first 1–2 days of hospitalization for acute variceal bleeding in patients with advanced liver disease (Child-Pugh class B, Child-Pugh class C with score 10–13), because randomized trials show significant decreases in rebleeding and mortality compared with standard endoscopic and medical therapy.

Portal hypertension is also responsible for bleeding from gastric varices, varices in the small and large intestine, and portal hypertensive gastropathy and enterocolopathy. Bleeding gastric varices are treated with endoscopic injection of tissue adhesive (e.g., *n*-butyl cyanoacrylate), if available; if not, TIPS is performed.

EROSIVE DISEASE

Erosions are endoscopically visualized breaks that are confined to the mucosa and do not cause major bleeding because arteries and veins are not present in the mucosa. Erosions in the esophagus, stomach, or duodenum commonly cause mild UGIB, with erosive gastritis and duodenitis accounting for perhaps ~10–15% and erosive esophagitis (primarily due to gastroesophageal reflux disease) accounting for ~1–10% of UGIB hospitalizations. The most important cause of gastric and duodenal erosions is NSAID use: ~50% of patients who chronically ingest NSAIDs may have gastric erosions. Other potential causes of gastric erosions include alcohol intake, *H. pylori* infection, and stress-related mucosal injury.

Stress-related gastric mucosal injury occurs only in extremely sick patients, such as those with serious trauma, major surgery, burns covering more than one-third of the body surface area, major intracranial disease, or severe medical illness (e.g., ventilator dependence, coagulopathy). Severe bleeding should not develop unless ulceration occurs. The mortality rate in these patients is high because of their serious underlying illnesses.

The incidence of bleeding from stress-related gastric mucosal injury has decreased dramatically in recent years, most likely due to better care of critically ill patients. A recent double-blind placebo-controlled randomized trial in 3282 intensive care patients with risk factors for GIB showed a small benefit of PPI in clinically important bleeding (2.5% vs 4.2%) without a difference in mortality or infections (e.g., *Clostridium difficile*, pneumonia). Thus, pharmacologic prophylaxis for bleeding has limited benefit but may be considered in the high-risk patients mentioned above. Meta-analyses of randomized trials suggest PPIs are more effective than H_2-receptor antagonists in reduction of overt and clinically important UGIB without differences in mortality or nosocomial pneumonia.

OTHER CAUSES

Less common causes of UGIB include neoplasms, vascular ectasias (including hereditary hemorrhagic telangiectasias [Osler-Weber-Rendu] and gastric antral vascular ectasia ["watermelon stomach"]), Dieulafoy's lesion (in which an aberrant vessel in the mucosa bleeds from a pinpoint mucosal defect), prolapse gastropathy (prolapse of proximal stomach into esophagus with retching, especially in alcoholics), aortoenteric fistulas, and hemobilia or hemosuccus pancreaticus (bleeding from the bile duct or pancreatic duct).

Small-Intestinal Sources of Bleeding

Patients without a source of GIB identified on upper endoscopy and colonoscopy were previously labeled as having obscure GIB. With the advent of improved diagnostic modalities, ~75% of GIB previously labeled obscure is now estimated to originate in the small intestine beyond the extent of a standard upper endoscopic exam. Small-intestinal GIB may account for ~5% of GIB cases. The most common causes in adults include vascular ectasias, neoplasm (e.g., gastrointestinal stromal tumor, carcinoid, adenocarcinoma, lymphoma, metastases), and NSAID-induced erosions and ulcers. Meckel's diverticulum is the most common cause of significant small-intestinal GIB in children, decreasing in frequency as a cause of bleeding with age. Other less common causes of small-intestinal GIB include Crohn's disease, infection, ischemia, vasculitis, small-bowel varices, diverticula, intussusception, Dieulafoy's lesions, aortoenteric fistulas, and duplication cysts.

Small-intestinal vascular ectasias are treated with endoscopic therapy, if possible, based on observational studies suggesting initial efficacy. However, rebleeding is common: 45% over a mean follow-up of 26 months in a systematic review. Estrogen/progesterone compounds are not recommended

because a multicenter double-blind trial found no benefit in prevention of recurrent bleeding. Octreotide is used, based on positive results from case series but no randomized trials. A randomized trial reported significant benefit of thalidomide and awaits further confirmation. Other isolated lesions, such as tumors, generally require surgical resection.

Colonic Sources of Bleeding

Hemorrhoids are probably the most common cause of lower GIB (LGIB); anal fissures also cause minor bleeding and pain. If these local anal processes, which rarely require hospitalization, are excluded, the most common cause of LGIB in adults is diverticulosis. Other causes include vascular ectasias (especially in the proximal colon of patients >70 years), neoplasms (primarily adenocarcinoma), colitis (ischemic, infectious, Crohn's or ulcerative colitis, NSAID-induced colitis or ulcers), postpolypectomy bleeding, and radiation proctopathy. Rarer causes include solitary rectal ulcer syndrome, varices (most commonly rectal), lymphoid nodular hyperplasia, vasculitis, trauma, and aortocolic fistulas. In children and adolescents, the most common colonic causes of significant GIB are inflammatory bowel disease and juvenile polyps.

Diverticular bleeding is abrupt in onset, usually painless, sometimes massive, and often from the right colon; chronic or occult bleeding is not characteristic. Case series from the United States and Europe suggest colonic diverticula stop bleeding spontaneously in ≥90% of patients, with rebleeding on long-term follow-up as low as ~15% over 4-5 years. Rebleeding is substantially higher in reports from Asia. Case series suggest endoscopic therapy may decrease recurrent bleeding in the uncommon case when colonoscopy identifies the specific bleeding diverticulum. When diverticular bleeding is found at angiography, transcatheter arterial embolization by superselective technique stops bleeding in a majority of patients. Segmental surgical resection is recommended for persistent or refractory diverticular bleeding.

Bleeding from colonic vascular ectasias may be overt or occult; it tends to be chronic and only occasionally hemodynamically significant. Endoscopic hemostatic therapy may be used in the treatment of vascular ectasias, as well as discrete bleeding ulcers and postpolypectomy bleeding. Transcatheter arterial embolization also may be attempted for persistent bleeding from vascular ectasias and other discrete lesions. Surgical therapy is generally required for major persistent or recurrent bleeding from colonic sources that cannot be treated medically, endoscopically, or angiographically. Patients with Heyde's syndrome (bleeding vascular ectasias and aortic stenosis) appear to benefit from aortic valve replacement.

APPROACH TO THE PATIENT WITH GASTROINTESTINAL BLEEDING

Initial Assessment

Measurement of the heart rate and blood pressure is the best way to initially assess a patient with GIB. Clinically significant bleeding leads to postural changes in heart rate or blood pressure, tachycardia, and, finally, recumbent hypotension. In contrast, hemoglobin does not fall immediately with acute GIB, due to proportionate reductions in plasma and red cell volumes ("people bleed whole blood"). Thus, hemoglobin may be normal or only minimally decreased at initial presentation of a severe bleeding episode. As extravascular fluid enters the vascular space to restore volume, the hemoglobin falls, but this process may take up to 72 h. Transfusion is recommended when the hemoglobin drops below 7 g/dL, based on a large randomized trial showing this restrictive transfusion strategy decreases rebleeding and death in acute UGIB compared with a transfusion threshold of 9 g/dL. Patients with slow, chronic GIB may have very low hemoglobin values despite normal blood pressure and heart rate. With the development of iron-deficiency anemia, the mean corpuscular volume is low and red blood cell distribution width is increased.

Differentiation of UGIB from LGIB

Hematemesis indicates an UGIB source. Melena indicates blood has been present in the gastrointestinal (GI) tract for ≥14 h and as long as 3–5 days. The more proximal the bleeding site, the more likely melena will occur. Hematochezia usually represents a lower GI source of bleeding, although an upper GI lesion may bleed so briskly that blood transits the bowel before melena develops. When hematochezia is the presenting symptom of UGIB, it is associated with hemodynamic instability and dropping hemoglobin. Bleeding lesions of the small bowel may present as melena or hematochezia. Other clues to UGIB include hyperactive bowel sounds and an elevated blood urea nitrogen (due to volume depletion and blood proteins absorbed in the small intestine).

A nonbloody nasogastric aspirate may be seen in ~15% of patients with UGIB who present with clinically serious hematochezia. A bile-stained appearance does not exclude UGIB because reports of bile in the aspirate are incorrect in ~50% of cases. Testing of aspirates that are not grossly bloody for occult blood is not useful.

Evaluation and Management of UGIB

(FIG. 48-1)

INITIAL RISK ASSESSMENT

Baseline characteristics predictive of rebleeding and death include hemodynamic compromise (tachycardia or hypotension), increasing age, and comorbidities. Risk assessment tools may be used to identify patients with very low risk. Discharge from the emergency room with outpatient management has been suggested for patients with a Glasgow-Blatchford score (possible range 0–23, **Table 48-1**) of 0–1 because only ~1% of patients who require transfusion, require hemostatic intervention, or die have a score of 0–1.

TABLE 48-1

Glasgow-Blatchford Score

RISK FACTORS AT ADMISSION	SCORE
Blood urea nitrogen (mg/dL)	
18.2 to <22.4	2
22.4 to <28.0	3
28.0 to <70.0	4
≥70.0	6
Hemoglobin (g/dL)	
12.0 to <13.0 (men); 10.0 to <12.0 (women)	1
10.0 to <12.0 (men)	3
<10.0	6
Systolic blood pressure (mmHg)	
100–109	1
90–99	2
<90	3
Heart rate (beats per minute)	
≥100	1
Melena	1
Syncope	2
Hepatic disease	2
Cardiac failure	2

PRE-ENDOSCOPIC MEDICATIONS

PPI infusion may be considered at presentation; it decreases high-risk ulcer stigmata (e.g., active bleeding) and need for endoscopic therapy but does not improve clinical outcomes such as further bleeding, surgery, or death. The promotility agent erythromycin, 250 mg intravenously ~30–90 min before endoscopy, is suggested to improve visualization at endoscopy, thereby reducing the need for repeat endoscopy and hospital stay. Cirrhotic patients presenting with UGIB should be given an antibiotic (e.g., ceftriaxone) and IV vasoactive medication (e.g., octreotide) upon presentation. Antibiotics decrease bacterial infections, rebleeding, and mortality, and vasoactive medications may improve control of bleeding in the 12 h after presentation.

ENDOSCOPY

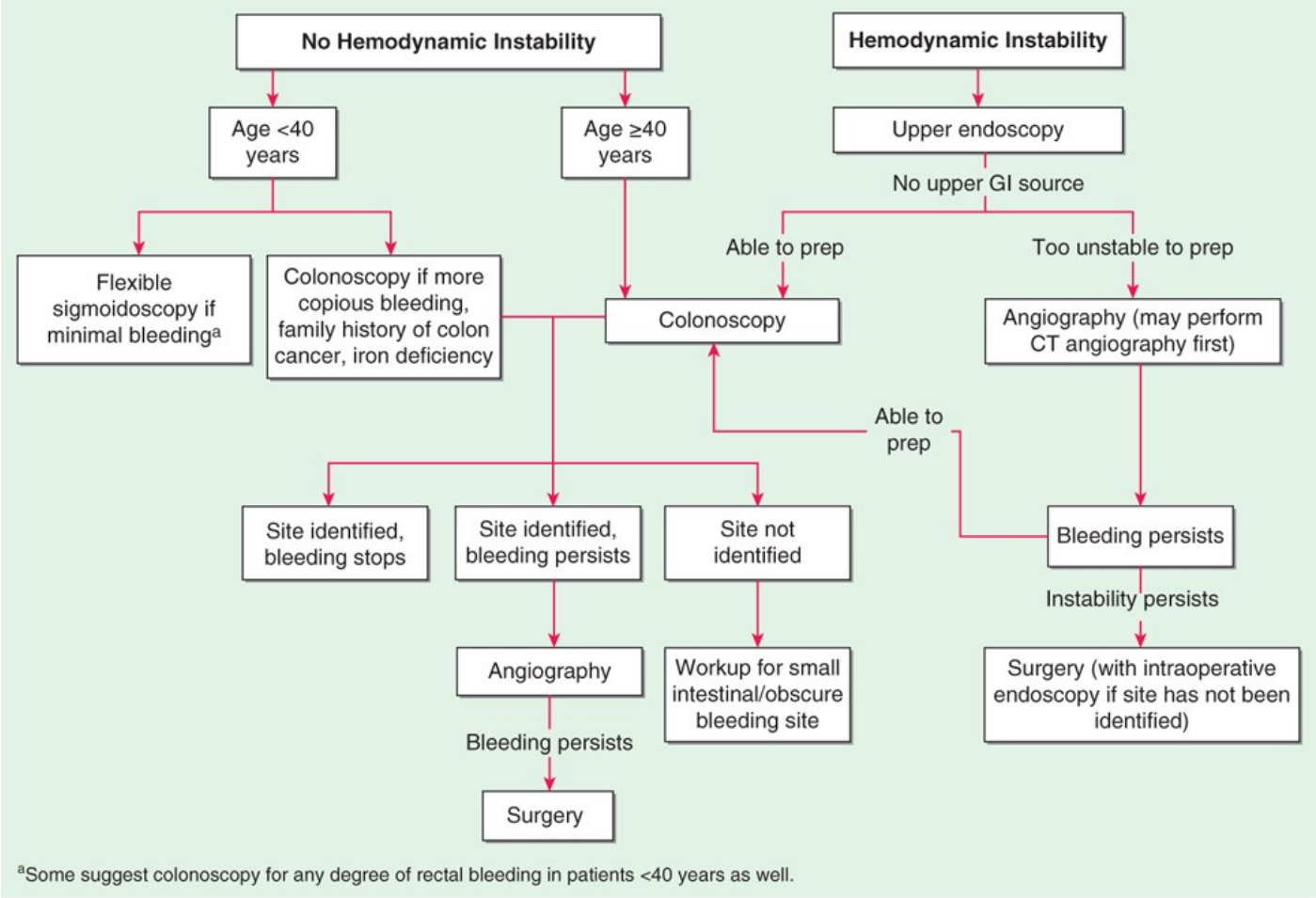
Upper endoscopy should be performed within 24 h in most patients hospitalized with UGIB whether they have clinical features predicting low risk or high risk of further bleeding and death. Even in high-risk patients, more urgent endoscopy (performed within 6 h of gastroenterology consultation) does not improve clinical outcomes. Early endoscopy in low-risk patients (e.g., hemodynamically stable without severe comorbidities) identifies low-risk findings (e.g., clean-based ulcers, erosions, nonbleeding Mallory-Weiss tears) that allow discharge in ≥40% of patients, thereby reducing hospital stay and costs. Patients with high-risk endoscopic findings (e.g., varices, ulcers with active bleeding or a visible vessel) benefit from hemostatic therapy at endoscopy.

Evaluation and Management of LGIB

Patients with hematochezia and hemodynamic instability should have upper endoscopy to rule out an upper GI source before evaluation of the lower GI tract **(FIG. 48-2)**.

FIGURE 48-2

Suggested algorithm for patients with acute lower gastrointestinal bleeding.



Colonoscopy after an oral lavage solution is the procedure of choice in most patients admitted with LGIB unless bleeding is too massive, in which case angiography is recommended. Computed tomography (CT) angiography is often suggested prior to angiography to document evidence and location of active bleeding. Sigmoidoscopy is used primarily in patients <40 years old with minor bleeding. In patients with no source identified on colonoscopy, imaging studies may be employed. ^{99m}Tc-labeled red cell scan allows repeated imaging for up to 24 h and may identify the general location of bleeding. However, CT angiography is increasingly used instead because it is likely superior and more readily available. In active LGIB, angiography can detect the site of bleeding (extravasation of contrast into the gut) and permits treatment with transcatheter arterial embolization.

Evaluation and Management of Small-Intestinal or Obscure GIB

In patients with massive bleeding suspected to be from the small intestine, current guidelines suggest angiography as the initial test, with CT angiography or ^{99m}Tc-labeled red cell scan prior to angiography if the patient's clinical status permits. For others, repeat upper and lower endoscopy may be considered as the initial evaluation because second-look procedures identify a source in up to ~25% of upper endoscopies and colonoscopies; a push enteroscopy, usually performed with a pediatric colonoscope to inspect the entire duodenum and proximal jejunum, may be substituted for a repeat standard upper endoscopy. If second-look procedures are negative, evaluation of the entire small intestine is performed, usually with video capsule endoscopy. A systematic review of comparative studies showed the yield of "clinically significant findings" to be greater with capsule than push enteroscopy (56% vs 26%) or small bowel barium radiography (42% vs 6%). However, capsule endoscopy does not allow full visualization of the small intestine, tissue sampling, or application of therapy.

CT enterography may be used initially instead of video capsule in patients with possible small bowel narrowing (e.g., stricture, prior surgery or radiation, Crohn's disease) and may follow a negative video capsule for suspected small-intestinal GIB, given its higher sensitivity for small-intestinal masses.

If capsule endoscopy is positive, management is dictated by the finding. If capsule endoscopy is negative, clinically stable patients may be observed and

treated with iron if iron deficiency is present, while those with ongoing bleeding (e.g., need for transfusions) undergo further testing. A second capsule endoscopy may be considered because it is reported to identify a source in up to ~50% of cases. “Deep” enteroscopy (double-balloon, single-balloon, or spiral enteroscopy) is commonly the next test after capsule endoscopy for clinically important GIB documented or suspected to be from the small intestine because it allows the endoscopist to examine, obtain specimens from, and provide therapy to much or all of the small intestine. Other imaging techniques sometimes used in evaluation of obscure GIB include ^{99m}Tc-labeled red blood cell scintigraphy, CT angiography, angiography, and ^{99m}Tc-pertechnetate scintigraphy for Meckel’s diverticulum (especially in young patients). If all tests are unrevealing, intraoperative endoscopy is indicated in patients with severe recurrent or persistent bleeding requiring repeated transfusions.

Positive Fecal Occult Blood Test

Fecal occult blood testing is recommended only for colorectal cancer screening, beginning at age 45–50 years in average-risk adults. A positive test necessitates colonoscopy. If evaluation of the colon is negative, further workup is not recommended unless iron-deficiency anemia or GI symptoms are present.

FURTHER READING

Garcia-Tsao G et al: Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the Study of Liver Diseases. Hepatology 65:310, 2017. [PubMed: 27786365]

Gurudu SR et al: The role of endoscopy in the management of suspected small-bowel bleeding. Gastrointest Endosc 85:22, 2017. [PubMed: 27374798]

Krag M et al: Pantoprazole in patients at risk for gastrointestinal bleeding in the ICU. N Engl J Med 379:2199, 2018. [PubMed: 30354950]

Laine L et al: ACG clinical guideline: Upper gastrointestinal and ulcer bleeding. Am J Gastroenterol 116:899, 2021. [PubMed: 33929377]

Lau JYW et al: Timing of endoscopy for acute upper gastrointestinal bleeding. N Engl J Med 382:1299, 2020. [PubMed: 32242355]

Peery AF et al: Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: Update 2018. Gastroenterology 156:254, 2019. [PubMed: 30315778]

Stanley AJ, Laine L: Management of acute upper gastrointestinal bleeding. BMJ 364:l536, 2019. [PubMed: 30910853]

Strate LL, Gralnek KM: ACG clinical guideline: Management of patients with acute lower gastrointestinal bleeding. Am J Gastroenterol 111:459, 2016. [PubMed: 26925883]

Villaneuva C et al: Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med 368:11, 2013. [PubMed: 23281973]