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Wolters Kluwer

Approach to acute upper gastrointestinal bleeding in adults

Author: John R Saltzman, MD, FACP, FACG, FASGE, AGAF
Section Editor: Mark Feldman, MD, MACP, AGAF, FACG
Deputy Editor: Anne C Travis, MD, MSc, FACG, AGAF

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INTRODUCTION

Patients with acute upper gastrointestinal (GI) bleeding commonly present with hematemesis (vomiting of blood or coffee-ground-like material) and/or melena (black, tarry stools). The initial evaluation of patients with acute upper GI bleeding involves an assessment of hemodynamic stability and resuscitation if necessary. Diagnostic studies (usually endoscopy) follow, with the goal of both diagnosis, and when possible, treatment of the specific disorder.

The diagnostic and initial therapeutic approach to patients with clinically significant (ie, the passage of more than a scant amount of blood) acute upper GI bleeding will be reviewed here. This approach is consistent with a multidisciplinary international consensus statement updated in 2010, a 2012 guideline issued by the American Society for Gastrointestinal Endoscopy, a 2012 guideline issued by the American College of Gastroenterology, and a 2015 guideline issued by the European Society of Gastrointestinal Endoscopy [1-5]. The causes of upper GI bleeding, the endoscopic management of acute upper GI bleeding, and the management of active variceal hemorrhage are discussed separately. (See "Causes of upper gastrointestinal bleeding in adults" and "Overview of the treatment of bleeding peptic ulcers" and "Overview of the management of patients with variceal bleeding" and "Methods to achieve hemostasis in patients with acute variceal hemorrhage".)

A table outlining the major causes, clinical features, and emergency management of acute severe upper gastrointestinal bleeding in adults is provided (table 1).

INITIAL EVALUATION

The initial evaluation of a patient with a suspected clinically significant acute upper GI bleed includes a history, physical examination, laboratory tests, and in some cases, nasogastric lavage (see 'Nasogastric lavage' below). The goal of the evaluation is to assess the severity of the bleed, identify potential sources of the bleed, and determine if there are conditions present that may affect subsequent management. The information gathered as part of the initial evaluation is used to guide decisions regarding triage, resuscitation, empiric medical therapy, and diagnostic testing.

Factors that are predictive of a bleed coming from an upper GI source identified in a meta-analysis included a patient-reported history of melena (likelihood ratio [LR] 5.1-5.9), melenic stool on examination (LR 25), blood or coffee grounds detected during nasogastric lavage (LR 9.6), and a ratio of blood urea nitrogen to serum creatinine greater than 30 (LR 7.5) [6]. On the other hand, the presence of blood clots in the stool made an upper GI source less likely (LR 0.05). Factors associated with severe bleeding included red blood detected during nasogastric lavage (LR 3.1), tachycardia (LR 4.9), or a hemoglobin level of less than 8 g/dL (LR 4.5-6.2).

Bleeding manifestations — Hematemesis (either red blood or coffee-ground emesis) suggests bleeding proximal to the ligament of Treitz. The presence of frankly bloody emesis suggests moderate to severe bleeding that may be ongoing, whereas coffee-ground emesis suggests more limited bleeding.

The majority of melena (black, tarry stool) originates proximal to the ligament of Treitz (90 percent), though it may also originate from the oropharynx or nasopharynx, small bowel, or right colon [7]. Melena may be seen with variable degrees of blood loss, being seen with as little as 50 mL of blood [8].

Hematochezia (red or maroon blood in the stool) is usually due to lower GI bleeding. However, it can occur with massive upper GI bleeding [9], which is typically associated with orthostatic hypotension. (See 'Physical examination' below.)

Past medical history — Patients should be asked about prior episodes of upper GI bleeding, since up to 60 percent of patients with a history of an upper GI bleed are bleeding from the same lesion [10]. In addition, the patient's past medical history should be reviewed to identify important comorbid conditions that may lead to upper GI bleeding or may influence the patient's subsequent management.

Potential bleeding sources suggested by a patient's past medical history include:

- Varices or portal hypertensive gastropathy in a patient with a history of liver disease or alcohol abuse
- Aorto-enteric fistula in a patient with a history of an abdominal aortic aneurysm or an aortic graft
- Angiodysplasia in a patient with renal disease, aortic stenosis, or hereditary hemorrhagic telangiectasia

- Peptic ulcer disease in a patient with a history of *Helicobacter pylori* infection, nonsteroidal anti-inflammatory drug (NSAIDs) use, or smoking
- Malignancy in a patient with a history of smoking, alcohol abuse, or *H. pylori* infection
- Marginal ulcers (ulcers at an anastomotic site) in a patient with a gastroenteric anastomosis

Comorbid illnesses may influence patient management in the setting of an acute upper GI bleed. Comorbid illnesses may:

- Make patients more susceptible to adverse effects of anemia (eg, coronary artery disease, pulmonary disease). Such patients may need to be maintained at higher hemoglobin levels than patients without these disorders. (See 'Blood product transfusions' below.)

- Predispose patients to volume overload in the setting of vigorous fluid resuscitation or blood transfusions (eg, renal disease, heart failure). Such patients may need more invasive monitoring during resuscitation. (See 'General support' below.)

- Result in bleeding that is more difficult to control (eg, coagulopathies, thrombocytopenia, significant hepatic dysfunction). Such patients may need transfusions of fresh frozen plasma or platelets. (See 'Blood product transfusions' below.)

- Predispose to aspiration of GI contents into the lungs (eg, dementia, hepatic encephalopathy). Endotracheal intubation should be considered in such patients. (See 'General support' below.)

Medication history — A thorough medication history should be obtained, with particular attention paid to drugs that:

- Predispose to peptic ulcer formation, such as aspirin and other NSAIDs, including COX-2 inhibitors (see "NSAIDs (including aspirin): Pathogenesis of gastroduodenal toxicity")
- Are associated with pill esophagitis (see "Medication-induced esophagitis")
- Promote bleeding, such as antiplatelet agents (eg, clopidogrel) and anticoagulants
- May alter the clinical presentation, such as bismuth and iron, which can turn the stool black

Symptom assessment — Patients should be asked about symptoms as part of the assessment of the severity of the bleed and as a part of the evaluation for potential bleeding sources. Symptoms that suggest the bleeding is severe include orthostatic dizziness, confusion, angina, severe palpitations, and cold/clammy extremities.

Specific causes of upper GI bleeding may be suggested by the patient's symptoms [7]:

- Peptic ulcer: Upper abdominal pain
- Esophageal ulcer: Odynophagia, gastroesophageal reflux, dysphagia
- Mallory-Weiss tear: Emesis, retching, or coughing prior to hematemesis

- Variceal hemorrhage or portal hypertensive gastropathy: Jaundice, abdominal distention (ascites)
- Malignancy: Dysphagia, early satiety, involuntary weight loss, cachexia

Physical examination — The physical examination is a key component of the assessment of hemodynamic stability. Signs of hypovolemia include [7]:

- Mild to moderate hypovolemia (less than 15 percent of blood volume lost): Resting tachycardia.
- Blood volume loss of at least 15 percent: Orthostatic hypotension (a decrease in the systolic blood pressure of more than 20 mmHg and/or an increase in heart rate of 20 beats per minute when moving from recumbency to standing).
- Blood volume loss of at least 40 percent: Supine hypotension.

Examination of the stool color may provide a clue to the location of the bleeding, but it is not a reliable indicator. In a series of 80 patients with severe hematochezia (red or maroon blood in the stool), 74 percent had a colonic lesion, 11 percent had an upper GI lesion, 9 percent had a presumed small bowel source, and no site was identified in 6 percent [9]. Nasogastric lavage may be carried out if there is doubt as to whether a bleed originates from the upper GI tract. (See 'Nasogastric lavage' below.)

The presence of abdominal pain, especially if severe and associated with rebound tenderness or involuntary guarding, raises concern for perforation. If any signs of an acute abdomen are present, further evaluation to exclude a perforation is required prior to endoscopy.

Finally, as with the past medical history, the physical examination should include a search for evidence of significant comorbid illnesses. (See 'Past medical history' above.)

Laboratory data — Laboratory tests that should be obtained in patients with acute upper gastrointestinal bleeding include a complete blood count, serum chemistries, liver tests, and coagulation studies. In addition, serial electrocardiograms and cardiac enzymes may be indicated in patients who are at risk for a myocardial infarction, such as older adults, patients with a history of coronary artery disease, or patients with symptoms such as chest pain or dyspnea. (See "Diagnosis of acute myocardial infarction".)

The initial hemoglobin level in patients with acute upper GI bleeding will often be at the patient's baseline because the patient is losing whole blood. With time (typically after 24 hours or more) the hemoglobin level will decline as the blood is diluted by the influx of extravascular fluid into the vascular space and by fluid administered during resuscitation. It should be kept in mind that excessive volume administration can lead to a falsely low hemoglobin value. The initial hemoglobin level is monitored every two to eight hours, depending upon the severity of the bleed.

Patients with acute bleeding should have normocytic red blood cells. Microcytic red blood cells or iron deficiency anemia suggest chronic bleeding. Because blood is absorbed as it passes through the small bowel and patients may have decreased renal perfusion, patients with acute upper GI bleeding typically have an elevated blood urea nitrogen (BUN)-to-creatinine or urea-to-creatinine ratio. Values >36:1 or >100:1, respectively, suggest upper GI bleeding as the cause [11-13]. The higher the ratio, the more likely the bleeding is from an upper GI source [11].

Nasogastric lavage — Whether all patients with suspected acute upper GI bleeding require nasogastric tube (NGT) placement is controversial, in part because studies have failed to demonstrate a benefit with regard to clinical outcomes [14]. As an example, a retrospective study looked at whether there were clinical benefits from NGT lavage in 632 patients admitted with gastrointestinal bleeding [15]. Patients who underwent NGT lavage were matched with patients with similar characteristics who did not undergo NGT lavage. NGT lavage was associated with a shorter time to endoscopy. However, there were no differences between those who underwent NGT lavage and those who did not with regard to mortality, length of hospital stay, surgery, or transfusion requirement. Similarly, in a randomized trial with 280 patients with upper GI bleeding, there were no differences in rebleeding rates or mortality between patients who underwent NGT lavage and those who did not [16].

More often, NGT lavage is used when it is unclear if a patient has ongoing bleeding and thus might benefit from an early endoscopy. In addition, NGT lavage can be used to remove particulate matter, fresh blood, and clots from the stomach to facilitate endoscopy. (See "Inpatient placement and management of nasogastric and nasoenteric tubes in adults", section on 'Tube placement'.)

The presence of red blood or coffee ground material in the nasogastric aspirate also confirms an upper GI source of bleeding and predicts whether the bleeding is caused by a lesion at increased risk for ongoing or recurrent bleeding [15,17]. However, lavage may not be positive if bleeding has ceased or arises beyond a closed pylorus. Nasogastric aspiration of nonbloody bilious fluid suggests that the pylorus is open and that there is no active upper GI bleeding distal to the pylorus [9].

We suggest that patients only undergo NGT lavage if particulate matter, fresh blood, or clots need to be removed from the stomach to facilitate endoscopy.

GENERAL MANAGEMENT

Hemodynamically unstable patients — While the principles behind the management of all patients with upper gastrointestinal bleeding are similar, there are some special considerations when it comes to patients presenting with hemodynamic instability (shock, orthostatic hypotension) (table 1).

Intravenous access — Adequate peripheral access should be attained with either two 18 gauge or larger intravenous catheters and/or a large-bore, single-lumen central cordis.

Fluid resuscitation — Fluid resuscitation should begin immediately and should not be delayed pending transfer of the patient to an intensive care unit. The approach to fluid resuscitation in patients who are hemodynamically unstable is discussed in detail elsewhere. (See "Evaluation of and initial approach to the adult patient with undifferentiated hypotension and shock", section on 'Hemodynamic support'.)

Transfusion — Patients with active bleeding and hypovolemia may require red blood cell transfusion despite an apparently normal hemoglobin, particularly if the patient remains hemodynamically unstable despite appropriate fluid resuscitation.

Patients without active bleeding who become hemodynamically stable with fluid resuscitation should receive a blood transfusion if the hemoglobin is <9 g/dL (90 g/L) for high-risk patients and if it is <7 g/dL (70 g/L) in low-risk patients. (See 'Blood product transfusions' below.)

However, it is important to avoid overtransfusion in patients with suspected variceal bleeding, as it can precipitate worsening of the bleeding [18-22]. Transfusing patients with suspected variceal bleeding to a hemoglobin >10 g/dL (100 g/L) should be avoided. (See "Overview of the management of patients with variceal bleeding", section on 'Resuscitation and support'.)

Transfusion of platelets may be required if the platelet count is <50,000/microL and prothrombin complex concentrate is indicated if the INR is >2 (we will proceed with endoscopy once the INR is <2.5 [23]). In addition, because packed red blood cells do not contain coagulation factors, transfusion of a unit of fresh frozen plasma (FFP) should be given after every four units of packed red blood cells [24]. (See 'Thrombocytopenia' below and 'Coagulopathy' below.)

Medications and endoscopy — The approach to medications (eg, proton pump inhibitors) and endoscopy are similar for patients with hemodynamic instability compared with patients who are hemodynamically stable. It is particularly important to ensure that these patients are adequately resuscitated prior to undergoing upper endoscopy. (See 'Medications' below and 'Upper endoscopy' below.)

Triage — All patients with hemodynamic instability or active bleeding (manifested by hematemesis, bright red blood per nasogastric tube, or hematochezia) should be admitted to an intensive care unit for resuscitation and close observation with automated blood pressure monitoring, electrocardiographic monitoring, and pulse oximetry.

A table outlining the emergency management of acute severe upper gastrointestinal bleeding is provided (table 1).

Other patients can be admitted to a regular medical ward, though we suggest that all admitted patients with the exception of low-risk patients receive electrocardiographic monitoring. Outpatient management may be appropriate for some low-risk patients. (See 'Risk stratification' below.)

General support — Patients should receive supplemental oxygen by nasal cannula and should receive nothing per mouth. Two large caliber (18 gauge or larger) peripheral intravenous catheters or a central venous line should be inserted. For patients who are hemodynamically unstable, two 16 gauge intravenous catheters and/or a large-bore, single-lumen central cordis should be placed.

Elective endotracheal intubation in patients with ongoing hematemesis or altered respiratory or mental status may facilitate endoscopy and decrease the risk of aspiration. However, among patients who are critically ill, elective endotracheal intubation has been associated with worse outcomes. A case control study with 200 patients with upper GI bleeding who were critically ill found that patients who had elective endotracheal intubation were more likely than patients who were not intubated to have adverse cardiopulmonary outcomes based on a composite outcome that included pneumonia, pulmonary edema, acute respiratory distress syndrome, and cardiac arrest [25]. Of note, the presence of respiratory distress prior to intubation was not reported and the mean Glasgow Coma Scale score was 14.7 (+/- 0.95), indicating that altered mental status was absent in the majority of patients. Patients who were electively intubated were more likely to suffer cardiopulmonary complications compared with patients who were not intubated (20.0 versus 6.0 percent). In particular, patients who were intubated were more likely to be diagnosed with pneumonia within 48 hours (14.0 versus 2.0 percent). Pending additional studies in broader patient populations, our approach is still to proceed with intubation in patients deemed high-risk for aspiration, including those with massive upper GI bleeding or altered mental status.

Fluid resuscitation — Adequate resuscitation and hemodynamic stabilization is essential prior to endoscopy to minimize treatment-associated complications [26]. Patients with active bleeding should receive intravenous fluids (eg, 500 mL of normal saline or lactated Ringer's solution over 30 minutes) while being typed and cross-matched for blood transfusion. The rate of fluid resuscitation will in part depend on whether the patient is hemodynamically unstable. Patients at risk of fluid overload may require intensive monitoring.

If the blood pressure fails to respond to initial resuscitation efforts, the rate of fluid administration should be increased. In some patients, temporary support with vasopressor drugs may be required. (See "Evaluation of and initial approach to the adult patient with undifferentiated hypotension and shock", section on 'Hemodynamic support' and "Treatment of severe hypovolemia or hypovolemic shock in adults", section on 'Initial rate of fluid repletion'.)

Blood product transfusions

Anemia — The decision to initiate blood transfusion must be individualized. Our approach is to initiate blood transfusion if the hemoglobin is <7 g/dL (70 g/L) for most patients (including those

with stable coronary artery disease), with a goal of maintaining the hemoglobin at a level ≥7 g/dL (70 g/L) [4,21,27,28]. However, our goal is to maintain the hemoglobin at a level of ≥9 g/dL (90 g/L) for patients at increased risk of suffering adverse events in the setting of significant anemia, such as those with unstable coronary artery disease or in those with evidence of ongoing active bleeding. We do not have an age cutoff for determining which patients should have a goal hemoglobin of ≥9 g/dL (90 g/L), and instead base the decision on the patient's comorbid conditions. Patients with active bleeding and hypovolemia may require blood transfusion despite an apparently normal hemoglobin. In addition, because packed red blood cells do not contain coagulation factors, transfusion of a unit of fresh frozen plasma (FFP) should be given after every four units of packed red blood cells [24]. (See 'Laboratory data' above.)

It is particularly important to avoid overtransfusion in patients with suspected variceal bleeding, as it can precipitate worsening of the bleeding [18-22]. Transfusing patients with suspected variceal bleeding to a hemoglobin >10 g/dL (100 g/L) should be avoided. (See "Overview of the management of patients with variceal bleeding", section on 'Resuscitation and support'.)

Several randomized trials have compared liberal transfusion strategies (transfusing all patients or patients with a hemoglobin <9 to 10 g/dL [90 to 100 g/L]) with restrictive transfusion strategies (transfusing patients with a hemoglobin <7 to 8 g/dL [70 to 80 g/L]) [21,29-32].

In a meta-analysis of five randomized trials with a total of 1965 patients with acute upper gastrointestinal bleeding, patients assigned to a restrictive transfusion strategy were at lower risk than those assigned to a liberal transfusion strategy for mortality (absolute risk reduction [ARR] 2.2 percent, relative risk [RR] 0.65, 95% CI 0.44-0.97) and rebleeding (ARR 4.4 percent, RR 0.58, 0.40-0.84) [33]. There were no differences between patients with cirrhosis and those with non-variceal bleeding. With regard to mortality, there were non-statistically significant trends toward a higher risk of mortality with a restrictive transfusion strategy among patients with ischemic heart disease (RR 4.4, 95% CI 0.27-22) and a lower risk of mortality among patients without ischemic heart disease (RR 0.58, 95% CI 0.86-1.3). With regard to rebleeding, the risk was similar between those with and without ischemic heart disease (RR 0.50 and 0.69, respectively).

The meta-analysis did not detect a difference between a restrictive and a liberal transfusion strategy in the risk of myocardial infarction (RR 0.79, 95% CI 0.33-1.89), stroke (RR 0.49, 95% CI 0.12-2.01), or acute kidney injury (RR 0.77, 0.56-1.05), but not all of the included trials reported these outcomes.

Thrombocytopenia — Patients with active bleeding and a low platelet count (<50,000/microL) should be transfused with platelets. Limited data suggest that proceeding with upper endoscopy in patients with thrombocytopenia is generally safe [34], though whether there is a lower limit below which endoscopy should be delayed is unclear [35]. Our approach is to perform an upper endoscopy if the platelet count is >20,000/microL, though if the patient is suspected to have active bleeding, we attempt to raise the platelet count to >50,000/microL prior to endoscopy.

In the past, platelet transfusions were considered in non-thrombocytopenic or mildly thrombocytopenic patients with life-threatening bleeding who had been taking antiplatelet agents such as aspirin or clopidogrel [36]. However, high-quality evidence regarding the benefit of platelet transfusion is lacking, and some evidence suggests that platelet transfusion may be deleterious [37]. Because these cases can be complex, an individualized approach based on the complete clinical picture is required.

If the patient is taking antiplatelet medications because of a recent (less than one year) vascular stent placement or acute coronary syndrome, when possible, a cardiologist should be consulted prior to stopping the medications.

Coagulopathy — Patients with a coagulopathy that is not due to cirrhosis and with a prolonged prothrombin time with INR >2.0 should generally be transfused with FFP. We will perform upper endoscopy once the INR is <2.5 [23]. More rapid reversal of anticoagulation can be achieved if needed by the use of prothrombin complex concentrate infusions and is the preferred approach for patients with serious/life-threatening bleeding. A unit of FFP should also be given after every four units of packed red blood cells because packed red blood cells do not contain coagulation factors [24]. (See "Management of warfarin-associated bleeding or supratherapeutic INR", section on 'Treatment of bleeding'.)

The management of coagulopathies in patients with cirrhosis is more complicated because the INR is not an accurate measure of hemostasis in patients with cirrhosis, because it only reflects changes in procoagulant factors. The management of coagulopathies in patients with cirrhosis who have acute bleeding is discussed separately. (See "Hemostatic abnormalities in patients with liver disease", section on 'Bleeding'.)

Provided the patient is hemodynamically stable, urgent endoscopy can usually proceed simultaneously with transfusion and should not be postponed until the coagulopathy is corrected. However, as noted above, in patients with an INR ≥2.5, we attempt to correct the INR to <2.5 prior to starting an endoscopy, with additional FFP or prothrombin complex concentrate being given after the endoscopy if high-risk stigmata for recurrent bleeding were found or if endoscopic therapy was performed and the INR is still >2.0. This approach is based on data that suggest endoscopy is safe in patients who are mildly to moderately anticoagulated [38].

Medications

Acid suppression — Patients admitted to the hospital with acute upper GI bleeding are typically treated with a proton pump inhibitor (PPI). We suggest that patients with acute upper GI bleeding be started empirically on an intravenous (IV) PPI (eg, esomeprazole 40 mg IV twice daily after an initial bolus of 80 mg IV). The PPI can be started at presentation and continued until confirmation of the cause of bleeding. Once the source of the bleeding has been identified and

treated (if possible), the need for ongoing acid suppression can be determined. (See "Overview of the treatment of bleeding peptic ulcers", section on 'Acid suppression'.)

Several studies have examined the role of acid suppression given before or after endoscopy (with or without therapeutic intervention) [39]. In the setting of active upper GI bleeding from an ulcer, acid suppressive therapy with H2 receptor antagonists has **not** been shown to significantly lower the rate of ulcer rebleeding [40-42]. By contrast, high dose antisecretory therapy with an intravenous infusion of a PPI significantly reduces the rate of rebleeding compared with standard treatment in patients with bleeding ulcers [43]. In addition, PPIs given as intermittent boluses appear to be at least as effective as PPIs given as a continuous infusion (see "Overview of the treatment of bleeding peptic ulcers", section on 'Continuous versus intermittent dosing'). Oral and intravenous PPI therapy also decrease the length of hospital stay, rebleeding rate, and need for blood transfusion in patients with high-risk ulcers treated with endoscopic therapy. (See "Overview of the treatment of bleeding peptic ulcers", section on 'Acid suppression'.)

PPIs may also promote hemostasis in patients with lesions other than ulcers. This likely occurs because neutralization of gastric acid leads to the stabilization of blood clots [44].

Prokinetics — Both erythromycin and metoclopramide have been studied in patients with acute upper GI bleeding. The goal of using a prokinetic agent is to improve gastric visualization at the time of endoscopy by clearing the stomach of blood, clots, and food residue. We suggest that erythromycin be considered in patients who are likely to have a large amount of blood in their stomach, such as those with severe bleeding. A reasonable dose is 3 mg/kg intravenously over 20 to 30 minutes, 30 to 90 minutes prior to endoscopy.

Erythromycin promotes gastric emptying based upon its ability to be an agonist of motilin receptors. Using erythromycin to improve gastric visualization has been studied in at least four randomized controlled trials [45-48]. The studies suggested that a single dose of intravenous erythromycin given 20 to 120 minutes before endoscopy can significantly improve visibility, shorten endoscopy time, and reduce the need for second-look endoscopy. Treatment appears to be safe.

A meta-analysis examined five trials with 316 patients who were assigned to erythromycin, metoclopramide, or placebo [49]. The analysis found that the use of a prokinetic agent decreased the need for second-look endoscopy, but did not affect the number of units of blood transfused, length of hospital stay, or need for surgery. In subgroup analyses, erythromycin continued to show a benefit with regard to the need for second-look endoscopy, but metoclopramide did not.

A second meta-analysis examined four trials with 335 patients who were assigned to either erythromycin or a control group [50]. The meta-analysis found that patients who received erythromycin were significantly more likely to have an empty stomach at the time of endoscopy compared with patients in the control group (69 versus 37 percent). Patients treated with erythromycin also had significant reductions in the need for second endoscopy, volume of blood

transfused, and length of hospital stay. Finally, there was a trend toward shorter endoscopic procedure times and decreased mortality for patients treated with erythromycin.

Erythromycin has also been compared with nasogastric lavage. A randomized trial with 253 patients that compared erythromycin alone with nasogastric lavage alone and nasogastric lavage plus erythromycin found that the quality of visualization did not differ significantly among the three groups [51]. In addition, there were no differences among the groups with regard to procedure duration, rebleeding rates, need for second endoscopy, number of transfused units of blood, and mortality. (See 'Nasogastric lavage' above.)

Vasoactive medications — Somatostatin, its analog octreotide, and terlipressin (not available in the United States) are used in the treatment of variceal bleeding and may also reduce the risk of bleeding due to nonvariceal causes. In patients with suspected variceal bleeding, octreotide is given as an intravenous bolus of 20 to 50 mcg, followed by a continuous infusion at a rate of 25 to 50 mcg per hour. (See "Methods to achieve hemostasis in patients with acute variceal hemorrhage", section on 'Somatostatin and its analogs'.)

Octreotide is not recommended for routine use in patients with acute nonvariceal upper GI bleeding, but it can be used as adjunctive therapy in some cases. Its role is generally limited to settings in which endoscopy is unavailable or as a means to help stabilize patients before definitive therapy can be performed. (See "Overview of the treatment of bleeding peptic ulcers", section on 'Somatostatin and octreotide'.)

Antibiotics for patients with cirrhosis — Bacterial infections are present in up to 20 percent of patients with cirrhosis who are hospitalized with gastrointestinal bleeding; up to an additional 50 percent develop an infection while hospitalized. Such patients have increased mortality.

Multiple trials evaluating the effectiveness of prophylactic antibiotics in cirrhotic patients hospitalized for GI bleeding suggest an overall reduction in infectious complications and possibly decreased mortality. Antibiotics may also reduce the risk of recurrent bleeding in hospitalized patients who bled from esophageal varices. A reasonable conclusion from these data is that patients with cirrhosis who present with acute upper GI bleeding (from varices or other causes) should be given prophylactic antibiotics, preferably before endoscopy (although effectiveness has also been demonstrated when given after endoscopy). (See "Overview of the management of patients with variceal bleeding".)

Tranexamic acid — Tranexamic acid is an antifibrinolytic agent that has been studied in patients with upper GI bleeding. A meta-analysis that included eight randomized trials of tranexamic acid in patients with upper GI bleeding found a benefit with regard to mortality but not with regard to bleeding, surgery, or transfusion requirements [52]. When only studies that used antiulcer drugs and/or endoscopic therapy were included, there was no beneficial effect. This suggests that there is no role for tranexamic acid in the treatment of upper GI bleeding, since the

current standard of care is to treat patients with proton pump inhibitors and endoscopic therapy (if indicated).

Anticoagulants and antiplatelet agents — When possible, anticoagulants and antiplatelet agents should be held in patients with upper GI bleeding. However, the thrombotic risk of reversing anticoagulation should be weighed against the risk of continued bleeding without reversal, and thus the decision to discontinue medications or administer reversal agents needs to be individualized. In some cases (eg, stopping a nonsteroidal anti-inflammatory drug in a patient who is taking it for mild joint pain), the decision to stop these agents may be straightforward. However, in more complicated cases, consultation with the provider who prescribed the anticoagulant/antiplatelet medication should be considered. (See "Management of anticoagulants in patients undergoing endoscopic procedures", section on 'Urgent procedures' and "Gastrointestinal endoscopy in patients with disorders of hemostasis" and "Management of warfarin-associated bleeding or supratherapeutic INR", section on 'Resumption of anticoagulation after bleeding' and "Management of antiplatelet agents in patients undergoing endoscopic procedures".)

The approach to the reversal of anticoagulation in patients on warfarin (table 2) or direct-acting oral anticoagulants (table 3) is discussed in detail elsewhere. (See "Management of warfarin-associated bleeding or supratherapeutic INR", section on 'Serious/life-threatening bleeding' and "Management of bleeding in patients receiving direct oral anticoagulants", section on 'Anticoagulant reversal'.)

When to resume these medications once hemostasis has been achieved will also depend on the patient's risks for thrombosis and recurrent bleeding. (See "Management of anticoagulants in patients undergoing endoscopic procedures", section on 'Resuming anticoagulants after hemostasis' and "Overview of the treatment of bleeding peptic ulcers", section on 'Risk factors for persistent or recurrent bleeding'.)

Consultations — Gastroenterological consultation should be obtained in all patients with suspected clinically significant acute upper GI bleeding. The decision to obtain surgical and interventional radiology consultations prior to endoscopy should be based upon the likelihood of persistent or recurrent bleeding, or risks/complications stemming from endoscopic therapy (perforation, precipitation of massive bleeding).

As a general rule, we obtain surgical and interventional radiology consultation if endoscopic therapy is unlikely to be successful, if the patient is deemed to be at high risk for rebleeding or complications associated with endoscopy, or if there is concern that the patient may have an aorto-enteric fistula. In addition, a surgeon and an interventional radiologist should be promptly notified of all patients with severe acute upper GI bleeding [53].

DIAGNOSTIC STUDIES

An algorithm providing an overview of the diagnostic approach to patients with suspected upper gastrointestinal bleeding is provided (algorithm 1).

Upper endoscopy — Upper endoscopy is the diagnostic modality of choice for acute upper GI bleeding (algorithm 1) [54,55]. Endoscopy has a high sensitivity and specificity for locating and identifying bleeding lesions in the upper GI tract. In addition, once a bleeding lesion has been identified, therapeutic endoscopy can achieve acute hemostasis and prevent recurrent bleeding in most patients. Early endoscopy (within 24 hours) is recommended for most patients with acute upper GI bleeding, though whether early endoscopy affects outcomes and resource utilization is unsettled. (See 'Early endoscopy' below and "Methods to achieve hemostasis in patients with acute variceal hemorrhage", section on 'Initial management' and "Overview of the treatment of bleeding peptic ulcers", section on 'Endoscopic therapy'.)

Endoscopic findings in patients with bleeding peptic ulcers may be described using the Forrest classification [56]. Findings include spurting hemorrhage (class Ia) (picture 1), oozing hemorrhage (class Ib), a nonbleeding visible vessel (class IIa) (picture 2), an adherent clot (class IIb) (picture 3), a flat pigmented spot (class IIc) (picture 4), and a clean ulcer base (class III) (picture 4). The endoscopic appearance helps determine which lesions require endoscopic therapy. (See "Overview of the treatment of bleeding peptic ulcers", section on 'Endoscopic therapy'.)

It may be helpful to irrigate the stomach prior to endoscopy to help remove residual blood and other gastric contents. However, despite irrigation, the stomach can be obscured with blood, potentially making it difficult to establish a clear diagnosis and/or perform therapeutic maneuvers. In patients in whom blood obscures the source of bleeding, a second endoscopy may be required to establish a diagnosis and to potentially apply therapy, but routine second-look endoscopy is not recommended. (See 'Nasogastric lavage' above and "Overview of the treatment of bleeding peptic ulcers", section on 'Second-look endoscopy'.)

Early endoscopy — Studies have reached variable conclusions when determining whether the application of early endoscopy (typically within 24 hours) for risk stratification and treatment reduces resource utilization or affects patient outcomes [57-66]. Some studies have demonstrated reduced resource utilization and improved outcomes from early endoscopy [60,61,63,65,66], while other studies, including a randomized trial, did not [57,58,62]. In addition, emergency endoscopy (within 12 hours) has been associated with poor outcomes [62,64], possibly due to inadequate resuscitation in patients undergoing emergency endoscopy. Our approach is to perform upper endoscopy within 24 hours for most patients with upper GI bleeding, but only after adequate resuscitation has been provided.

Risks of endoscopy — Risks of upper endoscopy include pulmonary aspiration, adverse reactions to medications used to achieve conscious sedation, GI perforation, and increasing

bleeding while attempting therapeutic intervention.

While patients need to be hemodynamically stable prior to undergoing endoscopy, data suggest that most patients do not need to have a normal hematocrit in order to safely undergo endoscopy [67]. In addition, endoscopy appears to be safe in patients who are mildly to moderately anticoagulated [38]. In a retrospective study of 920 patients with upper GI bleeding undergoing upper endoscopy, patients with low hematocrits (<30 percent) were similar to those with high hematocrits (>30 percent) with regard to cardiovascular complications and mortality [67]. In another retrospective study with 233 patients with upper GI bleeding who received endoscopic therapy, an elevated INR was not associated with an increased risk of rebleeding, transfusion requirement, surgery, length of stay, or mortality [38]. The INR was between 1.3 and 2.7 in 95 percent of the patients, so the results of the study may only apply to patients who are mildly to moderately anticoagulated.

The risks versus benefits of upper endoscopy should be considered in high-risk patients, such as those who have had a recent myocardial infarction. In one study, for example, 200 patients who underwent endoscopy within 30 days after myocardial infarction (MI) were compared with 200 controls matched for age, sex, and endoscopic indication [68]. Complications (including fatal ventricular tachycardia, near respiratory arrest, and mild hypotension) occurred more often in patients who had a recent MI (8 versus 2 percent). Complications occurred more often (21 versus 2 percent) in patients who were very ill (Apache II score >16 or hypotension prior to endoscopy). However, such patients are at increased risk for complications even without endoscopy and may be particularly vulnerable to complications from continued bleeding without endoscopy. (See "Predictive scoring systems in the intensive care unit".)

Other diagnostic tests — Other diagnostic tests for acute upper GI bleeding include angiography, which can detect active bleeding [69,70], deep small bowel enteroscopy, and rarely, intraoperative enteroscopy (algorithm 1). Upper GI barium studies are **contraindicated** in the setting of acute upper GI bleeding because they will interfere with subsequent endoscopy, angiography, or surgery [54]. There is also interest in using wireless capsule endoscopy for patients who have presented to the emergency department with suspected upper GI bleeding. An esophageal capsule (which has a recording time of 20 minutes) can be given in the emergency department and reviewed immediately for evidence of bleeding. Confirming the presence of blood in the stomach or duodenum may aid with patient triage and identify patients more likely to benefit from early endoscopy [71-75]. Small bowel capsule endoscopy has also been employed to help localize bleeding in patients with acute gastrointestinal bleeding without hematemesis. (See "Angiographic control of nonvariceal gastrointestinal bleeding in adults" and "Evaluation of suspected small bowel bleeding (formerly obscure gastrointestinal bleeding)" and "Wireless video capsule endoscopy", section on 'Esophageal capsule endoscopy' and "Wireless video capsule endoscopy", section on 'Indications' and "Wireless video capsule endoscopy", section on 'Acute gastrointestinal bleeding'.)

A colonoscopy is generally required for patients with hematochezia and a negative upper endoscopy unless an alternative source for the bleeding has been identified. In addition, patients with melena and a negative upper endoscopy frequently undergo colonoscopy to rule out a right-sided colonic source for the bleeding, as such lesions may present with melena. In a study that included 1743 colonoscopies performed for the evaluation of melena following a non-diagnostic upper endoscopy, a suspected bleeding source was identified in 5 percent of patients, a rate that was higher than that seen in 194,979 average-risk screening controls (1 percent) [76]. Despite the relatively low yield in patients with melena, we routinely perform a colonoscopy in patients with melena and a negative upper endoscopy, as well as in patients with hematochezia. (See "Approach to acute lower gastrointestinal bleeding in adults", section on 'Colonoscopy'.)

RISK STRATIFICATION

Endoscopic, clinical, and laboratory features may be useful for risk stratification of patients who present with acute upper GI bleeding (table 4 and picture 1 and picture 2 and picture 3 and picture 4) [77-86], and the use of risk stratification tools is recommended by the International Consensus Upper Gastrointestinal Bleeding Conference Group [2]. Factors associated with rebleeding identified in a meta-analysis included [87]:

- Hemodynamic instability (systolic blood pressure less than 100 mmHg, heart rate greater than 100 beats per minute)
- Hemoglobin less than 10 g/L
- Active bleeding at the time of endoscopy
- Large ulcer size (greater than 1 to 3 cm in various studies)
- Ulcer location (posterior duodenal bulb or high lesser gastric curvature)

An increase in the blood urea nitrogen (BUN) level at 24 hours compared with baseline may be another predictor of poor outcomes. A study of 357 patients with acute nonvariceal upper GI bleeding found that an increase in the BUN at 24 hours was a predictor of a composite outcome that included rebleeding and mortality [88]. The authors speculate that the association of poor outcomes with an increase in BUN may be the result of inadequate resuscitation.

Several investigators have developed decision rules and predictive models that permit identification of patients who are at low risk for recurrent or life-threatening hemorrhage [89]. Such patients may be suitable for early hospital discharge or even outpatient care. The effectiveness of such rules has been evaluated in a variety of clinical settings, with most studies suggesting that patients deemed to be low-risk can safely be discharged early or treated as outpatients [58,77-83,89-96]. In addition, this approach is associated with reduced resource utilization compared with universal hospitalization of patients with acute upper GI bleeding.

Risk scores — Two commonly cited scoring systems are the Rockall score and the Blatchford score:

- The Rockall score is based upon age, the presence of shock, comorbidity, diagnosis, and endoscopic stigmata of recent hemorrhage (calculator 1) [77]. In one validation study, only 32 of 744 patients (4 percent) who scored 2 or less (out of a maximum of 11) rebled and only one died.

  On the other hand, in a later study of 247 patients who underwent endoscopic therapy for bleeding peptic ulcers, the model performed poorly when predicting recurrent bleeding, underscoring the need for validation of this model [97].

- The Blatchford score (also known as the Glasgow Blatchford score), unlike the Rockall score, does not take endoscopic data into account and thus can be used when the patient first presents (calculator 2) [82]. The score is based upon the blood urea nitrogen, hemoglobin, systolic blood pressure, pulse, and the presence of melena, syncope, hepatic disease, and/or cardiac failure. The score ranges from zero to 23 and the risk of requiring endoscopic intervention increases with increasing score. One meta-analysis found that a Blatchford score of zero was associated with a low likelihood of the need for urgent endoscopic intervention (likelihood ratio 0.02, 95% confidence interval [CI] 0-0.05) [6]. A second study with 3012 patients found that a score ≤1 could be used to identify a low-risk cohort [98].

  A simpler version of the score, known as the modified Glasgow Blatchford score, is calculated using only the blood urea nitrogen, hemoglobin, systolic blood pressure, and pulse. The score ranges from 0 to 16. A prospective study of the modified score found that it performed as well as the full Blatchford score and that it outperformed the Rockall score with regard to predicting the need for clinical intervention, rebleeding, and mortality [99].

AIMS65 is another scoring system that uses data available prior to endoscopy. Studies suggest it has high accuracy for predicting inpatient mortality among patients with upper GI bleeding [86,100,101]. The score was derived using data from a database that contained information from 187 United States hospitals. The derivation cohort used data from 29,222 hospital admissions. The score was then validated using a separate data set containing information from 32,504 admissions. The study found that five factors were associated with increased inpatient mortality:

- **A**lbumin less than 3.0 g/dL (30 g/L)
- **I**NR greater than 1.5
- Altered **M**ental status (Glasgow coma score less than 14, disorientation, lethargy, stupor, or coma)
- **S**ystolic blood pressure of 90 mmHg or less
- Age older than **65** years

In the validation cohort, the mortality rate increased significantly as the number of risk factors present increased:

- Zero risk factors: 0.3 percent
- One risk factor: 1 percent
- Two risk factors: 3 percent
- Three risk factors: 9 percent
- Four risk factors: 15 percent
- Five risk factors: 25 percent

In addition to predicting mortality, an increasing score was also associated with increased length of stay (from 3.4 days for zero risk factors to 8.1 days for five risk factors) and increased cost (average cost of $5647 USD with zero risk factors to $15,776 USD with five risk factors). Prospective studies are needed to confirm the ability of the score to predict mortality, length of stay, and cost. In addition, it is not yet known if the score predicts rebleeding following endoscopic therapy.

Implementation — The data presented above suggest that risk stratification is feasible and permits identification of patients who can be managed safely without hospitalization. However, for these systems to be successful, the risk stratification system must be tied directly to decisions regarding patient discharge. None of the published risk scores has yet been adopted widely.

As a general rule, we discharge patients who meet all of the following criteria:

- Have no comorbidities.
- Have stable vital signs.
- Have a normal hemoglobin level.
- Have a likely bleeding source identified on upper endoscopy that is not associated with a high risk of rebleeding (eg, variceal bleeding, active bleeding, bleeding from a Dieulafoy's lesion, or ulcer bleeding with high-risk stigmata) (table 4).

If a patient meets these criteria, the decision to discharge the patient also depends on individual-patient factors, such as reliability for follow-up and confidence of the endoscopists in the diagnosis.

If patients do not meet these criteria we admit them to a monitored setting or intensive care unit (depending upon the severity of bleeding, comorbidities, and stability of vital signs). Most patients who have received endoscopic treatment for high-risk stigmata should be hospitalized for 72 hours to monitor for rebleeding, since most rebleeding occurs during this time [2].

TREATMENT

The treatment of patients with upper GI bleeding is discussed separately:

- (See "Overview of the treatment of bleeding peptic ulcers".)
- (See "Methods to achieve hemostasis in patients with acute variceal hemorrhage".)
- (See "Angiodysplasia of the gastrointestinal tract", section on 'Treatment'.)
- (See "Portal hypertensive gastropathy", section on 'Management'.)
- (See "Causes of upper gastrointestinal bleeding in adults", section on 'Vascular lesions'.)
- (See "Causes of upper gastrointestinal bleeding in adults", section on 'Aortoenteric fistulas'.)
- (See "Causes of upper gastrointestinal bleeding in adults", section on 'Upper gastrointestinal tumors'.)
- (See "Argon plasma coagulation in the management of gastrointestinal hemorrhage".)
- (See "Angiographic control of nonvariceal gastrointestinal bleeding in adults".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Gastrointestinal bleeding in adults".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Upper endoscopy (The Basics)" and "Patient education: GI bleed (The Basics)")

- Beyond the Basics topics (see "Patient education: Upper endoscopy (Beyond the Basics)" and "Patient education: Peptic ulcer disease (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- A table outlining the emergency management of acute severe upper gastrointestinal bleeding is provided (table 1). (See 'Introduction' above.)
- A careful history should be obtained to identify potential sources of the upper GI bleed, assess the severity of the bleed, and to identify comorbid conditions that may influence the patient's subsequent management. (See 'Initial evaluation' above.)
- The physical examination should focus on signs that indicate the severity of blood loss, help localize the source of the bleeding, and suggest complications. (See 'Physical examination' above.)
- The presence of abdominal pain, especially if severe and associated with rebound tenderness or involuntary guarding raises concern for perforation. If any signs of an acute abdomen are present, further evaluation to exclude a perforation is required prior to endoscopy. (See 'Physical examination' above.)
- Laboratory tests obtained in patients with acute upper gastrointestinal bleeding include a complete blood count, serum chemistries, liver tests, and coagulation studies. In addition, we suggest ruling out a myocardial infarction in older adult patients and those with known cardiovascular disease who have severe bleeding, especially if there has been hemodynamic instability. (See 'Laboratory data' above.)
- Patients should not routinely undergo NGT lavage as part of in the management if acute upper gastrointestinal bleeding. (See 'Nasogastric lavage' above.)
- Patients who require hospitalization should be admitted to a monitored bed or intensive care unit depending upon the severity of bleeding. (See 'Triage' above.)
- We suggest incorporation of a validated risk score for upper gastrointestinal bleeding into routine clinical practice to facilitate optimal triage decisions. (See 'Risk scores' above.)
- General supportive measures include:
  - Provision of supplemental oxygen by nasal cannula
  - Nothing per mouth
  - Two large caliber (18 gauge or larger) peripheral catheters or a central venous line
- For the majority of patients with acute upper gastrointestinal bleeding who do not have significant comorbid illnesses, we recommend giving blood transfusions to maintain the hemoglobin at ≥7 g/dL (70 g/L) rather than ≥9 g/dL (90 g/L) (**Grade 1B**). However, patients with active bleeding and hypovolemia may require blood transfusion despite an apparently normal hemoglobin. For patients at increased risk of suffering adverse events in the setting of

significant anemia, such as those with unstable coronary artery disease, we suggest transfusing to maintain the hemoglobin at ≥9 g/dL (90 g/L) rather than ≥7 g/dL (70 g/L) (**Grade 2C**). (See 'Blood product transfusions' above and "Overview of the non-acute management of unstable angina and non-ST elevation myocardial infarction", section on 'Red cell transfusion'.)

In patients with suspected variceal bleeding, we suggest transfusing to a hemoglobin of no more than 10 g/dL (100 g/L) (**Grade 2C**). It is particularly important to avoid overtransfusion in patients with suspected variceal bleeding, as it can precipitate worsening of the bleeding. (See 'Blood product transfusions' above.)

- We suggest that patients with acute upper GI bleeding be treated with an intravenous PPI at presentation until confirmation of the cause of bleeding, after which the need for specific therapy and the duration of PPI use can be determined (**Grade 2B**). (See 'Acid suppression' above and "Overview of the treatment of bleeding peptic ulcers", section on 'Acid suppression'.)

- We suggest that erythromycin be given prior to endoscopy in patients who are likely to have a large amount of blood in their stomach, such as those with severe bleeding. A reasonable dose is 3 mg/kg intravenously over 20 to 30 minutes, 30 to 90 minutes prior to endoscopy. (See 'Prokinetics' above.)

- Somatostatin, its analog octreotide, or terlipressin (not available in the United States) should be started if variceal bleeding is suspected. (See "Methods to achieve hemostasis in patients with acute variceal hemorrhage", section on 'Pharmacologic therapy'.)

- Patients with cirrhosis who present with acute upper GI bleeding (from varices or other causes) should be given prophylactic antibiotics, preferably before endoscopy. (See "Overview of the management of patients with variceal bleeding".)

- We recommend upper endoscopy within 24 hours for the evaluation and management of clinically significant (ie, more than a scant amount of blood) acute upper GI bleeding (**Grade 1A**). Additional diagnostic tests may be required in specific circumstances. An algorithm providing an overview of the diagnostic approach to patients with suspected upper gastrointestinal bleeding is provided (algorithm 1). (See 'Diagnostic studies' above.)

- The treatment of patients with upper GI bleeding due to various causes is discussed separately. (See "Overview of the treatment of bleeding peptic ulcers" and "Contact thermal devices for the treatment of bleeding peptic ulcers" and "Methods to achieve hemostasis in patients with acute variceal hemorrhage".)

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Topic 2548 Version 68.0

GRAPHICS

Rapid overview: Emergency management of severe upper GI bleeding in adults

Major causes*
Peptic ulcer, esophagogastric varices, arteriovenous malformation, tumor, esophageal (Mallory-Weiss) tear
Clinical features
History
Use of: NSAIDs, aspirin, anticoagulants, antiplatelet agents
Alcohol abuse; previous GI bleed; liver disease; coagulopathy
Symptoms and signs: Abdominal pain; hematemesis or "coffee ground" emesis; passing melena/tarry stool (stool may be frankly bloody or maroon with massive or brisk upper GI bleeding)
Examination
Tachycardia, orthostatic blood pressure changes suggest moderate to severe blood loss; hypotension suggests life-threatening blood loss (hypotension may be late finding in healthy younger adult)
Rectal examination is performed to assess stool color (melena versus hematochezia versus brown)
Significant abdominal tenderness accompanied by signs of peritoneal irritation (eg, involuntary guarding) suggests perforation
Diagnostic testing
Obtain type and screen (or type and crossmatch for hemodynamic instability, severe bleeding, or high-risk patient)
Obtain hemoglobin concentration (normal measurement may be inaccurate with acute severe hemorrhage), platelet count, coagulation studies (prothrombin time with INR), liver enzymes (AST, ALT), albumin, BUN and creatinine
Nasogastric lavage may be helpful if the source of bleeding is unclear (upper or lower GI tract) or to clean the stomach prior to endoscopy
Treatment
Closely monitor airway, clinical status, vital signs, cardiac rhythm, urine output, nasogastric output (if nasogastric tube in place)
Do NOT give patient anything by mouth
Establish two large bore IV lines (16 gauge or larger)
Provide supplemental oxygen
Treat hypotension initially with rapid, bolus infusions of isotonic crystalloid
Transfuse for:
Hemodynamic instability despite crystalloid resuscitation
Hemoglobin <9 g/dL (90 g/L) in high-risk patients (eg, elderly, coronary artery disease)
Hemoglobin <7 g/dL (70 g/L) in low-risk patients
Avoid over-transfusion with possible variceal bleeding
Give fresh frozen plasma for coagulopathy; give platelets for thrombocytopenia (platelets <50,000) or platelet dysfunction (eg, chronic aspirin therapy)
Obtain immediate consultation with gastroenterologist; obtain surgical and interventional radiology consultation for any large-scale bleeding¶
Pharmacotherapy for all patients with suspected or known severe bleeding:
Give a proton pump inhibitor (eg, esomeprazole 40 mg IV twice daily or pantoprazole 40 mg IV twice daily)
Pharmacotherapy for known or suspected esophagogastric variceal bleeding and/or cirrhosis:
Give somatostatin or an analogue (eg, octreotide 50 mcg IV bolus, followed by 50 mcg/hour continuous IV infusion)
Give an IV antibiotic (eg, ceftriaxone or fluoroquinolone)
Balloon tamponade may be performed as a temporizing measure for patients with uncontrollable hemorrhage likely due to varices using any of several devices (eg, Sengstaken-Blakemore tube, Minnesota tube); tracheal intubation is necessary if such a device is to be placed; ensure proper device placement prior to inflation to avoid esophageal rupture

GI: gastrointestinal; INR: international normalized ratio; AST: aspartate aminotransferase; ALT: alanine aminotransferase; BUN: blood urea nitrogen; IV: intravenous.
* An important but uncommon cause of gastrointestinal hemorrhage is vascular-enteric fistula, typically aortoduodenal

fistula related to erosion of a prosthetic aortic graft.

¶ Minimally invasive techniques to control bleeding include sclerotherapy, embolization and other vascular occlusion techniques. For patients with massive hemorrhage, resuscitative endovascular balloon occlusion of the aorta (REBOA) can be used to limit blood loss and support perfusion of vital organs until the sites of bleeding can be directly controlled.

Graphic 72195 Version 9.0

Emergency reversal of anticoagulation from warfarin for life-threatening hemorrhage in adults: Suggested approaches based upon available resources

A. If 4-factor prothrombin complex concentrate (4F PCC) is available (preferred approach):
1. Give 4F PCC* 1500 to 2000 units¶ IV over 10 minutes. Check INR 15 minutes after completion of the infusion. If INR is not ≤1.5, give additional 4F PCC (refer to topic or drug reference for details).
2. Give vitamin K 10 mg IV over 10 to 20 minutes.
B. If 3-factor prothrombin complex concentrate (3F PCC) is available but 4F PCC is not available:
1. Give 3F PCC* 1500 to 2000 units¶ IV over 10 minutes. Check INR 15 minutes after completion of the infusion. If INR is not ≤1.5, give additional 3F PCC (refer to topic or drug reference for details).
2. Give Factor VIIa 20 mcg/kg IV **OR** give FFP 2 units IV by rapid infusion. Factor VIIa may be preferred if volume overload is a concern.
3. Give vitamin K 10 mg IV over 10 to 20 minutes.
C. If neither 3F PCC nor 4F PCC is available:
1. Give FFP 2 units IV by rapid infusion. Check INR 15 minutes after completion of infusion. If INR ≥1.5, administer 2 additional units of FFP IV rapid infusion. Repeat process until INR ≤1.5. May wish to administer loop diuretic between FFP infusions if volume overload is a concern.
2. Give vitamin K 10 mg IV over 10 to 20 minutes.

These products and doses are for use in life-threatening bleeding only. Evidence of life-threatening bleeding and over-anticoagulation with a vitamin K antagonist (eg, warfarin) are required. Anaphylaxis and transfusion reactions can occur.
It may be reasonable to thaw 4 units of FFP while awaiting the PT/INR. The transfusion service may substitute other plasma products for FFP (eg, Plasma Frozen Within 24 Hours After Phlebotomy [PF24]); these products are considered clinically interchangeable. PCC will reverse anticoagulation within minutes of administration; FFP administration can take hours due to the volume required; vitamin K effect takes 12 to 24 hours, but administration of vitamin K is needed to counteract the long half-life of warfarin. Subsequent monitoring of the PT/INR is needed to guide further therapy. Refer to topics on warfarin reversal in individual situations for further management.

PCC: unactivated prothrombin complex concentrate; 4F PCC: PCC containing coagulation factors II, VII, IX, X, protein S and protein C; 3F PCC: PCC containing factors II, IX, and X and only trace factor VII; FFP: fresh frozen plasma; PT: prothrombin time; INR: international normalized ratio; FEIBA: factor eight inhibitor bypassing agent.
* Before use, check product label to confirm factor types (3 versus 4 factor) and concentration. Activated complexes and single-factor IX products (ie, FEIBA, AlphaNine, Mononine, Immunine, BeneFix) are NOT used for warfarin reversal.
¶ PCC doses shown are those suggested for initial treatment of emergency conditions. Subsequent treatment is based on INR and patient weight if available. Refer to topic and Lexicomp drug reference included with UpToDate for INR-based dosing.

Graphic 89478 Version 10.0

Direct oral anticoagulant-associated bleeding reversal strategies

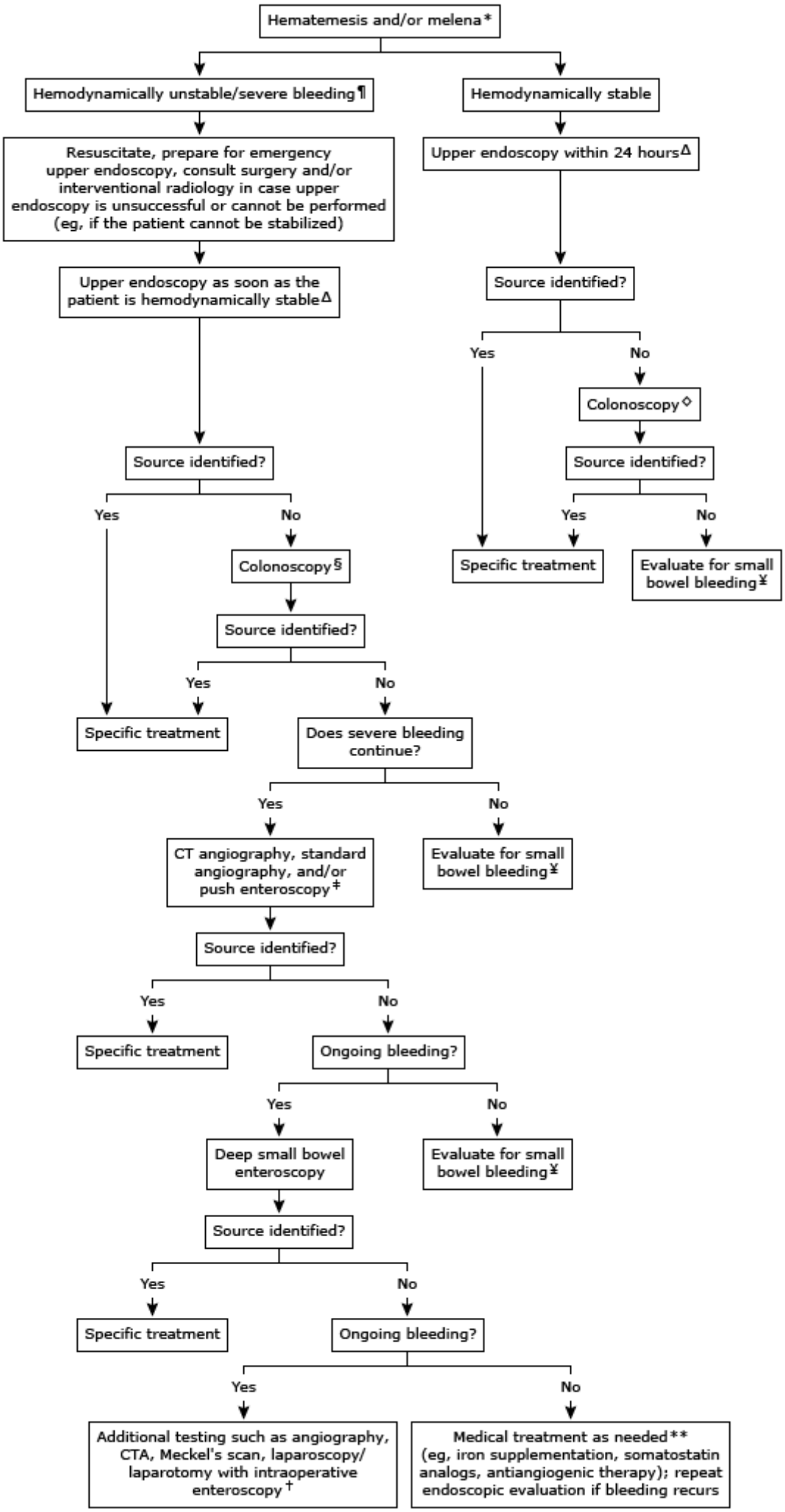
Type of bleeding	Agent	Possible interventions
Life-threatening or imminently fatal bleeding (eg, intracranial, retroperitoneal, compartment syndrome, massive gastrointestinal)	Dabigatran (Pradaxa)	▪ Idarucizumab ▪ Activated PCC* (eg, FEIBA) ▪ Antifibrinolytic agent (eg, tranexamic acid, epsilon-aminocaproic acid) ▪ Anticoagulant discontinuation ▪ Oral activated charcoal (if last dose within prior two hours) ▪ Hemodialysis ▪ RBC transfusions if needed for anemia ▪ Platelet transfusions if needed for thrombocytopenia or impaired platelet function (eg, due to aspirin) ▪ Surgical/endoscopic intervention if appropriate
	Rivaroxaban (Xarelto), apixaban (Eliquis), edoxaban (Lixiana), betrixaban (Bevyxxa)	▪ Andexanet alfa (AndexXa), if available ▪ 4-factor unactivated PCC* (eg, Kcentra) ▪ Antifibrinolytic agent (eg, tranexamic acid, epsilon-aminocaproic acid) ▪ Anticoagulant discontinuation ▪ Oral activated charcoal (if last dose recent enough) ▪ RBC transfusions if needed for anemia ▪ Platelet transfusions if needed for thrombocytopenia or impaired platelet function (eg, due to aspirin) ▪ Surgical/endoscopic intervention if appropriate
Minor bleeding (eg, epistaxis, uncomplicated soft tissue bleeding, minor [slow] gastrointestinal bleeding)	Dabigatran (Pradaxa)	▪ Local hemostatic measures ▪ Possible anticoagulant discontinuation • Half-life (normal renal function¶): 12 to 17 hours ▪ Possible antifibrinolytic agent (eg, tranexamic acid, epsilon-aminocaproic acid)
	Rivaroxaban (Xarelto), apixaban (Eliquis), edoxaban (Lixiana), betrixaban (Bevyxxa)	▪ Local hemostatic measures ▪ Possible anticoagulant discontinuation • Half-lives (normal renal function¶): ○ Rivaroxaban 5 to 9 hours ○ Apixaban 8 to 15 hours ○ Edoxaban 6 to 11 hours ▪ Possible antifibrinolytic agent (eg, tranexamic acid, epsilon-aminocaproic acid)

The table describes measures that may be used to manage bleeding associated with DOACs. Clinical judgment is essential in all cases of DOAC-associated bleeding in order to assess the risks of bleeding and weigh these against the risks of thrombosis if anticoagulation is discontinued or reversed. Refer to UpToDate topics on the use of direct thrombin inhibitors and direct factor Xa inhibitors and management of DOAC-associated bleeding for further details and dosing. The onset of all of the agents discussed herein is approximately 2 to 4 hours.

PCC: prothrombin complex concentrate; FEIBA: factor eight inhibitor bypassing activity; RBC: red blood cell; DOAC: direct oral anticoagulant.
* Use PCC product only if a specific reversal agent is unavailable and/or if continued bleeding is reasonably likely to be fatal within hours.
¶ The anticoagulant effect of these agents (especially dabigatran) will dissipate more slowly as renal function declines. Severe hepatic failure may also prolong the half-life for rivaroxaban, apixaban, edoxaban, and betrixaban.

Graphic 96230 Version 15.0

Evaluation of suspected upper gastrointestinal bleeding


Hematemesis and/or melena*
Hemodynamically unstable/severe bleeding¶
Hemodynamically stable
Resuscitate, prepare for emergency upper endoscopy, consult surgery and/or interventional radiology in case upper endoscopy is unsuccessful or cannot be performed (eg, if the patient cannot be stabilized)
Upper endoscopy as soon as the patient is hemodynamically stable∆
Upper endoscopy within 24 hours∆
Source identified?
Yes
No
Colonoscopy◇
Source identified?
Yes
No
Specific treatment
Evaluate for small bowel bleeding¥
Source identified?
Yes
No
Colonoscopy§
Source identified?
Yes
No
Specific treatment
Does severe bleeding continue?
Yes
No
CT angiography, standard angiography, and/or push enteroscopy‡
Evaluate for small bowel bleeding¥
Source identified?
Yes
No
Specific treatment
Ongoing bleeding?
Yes
No
Deep small bowel enteroscopy
Evaluate for small bowel bleeding¥
Source identified?
Yes
No
Specific treatment
Ongoing bleeding?
Yes
No
Additional testing such as angiography, CTA, Meckel's scan, laparoscopy/ laparotomy with intraoperative enteroscopy†
Medical treatment as needed** (eg, iron supplementation, somatostatin analogs, antiangiogenic therapy); repeat endoscopic evaluation if bleeding recurs

GI: gastrointestinal; CT: computed tomographic; CTA: computed tomographic angiography; MR: magnetic resonance.
* The presence of both hematemesis and melena suggests that brisk bleeding is present.
¶ Bleeding associated with signs such as hypotension, tachycardia, or orthostatic hypotension.
Δ Consider evaluation with a side-viewing duodenoscope if there are risk factors for hemobilia or hemosuccus pancreaticus; consider CTA (followed by push enteroscopy if the CTA is negative) in patients at risk for an aortoenteric fistula. Conventional angiography is typically performed if the patient remains hemodynamically unstable despite attempts at resuscitation.
◇ Patients who present with hematemesis do not need to undergo colonoscopy, since hematemesis suggests the bleeding is proximal to the ligament of Treitz. They should proceed directly to an evaluation for small bowel bleeding if upper endoscopy is negative. Colonoscopy is the next step in the evaluation of patients with melena.
§ If the patient becomes hemodynamically unstable following initial resuscitation, conventional angiography can be performed. Patients who present with hematemesis do not need to undergo colonoscopy and can skip this step in the evaluation because hematemesis suggests the bleeding is proximal to the ligament of Treitz.
¥ If the initial endoscopic evaluation was inadequate (eg, fair or poor visualization, failure to reach the cecum), repeat examination should be considered before initiating an evaluation for small bowel bleeding. Refer to UpToDate topic review on suspected small bowel bleeding for details.
‡ If not already done. If the patient remains hemodynamically stable and does not have evidence of aggressive bleeding (eg, ongoing hematochezia), perform a CTA or push enteroscopy (CTA is the initial test of choice if there is concern for an aortoenteric fistula). If the patient becomes hemodynamically unstable following initial resuscitation or has signs of aggressive bleeding, perform conventional angiography.
† If not already done, angiography or CTA may be obtained. If angiography or CTA has been performed and no source is identified, a Meckel's scan should be obtained in younger patients with overt bleeding, unless the only manifestation of bleeding was hematemesis. Surgical exploration is appropriate if no other studies have revealed a source and significant bleeding continues or if there is high suspicion for a small bowel neoplasm.
** If the deep small bowel enteroscopy was incomplete, a video capsule endoscopy study should be obtained, followed by CT enterography or MR enterography if the capsule endoscopy is negative.

Graphic 105093 Version 3.0

Bleeding gastric ulcer

Endoscopy shows an actively bleeding gastric ulcer (Forrest classification Ia) along the lesser curvature.

Courtesy of Rome Jutabha, MD and Dennis M Jensen, MD.

Graphic 61646 Version 2.0

Duodenal ulcer with visible vessel

Upper endoscopy showing a duodenal ulcer with a nonbleeding visible vessel (arrow) in a large circumferential ulcer (Forrest classification IIa).

Courtesy of Rome Jutabha.

Graphic 54960 Version 4.0

Gastric ulcer with adherent clot

Upper endoscopy showing a gastric ulcer with an adherent clot (Forrest classification IIb).

Courtesy of Rome Jutabha, MD.

Graphic 76246 Version 1.0

Peptic ulcers at low risk for rebleeding

Ulcers with a flat pigmented spot (Forrest classification IIc; panel A) or a clean base (Forrest classification III, panel B) are at low risk for rebleeding and do not need to be treated endoscopically.

Courtesy of Rome Jutabha, MD and Dennis M Jensen, MD.

Graphic 52497 Version 2.0

Endoscopic predictors of recurrent peptic ulcer hemorrhage

Endoscopic stigmata of recent hemorrhage	Prevalence, percent	Risk of rebleeding on medical management, percent
Active arterial bleeding (Forrest Ia)	10	90
Oozing without visible vessel (Forrest Ib)	10	10 to 20
Non-bleeding visible vessel (Forrest IIa)	25	50
Adherent clot (Forrest IIb)	10	25 to 30
Flat spot (Forrest IIc)	10	7 to 10
Clean ulcer base (Forrest III)	35	3 to 5

Adapted from: Katschinski B, Logan R, Davies J, et al. Dig Dis Sci 1994; 39:706.

Graphic 78607 Version 6.0

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