

INTRODUCTION

Hematemesis is defined as vomiting of blood, which is indicative of bleeding from the esophagus, stomach, or duodenum.¹ Hematemesis includes vomiting of bright red blood, suggestive of recent or ongoing bleeding, and dark material (coffee-ground emesis), which suggests bleeding that had stopped some time ago. Hematemesis is often accompanied by melena which is black tarry stool that results from degradation of blood to hematin or other hemochromes by intestinal bacteria.

Gastrointestinal bleeding can be classified as overt, occult or obscure.

Overt Gastro-Intestinal (GI) bleeding is visible and can present in the form of hematemesis, “coffee-ground” emesis, melena, or hematochezia. Occult bleeding refers to bleeding which is not clinically visible as it is microscopic bleeding. Obscure GI bleeding refers to recurrent bleeding in which a source is not identified after upper endoscopy and colonoscopy. It may be either overt or occult.

Depending upon the site, gastrointestinal bleeding can be classified as either upper or lower GI bleed. Upper GI bleeding is hemorrhage originating from the esophagus to the ligament of Treitz, at the duodenojejunal flexure and lower GI bleeding originates from a site distal to the ligament of Treitz.

Hematemesis is a manifestation of acute severe upper Gastro-Intestinal bleed. Acute GI bleeding is a major cause of hospital admissions in the United States, which is estimated at 300,000 patients annually. **Upper GI tract bleed is approximately four times more common than that of lower GI tract and is a major cause of morbidity and mortality.** Acute GI bleeding is more common in men than women and its prevalence increases with age. The most common causes of acute upper GI bleeding are peptic ulcer disease including from the use of aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs), variceal hemorrhage, Mallory-Weiss tear and neoplasms including gastric cancers. Other relatively common causes include esophagitis, erosive gastritis/duodenitis, vascular ectasias and Dieulafoy’s lesions.¹ Esophageal varices and peptic ulcer disease are major causes of upper GI bleeding in both Eastern and Western societies.

Severe GI bleed is defined as documented gastrointestinal bleeding accompanied by shock or orthostatic hypotension, and a decrease in the hematocrit value by at least 6% or a decrease in the hemoglobin level of at least 2 g/dL, or requires transfusion of at least two units of packed red blood cells.¹ Patients with severe GI bleeding

require admission for resuscitation and treatment.

INITIAL EVALUATION (FIGURE 1)

The initial evaluation of the patient with bloody vomiting involves an assessment of the hemodynamic stability and resuscitation, and if necessary diagnostic studies (usually endoscopy) with the goal of both diagnoses and when possible, treatment of the specific disorder.

Evaluation of the patient includes a history, physical examination, laboratory tests, and in some cases, nasogastric lavage. The information gathered as a part of initial evaluation is used to guide decisions regarding triage, resuscitation, empiric medical therapy and diagnostic testing.

Past Medical History - Patients should be asked about prior episodes of upper GI bleeding, since up to 60 percent of patients bleed from the same lesion.² In addition, the patient’s past medical history should be reviewed to identify important co-morbid conditions.

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.
- Peptic ulcer disease in a patient with a history of *Helicobacter pylori*, nonsteroidal anti-inflammatory drug (NSAIDs) use, or smoking and epigastric discomfort.
- Cameron’s erosions in patient with history of large hiatal hernia.
- 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.
- 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 hypoxemia (eg, coronary artery disease, pulmonary disease). Such patients may need to be maintained at higher hemoglobin levels than patients without these

disorders.

- Predispose patients to volume overload in the setting of fluid resuscitation or blood transfusions (eg, renal disease, heart failure). Such patients may need more invasive monitoring during resuscitation.
- 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.
- Predispose to aspiration (eg, dementia, hepatic encephalopathy). Endotracheal intubation should be considered in such patients.

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:³

- Peptic ulcer: Epigastric or right upper quadrant pain
- Esophageal ulcer: Odynophagia, gastroesophageal reflux, dysphagia.
- Mallory-Weiss tear: Emesis, retching, or coughing prior to hematemesis.
- Variceal hemorrhage or portal hypertensive gastropathy: Jaundice, weakness, fatigue, anorexia, abdominal distention.
- 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:³

- Mild to moderate hypovolemia: 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.

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.

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.

The initial hemoglobin 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 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 overhydration 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 (>20:1 or >100:1, respectively).^{4,5} The higher the ratio, the more likely the bleeding is from an upper GI source.⁴

GENERAL MANAGEMENT (FIGURE 2)

Triage — Resuscitation of a hemodynamically unstable patient begins with assessing and addressing the ABCs (ie, airway, breathing, circulation) of initial management. All patients with hemodynamic instability (shock, orthostatic hypotension) 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, electrocardiogram monitoring, and pulse oximetry. Foley catheter placement is mandatory to allow a continuous evaluation of the urinary output as a guide to renal perfusion.

Other patients can be admitted to a regular medical ward, all admitted patients with the exception of low-risk patients receive electrocardiogram monitoring. Outpatient management may be appropriate for some low-risk patients.

General support — Patients should receive supplemental oxygen by nasal cannula and should receive nothing per mouth. Two large caliber (16 gauge or larger) peripheral intravenous catheters or a central venous line should be inserted who need close monitoring during resuscitation.

Elective endotracheal intubation in patients with ongoing hematemesis or altered respiratory or mental status may facilitate endoscopy and decrease the risk of aspiration.

Fluid resuscitation — Adequate resuscitation and stabilization is essential prior to endoscopy to minimize treatment-associated complications.⁶ According to the 2008 SIGN guideline, either colloid or crystalloid solutions may be used to attain volume restoration prior to administering blood products.⁷ A rough guideline for the total amount of crystalloid fluid volume needed to correct

the hypovolemia is the 3-for-1 rule. Replace each milliliter of blood loss with 3 mL of crystalloid fluid. This restores the lost plasma volume. Patients with severe coexisting medical illnesses, such as cardiovascular and pulmonary diseases, may require pulmonary artery catheter insertion to closely monitor hemodynamic cardiac performance profiles during the early resuscitative phase.

If the blood pressure fails to respond to initial resuscitation efforts, the rate of fluid administration should be increased.

Blood transfusions — The decision to initiate blood transfusions must be individualized. Initiate blood transfusions 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 (70g/L).⁸⁻¹⁰ Try 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. However, patients with active bleeding and hypovolemia may require blood transfusion despite an apparently normal hemoglobin

It is particularly important to avoid overtransfusion in patients with suspected variceal bleeding, as it can precipitate worsening of the bleeding [9]. Transfusing patients with suspected variceal bleeding to a hemoglobin >10 g/dL (100 g/L) should be avoided.

Patients with active bleeding and a low platelet count ($< 50,000/\text{microL}$) should be transfused with platelets. Patients with a coagulopathy that is not due to cirrhosis (prolonged prothrombin time with INR >1.5) should be transfused with fresh frozen plasma (FFP). 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.

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, in patients with an INR ≥ 3 , attempt to correct the INR to <3 prior to starting an endoscopy, with additional FFP 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 >1.5 . This approach is based on data that suggest endoscopy is safe in patients who are mildly to moderately anticoagulated.¹¹ In addition, because packed red blood cells do not contain coagulation factors, transfusion of a unit of FFP should be considered after every four units of packed red blood cells.¹²

Platelet transfusions should also be considered in patients with life-threatening bleeding who have received antiplatelet agents such as aspirin or clopidogrel.¹³ If the patient is taking the 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 agent or giving a platelet transfusion.

MEDICATIONS

Acid suppression

Patients admitted to the hospital with acute upper GI bleeding are typically treated with a proton pump inhibitor (PPI). Patients with acute upper GI bleeding can be started empirically on an intravenous (IV) PPI. It 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.

Several studies have examined the role of acid suppression given before or after endoscopy (with or without therapeutic intervention).¹⁴ 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.¹⁵⁻¹⁷ 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.¹⁸ Lao et al have demonstrated that high-dose intravenous omeprazole can accelerate the resolution of stigmata of recent hemorrhage and reduce the need for endoscopic therapy.¹⁹

The suggested dosing of intravenous pantoprazole and esomeprazole is 80-mg bolus followed by 8-mg/h infusion. The infusion is continued for 48-72 hours. 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.

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.²⁰

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. Erythromycin should 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

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.²¹ 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.

Somatostatin and its analogs

Somatostatin, or its analog octreotide, is used in the treatment of variceal bleeding and may also reduce the risk of bleeding due to nonvariceal causes.²² In patients

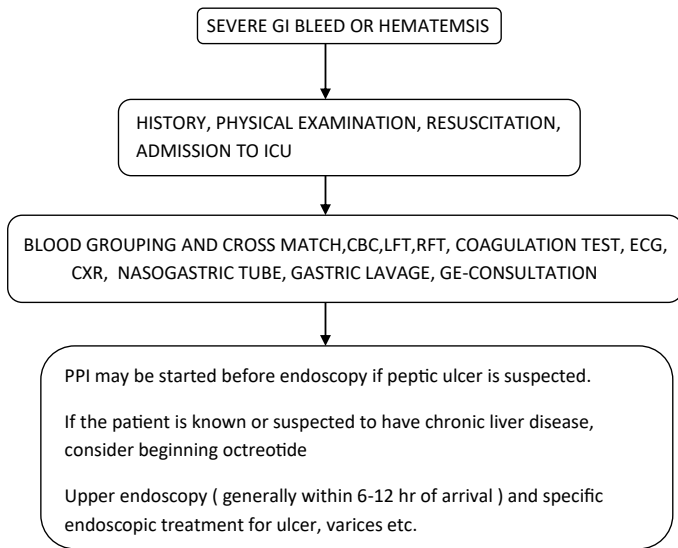


Fig. 1: Algorithm for the initial management of severe upper gastrointestinal (UGI) bleeding. CBC-Complete blood count, LFT – liver function test, RFT – renal function test, ECG-electrocardiogram, CXR – Chest X-Ray, GE- Gastroenterologist.

with suspected variceal bleeding, octreotide is given as an intravenous bolus of 50 mcg, followed by a continuous infusion at a rate of 50 mcg per hour. 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.

A meta-analysis has shown that vasoactive drugs (e.g., octreotide, somatostatin, terlipressin [a long-acting vasopressin analog]) are as effective as sclerotherapy for controlling variceal bleeding and cause fewer adverse events.²³

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. Meta-analyses have suggested that administration of an antibiotic to cirrhotic patients with variceal bleeding is associated with a decrease in the rates of mortality and bacterial infections.²⁴⁻²⁵ The optimal type and duration of antibiotic is unknown. The most commonly prescribed antibiotics are fluoroquinolones, including oral norfloxacin, 400 mg twice daily, intravenous ciprofloxacin, 400 mg every 12 hours, intravenous levofloxacin, 500 mg every 24 hours, and intravenous ceftriaxone, 1 g every 24 hours, administered for seven days.

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.

SPECIFIC DIAGNOSTIC STUDY AND MANAGEMENT

Upper endoscopy

In patients with acute upper GI bleeding, upper endoscopy is considered the investigation of choice.²⁶ Early upper endoscopy within 24 h of presentation is recommended in most patients with acute upper GI bleeding to confirm diagnosis and has the benefit of targeted endoscopic treatment, resulting in reduced morbidity, hospital length of stay, risk of recurrent bleeding and the need for surgery.²⁷ Patients with major bleeding and high-risk endoscopic findings (e.g., varices, ulcers with active bleeding or a visible vessel) benefit from endoscopic hemostatic therapy, while patients with low-risk lesions (e.g., clean-based ulcers, nonbleeding Mallory-Weiss tears, erosive or hemorrhagic gastropathy) who have stable vital signs and hemoglobin, and no other medical problems, can be discharged home.

The Forrest classification (Fig. 3) is used to categorize findings during endoscopic evaluation of bleeding peptic ulcers, as follows: active spurting bleeding (Forrest IA); oozing bleeding (Forrest IB); pigmented protuberance or nonbleeding visible vessel (NBVV; Forrest IIA); adherent clot (Forrest IIB); flat pigmented spot (Forrest IIC); and clean-based ulcer (Forrest III).¹ Patients with major stigmata of ulcer hemorrhage (spurting, NBVV, or adherent clot) benefit most from endoscopic hemostasis, whereas those with a flat spot or clean based ulcer do not.

Endoscopic grading of esophageal varices is subjective. Small varices that is, those occupying less than one third of the lumen, are less than 5 mm in diameter, whereas large varices are greater than 5 mm in diameter. Patients with large esophageal varices, Child (or Child-Pugh) class C cirrhosis, and red color signs on varices have the highest risk of variceal bleeding within 1 year.¹ Endoscopic variceal ligation combined with Pharmacological therapy (somatostatin or its analogues octreotide and vapreotide; terlipressin) is the preferred therapy for control of acute esophageal variceal bleeding. Endoscopic variceal ligation is preferred therapy for initial control of bleeding and prevention of rebleeding, and is associated with fewer complications than endoscopic sclerotherapy and requires fewer sessions to achieve variceal obliteration.¹

Most commonly used endoscopic classification of Gastric varices, described by Sarin et al. divides gastric varices into four groups:

- GOV1 (74%) – when esophageal varices extend into the lesser curvature
- GOV2 (16%) – when esophageal varices extend into the fundus
- IGV1 (8%) – isolated fundic varices without esophageal varices
- IGV2 (2%) – isolated antral varices

In patients who bleed from gastric fundal varices, endoscopic variceal obturation using tissue adhesives such as cyanoacrylate is preferred, where available. Otherwise, EVL is an option. A TIPS (transjugular intrahepatic portosystemic shunt) should be considered in patients in whom hemorrhage from fundal varices

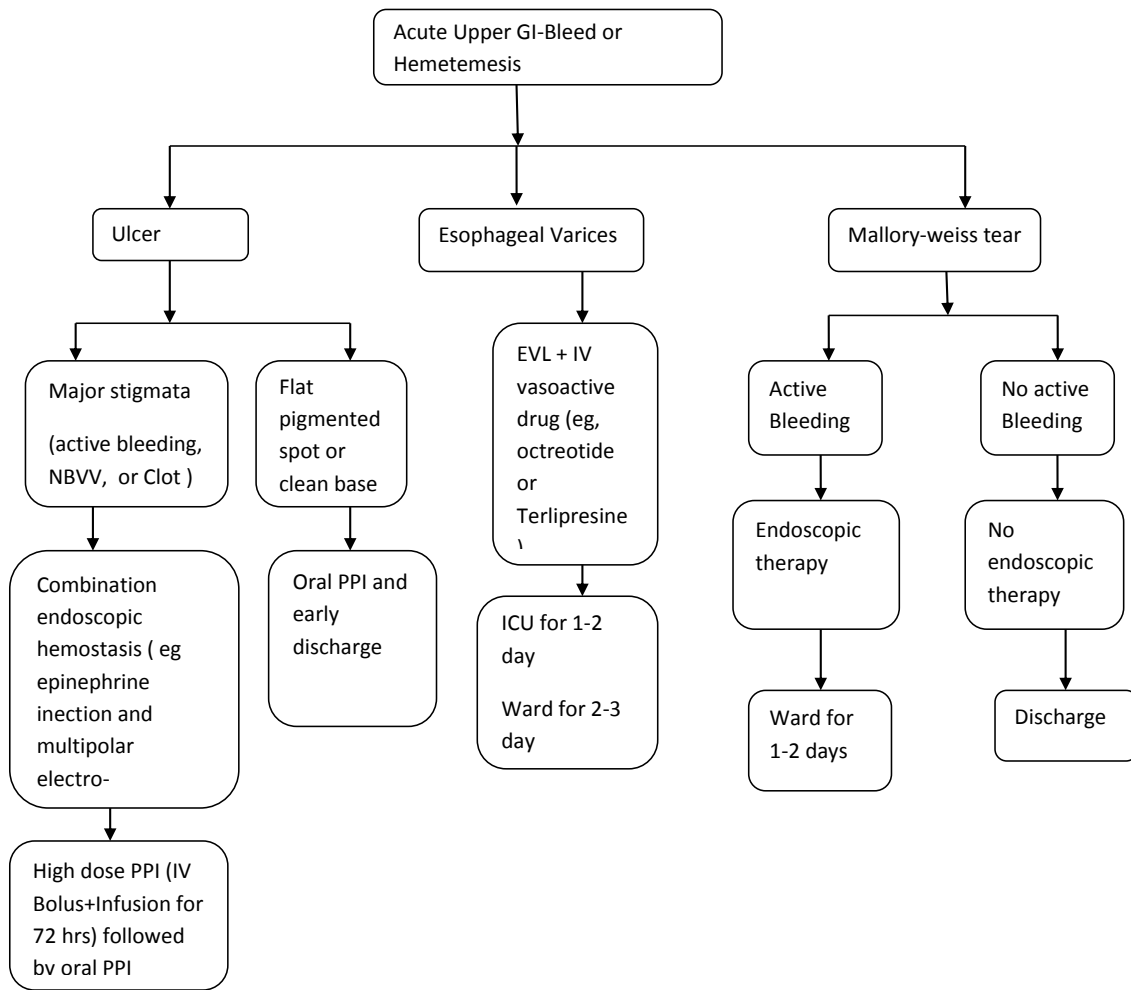


Fig. 2: Algorithm for the endoscopic and medical management of severe GI – hemorrhage, following hemodynamic stabilization. IV, intravenous; NBVV, nonbleeding visible vessel; PPI, proton pump inhibitor; EVL, Endoscopic Variceal Ligation

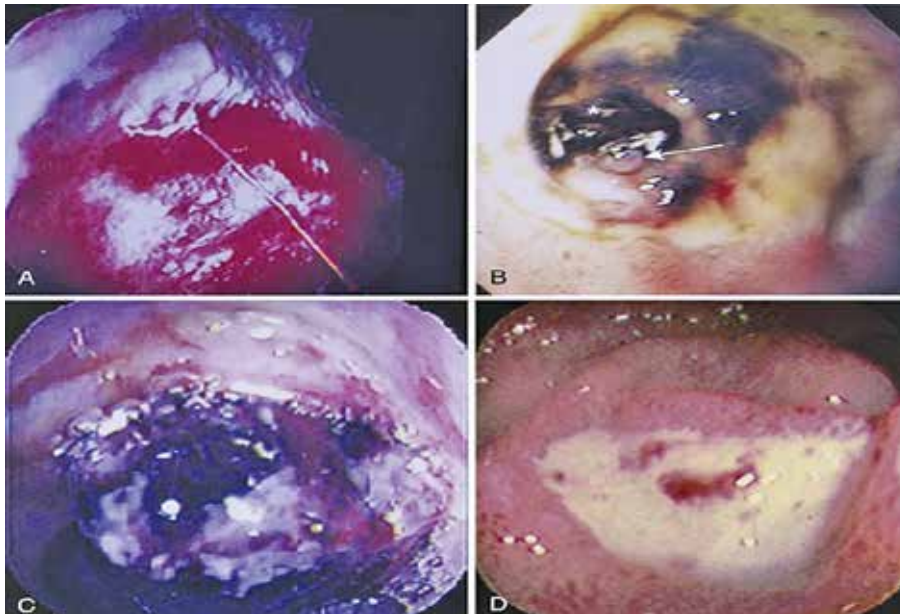


Fig. 3: Endoscopic stigmata of recent peptic ulcer bleeding. A, Active bleeding with spurting. B, Visible vessel (arrow) with an adjacent clot. C, An adherent clot. D, Slight oozing of blood after washing in the center of an ulcer without a clot or visible vessel.

cannot be controlled or in whom bleeding recurs despite combined pharmacological and endoscopic therapy.

The reported sensitivity and specificity of endoscopy for

upper gastroduodenal bleeding are 92%-98% and 30%-100%, respectively.²⁶

Risks of upper endoscopy include aspiration, side-effects

192 from sedation, perforation, and increased bleeding while attempting therapeutic intervention. The airway should be secured by endotracheal intubation in the case of massive upper GI bleeding.

The practice of routine second look endoscopy after hemostasis is achieved on first endoscopy remains controversial. The 2010 International Consensus Recommendations did not recommend routine use of second look endoscopy but stated it may be useful in selected patients with high risk of re-bleeding²⁷

Other diagnostic tests - In cases of acute upper GI bleeding where upper endoscopy is non-diagnostic in which a bleeding site cannot be identified or treated, the next investigation depends on the patient's hemodynamic stability. If the patient is unstable with large volume upper GI blood loss, patient should proceed to urgent surgery, such as an exploration and partial gastrectomy for uncontrolled bleeding gastric ulcer.²⁸ Intraoperative endoscopy may be a useful adjunct during surgery to help localize the source of bleeding. If the patient is hemodynamically stable with low volume bleeding, repeat endoscopy may be considered.

Other diagnostic tests for acute upper GI bleeding include CT angiography, catheter angiography and nuclear scintigraphy, which can detect active bleeding, deep small bowel enteroscopy, and rarely, intraoperative enteroscopy.²⁹

Upper GI barium studies are contraindicated in the setting of acute upper GI bleeding because they may interfere with subsequent investigations or surgery,³⁰ and due to the risk of barium peritonitis if there is a pre-existing perforation of the bowel wall.

RISK STRATIFICATION

Endoscopic, clinical, and laboratory features may be useful for risk stratification of patients who present with acute upper GI bleeding, and the use of risk stratification tools is recommended by the International Consensus Upper Gastrointestinal Bleeding Conference Group.²⁷ Factors associated with rebleeding identified in a meta-analysis included:³¹

- 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)

Risk scores — For acute upper GI bleeding, risk scores such as the Rockall Score and Glasgow Blatchford Score (GBS) have been developed and validated.³² While the Rockall score uses endoscopic findings, the GBS is based upon the patient's clinical presentation such as systolic blood pressure, pulse, presence of melena, syncope, hepatic disease, cardiac failure and laboratory parameters such as blood urea nitrogen and hemoglobin. Therefore,

the GBS may be best suited for initial risk evaluation of suspected acute upper GI bleeding, such as in the emergency department setting

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.³³

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, patients who meet the following criteria can be discharged home:

- Have stable vital signs
- Have a normal hemoglobin
- Have a likely bleeding source identified on upper endoscopy
- Have a source of bleeding 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)
- Have no comorbidities

However, the decision to discharge a patient also depends upon individual-patient factors, such as reliability for follow-up and confidence in the diagnosis.

If patients do not meet these criteria, patient should be admitted in 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.

CONCLUSION

Hematemesis is a manifestation of acute severe GI bleeding can be caused by a wide range of pathologies. Esophageal varices and peptic ulcer disease are major causes of upper GI bleeding in both Eastern and Western societies. In patients with active GI bleeding who are unstable, acute resuscitation should precede any investigations. Upper endoscopy is the mainstay of initial investigations and deciding the specific therapy.

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