Portal hypertensive gastropathy

AUTHOR: Don C Rockey, MD
SECTION EDITOR: Mark Feldman, MD, MACP, AGAF, FACG
DEPUTY EDITOR: Kristen M Robson, MD, MBA, FACG

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Sep 2023.**
This topic last updated: **Dec 20, 2022.**

INTRODUCTION

Portal hypertension most commonly develops in the setting of chronic liver injury with cirrhosis and typically is the result of a combination of an increase in resistance to portal blood flow and an increase in portal blood flow. Other less common causes of portal hypertension include noncirrhotic portal hypertension and extrahepatic portal vein thrombosis. (See "Portal hypertension in adults".)

Portal hypertension may lead to complications such as the following:

- Variceal hemorrhage
- Ascites
- Portal hypertensive gastropathy (PHG)
- Spontaneous bacterial peritonitis (a complication of ascites)
- Hepatic hydrothorax

Portal hypertension may also be associated with several other complications in patients with chronic liver disease, although the pathogenesis of these complications when they are associated with portal hypertension remains unclear.

- Hepatorenal syndrome
- Hepatopulmonary syndrome
- Portopulmonary hypertension

- Cirrhotic cardiomyopathy

This topic will review the pathogenesis, clinical manifestations, diagnosis, and management of PHG. Other complications of portal hypertension and cirrhosis are discussed elsewhere. (See "Portal hypertension in adults" and "Cirrhosis in adults: Overview of complications, general management, and prognosis".)

EPIDEMIOLOGY

Portal hypertensive gastropathy (PHG) has been estimated to occur in 20 to 98 percent of patients with cirrhosis [1-7]. Some of the variability in prevalence estimates may be related to the study of different patient populations and variable definitions of PHG used in different studies. In one of the larger studies that included 1016 patients with severe hepatic fibrosis or cirrhosis who had no prior history of gastrointestinal bleeding, PHG was detected in 37 percent of patients [1].

PHG appears to be more common in patients with advanced liver disease, more severe portal hypertension, esophageal varices, or a history of treatment for esophageal varices with sclerotherapy or band ligation [4-6,8].

PATHOGENESIS

Portal hypertension is a prerequisite for the development of portal hypertensive gastropathy (PHG). However, the correlation between the severity of portal hypertension and the severity of PHG appears to be weak, and it is unclear as to the relationship between clinically significant portal hypertension and PHG [9]. The pathogenesis of PHG may be related to both congestion and hyperemia in the stomach. This is supported by the finding that gastric mucosal blood flow is increased in patients with cirrhosis and PHG compared with those without PHG [10]. Other possible mechanisms include mucosal ischemia and increased nitric oxide synthase activity or inflammation associated with abnormal blood flow due to portal hypertension, but their etiologic role is uncertain [11,12]. The severity of gastropathy is related to portal pressure, the level of hepatic vascular resistance, and the degree of reduction in hepatic perfusion [13].

Some studies have suggested that endoscopic sclerotherapy or ligation of esophageal varices increases the risk of developing PHG, though this issue remains controversial [14]. It has been hypothesized that variceal obliteration results in hyperdynamic congestion, which then gives rise to PHG [2]. In a prospective series with 107 patients with portal hypertension from various causes who were studied before and after sclerotherapy [2], PHG was evident in 4 of 35 patients

with cirrhosis before sclerotherapy. After sclerotherapy, 21 additional patients (20 percent) developed PHG during a follow-up of 23 months. The risk of developing PHG appeared to be influenced by prior sclerotherapy, the severity of liver disease, the etiology of portal hypertension, and the coexistence of gastric varices, but the risk was not directly correlated with intravariceal pressure.

CLINICAL MANIFESTATIONS

Patients with portal hypertensive gastropathy (PHG) are often asymptomatic and are diagnosed when endoscopy is performed for other reasons (eg, to screen for esophageal varices) [15]. However, because the gastric mucosa in the setting of PHG is friable, bleeding may occur when ectatic vessels rupture (though PHG is an uncommon cause of significant bleeding in patients with portal hypertension). When bleeding occurs it is typically chronic, though it can be acute and massive. Patients with chronic bleeding may have occult blood in their stool and/or iron deficiency anemia. Patients with acute bleeding may present with hematemesis, melena, or if the bleeding is massive, hematochezia.

Chronic bleeding is estimated to develop in 3 to 60 percent of patients with PHG [3,4,16,17], and acute bleeding is estimated to occur in 2 to 12 percent [3-5]. Among patients with acute bleeding, the majority (90 to 95 percent) have severe PHG [4,5]. (See 'Classification' below.)

The natural history of PHG has been evaluated in prospective studies [3,4]. One study included 315 patients who were followed with clinical and endoscopic examinations every six months for three years [3]. During follow-up, endoscopic PHG remained stable in 29 percent, worsened in 23 percent, improved in 23 percent, and fluctuated in 25 percent. Acute bleeding from PHG was observed in only eight patients (2.5 percent), with one death. Chronic bleeding occurred in 34 patients (11 percent).

DIAGNOSIS

Diagnostic approach — Portal hypertensive gastropathy (PHG) should be suspected in patients with risk factors for portal hypertension who have signs of acute or chronic gastrointestinal bleeding. If PHG is suspected, patients should undergo upper gastrointestinal endoscopy to confirm the diagnosis. PHG should also be suspected in patients with portal hypertension who are undergoing endoscopy for other reasons and have characteristic endoscopic findings (a mosaic-like or "snakeskin" appearance of the gastric mucosa, predominantly in the fundus and body). Mild PHG can be mimicked by a number of other disorders that cause mucosal injury to

the stomach. Mucosal biopsies are generally not required but may be helpful if the diagnosis is unclear; however, care should be taken in the setting of coagulopathy. Diagnostic uncertainty most often occurs when gastrointestinal vascular ectasia (GAVE) is also being considered in the differential diagnosis. (See 'Differential diagnosis' below.)

Upper endoscopy — PHG is typically diagnosed endoscopically. PHG characteristically appears as a fine, white, reticular pattern separating areas of pinkish mucosa, giving the gastric mucosa a snakeskin appearance (picture 1) [18]. Other findings may include flat or bulging red marks or red spots that resemble vascular ectasias, or black-brown spots [15]. Mucosal changes are usually most evident in the fundus and body (proximal part) of the stomach. In more severe cases, oozing, bleeding, subepithelial hemorrhages, and increased vascularity similar to angiomas are evident, often involving the gastric fundus, gastric body, and antrum.

Histologic findings — Biopsies are generally not needed to make a diagnosis of PHG because the combination of the appropriate clinical setting and endoscopic appearance of the lesion is usually sufficient. If biopsies are obtained because of a suspicion of PHG, care should be taken in the setting of coagulopathy. If biopsies are obtained, typical histologic findings include dilated submucosal and mucosal veins and ectatic capillaries [19]. Findings such as inflammation and thrombi are absent.

CLASSIFICATION

Portal hypertensive gastropathy (PHG) is typically categorized as either mild or severe [15]. Mild PHG is characterized by a mosaic-like pattern without other findings. Severe PHG is characterized by a mosaic-like pattern with flat or bulging red or black-brown spots and/or active bleeding.

DIFFERENTIAL DIAGNOSIS

Chronic bleeding — The differential diagnosis for patients with chronic bleeding encompasses different lesions throughout the gastrointestinal tract, including peptic ulcer disease, angiodysplasia, and malignancies (table 1) [20]. When diffuse mucosal changes are seen on endoscopy, gastritis (often related to drugs or toxins such as alcohol) is a potential source. The evaluation of occult bleeding includes upper endoscopy, colonoscopy, possible evaluation of the small bowel, other testing (such as cross-sectional imaging), and this is discussed separately. (See "Evaluation of occult gastrointestinal bleeding".)

Acute bleeding — Patients with risk factors for portal hypertensive gastropathy (PHG) (eg, cirrhosis) may bleed from other upper gastrointestinal tract lesions, especially esophagogastric varices, but also from peptic ulcer disease and esophagitis [21]. Upper endoscopy permits differentiation among these different bleeding sources (table 1). (See "Causes of upper gastrointestinal bleeding in adults" and "Approach to acute upper gastrointestinal bleeding in adults".)

Endoscopic findings — Gastrointestinal vascular ectasia (GAVE) is also associated with cirrhosis and may be difficult to differentiate from PHG. It is important to differentiate between the two entities because they are treated differently. GAVE is treated with thermoablative therapy, whereas PHG is treated with measures aimed at reducing portal pressure. Findings that favor a diagnosis of GAVE include an antral-predominant location of the lesions and a classic linear pattern of lesions. In situations where the diagnosis remains unclear, histological analysis may be helpful. Histologic findings that suggest GAVE include extensive vascular ectasia, spindle cell proliferation, fibrin thrombi, and fibrohyalinosis [22]. (See "Causes of upper gastrointestinal bleeding in adults", section on 'Gastric antral vascular ectasia'.)

MANAGEMENT

Management overview — An overview of the management of portal hypertensive gastropathy (PHG) is presented in the table (table 2). In general, the management of PHG is directed at decreasing portal pressure [15], and depends on the acuity and severity of bleeding:

- Primary prophylaxis – Primary prophylaxis to prevent bleeding with a nonselective beta blocker may be appropriate in patients with severe PHG or in patients who have other indications for nonselective beta blocker therapy (eg, varices). (See 'Primary prophylaxis' below.)

- Chronic bleeding – Among patients with chronic bleeding, treatment typically consists of a nonselective beta blocker as well as iron repletion and/or blood transfusions. If medical therapy is successful at controlling the bleeding, secondary prophylaxis with a nonselective beta blocker should be continued indefinitely. (See 'Chronic bleeding' below.)

- Acute bleeding – For patients with acute bleeding, treatment includes administration of a vasoactive medication, resuscitation/blood transfusion as needed, and, for patients with cirrhosis, antibiotic prophylaxis. Once the bleeding is controlled, a nonselective beta blocker is started and continued indefinitely. (See 'Acute bleeding' below and "Approach to acute upper gastrointestinal bleeding in adults".)

- Refractory bleeding – If initial therapy fails and bleeding is severe and refractory, transjugular intrahepatic portosystemic shunt (TIPS) placement or shunt surgery may be considered. Liver transplantation is an option for patients with decompensated liver disease. In patients who fail medical therapy but have less severe bleeding, management with iron repletion and/or blood transfusions is an alternative. (See 'Refractory bleeding' below.)

Nonselective beta blockers include propranolol and nadolol. Carvedilol is a mixed beta (beta-1 and beta-2) and alpha (alpha-1) adrenergic receptor blocker and has been shown to reduce portal pressure, though it has not been studied specifically with regard to PHG. It appears to be well tolerated and simple to use, and we find it useful in patients who are not able to tolerate propranolol or nadolol. Beta blockers should be titrated to a heart rate of 50 to 55 beats per minute or to the maximum tolerated dose:

- Propranolol – Starting dose 20 mg orally twice daily; maximum 160 mg twice daily
- Nadolol – Starting dose 40 mg orally once daily; maximum 160 mg once daily
- Carvedilol – Starting dose 3.125 mg orally twice daily; maximum 25 mg twice daily

We generally avoid beta blockers in patients with hypotension (systolic blood pressure <100 mmHg) or with severe ascites. (See "Ascites in adults with cirrhosis: Diuretic-resistant ascites", section on 'Discontinuing beta blockers'.)

Vasoactive medications include octreotide, somatostatin, and terlipressin, and are given as follows in patients with acute bleeding:

- Octreotide – 100 mcg intravenous (IV) bolus followed by an IV infusion of 25 mcg/hour for 48 hours.
- Somatostatin – 250 mcg IV bolus followed by an IV infusion of 250 mcg/hour for three days.
- Terlipressin (available in the United States; gastrointestinal bleeding is an off-label indication) – 2 mg IV every four hours initially, then titrated down to 1 mg every four hours once bleeding is controlled. It is continued for up to five days.

Primary prophylaxis — Patients with mild PHG who do not have signs of bleeding and who do not have esophagogastric varices do not require treatment. On the other hand, patients with severe PHG may benefit from treatments aimed at reducing portal pressure, though high-quality studies in the setting are lacking. We treat patients with severe PHG with a nonselective beta blocker if they have other factors that increase their risk of bleeding (eg, a coagulopathy, thrombocytopenia) (table 2). (See 'Chronic bleeding' below.)

Patients with PHG and small esophageal varices should receive a nonselective beta blocker if there are no contraindications. This is because nonselective beta blockers are generally indicated for primary prophylaxis against variceal hemorrhage in patients with small varices and may also be beneficial for PHG in this setting [8,23,24]. (See "Primary prevention of bleeding from esophageal varices in patients with cirrhosis", section on 'Selecting a strategy'.)

Options for primary prophylaxis to prevent variceal hemorrhage in patients with medium or large varices include a nonselective beta blocker or endoscopic variceal ligation. Our approach in patients with PHG and medium or large varices is to treat with a nonselective beta blocker because of the potential therapeutic benefit for varices and PHG. We reserve endoscopic therapy for patients who are intolerant of or who have contraindications to beta blocker therapy. This often includes patients with advanced liver disease (Child-Pugh class C).

Chronic bleeding — In patients with chronic bleeding, our approach is to start therapy aimed at lowering portal pressure (typically a nonselective beta blocker such as propranolol, nadolol [16,19,25], or carvedilol), and to replete the patients' iron stores if needed (typically orally, although intravenous iron is also an effective option) (table 2). Patients with a hemoglobin <7 g/dL also typically require blood transfusion. (See "Treatment of iron deficiency anemia in adults", section on 'Oral iron' and "Treatment of iron deficiency anemia in adults", section on 'Intravenous iron'.)

The use of nonselective beta blockers for patients with bleeding from PHG was examined in a trial with 54 patients with PHG and acute or chronic bleeding from severe PHG [16]. Propranolol reduced the rate of recurrent bleeding compared with placebo (9 of 26 patients [35 percent] versus 17 of 28 patients [62 percent] at one year).

Acute bleeding — Patients with acute bleeding should be managed as other patients with acute upper gastrointestinal bleeding (UGIB), including obtaining adequate intravenous access, fluid resuscitation, blood transfusion, starting an intravenous proton pump inhibitor (PPI), and performing early upper endoscopy (algorithm 1). In addition, vasoconstrictor therapy with a medication such as terlipressin or octreotide should be initiated as soon as possible (prior to endoscopy) (table 2). Patients with cirrhosis also require antibiotic prophylaxis. The general approach to patients with UGIB is discussed in detail separately. (See "Approach to acute upper gastrointestinal bleeding in adults".)

If the bleeding is confirmed to be from PHG, the vasoconstrictor should be continued (or started if it was not given initially). The use of PPIs in this setting remains controversial, but because acid is not likely to play a major role in patients with bleeding from PHG, the PPI can be discontinued unless it is indicated for another reason.

The efficacy of vasoconstrictors for acute bleeding from PHG was demonstrated in a trial of 68 patients [26]. Patients were assigned to receive octreotide, vasopressin, or omeprazole. Bleeding was controlled in all 24 of the patients who received octreotide, in 14 of 22 (64 percent) of the patients who received vasopressin, and in 13 of 22 (59 percent) of patients who received omeprazole. In a second trial with 86 patients with bleeding from PHG or varices, those who received higher doses of terlipressin had better bleeding control and lower recurrence rates than patients who received lower doses [27].

Because PHG is a diffuse process, endoscopic therapy is typically not effective. However, endoscopic thermal coagulation may be effective for patients with focally bleeding lesions. Banding, injection therapy, H2 blockers, and topical agents such as sucralfate are ineffective for controlling diffuse bleeding or for preventing rebleeding from extensive PHG. A case series has described the successful use of hemostatic nanopowder in patients with acute bleeding from PHG [28]. (See "Overview of the treatment of bleeding peptic ulcers", section on 'Hemostatic sprays'.)

Once the acute bleeding episode has resolved, the patient should be started on a nonselective beta blocker, as is done for secondary prophylaxis of acute variceal hemorrhage [19,29]. (See "Prevention of recurrent bleeding from esophageal varices in patients with cirrhosis", section on 'Specific interventions'.)

Refractory bleeding — The most challenging patients with PHG are those who fail to respond to initial pharmacologic therapy. Alternative and additional treatment options include TIPS placement, shunt surgery, and liver transplantation (table 2). The choice of therapy will depend on local expertise with TIPS placement and surgical shunting and whether the patient is a candidate for liver transplantation. However, not all patients with refractory bleeding will require such invasive intervention. Patients with less severe chronic bleeding may be adequately managed with iron repletion and/or blood transfusion. (See "Treatment of iron deficiency anemia in adults".)

Information on the efficacy of TIPS placement for PHG is limited. In one series involving 40 patients, TIPS placement was associated with an improvement in endoscopic findings and a decrease in transfusion requirement in 89 and 75 percent of patients with mild and severe PHG, respectively [30]. Endoscopic improvement in patients with mild PHG was visible within six weeks in most patients and by three to six months in approximately 85 percent of patients. The response was slower in patients with severe PHG.

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" and "Society guideline links: Portal hypertension and ascites".)

SUMMARY AND RECOMMENDATIONS

- **Epidemiology –** Portal hypertensive gastropathy (PHG) is estimated to occur in 20 to 98 percent of patients with cirrhosis. (See 'Epidemiology' above.)

- **Clinical features –** Patients with PHG are often asymptomatic and are diagnosed when endoscopy is performed for other reasons (eg, to screen for esophageal varices). Bleeding is typically chronic, though it can be acute and massive in some patients. (See 'Clinical manifestations' above.)

- **Diagnosis –** PHG should be suspected in patients with risk factors for portal hypertension who have symptoms and/or signs of acute or chronic gastrointestinal bleeding (UGIB). Patients with evidence of UGIB should undergo upper GI endoscopy to confirm the diagnosis. PHG should also be suspected in patients with portal hypertension who are undergoing endoscopy for other reasons and have characteristic endoscopic findings (a mosaic-like or "snakeskin" appearance of the gastric mucosa, especially in the cardia, fundus, and/or body). Biopsies may be required if the diagnosis is unclear (especially if gastric antral vascular ectasia is also being considered in the differential diagnosis). (See 'Diagnosis' above.)

- **Classification –** PHG is most commonly categorized endoscopically as either mild or severe. Mild PHG is characterized by a mosaic-like pattern without other findings. Severe PHG is characterized by a mosaic-like pattern with flat or bulging red or black-brown spots, or by active hemorrhage. (See 'Classification' above.)

- **Management –** The goal of management of PHG is to reduce portal pressure (table 2). The specific approach depends on the acuity and severity of bleeding (see 'Management' above):

  - **Primary prophylaxis** – In patients with severe PHG and other risk factors for GI bleeding (eg, a coagulopathy, thrombocytopenia), we suggest primary prophylaxis with a nonselective beta blocker rather than giving no prophylaxis (**Grade 2C**). Nonselective beta blockers should also be started in patients who have other indications for nonselective beta blocker therapy (eg, varices). Carvedilol is an alternative for patients

who cannot take beta blockers or do not tolerate them. For all other patients, we suggest **not** giving primary prophylaxis (**Grade 2C**). (See 'Primary prophylaxis' above.)

- **Chronic bleeding** – Patients with chronic bleeding should receive iron repletion/blood transfusions as needed. In addition, we suggest that patients with chronic bleeding also receive treatment with a nonselective beta blocker rather than treatment with iron repletion/blood transfusions alone (**Grade 2C**). Carvedilol is an alternative for patients who cannot take beta blockers or do not tolerate them. If medical therapy is successful at controlling the bleeding, the medication should be continued indefinitely. (See 'Chronic bleeding' above.)

- **Acute bleeding** – Patients with acute bleeding should be managed the same as patients with other causes of UGIB. Management includes resuscitation/blood transfusion as necessary, upper endoscopy, and, for patients with cirrhosis, antibiotic prophylaxis. For patients known to have PHG, we suggest additional treatment with a vasoactive medication (eg, terlipressin or octreotide) rather than supportive measures alone (**Grade 2B**). This suggestion is based both on studies that have examined the use of vasoactive medications in patients with acute bleeding from PHG as well as the efficacy of vasoactive medications in patients with bleeding from other complications of portal hypertension. Vasoactive medications should also be given to patients with known or suspected varices. Once bleeding is controlled, a nonselective beta blocker is started and continued indefinitely. (See 'Acute bleeding' above and "Approach to acute upper gastrointestinal bleeding in adults" and "Methods to achieve hemostasis in patients with acute variceal hemorrhage", section on 'Pharmacologic therapy'.)

- **Refractory bleeding** – For patients who fail to respond to initial therapy, further treatment options include transjugular intrahepatic portosystemic shunt (TIPS) placement, shunt surgery, and liver transplantation. The choice of therapy will depend on local expertise with TIPS placement and surgical shunting and whether the patient is a liver transplant candidate. However, not all patients with refractory bleeding will require invasive treatment. Patients with less severe chronic bleeding may be adequately managed with iron repletion and/or blood transfusion. (See 'Refractory bleeding' above.)

REFERENCES

1. Fontana RJ, Sanyal AJ, Mehta S, et al. Portal hypertensive gastropathy in chronic hepatitis C patients with bridging fibrosis and compensated cirrhosis: results from the HALT-C trial. Am J Gastroenterol 2006; 101:983.
2. Sarin SK, Sreenivas DV, Lahoti D, Saraya A. Factors influencing development of portal hypertensive gastropathy in patients with portal hypertension. Gastroenterology 1992; 102:994.
3. Primignani M, Carpinelli L, Preatoni P, et al. Natural history of portal hypertensive gastropathy in patients with liver cirrhosis. The New Italian Endoscopic Club for the study and treatment of esophageal varices (NIEC). Gastroenterology 2000; 119:181.
4. Merli M, Nicolini G, Angeloni S, et al. The natural history of portal hypertensive gastropathy in patients with liver cirrhosis and mild portal hypertension. Am J Gastroenterol 2004; 99:1959.
5. D'Amico G, Montalbano L, Traina M, et al. Natural history of congestive gastropathy in cirrhosis. The Liver Study Group of V. Cervello Hospital. Gastroenterology 1990; 99:1558.
6. Iwao T, Toyonaga A, Oho K, et al. Portal-hypertensive gastropathy develops less in patients with cirrhosis and fundal varices. J Hepatol 1997; 26:1235.
7. Thuluvath PJ, Yoo HY. Portal Hypertensive gastropathy. Am J Gastroenterol 2002; 97:2973.
8. Cubillas R, Rockey DC. Portal hypertensive gastropathy: a review. Liver Int 2010; 30:1094.
9. Marrache MK, Bou Daher H, Rockey DC. The relationship between portal hypertension and portal hypertensive gastropathy. Scand J Gastroenterol 2022; 57:340.
10. Ohta M, Hashizume M, Higashi H, et al. Portal and gastric mucosal hemodynamics in cirrhotic patients with portal-hypertensive gastropathy. Hepatology 1994; 20:1432.
11. El-Newihi HM, Kanji VK, Mihas AA. Activity of gastric mucosal nitric oxide synthase in portal hypertensive gastropathy. Am J Gastroenterol 1996; 91:535.
12. Piasecki C, Chin J, Greenslade L, et al. Endoscopic detection of ischaemia with a new probe indicates low oxygenation of gastric epithelium in portal hypertensive gastropathy. Gut 1995; 36:654.
13. Iwao T, Toyonaga A, Sumino M, et al. Portal hypertensive gastropathy in patients with cirrhosis. Gastroenterology 1992; 102:2060.
14. Hou MC, Lin HC, Kuo BI, et al. Comparison of endoscopic variceal injection sclerotherapy and ligation for the treatment of esophageal variceal hemorrhage: a prospective randomized trial. Hepatology 1995; 21:1517.
15. Urrunaga NH, Rockey DC. Portal hypertensive gastropathy and colopathy. Clin Liver Dis 2014; 18:389.

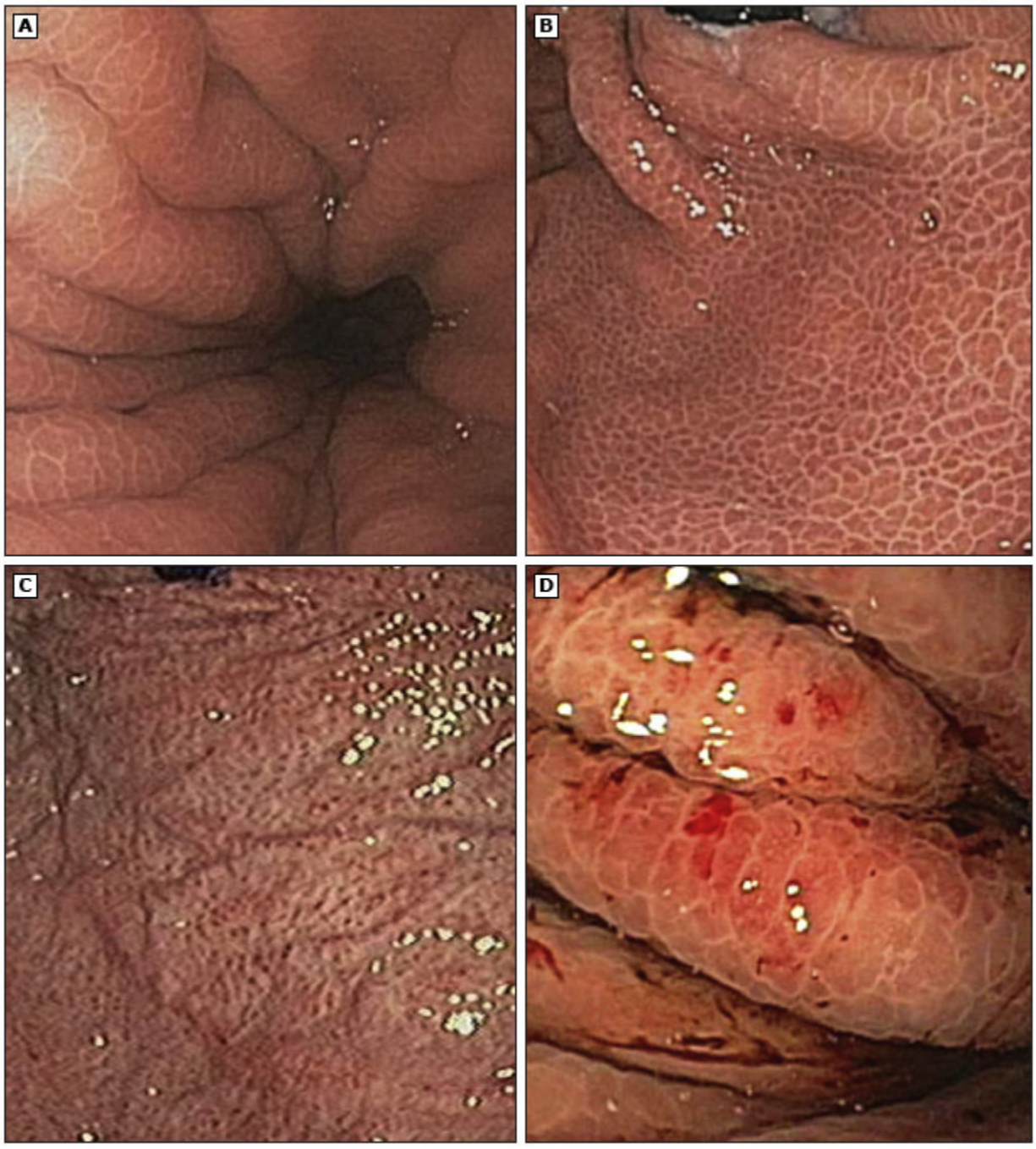
16. Pérez-Ayuso RM, Piqué JM, Bosch J, et al. Propranolol in prevention of recurrent bleeding from severe portal hypertensive gastropathy in cirrhosis. Lancet 1991; 337:1431.
17. Sarin SK, Shahi HM, Jain M, et al. The natural history of portal hypertensive gastropathy: influence of variceal eradication. Am J Gastroenterol 2000; 95:2888.
18. Wollenman CS, Chason R, Reisch JS, Rockey DC. Impact of ethnicity in upper gastrointestinal hemorrhage. J Clin Gastroenterol 2014; 48:343.
19. Patwardhan VR, Cardenas A. Review article: the management of portal hypertensive gastropathy and gastric antral vascular ectasia in cirrhosis. Aliment Pharmacol Ther 2014; 40:354.
20. Rockey DC. Occult and obscure gastrointestinal bleeding: causes and clinical management. Nat Rev Gastroenterol Hepatol 2010; 7:265.
21. Lyles T, Elliott A, Rockey DC. A risk scoring system to predict in-hospital mortality in patients with cirrhosis presenting with upper gastrointestinal bleeding. J Clin Gastroenterol 2014; 48:712.
22. Payen JL, Calès P, Voigt JJ, et al. Severe portal hypertensive gastropathy and antral vascular ectasia are distinct entities in patients with cirrhosis. Gastroenterology 1995; 108:138.
23. Merkel C, Marin R, Angeli P, et al. A placebo-controlled clinical trial of nadolol in the prophylaxis of growth of small esophageal varices in cirrhosis. Gastroenterology 2004; 127:476.
24. Bhardwaj A, Kedarisetty CK, Vashishtha C, et al. Carvedilol delays the progression of small oesophageal varices in patients with cirrhosis: a randomised placebo-controlled trial. Gut 2017; 66:1838.
25. Rockey DC. An Update: Portal Hypertensive Gastropathy and Colopathy. Clin Liver Dis 2019; 23:643.
26. Zhou Y, Qiao L, Wu J, et al. Comparison of the efficacy of octreotide, vasopressin, and omeprazole in the control of acute bleeding in patients with portal hypertensive gastropathy: a controlled study. J Gastroenterol Hepatol 2002; 17:973.
27. Bruha R, Marecek Z, Spicak J, et al. Double-blind randomized, comparative multicenter study of the effect of terlipressin in the treatment of acute esophageal variceal and/or hypertensive gastropathy bleeding. Hepatogastroenterology 2002; 49:1161.
28. Smith LA, Morris AJ, Stanley AJ. The use of hemospray in portal hypertensive bleeding; a case series. J Hepatol 2014; 60:457.
29. de Franchis R, Bosch J, Garcia-Tsao G, et al. Baveno VII - Renewing consensus in portal hypertension. J Hepatol 2022; 76:959.

30. Kamath PS, Lacerda M, Ahlquist DA, et al. Gastric mucosal responses to intrahepatic portosystemic shunting in patients with cirrhosis. Gastroenterology 2000; 118:905.

Topic 2645 Version 27.0

GRAPHICS

Portal hypertensive gastropathy



(Panels A and B) Representative images of mild portal hypertensive gastropathy (PHG). Panel A shows a forward-viewing image of the proximal stomach. Panel B shows a retroflex view of the cardia with the classic form of PHG, the typical "mosaic-like pattern" without significant stigmata of bleeding or erythema or edema.

(Panels C and D) Representative images of severe PHG. Red lesions of variable diameter are evident. There is often irregular mucosa. Cherry spots may be confluent or not. Slow oozing may also be seen as in panel D, an up-close view in the proximal stomach.

Reproduced from: Urrunaga NH, Rockey DC. Portal Hypertensive Gastropathy and Colopathy. Clin Liver Dis 2014; 18:389. Illustration used with the permission of Elsevier Inc. All rights reserved.

Graphic 105554 Version 1.0

Disorders that cause upper GI bleeding in adults

Cause	Bleeding manifestations	Associated signs and symptoms	Associated conditions or risk factors
Ulcerative or erosive			
Duodenal and/or gastric ulcer	Hematemesis Melena Hematochezia (indicates brisk bleeding) Occult blood loss	Upper abdominal pain Pain associated with eating (worse when eating suggests gastric ulcer, improvement with eating suggests duodenal ulcer) Dyspepsia¶	Infections: ▪ *Helicobacter pylori* ▪ CMV ▪ HSV NSAIDs Stress ulcer (eg, in patients who are critically ill) Excess gastric acid production (ZES) Idiopathic
Esophagitis	Hematemesis Melena Occult blood loss	Dysphagia/odynophagia Retrosternal pain Food impaction	Gastroesophageal reflux disease Medications that may cause "pill esophagitis": ▪ Erythromycin ▪ Tetracycline ▪ Doxycycline ▪ Clindamycin ▪ Trimethoprim-sulfamethoxazole ▪ NSAIDs ▪ Oral bisphosphonates ▪ Potassium chloride ▪ Quinidine ▪ Iron supplements Infections: ▪ HSV ▪ CMV

			▪ *Candida albicans* ▪ HIV
Gastritis/gastropathy Duodenitis/duodenopathy	Occult blood loss Hematemesis Melena	Dyspepsia¶	Risk factors: ▪ *H. pylori* ▪ NSAIDs ▪ Excessive alcohol consumption ▪ Radiation injury ▪ Physiologic stress ▪ Weight loss surgery ▪ Bile reflux Risk factors for bleeding: ▪ Anticoagulant use
Complications of portal hypertension			

Esophagogastric varices	Hematemesis Melena Hematochezia (indicates brisk bleeding)	Stigmata of chronic liver disease[Δ], in particular, signs of portal hypertension (splenomegaly, ascites, thrombocytopenia)	Portal hypertension from: ▪ Cirrhosis ▪ Portal vein thrombosis ▪ Noncirrhotic portal hypertension

Ectopic varices	Hematemesis Melena Hematochezia (indicates brisk bleeding)	Stigmata of chronic liver disease[Δ], in particular, signs of portal hypertension (splenomegaly, ascites, thrombocytopenia)	Portal hypertension from: ▪ Cirrhosis ▪ Portal vein thrombosis ▪ Noncirrhotic portal hypertension
Portal hypertensive gastropathy	Occult blood loss Hematemesis Melena Hematochezia (indicates brisk bleeding)	Stigmata of chronic liver disease[Δ], in particular, signs of portal hypertension (splenomegaly, ascites, thrombocytopenia)	Portal hypertension from: ▪ Cirrhosis ▪ Portal vein thrombosis ▪ Noncirrhotic portal hypertension
Vascular lesions			
Angiodysplasia	Hematemesis Melena Hematochezia Occult blood loss May have brisk bleeding	Cutaneous angiodysplasia in patients with hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome)	End-stage kidney disease Aortic stenosis Left ventricular assist device Hereditary hemorrhagic telangiectasia von Willebrand disease

			Radiation therapy Idiopathic
Dieulafoy's lesion	Hematemesis Melena Hematochezia (indicates brisk bleeding; bleeding is often particularly brisk)		Etiology unknown Bleeding may be associated with NSAIDs, cardiovascular disease, hypertension, chronic kidney disease, diabetes, or alcohol abuse
Gastric antral vascular ectasia (GAVE)	Hematemesis Melena Hematochezia (indicates brisk bleeding) Occult blood loss	In patients with cirrhosis, there may be stigmata of chronic liver disease[Δ], in particular, signs of portal hypertension (splenomegaly, ascites, thrombocytopenia)	Idiopathic Cirrhosis with portal hypertension Kidney disease/transplantation Diabetes mellitus Systemic sclerosis (scleroderma) Bone marrow transplantation
Blue rubber bleb nevus syndrome (Bean syndrome)	Hematemesis Melena Hematochezia (indicates brisk bleeding) Occult blood loss	Venous malformations and hemangiomas of any organ, including: ▪ Skin ▪ Central nervous system ▪ Liver	

		▪ Muscles ▪ Lymphatics Intussusception	
Traumatic or iatrogenic			
Mallory-Weiss syndrome	Hematemesis following an increase in intra-abdominal pressure Melena Hematochezia (indicates brisk bleeding)	Epigastric pain Back pain	Vomiting/retching (often related to alcohol consumption) Straining at stool or lifting Coughing Seizures Blunt abdominal trauma Hiatal hernia may increase the risk of developing a tear
Foreign body ingestion	Hematemesis Melena Hematochezia (indicates brisk bleeding) Occult blood loss	Dysphagia Odynophagia Neck or abdominal pain Choking Hypersalivation Retrosternal fullness	Psychiatric disorders Altered mental status (toxin induced, dementia, etc) Loose dentures
Post-surgical anastomotic bleeding ("marginal ulcers")	Occult blood loss Hematemesis Melena Hematochezia (indicates brisk bleeding)	Epigastric pain Nausea	Billroth II surgery Gastric bypass surgery NSAID use *H. pylori* infection Smoking
Post-polypectomy/endoscopic resection/endoscopic sphincterotomy	Hematemesis Melena Hematochezia (indicates brisk bleeding)	Past history of instrumentation (may be as long as three weeks prior to presentation)	Large lesions
Cameron lesions	Occult blood loss Hematemesis		Hiatal hernia Reflux esophagitis

	Melena Hematochezia (indicates brisk bleeding)		
Aortoenteric fistula	Hematemesis Melena Hematochezia (indicates brisk bleeding) May have a "herald" bleed followed by massive bleeding	Back pain Fever Signs of sepsis Pulsatile abdominal mass Abdominal bruit	Infectious aortitis (syphilis, tuberculosis) Prosthetic aortic graft Atherosclerotic aortic aneurysm Penetrating ulcers Tumor invasion Trauma Radiation injury Foreign body perforation
Tumors			
Upper GI tumors	Hematemesis Melena Hematochezia (indicates brisk bleeding) Occult blood loss	Weight loss Anorexia Nausea/vomiting Early satiety Epigastric pain Dysphagia (for tumors in the esophagus or proximal stomach) Gastric outlet obstruction Palpable mass Paraneoplastic manifestations: ▪ Diffuse seborrheic keratoses ▪ Acanthosis nigricans ▪ Membranous nephropathy	Virtually any tumor type may bleed Benign tumors: ▪ Leiomyoma ▪ Lipoma ▪ Polyp (hyperplastic, adenomatous, hamartomatous, inflammatory) Malignant tumors: ▪ Adenocarcinoma ▪ GI stromal tumors ▪ Lymphoma ▪ Kaposi sarcoma ▪ Carcinoid ▪ Melanoma ▪ Metastatic tumors

		▪ Coagulopathy	
Miscellaneous			
Hemobilia	Hematemesis Melena Hematochezia (indicates brisk bleeding)	Biliary colic Jaundice (obstructive) Sepsis (biliary)	Past history of liver or biliary tract instrumentation and/or injury, including the following: ▪ Liver biopsy ▪ Cholecystectomy ▪ Endoscopic biliary biopsies or stenting ▪ TIPS placement ▪ Angioembolization ▪ Blunt or penetrating abdominal trauma ▪ Gallstones ▪ Cholecystitis ▪ Hepatic or bile duct tumors ▪ Intrahepatic stents ▪ Hepatic artery aneurysms ▪ Hepatic abscesses
Hemosuccus pancreaticus	Hematemesis Melena Hematochezia (indicates brisk bleeding)	Abdominal pain Past evidence of symptoms/signs of pancreatitis Imaging evidence of pancreatitis (current or in the past) Elevated amylase and lipase (current or in the past)	Chronic pancreatitis Pancreatic pseudocysts Pancreatic tumors Pancreatic pseudoaneurysm Therapeutic endoscopy of the pancreas or pancreatic duct: ▪ Pancreatic stone removal ▪ Pancreatic duct sphincterotomy ▪ Pseudocyst drainage

			▪ Pancreatic duct stenting

CMV: cytomegalovirus; HSV: herpes simplex virus; ZES: Zollinger-Ellison syndrome; NSAID: nonsteroidal anti-inflammatory drug; HIV: human immunodeficiency virus; GI: gastrointestinal; TIPS: transjugular intrahepatic portosystemic shunt; ERCP: endoscopic retrograde cholangiopancreatography.

* If active bleeding or large amounts of residual blood are present, the characteristic endoscopic findings may be obscured.

¶ Postprandial fullness, early satiety, epigastric pain, or burning.

Δ Evidence of chronic liver disease includes jaundice, splenomegaly, ascites, thrombocytopenia, palmar erythema, spider angiomata, gynecomastia, testicular atrophy, and Dupuytren's contracture.

Graphic 103148 Version 6.0

Management of portal hypertensive gastropathy[1,2]

Clinical scenario	Medications to decrease portal hypertension	Management of anemia/blood loss	Comments
Primary prophylaxis	Nonselective beta blocker* titrated to HR of 50 to 55 BPM or highest tolerated dose, eg: ▪ Propranolol 20 mg orally twice daily (maximum 160 mg twice daily) **or** ▪ Nadolol 40 mg orally once daily (maximum 160 mg daily) Carvedilol starting at 3.25 mg orally twice daily (maximum 25 mg twice daily) is an alternative to nonselective beta blockers	N/A	Data supporting primary prophylaxis are lacking. We provide prophylaxis for the following patients: ▪ Patients with severe portal hypertensive gastropathy and other risk factors for bleeding (eg, a coagulopathy or thrombocytopenia) ▪ Patients with portal hypertensive gastropathy and varices
Chronic bleeding	Nonselective beta blocker* titrated to HR of 50 to 55 BPM or highest tolerated dose, eg: ▪ Propranolol 20 mg orally twice daily (maximum 160 mg twice daily) **or** ▪ Nadolol 40 mg orally once daily (maximum 160 mg daily) Carvedilol starting at 3.25 mg orally twice daily (maximum 25 mg twice daily) is an alternative to nonselective beta blockers	Iron repletion¶ Blood transfusion if hemoglobin <7 to 8 g/dL$^{\Delta}$	The nonselective beta blocker should be continued indefinitely
Acute bleeding	Vasoactive medication, eg: ▪ Octreotide 100 mcg IV bolus followed by an infusion of 25 mcg/hour for 48 hours **or** ▪ Somatostatin$^{\diamond}$ 250 mcg IV bolus followed by an infusion of 250 mcg/hour for three days **or**	Resuscitation with IV fluids and blood transfusion to maintain hemoglobin between 7 and 8 g/dL in patients with cirrhosis, or ≥8 g/dL in	Patients with cirrhosis should also receive antibiotic prophylaxis for SBP for seven days$^{¥}$, eg: ▪ Ceftriaxone 1 gram IV daily ▪ Ciprofloxacin 500 mg orally twice daily **or**

	▪ Terlipressin[§] 2 mg IV every four hours initially, then titrated down to 1 mg IV every four hours for up to five days	patients without cirrhosis	▪ Ciprofloxacin 400 mg IV twice daily **or** ▪ Trimethoprim-sulfamethoxazole 1 DS tablet orally twice daily **or** ▪ Norfloxacin[◇] 400 mg orally twice daily Once the acute bleeding episode is resolved, patients should be started on secondary prophylaxis with a nonselective beta blocker
Refractory bleeding (chronic or acute)	Shunt therapy: ▪ TIPS ▪ Surgical shunt Liver transplantation Endoscopic treatment/APC if a focal lesion is present	As above	Patients with chronic bleeding who respond appropriately to iron repletion or transfusion may be managed expectantly
Secondary prophylaxis	Nonselective beta blocker* titrated to HR of 50 to 55 BPM or highest tolerated dose, eg: ▪ Propranolol 20 mg orally twice daily (maximum 160 mg twice daily) **or** ▪ Nadolol 40 mg orally daily (maximum 160 mg daily) Carvedilol starting at 3.25 mg orally twice daily (maximum 25 mg twice daily) is an alternative to nonselective beta blockers	N/A	The nonselective beta blocker should be continued indefinitely

HR: heart rate; BPM: beats per minute; N/A: not applicable; IV: intravenous; SBP: spontaneous bacterial peritonitis; DS: double strength (ie, trimethoprim 160 mg and sulfamethoxazole 800 mg per tablet); TIPS: transjugular intrahepatic portosystemic shunt; APC: argon plasma coagulation.

Antibiotic doses shown are for use in patients with normal renal function. Some agents require dose adjustment in patients with renal impairment.

* Provided there are no contraindications to beta blocker therapy. Patients who cannot take or do not tolerate nonselective beta blockers or carvedilol are treated like those with refractory bleeding.

¶ Refer to UpToDate topics on treatment of iron deficiency for details on methods for iron repletion.

Δ The decision to transfuse blood is complicated and depends on multiple different variables, including the presence of underlying unstable cardiac disease, the acuity and volume of bleeding, the presence of cirrhosis, and other variables. In those with cirrhosis, the target hemoglobin is

typically 7 to 8 g/dL. Refer to UpToDate topics on the management of upper gastrointestinal bleeding for details.

◇ Not available in the United States.

§ In the United States, gastrointestinal bleeding is an off-label indication.

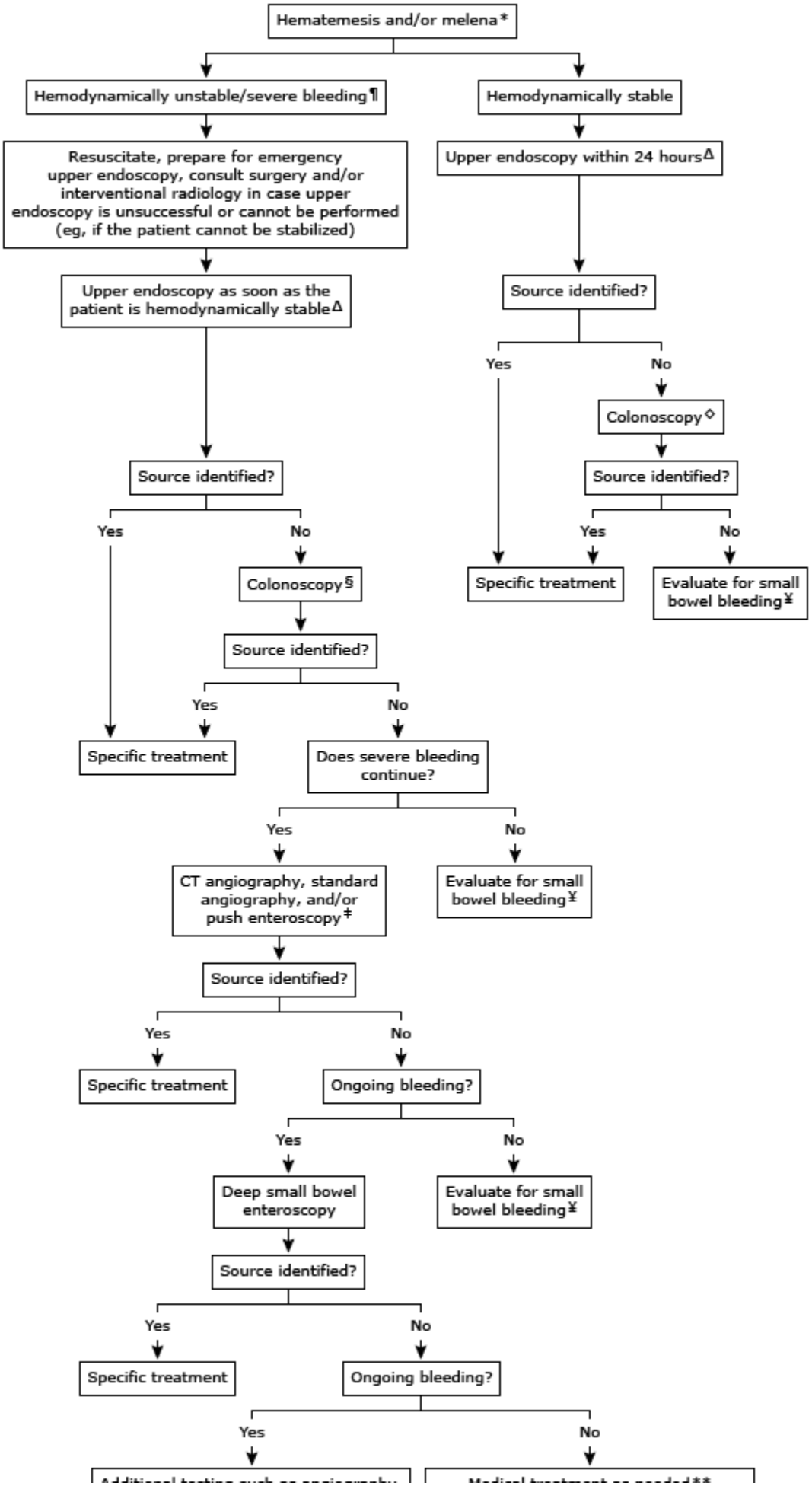
¥ Refer to UpToDate topics on the management of variceal hemorrhage for detailed discussions of antibiotic selection and administration.

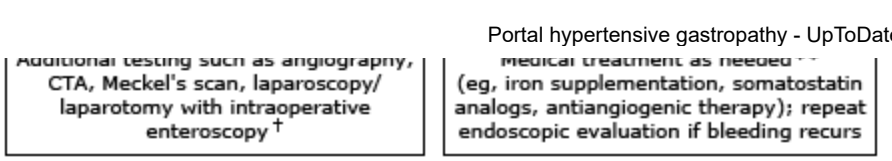
References:

1. *Urrunaga NH, Rockey DC. Portal hypertensive gastropathy and colopathy. Clin Liver Dis 2014; 18:389.*
2. *Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. Hepatology 2017; 65:310.*

Graphic 103137 Version 4.0

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 within 24 hours△
Upper endoscopy as soon as the patient is hemodynamically stable△
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



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 4.0

Contributor Disclosures

Don C Rockey, MD Grant/Research/Clinical Trial Support: Axella Therapeutics [HE trial]; AZ [PHTN study]; BI [PHTN study]; Durect [Alcoholic hepatitis trial]; Galectin Therapeutics [NASH trial]; Genfit [NASH trial]; Gilead Sciences [PBC trial]; Helio [Chronic disease recruitment]; Intercept Pharmaceuticals [NASH trial]; Inventiva [NASH trial]; Novo Nordisk [NASH trial]; Ocelot [ACLF trial]; Pfizer [NASH trial]; Salix [HE]; Sequana Medical [Alfapump]; Viking Therapeutics [NASH trial]. All of the relevant financial relationships listed have been mitigated. **Mark Feldman, MD, MACP, AGAF, FACG** No relevant financial relationship(s) with ineligible companies to disclose. **Kristen M Robson, MD, MBA, FACG** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy

→