# The Acute Upper Gastrointestinal Bleed

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**KEYWORDS**

• Upper gastrointestinal bleed • Peptic ulcer disease • Variceal bleeding • Endoscopy • Operative management

**KEY POINTS**

- Although only 2% to 8% of upper gastrointestinal (GI) bleeds require operative intervention, early surgeon involvement remains imperative.
- Initial evaluation and treatment of upper GI bleeding requires a systematic approach starting with airway, breathing, and circulation.
- Peptic ulcer disease remains the most common cause of upper GI bleeds despite the increased use of proton pump inhibitors and understanding of *Helicobacter pylori*.
- Endoscopy is the main diagnostic and therapeutic tool for most upper GI bleeds.
- Bleeding varices due to portal hypertension can fail medical and endoscopic treatment in 10% to 15% of cases in which transjugular intrahepatic portosystemic shunt may be required. Consideration of facility capabilities and need for transfer should be considered early.

## INTRODUCTION

Upper gastrointestinal bleeding (UGIB), defined as intraluminal hemorrhage proximal to the ligament of Treitz, can range from mild and asymptomatic to massive life-threatening hemorrhage.[1–3] For the purposes of this article, the authors define an acute UGIB to be one that results in new acute symptoms and is, therefore, potentially life-threatening. The incidence of UGIB is approximately 100 cases per 100,000 population per year.[4] Although the incidence of hospitalization for acute UGIB is decreasing (4% decrease from 1998–2006),[5] it remains a common problem encountered by the acute-care and general surgeon.

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The surgeon continues to play a key role in the outcome of patients with UGIBs. Even though only approximately 2.5% to 5% of UGIBs ultimately require operative intervention,[1,2] early surgeon consultation remains critical for a variety of reasons. In many practice settings, the surgeon represents the primary endoscopist, but even when this role is assumed by gastroenterology, early surgeon involvement allows for aid in appropriate resuscitation of unstable patients, streamlining of preoperative assessment, early establishment of the goals of the patient and family, and judgment regarding the limits of nonoperative management.

## PRESENTATION

UGIB typically presents with hematemesis or melena, but brisk UGIB can present with hematochezia. The redder the blood, the more rapid the bleed. Approximately 80% of all GI bleeds and 11% to 15% of cases of hematochezia are due to an upper source[6,7]; therefore, it is important to include upper sources in the differential diagnosis for all GI bleeds. Conversely, melena can occur from lower GI bleed that originate in the small bowel or right colon especially when there is slow transit time. Hematemesis almost always represents an upper source of bleeding, although nasal and oropharyngeal sources must also be kept in mind.

## TRIAGE

Effective initial evaluation and treatment of an UGIB requires a systematic approach. One organized approach is to divide priorities into a primary survey (airway, breathing, and circulation) and a secondary survey (completion of history and physical examination). The purpose of this division is to emphasize that lack of definitive diagnosis or detailed history and physical examination (H&P) should never impede initiation of airway protection and treatment of shock. Baradarian and colleagues[8] demonstrated that early intensive resuscitation with correction of hemodynamics, hemoglobin, and coagulopathy can reduce mortality in patients with UGIB. In the massively bleeding patient, it may not be possible to move beyond the primary survey until definitive source control of bleeding has been obtained. However, in most cases, the bleeding stops spontaneously[9] or the patient is stable enough to allow further details of the H&P to be obtained. Consideration must be given during the primary survey as to whether the health care facility is capable of providing definitive bleeding source control, and arrangements for transfer should be initiated if the facility is unable to care for the patient.

On the opposite extreme, if the patient is found to be stable on the primary survey and the secondary survey does not reveal comorbidities that increase the risk for complications, the patient can potentially be managed as an outpatient. Several clinical decision tools have been created to assist with risk stratification and triage. One is the Glascow-Blatchford Score (GBS) (**Table 1**). This scale is based on clinical parameters that are available before endoscopy. The GBS has been validated and can be used to safely manage patients with a GBS of either 0 or 1 as an outpatient.[10]

## INITIAL MANAGEMENT (THE PRIMARY SURVEY)

The primary survey is outlined in **Box 1**. The following key points are emphasized:

1. *Airway and breathing are always the initial priority*.[11] Assessment should be performed quickly, and if the airway is compromised a definitive airway is required. Ongoing reassessment of the airway must be performed. Mental status changes due to shock may lead to patient inability to protect their own airway. Pragmatic

**Table 1**
**Glasgow-Blatchford score**

| Admission Risk Marker | Score Component Value |
|---|---|
| Blood urea (mmol/L) | |
| ≥6.5 <8.0 | 2 |
| ≥8.0 <10.0 | 3 |
| ≥10.0 <25 | 4 |
| ≥25 | 6 |
| Hemoglobin (g/dL) for men | |
| ≥12 <13 | 1 |
| ≥10 <12 | 3 |
| <10 | 6 |
| Hemoglobin (g/dL) for women | |
| ≥10 <12 | 1 |
| <10 | 6 |
| Systolic blood pressure (mm Hg) | |
| 100–109 | 1 |
| 90–99 | 2 |
| <90 | 3 |
| Other markers | |
| Pulse ≥100 (per min) | 1 |
| Presentation with melena | 1 |
| Presentation with syncope | 2 |
| Hepatic disease | 2 |
| Cardiac failure | 2 |

*From* Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper gastrointestinal haemorrhage. Lancet 2000;356:1319; with permission.

**Box 1**
**The primary survey priorities**

1. Airway
2. Breathing
3. Circulation
   a. Access
   b. Blood volume restoration
   c. CBC, CMP, cross-match, and coagulation laboratory studies
   d. Drug history of anticoagulants/antiplatelets
   e. Source control and localization
      i. Preendoscopy initiation of PPI has a low risk to benefit ratio
      ii. Evaluate for portal hypertension/varices; consider need for transfer
      iii. Develop plan for endoscopy and treatment

*Abbreviations:* CBC, complete blood count; CMP, comprehensive metabolic panel; PPI, proton pump inhibitor.

consideration must be given to whether airway protection is required before the initiation of procedures such as endoscopy, but there is a lack of evidence that prophylactic intubation before endoscopy decreases complications.[12]

2. *Circulation is an issue in all acute GI bleeds. The degree of the problem must be quickly assessed.* Key data for this rapid assessment include presence of tachycardia, hypotension, anxiety/mental status changes, cool/clammy extremities, and recent syncope. Checking for orthopnea is a simple way to rapidly assess for hypovolemia when other clinical signs of shock are not present. However, it must be remembered that a patient can lose a significant blood volume without any clinical signs of shock.
   a. *Access—Establishing vascular access is the initial priority for treating the circulation problem.* Placement of at least 2 large-bore (18 or smaller gauge) peripheral intravenous devices is preferred because wide and short catheters offer the lowest resistance to flow for large volume resuscitation (flow is proportional to the radius to the fourth power and inversely proportional to length).
   b. *Blood volume restoration.* Hypotensive patients with active bleeding should be resuscitated with a 1:1:1 (packed red blood cell:fresh frozen plasma:platelet) transfusion strategy as translated from recent guidelines for treatment of traumatic bleeding.[13] Crystalloid may be used while blood products are being obtained, but the massively bleeding, hemodynamically unstable patient requires blood regardless of hemoglobin level. Uncross-matched blood may be used while waiting for completion of the cross-match. Foley catheter placement may be considered for hourly monitoring and guidance of resuscitation in an unstable patient. Finally, the principle of permissive hypotension should be followed with avoidance of overresuscitation beyond what is required to maintain perfusion and consciousness. Vasopressors should be avoided, other than for variceal bleeding. When the patient is hemodynamically stable, a restrictive transfusion strategy with a transfusion trigger of less than 7 g/dL is recommended.[14] In addition, recent evidence has not been able to demonstrate superiority of tranexamic acid in the treatment of UGIB when compared with current standard using proton pump inhibitors (PPIs) and endoscopic therapy.[15]
   c. Complete blood count, comprehensive metabolic panel, cross-match, and coagulation laboratory studies should be obtained. It should be emphasized that hemoglobin can remain normal in the setting of massive acute bleeding; therefore a normal value does not rule out massive hemorrhage. Assessment of total bilirubin and international normalized ratio are essential to screen for liver disease. In addition, coagulation studies provide information regarding potential coagulopathy associated with massive hemorrhage or due to medications. When available, thromboelastography can be useful for guiding product resuscitation in massive hemorrhage. All laboratory values should be trended based on the acuity of bleeding. Cross-match should be sent and units ordered to stay ahead of transfusion.
   d. *Drug history of any anticoagulant or antiplatelet medications is essential in the primary survey*. Depending on the severity of the bleeding and the indication for taking these medications, the patient may require emergent reversal. There are a growing number of anticoagulant and antiplatelet agents on the market, and specific reversal strategy is beyond the scope of this article. It should be remembered that GI bleeding in patients taking anticoagulant medications is still most commonly due to GI disease and should not be ascribed to the anticoagulant alone.[16] All nonsteroidal antiinflammatory drugs (NSAIDs) and selective

serotonin reuptake inhibitors (SSRIs) should be held due to their known association with increased risk of GI bleeding.[17]

e. *Source control. A plan for localization and source control should be developed during the primary survey.* The best way to help any bleeding patient is to stop the bleed. External soft-tissue hemorrhage bleeding can usually be stopped by applying pressure, but with bleeding in the GI tract, it is necessary to both localize the bleed and determine a method to stop it. Because this takes time (such as setting up endoscopy), the prior steps of initial management are listed earlier, but it must always be remembered that the primary goal is to stop the bleed. Therefore, a plan for localization and source control must be part of the primary survey.
   i. Because of the low risk to benefit ratio, the authors recommend starting a PPI during the early stage of workup because peptic ulcer disease represents the most common cause of UGIB.[18] Lau and colleagues[19] demonstrated that high-dose intravenous PPI in patients admitted for UGIB reduced the stigmata of recent hemorrhage and the need for intervention with endoscopy performed the following day. However, preendoscopy initiation did not change patient outcomes of rebleeding, need for surgery, or death.[19] Recommended intravenous dosing is an 80 mg bolus followed by an 8 mg/h infusion.
   ii. Nasogastric tube placement can be considered but is not required for diagnosis, prognosis, visualization, or therapeutic effect.[14] Intuitively, ongoing aspiration of bright red blood portends a more severe bleed, but there is no proven benefit for it. A Canadian study demonstrated that in retrospective review of the aspirate character did stratify risk, but there was low diagnostic accuracy. In addition, 13% of patients with known UGIB could have a clear or bile-stained aspirate.[20]
   iii. If portal hypertension/varices is known or suspected, the patient should be treated at a facility with an endoscopist experienced in banding. If this is not available or banding is not successful, the patient may require transjugular intrahepatic portosystemic shunt (TIPS) and should be transferred to a capable center. A Sengstaken–Blakemore tube or Minnesota tube can be a lifesaving temporizing device in unstable patients with bleeding varices requiring transfer. The patient should also have octreotide and antibiotics initiated before transfer.
   iv. The primary method for definitively localizing and treating most UGIB is endoscopy. Most of the UGIBs can be controlled with endoscopy alone. Urgent endoscopy is required for hemodynamically unstable patients, but studies have confirmed that for patients with stabilized acute bleeds there is no benefit from endoscopy at 6 to 12 hours compared with endoscopy within 24 hours.[21,22] Endoscopy may be performed in the intensive care unit or operating room setting (see specific causes of GI bleeds in the later discussion for further details of endoscopic treatment). If endoscopy is not available at the surgeon's institution within the necessary timeframe, the patient requires transfer to a capable facility. Plans for angiography or surgical intervention should be considered based on the cause of the bleed, patient comorbidities, and patient status.

## COMPLETION OF THE HISTORY AND PHYSICAL EXAMINATION (SECONDARY SURVEY)

Once the priorities of the primary survey are initiated or completed, there is then time to gather more information. The H&P can provide information to narrow the differential

diagnosis, tailor appropriate management, and conduct risk stratification of the patient based on probable cause and medical comorbidities.

Specific causes of UGIB may be suggested by the patient's symptoms:[23]

- Peptic ulcer: epigastric or right upper quadrant pain
- Esophageal ulcer: odynophagia, gastroesophageal reflux, dysphagia
- Mallory-Weiss tear: emesis, retching, or coughing before hematemesis
- Variceal hemorrhage or portal hypertensive gastropathy: jaundice, weakness, fatigue, anorexia, abdominal distention
- Malignancy: dysphagia, early satiety, involuntary weight loss, cachexia

History of recent trauma should be ruled out. A complete list of the medical comorbidities should be obtained. Knowledge of previous surgeries can help narrow the differential diagnosis and is important before any operative intervention. For example, history of aortic aneurysm repair provides a clue to possible aortoenteric fistula, and a history of GI anastomosis raises the possibility of a marginal ulcer. A complete medication list should again be verified for use of any anticoagulants, NSAIDs, salicylates, or SSRIs that are common in the elderly.[24]

## DEFINITIVE TREATMENT OF SPECIFIC CAUSES

### *Nonvariceal Bleeding*

Nonvariceal bleeding accounts for approximately 80% of all UGIBs.[25]

#### *Peptic Ulcer Disease*

Peptic ulcer disease is the most common cause of UGIB, representing nearly 40% of all cases.[26] The vast majority are related to *Helicobacter pylori* and NSAID use. The incidence has declined in the era of PPI use and the understanding of *H pylori*.[27]

Upper endoscopy is the diagnostic and therapeutic study of choice. Although most of the bleeds stop on their own, approximately 25% require an intervention at the time of endoscopy.[27] Endoscopic findings can be classified according to the Forrest classification[28] for guidance regarding need for intervention and risk of rebleeding (**Table 2**). Endoscopic treatment modalities include injection of epinephrine or sclerosants, bipolar electrocoagulation, band ligation, heater probe coagulation, constant probe pressure tamponade, argon plasma coagulator, laser photocoagulation, and hemoclips. Evidence has revealed improved rates of control when treatment modalities are used in combination than in isolation (eg, epinephrine injection followed by clipping). Injection of epinephrine is performed in 4 quadrants around the lesion, starting most distally in order to prevent obscuring the view for subsequent injections. Biopsies of all gastric ulcers should be performed due to their relatively high rate of

**Table 2**
**The Forrest classification**

| Class | Description | Endoscopic Intervention[14] | Rebleeding Rate[42] |
|---|---|---|---|
| 1A | Active spurting | Yes | 55% |
| 1B | Active oozing | Yes | 55% |
| 2A | Nonbleeding visible vessel | Yes | 43% |
| 2B | Adherent clot | Consider | 22% |
| 2C | Flat pigmented spot | No | 10% |
| 3 | Clean ulcer base | No | 5% |

malignancy (6%).[29] When duodenal ulcers are encountered, control of the bleeding should be performed, followed by biopsy not of the ulcer but of the antrum obtained for evidence of *H pylori*. *H pylori* testing may be falsely negative in the setting of an acute bleed, so repeat testing should be obtained later if the test is negative for *H pylori* followed by confirmation of eradication.

Risk of recurrent bleeding after endoscopic control is approximately 15% to 20%.[30] The risk of rebleeding can be predicted based on the initial endoscopic appearance of the ulcer (Forrest classification, see **Table 2**) When rebleeding does recur, repeat endoscopy should be attempted because long-term bleeding control can be obtained in approximately 75% of cases without increased risk of death and with fewer complications than those treated with surgery for first recurrent bleed.[30]

Operative intervention should be considered based on initial or recurrent magnitude of bleeding, ability of patient to withstand continued bleeding, and probability of recurrent bleeding. A Canadian review from 2004 to 2010 revealed a need for surgical intervention in 4.3% of cases of hospitalized UGIB caused by peptic ulcer disease.[31–33] In general, older patients with less physiologic reserve to withstand ongoing bleeding should undergo earlier operative intervention. Ulcers that are high-risk based on the Forrest classification, are larger than 2 cm, or are located in the stomach or posterior duodenum should all be considered for early surgical intervention.[34,35] The choice of operation depends on the location of the ulcer. Duodenal ulcers most commonly occur in the first portion (bulb) and erode posteriorly into the gastroduodenal artery. Approach for these ulcers consists of a longitudinal duodenotomy, oversewing of ulcer with triple stitch including the medially located transverse pancreatic artery, and closure transversely with Heineke-Mikulicz pyloroplasty. Historically, vagotomy $\pm$ antrectomy was also performed, but in the era of PPIs and understanding of H pylori, the utility of this acid-reducing procedure has greatly diminished. Gastric ulcers in favorable locations should be resected with primary closure of the gastrotomy site. Unfavorably located ulcers may have hemorrhage controlled with oversewing followed by biopsy to rule out malignancy.

The role of angiographic embolization for peptic ulcer disease is less well defined. Many patients now undergo an attempt at angiography and embolization before surgery, particularly in patients at high risk for surgery. Angiography is minimally invasive, it often allows precise localization of bleeding, and it enables the use of therapeutic options, which include embolization or vasopressin infusion. A hemorrhage rate of 0.5 to 1.0 mL/min is required before it can be visualized with angiography. Initial success rates for patients with acute peptic ulcer bleeding are between 52% and 98%, with recurrent bleeding rates of 10% to 20%.[36]

### *Mallory-Weiss Tears*

Mallory-Weiss tear is a laceration in the cardia caused by forceful emesis. These are commonly seen in alcoholic patients who retch after belching. Tears are usually single and longitudinal. The lesions have a high rate of spontaneous cessation of bleeding, and intervention is only required in only 10% of cases. It spontaneously resolves in 50% to 80% of the patients by the time endoscopy is performed. Rebleeding is rare (7%) and tears that are not actively bleeding can be managed with acid suppression and antiemetics alone. Endoscopic therapy is indicated for treatment of actively bleeding tears and should be treated with a combination of thermal coagulation, hemoclips, and/or endoscopic band ligation, with or without epinephrine injection. Patients who have failed endoscopic therapy should undergo angiography with transarterial embolization. Surgery with oversewing of the bleeding vessel is reserved for those who fail angiographic therapy.

### *Dieulafoy Lesions*

Dieulafoy vascular malformations consist of an unusually dilated submucosal vessel with erosion of a small portion of the overlying mucosa. The lesions typically occur along the lesser curve of the stomach within 6 cm of the gastroesophageal junction.[37] Because of the small size of the mucosal defect (2–5 mm) they can be difficult to identify.[38] Given the large size of the underlying artery, the bleeding can be massive. Usually they can be controlled endoscopically. If this fails, angiography and embolization is an excellent option. If both options are unsuccessful, which is rare, surgical intervention is required. An anterior gastrotomy should be performed with oversewing of the lesion. If the lesion cannot be identified, sometimes partial gastrectomy is required.

### *Aortoenteric Fistula*

Although primary aortoenteric fistulas can occur, primarily these are the result of prosthetic graft to duodenum fistula. Patients often present with an initial herald bleed before massive hemorrhage. Upper endoscopy to the ligament of Treitz is the diagnostic modality of choice. Treatment options for this challenging problem includes extra-anatomic bypass with resection of the infected graft and closure of the duodenal defect. Perioperative mortality rates are high.

### *Hemobilia and Hemosuccus Pancreaticus*

Hemobilia is bleeding into the biliary tract. Hemosuccus pancreaticus is bleeding in to the pancreatic ducts. These are rare causes of UGIB and are usually related to recent instrumentation or trauma. The treatment of choice for both entities is angiographic embolization.[39]

## VARICEAL BLEEDING

### *Gastroesophageal Varices*

For esophageal variceal bleeding, treatment consists of controlling the acute hemorrhage and reducing the risk of rebleeding. The 6-week mortality rate following the first episode of variceal bleeding is almost 20%.[40] Acute treatment consists of judicious fluid resuscitation, octreotide or vasopressin along with attempted endoscopic banding. When banding fails, TIPS can be lifesaving. This is required in approximately 10% of cases of variceal bleeding.[3] TIPS is associated with 50% rate of hepatic encephalopathy within 1 year.[41] Antibiotics are recommended for all acutely bleeding varices due to a high rate of underlying aggravating infection that led to the bleeding; there is evidence that a 7-day course of a broad spectrum antibiotic will lower the rebleeding rate.[40] A nonselective beta blocker such as propranolol should also be initiated for long-term prevention of rebleeding. Endoscopic banding should also be repeated every 10 to 14 days until all varices have been eradicated.

### *Portal Hypertensive Gastropathy*

Bleeding from portal hypertensive gastropathy is not amenable to endoscopic therapy due to its diffuse nature. It requires pharmacologic therapy to reduce portal venous pressure and if this fails, then TIPS.

### *Gastric Varices*

Gastric varices are isolated to the stomach and are caused by left-sided (sinistral) hypertension that usually results from splenic vein thrombosis in the setting of pancreatitis. The treatment of choice is splenectomy.

## SUMMARY

UGIB requires a systematic approach to evaluation and treatment, similar to the management of a trauma patient. Surgeon involvement in UGIBs remains integral despite the rare need for operative management. Endoscopy is the primary tool for diagnosis and treatment.

## REFERENCES

1. Clarke MG, Bunting D, Smart NJ, et al. The surgical management of acute upper gastrointestinal bleeding: a 12-year experience. Int J Surg 2010;8(5):377–80.
2. Botianu A, Matei D, Tantau M, et al. Mortality and need of surgical treatment in acute upper gastrointestinal bleeding: a one year study in a tertiary center with a 24 hours/day-7 days/week endoscopy call. Has anything changed? Chirurgia (Bucur) 2013;108(3):312–8.
3. Garcia-Pagan JC, Caca K, Bureau C, et al. Early use of TIPS in patients with cirrhosis and variceal bleeding. N Engl J Med 2010;362(25):2370–9.
4. Fallah MA, Prakash C, Edmundowicz S. Acute gastrointestinal bleeding. Med Clin North Am 2000;84(5):1183–208.
5. Zhao Y, Encinosa W. Hospitalizations for gastrointestinal bleeding in 1998 and 2006: statistical brief #65. Healthcare Cost and Utilization Project (HCUP) Statistical Briefs [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2006.
6. Barnert J, Messmann H. Management of lower gastrointestinal tract bleeding. Best Pract Res Clin Gastroenterol 2008;22(2):295–312.
7. Laine L, Shah A. Randomized trial of urgent vs. elective colonoscopy in patients hospitalized with lower GI bleeding. Am J Gastroenterol 2010;105(12):2636–41 [quiz: 42].
8. Baradarian R, Ramdhaney S, Chapalamadugu R, et al. Early intensive resuscitation of patients with upper gastrointestinal bleeding decreases mortality. Am J Gastroenterol 2004;99(4):619–22.
9. Wee E. Management of nonvariceal upper gastrointestinal bleeding. J Postgrad Med 2011;57(2):161–7.
10. Stanley AJ, Ashley D, Dalton HR, et al. Outpatient management of patients with low-risk upper-gastrointestinal haemorrhage: multicentre validation and prospective evaluation. Lancet 2009;373(9657):42–7.
11. Meltzer AC, Klein JC. Upper gastrointestinal bleeding: patient presentation, risk stratification, and early management. Gastroenterol Clin North Am 2014;43(4):665–75.
12. Rehman A, Iscimen R, Yilmaz M, et al. Prophylactic endotracheal intubation in critically ill patients undergoing endoscopy for upper GI hemorrhage. Gastrointest Endosc 2009;69(7):e55–9.
13. Baraniuk S, Tilley BC, del Junco DJ, et al. Pragmatic randomized optimal platelet and plasma ratios (PROPPR) Trial: design, rationale and implementation. Injury 2014;45(9):1287–95.
14. Laine L, Jensen DM. Management of patients with ulcer bleeding. Am J Gastroenterol 2012;107(3):345–60 [quiz: 61].
15. Bennett C, Klingenberg SL, Langholz E, et al. Tranexamic acid for upper gastrointestinal bleeding. Cochrane Database Syst Rev 2014;(11):CD006640.
16. Rubin TA, Murdoch M, Nelson DB. Acute GI bleeding in the setting of supratherapeutic international normalized ratio in patients taking warfarin: endoscopic diagnosis, clinical management, and outcomes. Gastrointest Endosc 2003;58(3):369–73.

17. Paton C, Ferrier IN. SSRIs and gastrointestinal bleeding. BMJ 2005;331(7516):529–30.
18. Barkun AN, Bardou M, Kuipers EJ, et al. International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med 2010;152(2):101–13.
19. Lau JY, Leung WK, Wu JC, et al. Omeprazole before endoscopy in patients with gastrointestinal bleeding. N Engl J Med 2007;356(16):1631–40.
20. Aljebreen AM, Fallone CA, Barkun AN. Nasogastric aspirate predicts high-risk endoscopic lesions in patients with acute upper-GI bleeding. Gastrointest Endosc 2004;59(2):172–8.
21. Tsoi KK, Ma TK, Sung JJ. Endoscopy for upper gastrointestinal bleeding: how urgent is it? Nat Rev Gastroenterol Hepatol 2009;6(8):463–9.
22. Sarin N, Monga N, Adams PC. Time to endoscopy and outcomes in upper gastrointestinal bleeding. Can J Gastroenterol 2009;23(7):489–93.
23. Cappell MS, Friedel D. Initial management of acute upper gastrointestinal bleeding: from initial evaluation up to gastrointestinal endoscopy. Med Clin North Am 2008;92(3):491–509, xi.
24. Tata LJ, Fortun PJ, Hubbard RB, et al. Does concurrent prescription of selective serotonin reuptake inhibitors and non-steroidal anti-inflammatory drugs substantially increase the risk of upper gastrointestinal bleeding? Aliment Pharmacol Ther 2005;22(3):175–81.
25. Enestvedt BK, Gralnek IM, Mattek N, et al. An evaluation of endoscopic indications and findings related to nonvariceal upper-GI hemorrhage in a large multicenter consortium. Gastrointest Endosc 2008;67(3):422–9.
26. Rockey DC. Gastrointestinal bleeding. Gastroenterol Clin North Am 2005;34(4):581–8.
27. Wang YR, Richter JE, Dempsey DT. Trends and outcomes of hospitalizations for peptic ulcer disease in the United States, 1993 to 2006. Ann Surg 2010;251(1):51–8.
28. Forrest JA, Finlayson ND, Shearman DJ. Endoscopy in gastrointestinal bleeding. Lancet 1974;2(7877):394–7.
29. Selinger CP, Cochrane R, Thanaraj S, et al. Gastric ulcers: malignancy yield and risk stratification for follow-up endoscopy. Endosc Int Open 2016;4(6):E709–14.
30. Lau JY, Sung JJ, Lam YH, et al. Endoscopic retreatment compared with surgery in patients with recurrent bleeding after initial endoscopic control of bleeding ulcers. N Engl J Med 1999;340(10):751–6.
31. Quan S, Frolkis A, Milne K, et al. Upper-gastrointestinal bleeding secondary to peptic ulcer disease: incidence and outcomes. World J Gastroenterol 2014;20(46):17568–77.
32. Sung JJ, Tsoi KK, Ma TK, et al. Causes of mortality in patients with peptic ulcer bleeding: a prospective cohort study of 10,428 cases. Am J Gastroenterol 2010;105(1):84–9.
33. Straube S, Tramer MR, Moore RA, et al. Mortality with upper gastrointestinal bleeding and perforation: effects of time and NSAID use. BMC Gastroenterol 2009;9:41.
34. Guglielmi A, Ruzzenente A, Sandri M, et al. Risk assessment and prediction of rebleeding in bleeding gastroduodenal ulcer. Endoscopy 2002;34(10):778–86.
35. Chung IK, Kim EJ, Lee MS, et al. Endoscopic factors predisposing to rebleeding following endoscopic hemostasis in bleeding peptic ulcers. Endoscopy 2001;33(11):969–75.
36. Gralnek IM. Will surgery be a thing of the past in peptic ulcer bleeding? Gastrointest Endosc 2011;73(5):909–10.

37. Lara LF, Sreenarasimhaiah J, Tang SJ, et al. Dieulafoy lesions of the GI tract: localization and therapeutic outcomes. Dig Dis Sci 2010;55(12):3436–41.
38. Nguyen DC, Jackson CS. The dieulafoy's lesion: an update on evaluation, diagnosis, and management. J Clin Gastroenterol 2015;49(7):541–9.
39. Millward SF. ACR Appropriateness Criteria on treatment of acute nonvariceal gastrointestinal tract bleeding. J Am Coll Radiol 2008;5(4):550–4.
40. Herrera JL. Management of acute variceal bleeding. Clin Liver Dis 2014;18(2):347–57.
41. Riggio O, Angeloni S, Salvatori FM, et al. Incidence, natural history, and risk factors of hepatic encephalopathy after transjugular intrahepatic portosystemic shunt with polytetrafluoroethylene-covered stent grafts. Am J Gastroenterol 2008;103(11):2738–46.
42. Laine L, Peterson WL. Bleeding peptic ulcer. N Engl J Med 1994;331(11):717–27.