Gastrointestinal Hemorrhage

16

Michael A. Samotowka

Introduction

There are over half a million patients hospitalized annually for gastrointestinal hemorrhage (GIH) in the USA [1]. The overall inpatient mortality rate in the USA is approximately 3 %. The majority of bleeds (~75 %) arise from the upper gastrointestinal tract, defined as proximal to the ligament of Treitz. GIH is most common in the elderly, and this population is prone to having a higher incidence of associated medical comorbidities. In the GIH patient population, 80 % of the mortality is attributable to their associated comorbidities rather than as a direct consequence of their GI hemorrhage. As the elderly population of America continues to expand, it can be expected that the incidence of GI hemorrhage patients will also increase in a proportionate fashion.

The presentation of acute upper GIH usually relates most commonly to the route of exodus of blood from the GI tract rather than hemodynamic abnormalities. In contrast, chronic UGIH may present with anemia, weakness, or dyspnea [2]. Active hematemesis is generally indicative of an upper and not lower GI tract source. Melena suggests a minimum blood loss of at least 200 ml and its presence is indicative of blood being present in the digestive tract for at least 12 h to allow RBC lysis and hemoglobin metabolism. Hematochezia may arise from either an upper or lower GI tract source and implies that blood has been present in the GI tract for less than 12 h.

Historically, bleeding that originates from the small bowel was included in the category of lower GIH, but today it is viewed as a separate entity and will be treated as such in this chapter. Bleeding from the small bowel may be occult or sporadic and thus very challenging to diagnose. It most often presents with chronic anemia or melena. Obscure GI hemorrhage refers to the patient population with persistent or recurrent GIH where the initial endoscopic evaluation did not identify the etiology of the bleed. This is estimated to be the case in about 5 % of patients with GIH [3]. Small bowel pathology accounts for up to 75 % of these patients. With the advent of capsule endoscopy and push enteroscopy as well as double-balloon endoscopy, many previously unidentifiable lesions are now readily localizable.

Lower GI (LGI) tract hemorrhage includes hemorrhage from the colon and rectum and typically presents with melena or hematochezia. Diverticular disease is the most common cause of lower gastrointestinal hemorrhage (LGIH); the incidence of this entity increases with advancing age. While severe hemorrhage progressing to shock does occur in UGIH, it is much less common in those with LGIH.

Upper Gastrointestinal Hemorrhage

Upper GI tract hemorrhage (UGIH) occurs at least fivefold more commonly than LGIH. Bleeding in the upper GI tract is separated into two distinct categories, those bleeds that are associated with varices (variceal) and those that are not associated with varices (non-variceal). Common causes of non-variceal UGIH are:

1. Peptic ulcer disease (PUD)
2. Esophagitis
3. Stress-related mucosal disease (SRMD)
4. Zollinger-Ellison syndrome
5. Vascular lesions
6. Mallory-Weiss tear
7. Tumors
8. Injury
9. Postsurgical
10. Other

M.A. Samotowka, MD, FCCM
Trauma/Surgical Critical Care, Cleveland Clinic,
Cleveland, OH 44195, USA
e-mail: Msamotowka@yahoo.com

N.D. Martin, L.J. Kaplan (eds.), *Principles of Adult Surgical Critical Care*, DOI 10.1007/978-3-319-33341-0_16

Peptic Ulcer Disease (PUD)

This is the most common cause of UGIH in both non-variceal and variceal hemorrhage patients. It accounts for an estimated 40–75 % of all episodes of upper tract hemorrhage [4]. The most common symptom is epigastric pain. Duodenal ulcers typically are characterized as a burning type of pain that is relieved by food or antacids. Gastric ulcers usually do not respond to food intake. In 1983 Warren and Marshall published a landmark paper demonstrating the association of the bacteria *Helicobacter pylori* and certain peptic ulcers [5]. *H. pylori* produces an intense local inflammatory response despite not invading the gastric mucosa. It also disrupts the normal gastric secretory physiology, which leads to high acid secretion in some areas and low acid secretion in others. The actual incidence of *H. pylori* involvement in PUD is not clear but studies have shown it to be in the range of 73–90 % [6].

Upper esophagoduodenal gastrointestinal endoscopy (EGD) remains the first-line mode for both diagnosis and therapy of bleeding ulcers. Severe hemorrhage is usually defined as greater than 1,000 ml of blood loss. It is important to remember that even in patients with a history of alcohol abuse and cirrhosis, the most likely etiology of acute UGIH is still peptic ulcer disease. Biopsies of an identified ulcer bed should be taken at the time of endoscopy to check for the presence of *H. pylori* as well as to rule out an underlying malignancy. If no endoscopy is performed, then serological or urea breath test or stool testing are also options to assess for the presence of *H. pylori*. The urea breath test can be adversely affected by the use of proton pump inhibitor medications. Serological tests are not useful to determine the efficacy of therapy as *H. pylori* antibodies remain detectable even after active infection has resolved.

Initial care of the patient with a significant UGIH begins with the basic principles of resuscitation. Securing the airway in those patients at risk for aspiration can be life saving. Establishment of large-bore and high-flow vascular access for volume resuscitation and discontinuation of any anticoagulants the patient may be taking should be done promptly. As the number of patients on various anticoagulants continues to increase, it is imperative to have the proper reversal agents available. For example, patients on aspirin will benefit from transfusion of platelets, while those on warfarin may require fresh frozen plasma, vitamin K, or a four-factor concentrate (PPC (plasma protein concentrate)). Chronic kidney disease (CKD) patients may require DDAVP to improve platelet function. Table 16.1 summarizes some of the currently available agents.

In patients who are *H. pylori* negative, the most common cause of PUD is chronic ingestion of nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin or ibuprofen. These drugs inhibit the formation of prostaglandins, which are essential in preserving gastric mucosal blood flow, the maintenance of the protective layer of mucus, as well as mucosal integrity. NSAIDs can also cause submucosal erosions by a direct cellular injury mechanism leading to destruction of gastric mucosa [7].

Aspirin is one of the most commonly used medications by prescription as well as over-the-counter use. The peak anti-platelet affect of aspirin is reached at a dose of just 31 mg in most patients; some patients require much higher doses for complete platelet inhibition. The anti-inflammatory affect increases with higher doses and most patients on aspirin are taking low-dose aspirin (81 mg/day). The use of aspirin and other nonsteroidal anti-inflammatory medications remains a major contributing factor to a peptic ulceration. Other risk factors for PUD include use of corticosteroids, tobacco abuse [8], chronic or binge alcohol abuse, as well as ulceration in association with cocaine intoxication [9]. In particular, alcohol and tobacco use increase gastric acid secretion and gastroesophageal reflux. Similar to NSAIDs, tobacco also inhibits prostaglandin production leading to defective gastric mucosal protection and an increased risk for mucosal erosion to expose the vulnerable submucosal vascular network. Cocaine use may induce local ischemia from intense vasoconstriction with resultant mucosal injury.

Table 16.1 Anticoagulant agents

	Mechanism of action	Duration of effect	Emergent reversal strategies
Warfarin	Inhibition of vitamin K-dependent clotting factors	Half-life ~40 h (highly variable)	Vitamin K
		Duration 2–5 days	KCENTRA (PCC)
			FFP
Dabigatran (Pradaxa)	Inhibitor of free and clot-bound thrombin	Half-life: 12–17 h (longer in acute kidney injury or CKD)	FEIBA-NF (PCC)
			~60 % dialyzable
			Praxbind recently FDA approved[a]
Rivaroxaban (Xarelto)	Factor Xa Inhibitor	Half-life: ~5–9 h	FEIBA-NF (PCC) may be considered
Apixaban (Eliquis)	Factor Xa Inhibitor	Half-life: ~12 h	FEIBA-NF (PCC) may be considered

[a]Idarucizumab (Praxbind) is a monoclonal antibody possessing an affinity for dabigatran 350×'s greater than that of thrombin

Esophagitis

Esophageal injury leading to hemorrhage accounts for about 2 % of UGIH [10]. Most causes of esophagitis develop from chronic reflux of gastric acid and irritation of the esophageal mucosa. Chemical (inadvertent or intentional) or therapeutic agent ingestion are other potential causes of esophageal injury and hemorrhage. Potassium supplement tablets are among the most common medication causing esophagitis. Serious bleeding that requires invasive intervention or transfer to the ICU is rare. Mechanical injury from indwelling drainage or enteral access catheters (or both) as well as post-instrumentation is more commonly implicated in hospitalized patients, especially those with critical illness. Non-massive hemorrhage from esophagitis is more common in the elderly and is generally repaired by cessation of the offending agent or treating previously undiagnosed or inadequately treated gastroesophageal reflux disease with acid suppression [11].

Stress-Related Mucosal Disease (SRMD)

Despite increased focus on stress ulcer prophylaxis in the ICU, this remains an important clinical problem in critically ill patients, having been initially described in 1969. A meta-analysis by Lin and colleagues found that 75–100 % of critically ill patients exhibit some degree of gross gastric lesions on upper endoscopy performed within 72 h of the onset of critical illness [12]. Most lesions were minor diffuse subepithelial hemorrhages or erosions and rarely progressed to massive bleeding [13]. Substantial GI hemorrhage (transfusion and intervention requiring) complicates approximately 1 % of all ICU admissions. The most important clinical factors that presage an increased risk of bleeding are acute respiratory failure defined as a need for mechanical ventilation for more than 48 h and the presence of coagulopathy. In this context, coagulopathy is defined as a platelet count <50,000 or an international normalized ratio (INR) >1.5 or an activated partial thromboplastin time of more than two times the control value. This data stems from a 1994 landmark study by Cook and colleagues that included over 2,000 ICU patients [14].

Subsequent inquiries identified acute kidney injury, age >50 years, hepatic injury, sepsis, shock, and male gender as less important risk factors [15]. The use of histamine-2 receptor antagonists (H2RA) or proton pump inhibitors (PPI) for stress ulcer prevention in high-risk critically ill patients is standard practice in most intensive care units, but the literature is not clear about their comparative efficacies or cost-effectiveness allowing clinical equipoise with regard to a preferred agent for prevention. Furthermore, acid suppression has in some studies been linked with an increased risk of ventilator-associated pneumonia [16].

Pooled results from ten randomized trials of prophylactic therapy spanning from 1980 to 1998 found an incidence of 17 % in the critically ill [17]. Analysis of trials published between 1993 and 2010 suggested a much reduced incidence of only 1 % [18]. This decrease in incidence is liberally attributed to improved critical care of, increased use of enteral nutritional support, and appropriate prophylactic therapy related in part to an increase in regulatory benchmarks driving prophylaxis. The pathophysiology of SRMD is not fully understood but is most likely multifactorial in etiology. Splanchnic hypoperfusion, as occurs during shock regardless of cause, is believed to be a major underlying cause contributing to the development of SRMD even with appropriate prophylaxis [19].

Zollinger-Ellison Syndrome (ZES)

This syndrome describes a specific hypersecretory state with antral G-cell hyperplasia and systemic mastocytosis that is associated with PUD [20]. It is a very rare cause of PUD accounting for less than 0.1 % of all duodenal ulcers. Typically it is associated with multiple duodenal ulcers or ulcers that fail to respond to conventional therapy. The ulcers can be found in unusual locations such as beyond the first portion of the duodenum. Most behave like typical ulcers that are associated with *H. pylori* although ZES patients may present with additional symptoms of cutaneous flushing, diarrhea, or heartburn. Treatment usually involves resection of the affected areas as ZES is not definitively treated using only medical therapy [21]. Hemorrhage in association with ZES-induced ulceration is generally not associated with perforation.

Vascular Lesions

Dieulafoy lesions lead to approximately 2 % of UGIH and are due to a large anomalous artery located in the digestive tract [22]. They are more common in the elderly and can be located anywhere in the GI tract but usually are located along the lesser curvature of the stomach. Most lesions can be diagnosed and then treated endoscopically with thermal coagulation, clips, as well as epinephrine injection. There are other vascular lesions of the UGI tract but they are much less common. Similar to hemorrhage in patients with ZES, resolution requires intervention as medical therapy alone is insufficient.

Mallory-Weiss Tear

A Mallory-Weiss tear refers to a longitudinal laceration of the mucosa that involves the distal esophagus or proximal

stomach or a combination of both with hemorrhage arising from the injured and exposed submucosal vessels [23]. In the vast majority of cases (90%), bleeding is self-limited. If bleeding persists the source area can usually be controlled with band ligation or clips. The etiology of the tear is thought to be related to changes in intraluminal pressure associated with violent retching and vomiting. Previously, therapy required operative management with an attendant increase in morbidity and mortality. One must remain cognizant that hemorrhage from a Mallory-Weiss tear may coexist with a full-thickness laceration, in particular of the esophagus, which when present drives a different therapeutic approach. Uncommonly, Mallory-Weiss tears may be associated with diagnostic intervention such as transesophageal echocardiography; such injuries may be considered as a separate entity due to the significantly higher mortality compared to patients with Mallory-Weiss tears that were not related to recent instrumentation [24].

Tumors

Tumors of the UGI tract do not characteristically present with acute massive hemorrhage but instead tend to a more insidious presentation. Indolent GIH is associated with both malignant and benign tumors. This group as a whole represents only a small percentage of UGI tract hemorrhage, but early diagnosis is essential especially for those with malignancy leading to the practice of routine biopsy of endoscopically identified ulceration or mass for diagnostic purposes. Examples of tumors associated with GIH include but are not limited to adenocarcinoma, gastrointestinal stromal tumors (GIST), lymphoma, leiomyoma, leiomyosarcoma, and lymphoma. Surgical resection, if not contraindicated by other patient comorbidities, is usually indicated although some cases of lymphoma may be treated with chemotherapy. Similarly, many cases of leiomyoma may be endoscopically resected as well.

Injury

Penetrating trauma (as opposed to blunt injury) to the upper GI tract can cause substantial bleeding. Gastric injury in particular may lead to substantial hemorrhage due to the multiple sources of blood supply to the stomach as well as the well-connected submucosal plexus. In this setting, endoscopic therapy is contraindicated and operative management is indicated. The clinician should remain aware that duodenal injury may not present with hemorrhage in an OGT in the presence of an intact pyloric sphincter mechanism, and the absence of blood should not be construed as evidence of the lack of injury. Injury from caustic ingestions cause widespread esophageal and gastric damage but uncommonly leads to major diffuse bleeding immediately after ingestion; hemorrhage hours to days after is instead more common. The surgical management of penetrating, blunt, and caustic ingestion injuries is beyond the scope of this text. However, the critical care aspects of management include distal enteral access for luminal nutritional support, acid suppression, and resuscitation to support mucosal blood flow.

Post-intervention and Postsurgical

Patients who undergo endoscopic intervention such as biopsy or polypectomy at the time of EGD are at risk for bleeding at the site of intervention, but these are almost always self-limiting and stop without intervention; similar bleeding risks are noted for those who undergo endoscopic sphincterotomy during endoscopic retrograde cholangiopancreatography. On occasion, angioembolization is required to control bleeding, but this is much less common than spontaneous cessation with supportive measures including ensuring an intact coagulation cascade.

In contradistinction, patients who have previously undergone aortic reconstruction with a synthetic graft are at risk for developing an aortoenteric fistula by erosion of the graft or stent directly into the lumen of the GI tract. If this occurs it is usually at the level of the third portion of the duodenum but can occur at any level of the GI tract. Massive hemorrhage can occur suddenly and is usually fatal. Many patients will have a history of a self-limited sentinel (or herald) bleed that occurred days or even weeks prior to the onset of life-threatening hemorrhage. The diagnosis is best made by CT scan or CT angiogram as endoscopy is frequently nondiagnostic. Definitive treatment involves emergent laparotomy with removal of the graft and creation of an extra-anatomic bypass such as an axillobifemoral bypass coupled with repair of the duodenal erosion; the options for surgical repair of the GI tract are multiple and are beyond the scope of this chapter. However, distal enteral access is rather useful to help avoid the need for TPN in the perioperative period and to help promote GI luminal health by providing essential glutamine. There are recent reports of repairing aortoenteric fistulas using covered endovascular stents [25], but this should only be a temporary step in stable patients until future definitive repair. Only in those patients with limited life expectancy or poor candidates for surgery should this be the sole treatment of the fistula.

Any operative intervention that involves intestinal resection and anastomosis embraces a risk for bleeding at the site of the anastomosis. This holds true whether the anastomosis was created using stapling or suture techniques or a combination of both. Bleeding at the anastomotic line is usually self-limited and may only require correction of coagulopathy

or discontinuing perioperative anticoagulants. Options for therapy depend on the timing of the bleed with regard to the operation as well as the hemodynamic impact of the bleeding. In general hemodynamic instability is best managed in the OR, especially when the event is in the immediate perioperative period; anastomosis revision or opening with suture control and reclosure are most commonly applied techniques. When more remote, endoscopic therapy is a viable option but often requires pre-intervention airway control. Such control also allows the procedure to be done at the bedside instead of moving the patient to the GI suite or OR. Endoscopic techniques including cautery and clip application with or without vasoconstrictor injection may afford control when the bleeding site is visualized. Similarly, angioembolization has been used for acute control as well but carries with it a risk of anastomotic ischemia (colon and small bowel > stomach). It should be noted that more often than not, anastomotic hemorrhage is arrested with correction of coagulopathy and control of elevated blood pressure when present.

As the number of patients in the USA who undergo operative intervention to control clinically severe obesity continues to rise, it is likely that the incidence of postoperative hemorrhage will rise in parallel. Those patients who have undergone gastric banding are at risk for erosion of the band through the gastric wall with subsequent hemorrhage and require prompt operative intervention; endoscopic or angioembolization techniques are not appropriate due to the combined hemorrhage and perforation; while uncommon, it is an important complication to recognize. In contrast, the most common operation for clinically severe obesity at present is gastric bypass with Roux-en-Y reconstruction. In this focused patient population, the incidence of postoperative GI tract bleeding complicates up to 4.4 % of patients [26]. The incidence is reported as threefold higher in those who were cared for using a laparoscopic approach versus in an open technique; the genesis of this difference remains unclear.

Early postoperative (>48 h) bleeding after gastric bypass is typically manifested by hematemesis or bright red blood per rectum in the presence of clinical signs of shock and is an indication for urgent surgical re-exploration. Hematemesis suggests that the gastrojejunal anastomosis is the origin of the bleed. Bright red blood per rectum could stem from the gastric remnant or the jejunojejunostomy anastomosis. In cases of late (<48 h postoperative) hemorrhage and hemodynamic stability, the patients can typically be treated nonoperatively with avoidance of anticoagulants and routine supportive critical care interventions. When the site is unclear and hemorrhage continues but is unaccompanied by hemodynamic compromise, some advocate using a tagged red blood cell nuclear scan to help identify the source, while others pursue a CTA as the initial step in site identification. It is likely that the selected diagnostic test is more related to availability and may vary from institution as a reflection of local resources. In gastric bypass patients who present with GI tract hemorrhage several months or even years after surgery, the most likely etiology is a marginal ulcer. Timely endoscopy (EGD) with therapeutic intervention is indicated in this situation and is generally coupled with acid suppression.

Other

There are several other potential causes of UGIH. Patients with a Crohn's exacerbation may present with GI tract hemorrhage and are generally self-limited. The pancreatic and hepatobiliary tract may rarely be the source of UGIH with patients presenting with hemobilia (post-injury or post-intervention) or hemosuccus pancreaticus, respectively. Additionally, Cameron lesions (linear erosions in the gastric portion of a hiatus hernia that is above the diaphragmatic orifice of the hernia) complicate approximately 3–5 % of such hernias and rise in proportion to the size of the hernia. Cameron lesions are very rare causes of over hemorrhage but may account for up to approximately 4 % of causes of occult GI bleeding [27].

Guideline-Derived Recommendations

To assist clinicians in the management of patients with nonvariceal upper gastrointestinal hemorrhage, a multidisciplinary consensus group was formed that reviewed relevant literature and constructed several evidence-based management recommendations [28]. Below is a brief synopsis of the group's findings:

Recommendation 1: Hospitals should develop institution-specific protocols for multidisciplinary management that should include access to an endoscopist with training in endoscopic hemostasis.

Recommendation 2: Support staff trained to assist in endoscopy should be available for urgent endoscopy. Patients identified as high risk for re-bleeding should be admitted to a monitored setting for at least the first 24 h.

Recommendation 3: Immediate evaluation and appropriate resuscitation are critical to proper management.

Recommendation 4: In selected patients, the placement of a nasogastric tube can be considered because the findings may have prognostic value.

Recommendation 5.1: Clinical (non-endoscopic) stratification of patients into low-risk and high-risk categories for re-bleeding and mortality is important for proper management. Available prognostic scales may be used to assist in decision-making.

Recommendation 5.2: Early stratification of patients into low-risk and high-risk categories for re-bleeding and mortality based on clinical *and* endoscopic criteria is important for proper management.

Recommendation 6: Early endoscopy (within the first 24 h) with risk classification by clinical and endoscopic criteria allows for safe and prompt discharge of patients classified as low risk.

Recommendation 7: A finding of low-risk endoscopic stigmata (a clear-based ulcer or a non-protuberant pigmented dot in an ulcer bed) is not an indication for endoscopic hemostatic therapy. A finding of a clot in an ulcer bed warrants targeted irrigation in an attempt at dislodgment, with appropriate treatment of the underlying lesion. A finding of high-risk endoscopic stigmata (active bleeding or a visible vessel in an ulcer bed) is an indication for immediate endoscopic hemostatic therapy.

Recommendation 8: No single solution for endoscopic injection therapy is superior to another for hemostasis.

Recommendation 9: No single method of endoscopic thermal coaptive therapy is superior to another.

Recommendation 10: Monotherapy, with injection or thermal coagulation, is an effective endoscopic hemostatic technique for high-risk stigmata; however, the combination is superior to either treatment alone.

Recommendation 11: The placement of clips is a promising endoscopic hemostatic therapy for high-risk stigmata.

Recommendation 12: Routine second-look endoscopy is not recommended.

Recommendation 13: In cases of re-bleeding, a second attempt at endoscopic therapy is generally recommended.

Recommendation 14: Surgical consultation should be sought for patients who have failed endoscopic therapy.

Recommendation 15: H-2 receptor antagonists are not recommended in the management of patients with acute upper GI bleeding.

Recommendation 16: Somatostatin and octreotide are not recommended in the routine management of patients with acute non-variceal UGIH.

Recommendation 17: An intravenous bolus followed by continuous infusion proton pump inhibitor is effective in decreasing re-bleeding.

Recommendation 18: In patients awaiting endoscopy, empirical therapy with a high-dose proton pump inhibitor should be considered.

Recommendation 19: Patients considered at low risk for re-bleeding after endoscopy can be fed within 24 h.

Recommendation 20: Patients with upper GI bleeding should be tested for *Helicobacter pylori* and receive eradication therapy if infection is present.

These recommendations were updated in 2010 [29]. There were only a few minor additions. More emphasis was placed on early risk stratification of patients for re-bleeding. Epinephrine injection alone is not advised. High-risk patients for re-bleeding should be hospitalized for at least 72 h. Blood transfusion for patients with a hemoglobin level <7 mg/dl is advised. A negative *H. pylori* test in the acute setting should be repeated. The most important addition addresses patients who need cardiovascular prophylaxis. Patients with an UGIH who require secondary cardiovascular prophylaxis should start receiving aspirin again as soon as cardiovascular risks outweigh gastrointestinal risks. This threshold is generally crossed within 7 days of cessation of hemorrhage. Aspirin plus a proton pump inhibitor therapy is preferred over clopidogrel alone to reduce re-bleeding.

Variceal Hemorrhage

Varices are thin-walled and dilated veins located in the distal esophagus that are characterized by a higher venous pressure than normal as well as a higher venous flow than normal; varices are not normally present and indicate the presence of a concomitant disease process. They are typically associated with a cirrhotic liver but the converse is not true as only about half of all cirrhotics have varices. The main factor that determines variceal rupture risk is the hepatic vein pressure gradient. Most variceal bleeds are esophageal with only 3 % having a gastric origin. Early (<12 h) esophagogastroduodenoscopy (EGD) is essential in the management of patients with known varices and active UGI hemorrhage. Early endoscopy accomplishes two key goals: (1) excludes a non-variceal source of hemorrhage and (2) provides endoscopic control for identified variceal hemorrhage (the mainstay of therapy for such bleeding).

Mortality after acute variceal hemorrhage remains high (15–20 %) despite advances in medical management. It is important to note that historical mortality rates were as high as 40 % in the 1980s. Historically, the Child-Pugh score and other subjective clinical data was used to estimate patient mortality. Reverter et al. showed that the MELD (model for end-stage liver disease) score demonstrated superior performance and a more strong correlation with 3-month mortality and is now the most commonly used and durable predictor of patient mortality associated with hepatic disease and decompensation [30]. Mortality is negatively influenced by recurrent hemorrhage.

Re-bleeding rates may reach 60 %, and the mortality associated with re-bleeding has been reported as high as 33 % [31].

Optimal care of the patient with acute variceal hemorrhage benefits from a multiprofessional approach including an intensivist. One should remain aware that those with variceal hemorrhage may require massive transfusion and a close relationship with the blood bank is essential; transfusion on a protocol with the involvement of a clot-focused hematologist in helpful in

guiding management and for participation in a quality improvement program for the massive transfusion protocol as well [32]. Early airway control may reduce pulmonary soilage and facilitate rapid diagnostic and therapeutic intervention using EGD. Administration of prophylactic antibiotics has been shown to be of some incremental benefit [33]. Early antibiotic administration has been shown to decrease the incidence of early re-bleeding and improve overall survival [34].

Endoscopic therapy offers several techniques to control hemorrhage and have in general replaced the Sengstaken-Blakemore or Linton tube for initial hemorrhage control in all but those with presentation hemodynamic instability. Esophageal varices may be treated using rubber banding or intra-variceal sclerotherapy with a sclerosing agent. There are several types of sclerosing agents that are FDA approved including 1.5 % sodium tetradecyl sulfate, absolute alcohol, ethanolamine, or sodium morrhuate. No single agent has been shown to be superior to others.

Concomitant medical management is essential to help reduce the likelihood of recurrent hemorrhage by reducing flow through the existing varices. A mainstay of such therapy is intravenous somatostatin. It was shown to be superior to placebo in controlling variceal hemorrhage when used in conjunction with endoscopic sclerotherapy [35]. Combined therapy using endoscopic intervention and vasoactive agents has been shown in several randomized controlled trials to be superior to either treatment alone [36]. If initial therapy fails, then consideration of an interventional radiologist placing a covered transjugular intrahepatic portosystemic shunt (TIPS) is indicated rather than any of the surgical procedures that are primarily of historic interest including a variety of systemic or selective shunts or esophageal devascularization procedures. The additional use of vasopressin as a vasoactive constrictive agent can be considered but it is associated with more side effects [37]. Adjunctive agents such as estrogen, long-acting nitrates, and bet-blockers may be considered as well with combination therapy outperforming monotherapy in preventing recurrent hemorrhage.

In the case of esophageal varices that are able to be initially endoscopically controlled, repeat therapeutic endoscopy is indicated if the patient is stable and has recurrent bleeding. For gastric varices repeat endoscopic treatment is not indicated. In this case a TIPS or other intervention should be considered. Garcia-Pagan et al. showed that in certain high-risk patients that included patients with Child B cirrhosis and active bleeding at endoscopy and Child C cirrhotics with less than 14 points after medical and endoscopic treatment was performed, the early placement of a covered TIPS (<72 h from admission) was associated with a better prognosis [38].

Additionally, when only gastric varices are noted, an evaluation for splenic vein thrombosis should be undertaken as appropriate therapy is splenectomy for gastric variceal hemorrhage due to unimpeded arterial inflow but blocked venous outflow. This condition has also been known as left-sided portal hypertension or sinistral hypertension. In a hybrid room or OR suite, initial control may be achieved with splenic artery embolization or balloon occlusion to allow resuscitation and achieve temporary hemorrhage control in those with prior abdominal surgery with the potential for the need for an extensive adhesiolysis to reach the spleen.

Hepatic Transplantation

Patients with variceal hemorrhage that requires intervention should be evaluated for transplant candidacy early in the course of their evaluation and therapy [39]. In particular, those with inadequate response to therapy may have few options other than hepatic transplantation to decrease variceal pressures and control bleeding. While the indications for acute transplantation are fairly consistent between centers in the USA, the use of supportive technologies such as CRRT for concomitant AKI or CKD, as well as bioartificial liver techniques, vary by center and are beyond the scope of this chapter.

Small Bowel Hemorrhage

The reported incidence of the small bowel as the source of hemorrhage is between 1 % and 7 % of patients who present with blood per rectum [40]. The most common cause is angiodysplasia. Other causes are:

1. Tumors (benign and malignant)
2. Crohn's disease
3. Meckel's diverticulum
4. Toxicity related to therapeutic agents
5. Toxicity related to illicit agents
6. Varices
7. Injury (blunt, penetrating, post-intervention)
8. Dieulafoy lesion

The most commonly used test to diagnose (presence and location) small intestinal hemorrhage is the ^{99m}Tc-tagged red blood cell scan. Unfortunately, the test is not very accurate due to the inability to spatially resolve location despite the test's excellent sensitivity to the presence of very small volume bleeding. Instead, there are now three relatively new modalities that improve localization quite substantially including:

1. Capsule endoscopy
2. Push enteroscopy
3. Double-balloon enteroscopy

Capsule endoscopy involves the patient swallowing a small pill with an embedded camera that takes images of the

bowel lumen during its aboral passage. The images are wirelessly sent to a monitor the patient wears allowing delayed image retrieval and analysis. The test is very sensitive and minimally invasive but cannot be used if there is any concern about the presence of a bowel obstruction that could preclude the patient passing the camera out the rectum; while the camera does not need to be recovered, intestinal obstruction will lead to an incomplete evaluation of luminal surfaces past the site of obstruction.

Double-balloon enteroscopy (DBE) uses a dedicated 200 cm enteroscope with two balloons. One of the balloons is attached to the tip of the endoscope and the other to the tip of a flexible overtube. By sequentially inflating and deflating the balloons, the scope can be advanced progressively more distally in the small bowel. The scope can be passed orally as well as transanally thus allowing for visualization of the entire length of small bowel. An advantage of DBE over capsule endoscopy is that it permits biopsies to be obtained of suspicious lesions and allows interventions to be deployed to control hemorrhage when discovered. In a meta-analysis comparing DBE to capsule endoscopy, Chen et al. found the yield of localizing the bleeding lesion was comparable for the two modalities [41], but there is clear asymmetry in terms of intervention.

Push enteroscopy uses an enteroscope that allows for visualization of the proximal 100 cm of small bowel. Push enteroscopy may be used in or out of the OR. Intraoperatively, push enteroscopy may be aided by manual of laparoscopic manipulation of small bowel, allowing telescoping for more than 100 cm of small intestine onto the enteroscope. In the ICU, similar manipulations may be made in those managed with an open abdomen, although the need for this is uncommon. In the GI suite, push enteroscopy may be aided by gravity and positional changes of the patient to facilitate passage of the enteroscope; airway control is essential in facilitating push enteroscopy. Like double-balloon enteroscopy, push enteroscopy also allows the operator to perform diagnostic and therapeutic interventions. Triester et al. in a meta-analysis comparing the yield of finding the source of small bowel hemorrhage with capsule endoscopy versus all other modalities found that capsule endoscopy was significantly superior with regard to diagnostic capacity to all other modalities [42].

Angiodysplasias are a common cause of small bowel hemorrhage and are small ectatic blood vessels that are found in the mucosa or submucosa of the GI tract. They are also called vascular ectasias or arteriovenous malformations (AVM). They are more common in the elderly and in patients with chronic kidney disease. Typically, they are multiple in number which can make it difficult to determine exactly which one is the source of hemorrhage. If the bleeding angiodysplasia is identified on endoscopy, it can be most effectively treated with clipping or thermal probe coagulation and injection of epinephrine. Argon plasma coagulation [43], as well as photodynamic therapies, has also been explored for these lesions.

If the exact one responsible cannot be identified, then surgical resection of the segment of involved small bowel can be considered, but patients with angiodysplasia are prone to develop new lesions and recurrence of bleeding in the remaining small bowel.

If a tumor is the etiology of small bowel hemorrhage, then resection is warranted if there are no other contraindications to surgery. Crohn's disease-associated bleeding is treated with immune suppression initially and only patients who fail conservative therapy go on to resection. Meckel's diverticulum-induced hemorrhage is best diagnosed with a Meckel's scan (99mTc-pertechnetate scintigraphy), and surgical resection is the treatment of choice. Varices and Dieulafoy lesions would be treated as discussed earlier.

Lower GI Hemorrhage (LGIH)

Patients with LGIH typically present with hematochezia or blood per rectum. Lower GI hemorrhage is one fifth as common as upper GI hemorrhage. The annual incidence in the USA is reported to be 20.5–27 cases per 100,000 adult population at risk. The majority of LGIH requires no intervention to stop [44]. The mean age of patients with LGIH ranges from 63 to 77 years of age. Mortality spans 2–4 %, and LGIH is more common in men than in women.

The basic principles of management are: (1) evaluation and resuscitation or hemodynamic stabilization of the patient (unlike UGIH cases the LGIH patients do not commonly present with massive hemorrhage), (2) localization of the bleeding site, and (3) site-specific therapeutic intervention. Patients with presentation hypotension, transfusion-requiring hemorrhage, all benefit from ICU admission and monitoring. Telemetry monitoring of preexisting arrhythmias, as well as known but not active coronary disease, does not require ICU admission. Patients with drug-eluting stents who have their antiplatelet therapy held may benefit from ICU admission for monitoring and potentially more rapid intervention as needed for myocardial ischemia.

Localization is the challenging step in this algorithm. Several large series have shown that colonoscopy has an overall diagnostic yield ranging from 53 to 97 % reflecting operator skill, intestinal preparation, and the intermittent nature of many etiologies of LGIH [45]. Early colonoscopy is considered the procedure of choice; however, its utility can be limited by massive ongoing bleeding. Arteriography is typically reserved for those patients. Jacovides et al. assessed the value of performing a computed tomographic angiogram (CTA) prior to visceral angiogram (VA) to improve the yield and found that it did in fact improve the efficacy of finding

the bleeding lesion [46]. To improve the yield of VA, some clinicians will use provocative angiography that entails systemic heparinization plus selective transcatheter injection of a vasodilator *and* tissue plasminogen activator into the suspected vessels. Push enteroscopy using a pediatric scope may be of benefit in certain stable patients [47].

Farrell et al. reviewed the utility of radionuclide imaging and found that although it was well tolerated by patients, it is an inconsistent technique for identifying the source of bleeding with a widely ranging accuracy of 24–91 % [48]. While demonstrating great sensitivity to the presence of small amounts of hemorrhage (0.1–0.2 ml blood loss per minute are identifiable), the patient must be bleeding at the time of the scan for it to be positive. Abnormal vasculature devoid of bleeding is not demonstrated by nuclear medicine studies and is better demonstrated on CTA or VA. The study should only be done in hemodynamically stable patients and when positive still requires a therapeutic intervention as this technique offers only diagnosis. The most common causes of LGIH are:

1. Diverticular disease
2. Angiodysplasia
3. Inflammatory bowel disease
4. Neoplasm
5. Hemorrhoids
6. Proctitis

Diverticulosis is common in the Western Hemisphere but rare in Asia and Africa. This difference has been attributed to a higher fat and processed substrate content in the US diet. The increased pressure required by the colon to aborally propel less well-hydrated stool results in pressure gradient-driven mucosal herniation through the muscular layer of the colon along the course of penetrating vessels. Expansion of the diverticulum during mass movement leads to vascular injury from stretch and tearing resulting in hemorrhage. Treatment of diverticular hemorrhage includes application of hemoclips, thermocoagulation, or epinephrine injection at the time of diagnostic and then therapeutic endoscopy. In the majority of cases, hemorrhage may be arrested endoscopically. In those who fail endoscopic management, options include angioembolization as well as resectional therapy. While previously believed to create very high risk for intestinal ischemia and perforation, angioembolization techniques infrequently require subsequent operative therapy for perforation [49]. Angiodysplasia-associated hemorrhage maybe treated in a similar fashion.

There are a host of less common causes of LGIH of which the clinician should be aware but which generally do not require ICU care; the majority of ICU care in these patients occurs after therapeutic intervention in the OR with less common care occurring during resuscitation. In patients with inflammatory bowel disease, severe life-threatening hemorrhage is uncommon, but it is the primary indication for 10 % of emergency colectomies in this patient population. Bleeding from a neoplasm is common but rarely massive. The vast majority of these bleeds can be treated endoscopically. Thus, if the patient has a malignant lesion, resection can be performed after the patient has been properly resuscitated and stabilized. Colonic polyps may bleed spontaneously (generally leading to fecal occult blood) or more commonly after biopsy.

Radiation proctitis may develop in patients who have previously undergone either external beam radiation therapy or the implantation of radioactive seeds for an unrelated system such as the prostate. Bleeding can occur at any time after radiation therapy, even years after treatment had been completed. Since radiation-induced changes in the microvasculature lead to friability, even minor mucosal challenges may lead to bleeding. In the elderly who have diminished thirst sensation and are more prone to stool dehydration, stercoral injury will more commonly occur in those with prior irradiation. Treatment of radiation proctitis is as outlined above for the other causes of LGIH. Proctitis that is due to inflammatory bowel disease may benefit from steroid enemas to reduce local inflammation. Proctitis that has an infectious underpinning generally responds to targeted anti-infective therapy. Periprocedural or autoerotic lacerations that are not full thickness but that are complicated by bleeding often respond to topical hemostatic agents. It is uncommon for any of the above to require ICU care.

Hemorrhoids are the most common cause of rectal bleeding. If unresponsive to topical agents, they are optimally band ligated, stapled using a circular stapler, or simply sutured. One must be aware of the relationship of hemorrhoidal hemorrhage to portal hypertension as mechanical hemorrhage control strategies alone may fail in that unique patient population. That group of patients often requires ICU admission for care of the portal hypertension.

Acute arterial or mesenteric venous occlusion may be complicated by LGIH, although this is quite rare. Hemorrhage in this setting occurs when there is enough ischemia to lead to mucosal death and slough. Bleeding from the junction of mucosa and submucosa may occur. Acute mesenteric ischemia is defined as a sudden decrease in blood flow to a level that is inadequate to meet the metabolic demands of the viscera [50]. The most common etiologies of acute mesenteric ischemia and their relative frequency are:

1. Arterial embolus (50 %)
2. Arterial thrombosis (20 %)
3. Low-flow state (20 %)
4. Mesenteric venous thrombosis (5 %)
5. Other (5 %)

There are many algorithms and approaches to identifying the presence of and impact of intestinal ischemia with regard

to intestinal viability and wall integrity. Techniques include CT, CTA, endoscopy, proctoscopy, and VA, with selection depending on the presence of pneumoperitoneum, peritonitis, hemodynamic instability, or hemorrhage, as well as local resources. Similarly there are a host of treatment options depending on the extent and impact of ischemia spanning therapeutic anticoagulation to resection with or without revascularization as well as lysis with or without stenting.

The intensivist should be cognizant of the association between several relationships including but not limited to:

1. New-onset atrial dysrhythmia and arterial embolization
2. Mesenteric venous thrombosis and hypercoagulability
3. Intestinal ischemia, resuscitation, and reperfusion injury to other viscera including the liver and kidneys
4. Intestinal ischemia operative therapy and a planned second-look procedure leading to open abdomen management for the initial 24–48 h after the index procedure
5. Risk for fistula formation with intestinal resection if the abdomen is unable to be closed primarily

Recognizing these relationships will help inform the intensivist with regard to diagnostic undertakings, likely procedural planning, risk, and outcome-based family discussions including the potential for hospital and ICU readmission, organ failure potential, and care coordination with the primary team.

Conclusion

GI hemorrhage spans a vast number of potential etiologies and overlaps with multiple organ systems. Key aspects in terms of diagnosis and temporary or definitive therapy including multiple hospital areas such as the GI suite, ICU, interventional radiology, and the operating room underscore the need for a team-based approach to the care of patients with GI tract hemorrhage.

References

1. Longstreth G. Epidemiology of hospitalization for acute upper gastrointestinal hemorrhage: a population-based study. Am J Gastroenterol. 1995;90:206–10.
2. Fllah M, Prakash C, Edmundowicz S. Acute gastrointestinal bleeding. Med Clin North Am. 2000;84:1183–208.
3. Delvaux M, Fassler I, Gray G. Clinical usefulness of the endoscopic video-capsule as the initial intestinal investigation in patients with obscure digestive bleeding validation of a diagnostic strategy based on the patient outcome after 12 months. Endoscopy. 2004; 36:1067–73.
4. Ramakrishnan K, Salinas RC. Peptic ulcer disease. Am Fam Phys. 2007;76(7):1005–12.
5. Warren JR, Marshall B. Unidentified curved bacilli on gastric epithelium in active gastritis. Lancet. 1983;1:1273.
6. Mercer DW, Robinson EK. Chapter 47. Peptic ulcer disease. In: Townsend CM et al., editors. Sabiston textbook of surgery. 18th ed. Philadelphia: Elsevier Saunders; 2008.
7. Harbison S, Dempsey D. Pepteic ulcer disease. Curr Prob Surg. 2005;42:346–454.
8. Svanes C. Trends in perforated peptic ulcer: incidence, etiology, treatment and prognosis. World J Surg. 2000;24(3):277–83.
9. Schuster KM, Fever WJ, Barquist ES. Outcomes of cocaine-induced gastric perforations repaired with an omental patch. J Gastrointest Surg. 2007;11(11):1560–3.
10. Vakil N, Van Zanten SV, et al. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. Am J Gastroenterol. 2006;101:1900–20.
11. Zimmerman J, Shohat V, Tsvang E, et al. Esophagitis is a major cause of upper gastrointestinal hemorrhage in the elderly. Scand J Gastroenterol. 1997;32:906–9.
12. Lin PC, Change CH, Hsu PL, et al. The efficacy and safety of proton pump inhibitors vs. histamine-2 receptor antagonists for stress ulcer bleeding prophylaxis among critical care patients: a meta-analysis. Crit Care Med. 2010;38:1197–205.
13. Stollman N, Metz DC. Pathophysiology and prophylaxis of stress ulcer in intensive care unit patients. J Crit Care. 2005;20:35–45.
14. Cook DJ, Fuller HD, Fuyatt GH, et al. Risk factors for gastrointestinal bleeding in critically ill patients. N Engl J Med. 1994;330: 377–81.
15. Cook DJ, et al. Risk factors for clinically important upper gastrointestinal bleeding in patients requiring mechanical ventilation. Canadian Critical Care Trials Group. Crit Care Med. 1999;27:2812–7.
16. Reilly J, Fennerty MB. Stress ulcer prophylaxis: the prevention of gastrointestinal bleeding and the development of nosocomial infections in critically ill patients. J Pharm Pract. 1998;11:418–32.
17. Laine L, Takevchi K, Tamawaski A. Gastric mucosal defence and cytoprotection: bench to bedside. Gastroenterology. 2008;135: 41–60.
18. Alhazzani W, Alanezi F, Jaeschke RZ, et al. Proton pump inhibitor versus Histamine 2 receptor antagonists for stress ulcer prophylaxis in critically ill patients: a systematic review and meta-analysis. Crit Care Med. 2013;41(3):693–705.
19. Fennerty MB. Pathophysiology of the upper gastrointestinal tract in the critically ill patient: rationale for the therapeutic benefits of acid suppression. Crit Care Med. 2002;30(6 Suppl):S351–5.
20. DelValle J. Zollinger-Ellison syndrome and other neuroendocrine tumors. In: Wolfe MM, editor. Therapy of digestive disorders. New York: Elsevier; 2006. p. 469–84.
21. Dolan JP, Norton JA. Chapter 58. Zollinger-Ellison syndrome. In: Yeo CL, editor. Schakelford's surgery of the alimentary tract. 6th ed. Philadelphia: Elsevier Saunders; 2007.
22. Hui AJ, Sung JJ. Endoscopic treatment of upper gastrointestinal bleeding. Curr Treat Options Gastroenterol. 2005;8:153–62.
23. Bharucha AE, Gostout CJ, et al. Clinical and endoscopic risk factors in the Mallory-Weiss syndrome. Am J Gastroenterol. 1997;92: 805–8.
24. Cappell MS, Dass K, Manickam P. Characterization of the syndrome of UGI bleeding from a Mallory-Weiss tear associated with transesophageal echocardiography. Dig Dis Sci. 2014;59:2381–9.
25. Burks JA, Faries PL, et al. Endovascular repair of bleeding aortoenteric fistulas: a 5 year experience. J Vasc Surg. 2001;34:1055–9.
26. Samotowka M. Bariatric surgery complications for the acute care surgeon. Bariatric Surg. 2016; In Press.
27. Keyur P, Ali MA, Wong RCK. Unusual causes of upper gastrointestinal bleeding. Gastroenterol Endoscop Clin N Am. 2015;25(3): 583–605.
28. Barkun A, Bardou M, Marshall JK, Nonvariceal Upper GI Bleeding Consensus Conference Group, et al. Consensus recommendations for managing patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med. 2003;139:843–57.

29. Barkun AN, Bardov M, et al. International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. Ann Intern Med. 2010;152:101–13.
30. Reverter E, et al. A MELD-based model to determine risk of mortality among patients with acute variceal bleeding. Gastroenterol. 2014;146:412–9.
31. Garcia–Pagán JC, Patch D. Trials and tribulations: the prevention of variceal rebleeding. Gastroenterology. 2015;149(3):528–31.
32. Young PP, Cotton BA, Goodnough LT. Massive transfusion protocol for patients with substantial hemorrhage. Transfus Med Rev. 2011;25(4):293–303.
33. Bernard B, Grange JD, et al. Antibiotic prophylaxis for the prevention of bacterial infections in cirrhotic patients with gastrointestinal bleeding: a meta-analysis. Hepatology. 1999;29:165–1661.
34. Chavez-Tapia N, et al. Antibiotic prophylaxis for cirrhotic patients with upper gastrointestinal bleeding. Cochrane Database Syst Rev. 2010; 9:CD002907.
35. Burrough A, McCormick P, et al. Randomized, double-blind, placebo-controlled trial of somatostatic for variceal bleeding: emergency control and prevention of early variceal re-bleeding. Gastroenterol. 1990;99:1388–95.
36. Carbonell N, Pauwels A, et al. Improved survival after variceal bleeding patients with cirrhosis over the past two decades. Hepatology. 2004;40:652–9.
37. Garcia-Tsao G, Bosch J. Management of varicies and variceal hemorrhage in cirrhosis. N Engl J Med. 2010;362:823–32.
38. Garcia-Pagan J, Pascoli M, et al. Use of early TIPS for high-risk variceal bleeding: results of a post-RCT surveillance study. J Hepatol. 2013;58:45–50.
39. Franchis R, on behalf of the Baveno VI faculty. Expanding consensus in portal hypertension: report of the Baveno VI consensus workshop: stratifying risk and individualizing care for portal hypertension. J Hepatol. 2015;63(3):743–52.
40. Gralnek IM. Obscure-overt gastrointestinal bleeding. Gastroenterol. 2005;128:1424–30.
41. Chen X, Zhi-Hua R, et al. A meta-analysis of the yield of capsule endoscopy compared to double-balloon enteroscopy in patients with small bowel diseases. World J Gastroenterol. 2007;13(32): 4372–8.
42. Triester SL, Leighton JA, et al. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with obscure gastrointestinal bleeding. Am J Gastroenterol. 2005; 100:2407–18.
43. Manner H. Argon plasma coagulation therapy. Curr Opin Gastroenterol. 2008;24(5):612–6.
44. Farrell JJ, Friedman LS. Gastrointestinal bleeding in the elderly. Gastroenterol Clin North Am. 2001;30:377–407.
45. Zuckerman GR, Prakash C. Acute lower intestinal bleeding: part 1: clinical presentation and diagnosis. Gastrointest Endosc. 1998; 48(6):606–17.
46. Jacovides CL, Nadolski G, et al. Arteriography for lower gastrointestinal hemorrhage role of preceding abdominal computed tomographic angiogram in diagnosis and localization. JAMA Surg. 2015;150(7):650–6.
47. Nguyen NQ, Rayner CK, et al. Push enteroscopy alters management in a majority of patients with obscure gastrointestinal bleeding. J Gastroenterol Hepatol. 2005;20(5):716–21.
48. Farrell JJ, Friedman LS. Review article: the management of lower gastrointestinal bleeding. Aliment Pharmacol Ther. 2005;21: 1281–98.
49. Tan KK, Nallathamby V, Wong D, Sim R. Can superselective embolization be definitive for colonic diverticular hemorrhage? An institutions experience over 9 years. J Gastrointest Surg. 2010; 14(1):112–8.
50. Oldenburg WA, Lau LL, et al. Acute mesenteric ischemia: a clinical review. Arch Intern Med. 2004;164(10):1054–62.