Gastrointestinal bleeding (GIB) in patients with known cancer can be a serious emergent problem with a wide variety of etiologies. GIB can also be the sentinel event in the discovery of a primary or metastatic cancer lesion to the gastrointestinal (GI) tract. Locating the site of bleeding is essential to its treatment and management. Upper gastrointestinal bleeding (UGIB) is defined as hemorrhage from a site proximal to the ligament of Treitz. UGIB bleeding can be because of peptic ulcer disease, variceal disease, and more obscure cancer-related etiologies. There are a wide variety of cancers that may metastasize to the stomach, proximal duodenum, or regional lymph nodes and can then erode into the GI lumen, leading to blood loss. Lower gastrointestinal bleeding (LGIB) also has a variety of etiologies in cancer patients. Cancer patients with GIB require a multidisciplinary approach to reduce morbidity and mortality. In this article, the authors have reviewed the literature on the etiology of gastrointestinal hemorrhage by location, including diagnostic and management strategies in the patient with suspected or known cancer. They have also reviewed special circumstances posed by various malignancies and some pediatric considerations.

UPPER GASTROINTESTINAL BLEEDING

Etiology

The major causes of UGIB in both cancer and noncancer patients are summarized in Box 1. Less commonly, cancer from various primary sources can metastasize to the esophagus, stomach, or duodenum and may be present with GIB ranging from an occult bleed to a significant hemorrhage. Lymph node disease from either primary GI lymphoma or metastatic disease can also erode through overlying mucosa and become a source of significant bleeding. In addition, mucositis related to...
chemotherapy can lead to clinically significant GIB. The approach to occult GI hemorrhage is not reviewed in this article.\textsuperscript{2,3}

Comparative data collected during the last 25 years has demonstrated that peptic ulcer disease (PUD) continues to be the most common cause of UGIB, but despite advances in treatment, mortality remains fairly constant. A prospective study of UGIB etiology between 1993/1994 and 2000 found a decrease in the incidence from 61.7 per 100,000 to 47.7 per 100,000.\textsuperscript{4} In this study, peptic ulcer–related bleeding was the most common cause in 46\% of patients, with half of these patients using nonsteroidal antiinflammatory drugs (NSAIDs). Despite the decrease in incidence, there was no significant change in mortality or the occurrence of rebleeding after treatment over time.\textsuperscript{5} Another population-based study in 2008 found that variceal bleeding accounts for 50\% to 60\% of UGIB in patients with cirrhosis and confirmed that the most common causes of UGIB were PUD (about 50\%), esophagitis, and erosive lesions.\textsuperscript{4} Neoplasms have been reported to be the source in 2.9\% to 4\% of patients presenting with a UGIB.\textsuperscript{7} In summary, patients presenting with UGIB have a relatively high mortality rate and risk of rebleeding. The etiologies are similar with cancer patients as compared with the general population, and neoplasms are less likely to be the primary underlying etiology.

**Presenting Signs and Symptoms**

UGIB typically presents with hematemesis, melena, or occult fecal blood. The presenting symptoms are dependent on the location of the bleeding lesion, amount of blood loss, and underlying etiology. Symptoms can range from a Mallory-Weiss tear with mild hematemesis after a period of retching to a hemodynamically unstable variceal hemorrhage in the setting of cirrhosis or massive hepatic neoplastic infiltration. Key risk factors to seek out include the use of NSAIDS, *Helicobacter pylori* infection, liver disease, history of abdominal surgery, history of prior GI bleeding, and history of cancer.\textsuperscript{8} The rate at which blood loss occurs and its effect on vital signs determine the pace of acute intervention.

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**Box 1**

Major causes of upper gastrointestinal bleeding\textsuperscript{6,8}

- Peptic ulcer disease (PUD)
- Esophageal and gastric varices
- Hemorrhagic gastritis
- Esophagitis
- Duodenitis
- Mallory-Weiss tears
- Angiodysplasia
- UGI malignancy
- Anastomotic ulcers
- Dieulafoy (abnormally large tortuous submucosal artery) lesions

UGIB may be seen with gastritis and esophagitis presenting with blood-streaked emesis. More commonly, these conditions present as epigastric pain with occult blood per rectum.\textsuperscript{1,8,9} Both are unlikely to represent a significant source of blood loss. However, in the setting of known cancer, occult blood in the stool must be fully evaluated. UGIB may be the result of metastasis to the upper gastrointestinal mucosa. Prompt referral to a gastroenterologist is appropriate to elucidate the source of luminal blood.

Mucositis has been identified as a significant complication from chemotherapy and the reason for emergency department (ED) visits for cancer patients. Although the symptoms are usually related to pain, dysphagia, and poor nutrition, severe mucositis can present with significant UGIB.\textsuperscript{10}

PUD can be a source of occult and major UGIB. The primary risk factors include the use of NSAIDs and smoking. Frequently, patients with cancer may use NSAIDs as an adjuvant to control cancer-related pain. For example, NSAIDs are used commonly in the setting of bony metastases from prostate or breast cancer. Patients with neoplasms in the thorax may also be at risk for mucosal ulceration secondary to radiation effects. Intensive care unit–related stress ulceration is a common complication in cancer patients. Brisk bleeding from stress ulcers, as with any UGI source, is likely to present as melena.

Bleeding from esophageal varices is one of the most dramatic and emergent sources of UGIB. Varices develop secondary to portal hypertension, most frequently in the setting of primary liver disease and cirrhosis. Cirrhosis and hepatitis may be associated with the development of hepatocellular carcinoma. Portal hypertension can also develop from metastatic tumor infiltration of the liver.\textsuperscript{11,12} Variceal bleeding typically presents as coffee ground hematemesis (because of oxidized blood) or frank blood. Rate of blood loss can be extremely fast as the varices are often large caliber veins. Patients may become hemodynamically unstable quickly and require rapid diagnosis and aggressive intervention.

**Diagnostic Evaluation**

Patients presenting with UGIB should be rapidly assessed with a focused history and physical examination in concert with initial resuscitation and diagnostic assessment. Information obtained should include history of pharmaceutical anticoagulation, bleeding diatheses, NSAID use, prior GI bleed, chemotherapy, and radiation treatment regimen; stool habits and nature of any recent emesis are particularly important.\textsuperscript{8} In the setting of malignancy, location of disease and extent of spread are important to elucidate. For example, a mediastinal malignancy presenting with hematemesis should prompt the clinician to consider invasion into a large vascular structure and impending vascular collapse.\textsuperscript{13–15} The presentation of upper GI bleed may represent either initial presentation of disease or significant advancement of known malignancy; therefore, a broad evaluation must be undertaken.

Initial stabilization must include rapid assessment of airway, breathing, and circulation, intravenous (IV) access, and laboratory collection. High-volume hematemesis with altered mental status may necessitate immediate airway management to prevent aspiration. Laboratory data should include complete blood count (CBC), chemistry panel, coagulation panel, blood type, and crossmatch. For cancer patients, multiple parameters in the CBC are useful. The hemoglobin and hematocrit values are used to establish a baseline and estimate blood loss by comparing to earlier values. The white blood count and differential can assess the effects of bone marrow suppression from tumor infiltration or chemotherapy. Finally, the platelet count is important for assessing risk of further hemorrhage and need for platelet transfusion. If this represents
an initial presentation of malignancy, the white blood count and differential may also be the first clue at a diagnosis of a hematologic malignancy. Coagulation parameters (especially international normalized ratio [INR]) may help assess the extent of disease if there are known or suspected liver metastases and raise suspicion for varices as the source of bleeding. These parameters also help to determine coagulation product replacement. The chemistry panel may help to assess other metabolic derangements to which cancer patients may be particularly susceptible, including acute renal failure, hyponatremia, hypercalcemia, hypophosphatemia/hyperphosphatemia, and hypokalemia/hyperkalemia. Liver tests (transaminases, bilirubin, and INR) may illustrate underlying pathology such as metastasis or functional obstruction. Additional studies should be tailored to the particular individual. For example, in patients with cardiovascular disease with hypotension, trending cardiac biomarkers and analyzing serial electrocardiograms may be appropriate to exclude associated cardiac ischemia; altered mental status with suspected liver involvement may be assessed with an ammonia level.

In addition to laboratory data, other interventions may be appropriate in assessing patients with suspected UGIB. Nasogastric aspiration with lavage may be useful in confirming the source and the briskness of bleeding, and it may increase the sensitivity of esophagogastroduodenoscopy (EGD). During lavage, bright red blood indicates active bleeding, whereas coffee ground gastric contents generally indicate recent bleeding as a result of oxidation of hemoglobin. Continued bright-red blood aspiration with repeated lavage is suggestive of severe bleeding. A nonbloody aspirate does not preclude recent gastric or duodenal hemorrhage. However, a nonbloody bilious aspirate may indicate bleeding distal to the ligament of Treitz or proximal bleeding that occurred several hours earlier.

Initial measures include volume resuscitation with crystalloids in addition to blood component therapy, along with large bore IV access, oxygen, and monitoring. Fluid resuscitation is initiated with a 500 to 1000 mL bolus of crystalloid depending on vital sign abnormalities. Repeat boluses can be initiated for persistent tachycardia and hypotension. Patients in shock that do not respond to initial fluid resuscitation of 2 L of crystalloid should be treated aggressively with packed red blood cells (PRBC) to maintain oxygen carrying capacity and tissue perfusion. PRBC transfusion is otherwise targeted to maintain a hematocrit at between 25 and 27 for most patients. Caution should be exercised to not overtransfuse certain patient populations. Transfusing to a hematocrit greater than 27 in cirrhotic patients has been shown to increase portal pressures and exacerbate bleeding. Coagulopathy can be treated with administration of fresh frozen plasma (FFP) or platelets as appropriate. Although there is debate on the ideal replacement ratio, 1 unit of FFP for every 4 units of PRBCs can be used as a guideline to prevent dilutional coagulopathy, with the goal of keeping the INR less than or equal to 1.5. Platelets should be replaced in the case of active bleeding when platelet counts are less than 50,000; otherwise a platelet count of greater than 20,000 is usually safe.

Initial empiric therapy with a proton pump inhibitor (PPI) is recommended before endoscopy. Although PPI therapy has benefits for endoscopy, it has not been shown to decrease mortality overall. PPI therapy has been beneficial in mitigating re-bleeding and the need for transfusions. Treatment with PPIs has been postulated to promote hemostasis by neutralizing pH even with bleeding that is not directly the result of acid exposure. PPI therapy is initiated intravenously (omeprazole or pantoprazole) with a bolus of 80 mg followed by a drip at a rate of 8 mg/h. Intravenous erythromycin 250 mg bolus or 3 mg/kg over 30 minutes can be given 30 to 90 minutes before EGD to facilitate gastric emptying of retained blood.
Therapeutic Interventions for Suspected Variceal Upper Gastrointestinal Bleeding

Variceal bleeding presents specific challenges because of the nature of vascular injury and the unique physiology of patients with cirrhosis. The American Association for the Study of Liver Disease (AASLD) and the American Society of Gastroenterologists have issued clinical guidelines for the management of variceal bleeding. Acute hemorrhage in patients with cirrhosis requires emergent intervention with volume support and blood transfusions to maintain a hemoglobin of 8 g/dL. Short-term antibiotic prophylaxis should also be initiated to reduce infectious complications and prevent variceal rebleeding. The AASLD recommends norfloxacin (400 mg orally twice a day), or ciprofloxacin (400 mg intravenously [IV] every 12 h). In centers of high fluoroquinolone resistance, 1 g of ceftriaxone daily may be preferable. Somatostatin (or analog) therapy should be initiated and continued for 3 to 5 days if the hemorrhage is suspected to be from varices because it decreases portal pressures. EGD should be performed within 12 hours to confirm the diagnosis and to treat an identified lesion. Uncontrolled or recurrent bleeding is an indication for a transjugular intrahepatic portosystemic shunt procedure. And finally balloon tamponade should be used as a temporizing measure for a maximum of 24 hours in patients with uncontrollable bleeding awaiting definitive management.

Patients with advanced hepatocellular carcinoma have an increased short-term mortality rate compared with other patients with variceal UGIB due to recurrent hemorrhage. Maintenance variceal ligation may be helpful in these patients to control recurrent hemorrhage. In addition, transarterial chemoembolization is another option to control bleeding in these patients. Injection sclerotherapy can also be used in patients with unresectable hepatocellular carcinoma.

Special Considerations in Cancer Patients

Nausea and vomiting is common in patients undergoing chemotherapy and can lead to hematemesis from Mallory-Weiss tears. Typically, the vomitus becomes blood-streaked after several episodes of emesis or wretching. In the absence of risk factors for portal hypertension, this can be managed conservatively. Vomiting and retching should be controlled. Chemotherapy-induced nausea and vomiting is a common complaint in the ED setting. Usually, metoclopramide is recommended if the patient is not already on 5-hydroxytryptamine 3A antagonist, such as ondansetron. Intravenous fluids are appropriate as significant vomiting may cause dehydration.

Radiation and chemotherapy are also risks for upper GI irritation, erosions, and bleeding. Radiation effects or direct extension of tumor can cause fistula development to the aorta and other vascular structures resulting in massive UGIB. Certain chemotherapeutic combinations have also been shown to cause acute gastroesophageal erosions. H2 blockers and proton pump inhibitors have been successfully shown to treat chemotherapy-related esophageal, gastric, and duodenal injury. EGD has been used to evaluate patients before and after PPI treatment and improvement in erosive and ulcerative lesions has been demonstrated. In a large, longitudinal study over 6 years of 451 patients with acute and chronic leukemias and other myeloproliferative disorders, 7.1% of patients suffered a GIB, mostly UGIB resulting from erosive gastritis, duodenal ulcers, and neutropenic enterocolitis. These disorders were frequently complicated by thrombocytopenia.

Finally, certain neoplasms have a propensity for erosion and hemorrhage. Gastric mucosa-associated lymphoid tissue lymphomas have been implicated as an important source of UGIB. These lymphoid tumors can infiltrate and extend into submucosal vascular structures and be a source of occult bleeding and massive GI

Gastrointestinal Bleeding in the Cancer Patient
hemorrhage. These lesions are also particularly susceptible to significant tumor necrosis after treatment and can lead to hemorrhage. There have been several case reports of UGIB from various tumors that have extended or eroded into mediastinal vascular structures requiring significant measures to control the bleeding, such as emergent thoracotomy.\textsuperscript{11–13,15,43} Known primary or metastatic disease in the mediastinum or near the surrounding vascular structures should raise the specter of erosion into a major vessel.\textsuperscript{13–15,43} These circumstances present with vital sign abnormalities, ongoing hematemesis, melena, or hematochezia and necessitate aggressive stabilization.

Patients who have had resection of pancreatic carcinoma and received intraoperative radiation therapy may present with UGIB complicated by portal system occlusion. Bleeding sources identified in these cases include esophageal and stomach varices as well as jejunal ulcers.\textsuperscript{44} Patients that have had endoscopic mucosal resection of gastric cancers are prone to immediate and recurrent hemorrhage, sometimes requiring repeated endoscopy to control bleeding.\textsuperscript{45}

Distinct from patients without known cancer, patients with gastric cancer may benefit from acute surgery to control hemorrhage and may not be amenable to endoscopic intervention.\textsuperscript{46–48} Despite the improvement in mortality rate with surgery, curative resection is relatively uncommon, and postoperative complications are common.

LOWER GASTROINTESTINAL BLEEDING

Acute LGIB is one of the most common GI indications for hospitalization, increasing dramatically with age.\textsuperscript{49} Colorectal cancer, commonly presenting with LGIB, is the fourth most commonly diagnosed cancer and second leading cause of cancer-related deaths in the United States.\textsuperscript{50} Approximately 147,000 cases are diagnosed annually with over 57,000 deaths.\textsuperscript{50} Depending on patient population, somewhere between 1% and 17% of acute LGIB is due to colonic neoplasms.\textsuperscript{51} Postpolypectomy bleeding accounts for an additional 2% to 6% of LGIB episodes.

Etiologies

Common etiologies for LGIB are summarized in Box 2. Patients with colon cancer are also susceptible to these causes. In a large study combining seven case series with a total of 1333 patients with LGIB, 19% were found to have a colorectal cancer or polyp, with these occurring more commonly in older patients.\textsuperscript{52} The source of the bleeding is usually erosion or ulceration of the mucosal surface and is the most

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<td><strong>Major causes of lower gastrointestinal bleeding</strong></td>
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<td>Diverticular disease</td>
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<td>Ischemic colitis</td>
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<td>Angiodysplasia</td>
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<td>Postpolypectomy bleeding</td>
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<td>Hemorrhoids</td>
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<td>Anal fissures</td>
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<td>Inflammatory bowel disease</td>
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common reason the patient comes to clinical attention. In addition, bleeding after polypectomy or biopsy is a significant cause of LGIB occurring in a biphasic fashion—immediately postprocedure and up to 15 days later due to sloughing of the eschar. The incidence of clinically significant postpolypectomy bleeding is decreasing from an initial rate of 2% to 3% to currently 0.2% to 0.6%.52

Other etiologies depend on the patient’s treatment modalities and time course of disease process. Neutropenic enterocolitis occurs in patients who have prolonged neutropenia; graft-versus-host disease (GVHD) appears any time after a stem cell transplant; infectious diarrhea can happen anytime during treatment with unusual species to be sought when the patient is immunosuppressed or exposed to nosocomial sources. Radiation-induced proctosigmoiditis is most frequent at 9 to 14 months (but can occur up to 2 years) after external radiation therapy or local brachytherapy. Arterial-luminal fistulas or tumor necrosis can occur at any time during therapy. In addition, any of these etiologies can be complicated by a superimposed coagulopathy from metastatic disease, therapeutic anticoagulation, or chemotherapy.

**Presenting Signs and Symptoms**

Traditionally, LGIB is defined as bleeding occurring distal to the ligament of Treitz.53 Identifying the approximate location of the bleeding source according to characteristics of the stool is usually imprecise. The appearance depends on the briskness of hemorrhage and the speed of passage of stool through the GI tract. Generally, bright-red blood per rectum suggests left-sided colonic lesions with maroon or melemic-appearing stool indicating a right-sided or UGI source. Important history obtained in the ED includes the nature and duration of bleeding; associated symptoms (abdominal pain, fever, or weight loss); history of constipation or diarrhea; known diverticulosis or previous PUD; current medications that might influence bleeding (NSAIDs, aspirin, coumadin, or heparin); history of cancer and treatment including surgery, endoscopic polypectomy, chemotherapy, or radiation therapy; family history of colon cancer; and history of comorbid conditions (chest pain or shortness of breath) that may affect further evaluation or disposition decisions. Chronic intermittent passage of small amounts of hematochezia is the most common presentation of LGIBs.51

Physical examination should concentrate on hemodynamic stability,53 comorbid conditions, abdominal tenderness for possible perforation or inflammation (ischemic colitis or inflammatory bowel disease), rectal examination for stool color and guaiac, and identification of anorectal lesions such as hemorrhoids or fistulas.

**Evaluation**

**Supportive care**

The initial goal of the ED physician in patients with LGIBs is to assess for hemodynamic stability with vital signs, including orthostatic blood pressure measurements where necessary, and to achieve reliable and large bore vascular access including a central line when appropriate for frequent blood draws and assessing central venous pressures. A nasogastric tube (NGT) is recommended to evaluate for potential brisk UGIB, which may present with similar signs and symptoms consistent with a LGIB. Irrigation with a NGT has a fairly good negative predictive value if there is visible bile in aspirate.51 The NGT can also be used to administer bowel-cleansing solutions for urgent colonoscopy.

The apparent briskness of bleeding, hemodynamic stability, and associated history and physical findings guide the laboratory workup of the patient with LGIB associated with suspected or known cancer.53 A CBC should be attained to assess hematocrit
and red blood cell indices, in addition to a white blood cell count with manual differential and platelet count. A bedside hemoglobin measurement (eg, Hemocue) can be helpful to get a quick estimate of blood loss and hasten the ordering of blood for transfusion. Coagulopathy is a frequent finding in patients with cancer and should be assessed with an INR and a partial thromboplastin time. Blood for type and cross should be sent if the patient is hemodynamically unstable, has a new low hematocrit, or shows other secondary effects of acute anemia such as myocardial ischemia. In addition, electrolytes and liver function tests are also sent because these patients frequently have comorbidities. Coagulopathy is a frequent finding in patients with cancer and should be assessed with an INR and a partial thromboplastin time. Blood for type and cross should be sent if the patient is hemodynamically unstable, has a new low hematocrit, or shows other secondary effects of acute anemia such as myocardial ischemia. In addition, electrolytes and liver function tests are also sent because these patients frequently have comorbidities. An ECG is recommended if cardiac ischemia or electrolyte abnormalities are suspected. Given that risk stratification is not as straightforward as in UGIB and that most LGIBs spontaneously stop, frequent monitoring and observation are key components of management.

**Colonoscopy**

As with UGIB, endoscopic evaluation is the key to the definitive diagnosis of LGIB in most patients. Though specific therapy is more limited than in UGIBs, colonoscopy usually localizes and diagnoses the cause of bleeding expeditiously. Biopsies can be obtained, and noncancer-related bleeding can be excluded. There are risks in the ED to emergent endoscopy, which include poor visualization due to lack of extensive bowel cleansing and the potential adverse events associated with procedural sedation. Rapid bowel cleansing can be obtained in 2 hours by administering a large volume of polyethylene glycol solution, but the optimal timing of colonoscopy is still controversial. Overall, complication rates are low (1%-2%), but fluid overload, perforation and subsequent sepsis can occur. A randomized controlled trial of urgent versus routine colonoscopy in patients with apparent LGIBs demonstrated that urgent colonoscopy improved detection of the source of bleeding but did not reduce mortality, hospital stay, transfusion requirements, need for surgery, or rebleeding episodes.

**Radionuclide imaging**

Other modalities for diagnosis are considered when colonoscopy is negative or the source is suspected to be in the small bowel. Radionuclide imaging is more sensitive than angiography because it requires a lower bleeding rate but is less specific. There are two modalities available, each with different strengths and limitations:

1) Technetium-99m sulfur colloid, which is rapidly cleared from intravascular space so the scan is made shortly after injection. Its uptake in the spleen, liver, and bone marrow may obscure the GI source.
2) 99mTc pertechnate-labeled red cells need to be imaged frequently including the first 30 minutes and then every few hours up to 24 hours to pick up intermittent bleeding.

A comparison of the two techniques found similar detection rates for LGIB. The two techniques mentioned localize only to an area of abdomen, and there are a significant number of false positive findings that may lead to unnecessary surgeries. Patients with a negative scan are likely to have negative arteriograms.

**Capsule endoscopy**

Several studies have found capsule endoscopy (swallowing a wireless camera to allow continuous video recording of the intestinal mucosa appearance) superior to other modalities for obscure GIB, especially in the small bowel, but it is less helpful in the colon because of stool retention, short battery life, and decreased visual field due to the large caliber of the colon.
Computed tomography angiography
Multidetector helical CT requires active bleeding for good localization. In one study, it was found to have a sensitivity and specificity of 90% and 99%, respectively, in the setting of massive bleeding compared to angiography as the gold standard.61 Other studies have confirmed its usefulness in a variety of patients with LGIB not localized by colonoscopy.62–65

Angiography
Mesenteric angiography requires ongoing blood loss of 1 to 1.5 mL/min to be well visualized.66 In addition, angiography offers therapeutic options to control bleeding that other modalities do not, including vasoconstriction with vasopressin or microembolization with a variety of substances. Frequently, bleeding due to cancer is not easily amenable to embolization, but it can be considered if the patient is a poor operative candidate.67 A significant number of patients with negative angiograms still require surgery, and there is a significant complication rate associated with intestinal and lower extremity ischemia, arterial dissection, renal failure due to contrast infusion, and catheter site infections.

Management

Colonoscopy
Colonoscopy is the primary evaluation and potential therapeutic modality for LGIB. Only 12% to 27% of patients have a lesion treatable by endoscopic therapy as compared to 51% of patients with UGIB.52

Emergent surgery
Emergent surgery may be indicated for colorectal cancer complications including perforation, fistulas, obstruction, and hemorrhage. Emergent surgery has a high mortality and morbidity, but outcomes have gradually improved with better supportive care.68,69 Better outcomes are found with more accurate preoperative localization resulting in less rebleeding. Surgery for patients with LGIB has defined risks and must take into account comorbidities.70 Patients in high-risk groups may have lesions amenable to less invasive treatment such as angiography.

Angiotherapy
Angiographical intervention with arterial embolization is usually reserved for high–surgical risk patients, but it carries a higher risk of colonic infarction compared to UGI angiography due to the lack of collateral circulation.71 Embolization is an optimal therapy for patients with vascular disease because vasopressin infusion may induce cardiac and cerebral ischemia.

Disposition
Patients with LGIBs are frequently hospitalized for diagnostic and therapeutic measures, and the potential for hemodynamic instability is high, especially in the elderly or patients with significant comorbidities. Identifiable high-risk patients (hemodynamically unstable, serious comorbid diseases, persistent bleeding, need for multiple transfusions, acute abdomen) should be hospitalized in an intensive care unit.

Special Situations

Neutropenic enterocolitis
This condition is also known as typhlitis, necrotizing enterocolitis, or ileocecal syndrome. Neutropenic enterocolitis likely occurs from the combination of GI mucosal injury from cytotoxic drugs, profound neutropenia, and other impaired host defenses allowing polymicrobial bacterial and fungal invasion.72 This leads to necrosis of the
bowel wall, almost always involving the cecum and often extending into the right colon and ileum. This disease should always be considered in a profoundly neutropenic patient (absolute neutrophil count < 500) with fever and abdominal pain that is usually located in the right lower quadrant. Other symptoms include distension, nausea, vomiting, diarrhea, and watery or bloody diarrhea. It can be diagnosed with abdominal CT that usually shows a dilated, fluid-filled, and distended cecum with bowel wall thickening, air, or hemorrhage that may progress to perforation or abscess. The initial treatment of patients without evidence of perforation is conservative with supportive care, bowel rest, and broad-spectrum antibiotics that should include the addition of antifungals if there is no improvement in 72 hours. Granulocyte colony stimulating factor may be effective in normalizing the white count, allowing containment of microbial invasion. Patients with perforation, peritonitis, or severe bleeding require surgical intervention with the complete removal of all affected bowel.

**Graft-versus-host disease**

The GI manifestations of GVHD may be severe with abdominal cramping and diarrhea with stool output that may reach up to 10 L a day. Patients may lose enough blood to require several units of PRBCs per day. A rectal biopsy may be helpful to distinguish this entity from cytomegalovirus (CMV) colitis, showing crypt cell necrosis with accumulation of debris. With severe disease, large mucosal areas of the colon may be denuded similar to the dermal manifestations of GVHD. Less frequently, UGI involvement with GVHD manifests with anorexia, dyspepsia, nausea, and vomiting. UGI GVHD is more amenable to immunosuppressive therapy than LGI involvement. Aminocaproic acid, a potent antifibrinolytic agent, may help to slow down blood loss from the GI tract associated with GVHD.

**Infectious diarrhea**

Community-acquired pathogens (salmonella, shigella, campylobacter, *Escherichia coli* O157) are also common in the patient with cancer. In addition, with diarrhea and LGIB the clinician should also evaluate for *Clostridium difficile* and other opportunistic infections such as CMV. CMV may cause an ulcerative colitis that is diagnosed with a mucosal biopsy and can be treated with ganciclovir or foscarnet.

**Radiation proctitis**

Acute external radiation injury to the rectosigmoid colon occurs within 6 weeks of therapy with symptoms of diarrhea, tenesmus, and, less commonly, bleeding that can result from friable, mucosal telangiectases. This entity can account for 1% to 5% of cases of LGIB that require hospitalization. A chronic, delayed form of radiation proctitis occurs at 9 to 15 months after radiation therapy with similar symptoms. For patients who have received prostatic brachytherapy, symptoms including LGIB peak at 4 and 16 months after placement. In addition, one needs to exclude a mucosal ulcer or cancer recurrence as late complications of radiation therapy of the distal colon. Not surprisingly, the severity of symptoms including the amount of LGIB is directly proportional to the delivered dose of radiation per volume of tissue, when prostatic brachytherapy is combined with external radiation therapy or when a patient has a comorbidity such as diabetes.

There are various therapy regimens for the treatment of significantly symptomatic radiation proctitis including topical formaldehyde or formalin to thrombose bleeding vessels; however, this therapy may induce acute colitis. Several studies, mostly with patients who have cervical cancer, have shown efficacy of sucralfate enemas to stop the LGIB of radiation proctitis. For LGIB refractory to topical treatment, colonoscopically applied argon laser plasma coagulation has been found useful in
multiple case series.89–92 One small case series of six patients demonstrated that a diverting loop colostomy seemed to help LGIB not stopped by the above methods.93

**Postprostatic biopsy bleeding**
A small case series found the use of a vaginal tampon for bleeding control to be helpful in patients with postprostatic biopsy bleeding.94

**Pediatric considerations**
Pediatric patients presenting with evidence of LGIB are much less likely to have an etiology associated with cancer or cancer-related therapies. Children are at risk for similar GI toxicities associated with cancer chemotherapy including typhlitis and GVHD. They have less exposure to abdominal/pelvic radiation therapy because genitourinary and colonic cancers are rare and there is a reluctance to use radiotherapy to avoid reproductive toxicity. Pediatric patients are also less likely to have a life-threatening cause of LGIB, and therefore a noninvasive evaluation is usually indicated.95 The differential diagnosis for pediatric LGIB is age and risk-factor dependent (Box 3).

### Box 3
**Most common pediatric causes of gastrointestinal bleeding**

- Neonates
- Swallowed maternal blood
- Anorectal fissures
- Necrotizing enterocolitis
- Malrotation
- Hirschsprung disease
- Coagulopathy
- *Infants*
- Anorectal fissures
- Allergic colitis
- Intussusception
- Meckel diverticulum
- Hemolytic uremic syndrome
- Henoch-Schönlein purpura
- Lymphonodular hyperplasia
- Gastrointestinal duplications
- *Children*
- Infectious diarrhea
- Juvenile polyps
- Inflammatory bowel disease

SUMMARY

UGIB has a relatively high mortality rate despite advances in treatment and detection. Although cancer is a less likely primary cause of upper GI bleeding, hematologic and anatomic cancer-related changes complicate the work-up and management of UGIB. Additionally, cancer treatments can have a variety of consequences that can lead to occult or massive hemorrhage. Initial management for GI bleeding is similar in patients with and without cancer; however, special consideration must be given to patients with cancer to address the various complicating factors that include related hematologic, metabolic, and structural abnormalities.

Patients with cancer that have LGIBs are usually stable, allowing a thorough evaluation including colonoscopy to localize the source of bleeding. A thorough history, physical examination, and laboratory work-up in the ED can help narrow the differential diagnosis. There are several additional imaging modalities if colonoscopy fails to define the etiology of LGIB in the cancer patient. Therapeutic interventions to stop LGIB require a multidisciplinary team that includes gastroenterologists, interventional radiologists, and surgeons. The ED physician can assist with initial stabilization, evaluation, and disposition of the cancer patient with bleeding of the gastrointestinal tract.

REFERENCES


