Lower gastrointestinal bleeding in patients with cirrhosis.

Maxwell M Chait[*]

The Columbia Doctors Medical Group, 180 East Hartsdale Avenue, Hartsdale, New York 10530, USA

Abstract

Lower gastrointestinal bleeding (LGIB) in patients with cirrhosis may be associated with life-threatening complications similar to upper GI bleeding (UGIB). The incidence, cause and severity of LGIB in patients with cirrhosis correspond to the child-Pugh class, the increase in portal hypertension, coagulopathy, age-specific gastrointestinal diseases, co-morbid diseases and polypharmacy. Bleeding may be chronic and mild or severe and life threatening, requiring endoscopic, radiologic or surgical intervention.

Introduction

Lower gastrointestinal bleeding (LGIB) in patients with cirrhosis may be associated with life-threatening complications similar to upper GI bleeding (UGIB). The data on LGIB in patients with cirrhosis is surprisingly small. The true incidence, diagnoses, risks of bleeding and results of treatment remain poorly defined, since there are no large epidemiologic studies available. Much of the data are from small studies and studies from the general population [1-3] LGIB in patients with cirrhosis occurs more often in younger patients than in the general population. This helps explain the variation in LGIB causes and why the age of the patient is such an important consideration, especially when a patient may have mild cirrhosis [4]. The most common causes of LGIB in patients with cirrhosis are portal hypertensive colopathy, colorectal varices and hemorrhoids. Whereas the most common causes of LGIB in the general population are diverticulosis coli and vascular ectasia [4]. LGIB is less common than UGIB in patients with cirrhosis. LGIB is a source of bleeding in 15-20% of cases of GI bleeding as compared to 80-85% of cases that occur from an upper GI source. In a longitudinal study by Brescia in which patients with cirrhosis were followed for two years, UGIB occurred in 34% and LGIB occurred in 6% of cases [5]. In the general, the incidence of LGIB increases with age and is more common in men than women [4]. In the United States the incidence of LGIB in the general population ranges from 20.5 to 27 per 100,000 persons per year with a greater than 200 fold increase from the third to the ninth decade of life [4].

The incidence and cause of LGIB in patients with cirrhosis corresponds to extent of liver disease with advancing Child-Pugh class, portal hypertension, coagulopathy, associated age-related gastrointestinal diseases, co-morbid diseases, and polypharmacy [1,4,6]. Gastrointestinal diseases that cause LGIB in patients with cirrhosis include portal hypertensive colopathy and enteropathy (PHC) and ileal, colorectal and anorectal varices. Less common causes are diverticulosis coli, vascular ectasia, inflammatory diseases, colonic neoplasia related disease and anorectal disorders which are more common in the general population [1-4]. Co-morbid diseases that are associated with an increased incidence and severity of LGIB include extent of liver disease with advancing Child-Pugh class, portal hypertension, coagulopathy, cardiovascular disease, cerebrovascular disease, renal disease, diabetes mellitus and malignancy. Polypharmacy that increases the risk of LGIB is important. The use of antibiotics, immunosuppressive agents, anticoagulants and non-steroidal anti-inflammatory drugs (NSAIDS) is common in these patients [1,4,6].

LGIB can be acute, occult or obscure in nature. Acute LGIB presents as melena or hematochezia. Although the source of melena is most often from the upper GI tract, it may also be from the small intestine or the right colon. Hematochezia is the passage of bright red blood per rectum, with or without stool. Occult bleeding is bleeding not apparent to the patient and is usually detected with stool guaiac testing. It is a common presentation of LGIB, occurring in 10% of the adult general population [4]. Remarkably, patients can loose up to 100 mL of blood per day and still have grossly normal appearing stools [7]. Obscure bleeding is bleeding in which the source of bleeding is difficult to detect on routine endoscopic and radiologic examinations and occurs in approximately 5% of all patients who present with LGIB [8].

Gastrointestinal diseases causing lower GI bleeding

The most common causes of LGIB in patients with cirrhosis are portal hypertensive colopathy, ileal, colorectal and anorectal varices and hemorrhoids [1-3]. Other gastrointestinal diseases that cause LGIB in these patients that are often age-specific include vascular ectasia, diverticulosis coli, inflammatory diseases, colonic neoplasia and anorectal disorders (Table 1) [4,9].

Vascular lesions associated with LGIB: Vascular lesions are the most common causes LGIB in patients with cirrhosis. They include PHC and ileal, colorectal and anorectal varices. Vascular lesions that can occur in cirrhosis but are seen more commonly in the general population are ischemic bowel disease, vascular ectasia, telangiectasia, hemangiomas, congenital arteriovenous malformations (AVM) and Dieulafoy's lesion.

Ileal, colorectal and anorectal varices: Portal hypertension increases venous pressure and can cause varices outside the esophagus, including the ileum, colon and rectum [10].

Table 1. Causes of LGIB in patients with liver disease.

Vascular diseases	Diverticulosis coli	Neoplasia related disease	Anorectal lesions
Portal hypertensive enteropathgy/colopathy	Inflammatory disease of the colon	Neoplasms	Hemorrhoids
Ileal, colorectal and anorectal varices	Infectious colitis	Post-polypectomy bleeding	Stercoral ulcer
Ischemic bowel disease	Idiopathic inflammatory bowel disease		Solitary ulcer syndrome
Vascular ectasia	Post-irradiation colitis		
Telangiectasia			
Hemangiomas			
Congenital arteriovenous malformations			
Dieulafoy's lesion			

The hepatic venous pressure gradient (HVPG) is normally 3-5 mmHg. HVPG greater than 12 mmHg is associated with development of varices. Greater than 20 mmHg it associated with a high risk of variceal hemorrhage [11]. Portal vein obstruction associated with mesenteric venous thrombosis and portal vein thrombosis may further exacerbate the risk of development of gastrointestinal varices and further promote bleeding. Portal hypertension causes venous dilation of the submucosal channels in the regions of the GI tract where splanchnic and systemic venous anastomoses occur. In one study 7.2% of patients studied angiograghically had colorectal varices [12].

Portal hypertensive colopathy (PHC): PHC is present in 48.5 to 66% of patients with cirrhosis. The incidence of PHC increases with worsening Child-Pugh class and coagulopathy, especially decreasing platelet count [1,10,11]. It is important to differentiate changes of PHC from vascular ectasia of the colon. PHC often occurs in a younger population with cirrhosis. These lesions are larger in number and more widely distributed than vascular ectasia of the colon. Histopathologically, there is dilatation of blood vessels in the submucosa, increased lymphocytes and plasma cells in the lamina propria and edema in the mucosa [13,14].

Ischemic bowel disease: Ischemic bowel disease accounts for 3% to 9% of all cases of LGIB in the general population and increases with advancing age [15]. The incidence of bowel ischemic in patients would be expected to be higher in older patients with cirrhosis or factors leading to ischemia. Colonic atherosclerosis predisposes to bowel ischemia and ischemic colitis [4]. Ischemic bowel disease occurs from reduced blood supply to the colon from a variety of factors as hypotension, portal vein obstruction, vascular constricting medications, such as vasopressin and vascular embolic events [16]. Although the precipitating event or factors leading to the lesion may not be identified, a history of a hypotension, the use of vasopressor agents to treat portal hypertension or bleeding, such as norepinephrine or vasopressin support the diagnosis. Patients often present with lower abdominal cramping type of pain followed by hematochezia or bloody diarrhea. LGIB in ischemic bowel disease is rarely severe. Ischemic bowel disease commonly involves the watershed areas of the colon. Although usually acute, some patients may develop a chronic colitis. It is often unresponsive to standard colitis treatment and may be complicated by perforation or stricture formation that requires surgical intervention [17].

Vascular ectasia: Vascular ectasia, also termed angiodysplasia can occur in the colon and small intestine. It is one of the leading causes of LGIB the general population [4]. Vascular ectasia occurs with much greater frequency in older patients.

Therefore, the incidence of vascular ectasia in patients with cirrhosis would vary with the age and is noted in over 25% of asymptomatic individuals over the age of 60 [4,18]. Vascular ectasia causes LGIB in 12% to 40% of patients in the general population, depending upon the study [4]. Vascular ectasia is the most common source of obscure GI bleeding, occurring up to 60% of cases in the general population of Western Europe and the United States [19,20]. Vascular ectasia is a degenerative lesion of previously normal blood vessels that may occur anywhere in the colon and small bowel. These lesions are noted to be ectatic, distorted veins, venules and capillaries, lined only by endothelium and occasionally by a small amount of smooth muscle [21,22]. Colonic lesions occur most commonly in the right colon because the right colon region has the largest luminal diameter with the highest resting wall tension. There is an association of vascular ectasia and aortic stenosis [23]. The bleeding from vascular ectasia is usually subacute, but can be chronic and recurrent, especially in lesions of the small bowel. LGIB may present as iron deficiency anemia and occult blood positive stools, but may be massive in up to 15% of patients with vascular ectasia.

Less common vascular lesions as a source of LGIB are telangiectasia, hemangiomas, congenital arteriovenous malformations (AVM) and Dieulafoy's lesion. Dieulafoy's lesion is a large superficial artery underlying a mucosal defect, which is rare and difficult to find when not bleeding [24].

Anorectal lesions: Anorectal lesions occur in up to 40% of patients with cirrhosis [2]. These include hemorrhoids, rectal fissure, stercoral ulcer and solitary rectal ulcer syndrome.

Hemorrhoids and rectal fissures: Hemorrhoids and rectal fissures are a common source of LGIB in patients with cirrhosis as well as in the general population. LGIB usually presents with intermittent low-volume hematochezia, which often coats the stool [25].

Stercoral ulcer and solitary rectal ulcer syndrome: Stercoral ulcers and the solitary rectal ulcer syndrome are an unusual source of LGIB that can occur in debilitated or elderly patients. Stercoral ulcers are the result of mucosal damage by hard impacted stool in the rectum, from manipulation or foreign body injury, such as from a rectal tube in the hospitalized patient. The solitary rectal ulcer syndrome is due to rectal prolapse and mucosal damage from constipation and straining [26].

Diverticulosis coli

The incidence of diverticulosis coli increases with age from approximately 5% of individuals at age 40 to 65% of individuals at age 85 in the countries of Western Europe and the United

States [27]. Therefore, the incidence of diverticular disease in patients with cirrhosis would vary according to the age of the patient. LGIB occurs in approximately 3% to 5% of patients with diverticular disease, usually in the form of hematochezia [28]. The incidence of LGIB ranges from 15% to 48% of the general population, depending upon the series [29,30]. Although about 90% of colonic diverticula are in the left colon, 50%-90% of diverticular LGIB occurs from right-sided colonic diverticula [31]. Diverticula may also arise in the small intestine where they may be source of obscure bleeding, such as from a small bowel diverticulum, such as Meckel's diverticulum.

LGIB from diverticula presents as painless, acute hematochezia. However, maroon colored stools or melena may occur in bleeding from right-sided colonic diverticula and small bowel diverticula. Although diverticular LGIB can be severe with significant morbidity and mortality, it usually ceases spontaneously, with less than 1% of patients requiring greater than four units of blood [4,27].

Inflammatory diseases of the colon: LGIB can occur from inflammatory diseases of the colon in 9-21% of cases in the general population and can occur in patients with cirrhosis [32]. Causes of inflammatory bowel disease in patients with LGIB include infectious colitis and idiopathic inflammatory bowel disease.

Infectious colitis: Patients with cirrhosis have a significant risk for infections, such as urinary tract infections, spontaneous bacterial peritonitis, spontaneous bacteremia, aspiration pneumonia, and infectious colitis [33]. Infectious colitis can be associated with LGIB. The mortality from infectious colitis increases with age and comorbid illness [34]. LGIB is rarely massive in patients with infectious colitis. Hematochezia is noted in less than 10% of cases [33]. The most common causes of enteric infections are Campylobacter, Salmonella, Shigella, *E. coli* 0157:H7 and *Clostridium difficile* [35]. *C. difficile* must be considered in patients who have recently been treated with antibiotics or have been in long-term care facilities and hospitals. Opportunistic infections are common in this population of patients. Cytomegalovirus (CMV) is an important cause of infectious colitis, especially in the immunocompromised patient, such as the post-liver transplant patient on immunosuppressives. Other infections as Tuberculosis involving the gastrointestinal tract leading to LGIB can occur in these patients. Infectious colitis often presents with a history of undercooked fish or meat consumption and during outbreaks of bloody diarrhea in the community and in long term care facilities or hospitals. *E. coli* 0157:H7 can cause significant complications, such as acute thrombotic thrombocytopenic purpura and death [36].

Idiopathic inflammatory bowel disease (IBD): IBD can be associated with liver disease and cirrhosis. Liver diseases that are known to be associated with IBD include NAFLD, chronic active hepatitis, primary biliary cirrhosis and primary sclerosing cholangitis (PSC) [37]. It occurs most often in younger individuals with a second peak occurring between the ages of 60 and 70 [38]. Although LGIB is common with IBD, severe hematochezia is infrequent [39,40].

Post irradiation colitis: Post irradiation colitis and proctitis are unusual source of LGIB and occur more often in the elderly patient with malignancy requiring irradiation, such as prostate cancer and gynecological malignancies. LGIB can be massive or occult with chronic iron deficiency anemia. It can develop acutely or many years after treatment [40].

Neoplasia related disease

Neoplasms: LGIB related to benign and malignant neoplasms of the colon and rectum and their treatment occurs in patients with cirrhosis as in the general population with the advancing age of the patient and occurs in 10% to 20% of cases of LGIB in the general population. The incidence of colon cancer in patients with cirrhosis is not well defined. In patients with PSC there is a higher risk of colon cancer [37,41]. LGIB is the initial presenting symptom in up to 26% of patients with colorectal neoplasms [41,42]. Although LGIB from colorectal neoplasms is usually occult or mild, it can be massive LGIB if there is erosion into a large vessel or if patients have coagulopathy or are taking anticoagulants or NSAIDS.

Post-polypectomy bleeding: Post-polypectomy hemorrhage is an unusual source of LGIB. It occurs in approximately 3% of patients in the general population. The incidence in patients with cirrhosis is unknown, but would be expected to be small. It presents as hematochezia soon after polypectomy, but it may be delayed in some cases for up to one week after the procedure [43-45].

Factors increasing the severity of LGIB (Table 2)

Factors that directly affect morbidity and mortality in patients with cirrhosis and LGIB are advancing Child-Pugh and portal hypertension, coagulopathy, co-morbid disease and polypharmacy [4,11,32].

Child-pugh class: Advancing Child-Pugh class with associated hepatic decompensation, hepatic encephalopathy and hepatorenal syndrome increase morbididty and mortality in LGIB [1-3,10,11]. Portal hypertension increases venous pressure and can cause vascular associated lesions in the ileum, colon and rectum [10]. Portal vein obstruction associated with mesenteric venous thrombosis and portal vein thrombosis may further exacerbate the risk of development of gastrointestinal lesions and further promote tendency towards bleeding.

Table 2. *Factors affecting the severity of LGIB in patients with liver disease.*

Child-Pugh class	Coagulopathy	Co-morbid diseases	Polypharmacy
Hepatic decompensation	Imbalance of procoagulation and anticoagulation factors	Cardiovascular disease	Anticoagulants
Hepatic encephalopathy	Thrombocytopenia	Cerebrovascular disease	NSAIDS
Hepatorenal syndrome	Clotting factor deficiency- elevated PT, INR, aPTT	Diabetes mellitus,	Antibiotics
		Infection	Immunosuppressive agents
		Hypertension	Antiviral agents
		Neoplasia	Vasopressors

Coagulopathy: Coagulopathy is common in cirrhosis due to an imbalance of pro-coagulants and anticoagulants leading to a bleeding diathesis, venous thrombosis and portal vein thrombosis and portal hypertension leading to hypersplenism. Management of thrombocytopenia due to platelet sequestration and liver disease and the alteration in production of factors necessary for coagulation monitored by the elevated prothrombin time (PT), international normalization ratio (INR) and activated partial thromboplastin time (aPTT) is critical for the control of hemorrhage. Hematologic consultation may often be necessary in patients with massive hemorrhage, especially those with concomitant venous thrombosis [46,47].

Co-morbid disease: Co-morbid diseases directly impact LGIB to increase morbidity and mortality in these patients [4,10,11]. After hemorrhage, the presence of serious concurrent illness is the second most important factor in predicting mortality among patients with LGIB [4]. Co-morbid diseases that are associated with an increased incidence and severity of LGIB include hepatic decompensation, hepatic encephalopathy, hepatorenal syndrome, cardiovascular disease, hypertension, renal disease, infection, diabetes mellitus and malignancy. Increasing portal hypertension increases the development of vascular lesions of the colon. Atherosclerotic cardiovascular disease affecting the splanchnic circulation is a cause of ischemic bowel disease [4,10,11]. Atrial fibrillation is associated with embolic events to the intestine leading to ischemic bowel disease [17]. Aortic valve disease is associated with vascular ectasia of the colon [23]. Cerebrovascular disease, diabetes mellitus and malignancy profoundly affect the course of LGIB, with prolonged hospitalizations and increased morbidity and mortality [4].

Polypharmacy: Polypharmacy, is common in this population [4,10,11]. Immunosuppressive agents and antiviral medication can lead to the development of thrombocytopenia, leukopenia and anemia promoting bleeding and enteric infections. Use of antibiotics is associated with the development of *C. difficile* and antibiotic associated colitis. Medications that aggravate LGIB are anticoagulants and NSAIDS. NSAIDS not only cause upper GI ulceration, but also ulceration of the small intestine and colon. NSAIDS and anticoagulants increase LGIB morbidity and mortality from hemorrhage due to their effect on blood clotting factors [29,30]. In patients given vasopressors for control of hemorrhage or hypotension, mesenteric ischemia may occur leading to ischemic colitis or bowel infarction.

Clinical course and diagnostic evaluation of LGIB

The clinical course of LGIB can vary widely in patients with cirrhosis from occult bleeding to massive life-threatening hemorrhage and death. The principles of management are similar to those with upper GI bleeding [10,11]. The history and physical examination is important, but may be complicated by cognitive impairment due to hepatic encephalopathy, age and co-morbid disease. Common presenting symptoms of LGIB may not be evident in the patient with portal encephalopathy or dementia. Abdominal pain may not be present and painless life-threatening hemorrhage can occur [48]. Physical examination to assess the severity of bleeding and status of the patient is important, with emphasis on the presence of orthostatic changes, signs of cardiopulmonary compromise, stigmata of chronic liver disease

and evidence of coagulopathy. Orthostatic changes in blood pressure imply a 20% to 40% loss of circulatory volume. Informed consent to procedures may be difficult to obtain in patients who suffer from cognitive dysfunction, since they cannot sufficiently participate in the informed consent process [49,50].

The timing of tests and the type of intervention depend upon the patient's functional status, the impact on clinical outcome and the available diagnostic strategies [4]. In patients with mild, chronic or occult bleeding with or without iron deficiency anemia, workup is usually performed as an outpatient. If LGIB is severe, the patient should be hospitalized and placed in an intensive care unit. Resuscitation efforts are the cornerstone in successful management of patients with acute LGIB. LGIB can stop spontaneously with appropriate resuscitation and supportive care or may be severe and life threatening. Laboratory data, including complete blood count, comprehensive metabolic profile, blood typing and cross matching, cardiac enzymes, PT, INR, aPTT, ammonia level, stool for occult-blood, electrocardiogram and chest x-ray should be obtained. In the appropriate setting, evaluation for infection must be done. Intravenous fluids, correction of clotting disorders with vitamin K, platelets, fresh frozen plasma, and blood transfusions are often required in patients with cirrhosis. Patients should be provided with an adequate airway and oxygenation, as necessary. Treatment of hepatic encephalopathy in patients with decompensated liver disease and LGIB may be necessary with rising ammonia level in patients with massive hemorrhage.

Approximately 15% of patients presenting with hematochezia may have an upper GI source of bleeding, such as esophageal varices. Esophageal variceal bleeding is much more common in this population and can present as hematochezia [4,32]. One should perform at least an NG lavage and confirm the presence of bilious or non-bloody aspirate in patients presenting with hematochezia to help rule out an upper GI source of bleeding [10,11,51]. However, even if NG lavage is negative, upper GI endoscopy should strongly be considered in all patients to rule out UGIB.

Plain x-ray films of the abdomen, CT scan of abdomen and barium enema are most often not helpful in the acute setting for the evaluation of LGIB. However, in the appropriate setting, plain x-ray films of the abdomen may reveal evidence for obstruction or perforation. In patients with severe ischemic bowel disease the "thumb printing" signs may be seen. In the evaluation of more chronic bleeding, flexible sigmoidoscopy, virtual colonoscopy and barium enema may be helpful in patients who cannot undergo a complete colonoscopy. When further investigation of intra-abdominal structures is warranted, CT scan of the abdomen and pelvis may be helpful.

Endoscopic and radiologic methods of evaluation of LGIB (Table 3)

The basic principles of endoscopic and radiologic methods for evaluation of LGIB are the same as for UGIB [10,11,16,32]. As in UGIB, endoscopy is the best approach to the evaluation of LGIB. Urgent colonoscopy performed within 24 h of hospitalization following a rapid purge should be performed for the evaluation of LGIB, once the patient has been resuscitated and hemodynamically stabilized [51-53]. Polyethylene sulfate purge

Table 3. *Endoscopic and radiologic modalities for the investigation of LGIB.*

Endoscopic Method	Radiologic methods
Colonoscopy	Radionuclide scan
Wireless capsule endoscopy	CT angiography
Push enteroscopy	MR angiography
Balloon enteroscopy	Abdominal angiography

causes less associated water and electrolyte abnormalities and may be preferable to saline purge for colonoscopic preparation in the patient with co-morbid renal or cardiovascular disease. If the patient is unable to take the purgative by mouth, NG tube administration may be necessary. The diagnostic accuracy of colonoscopy in the setting of acute LGIB ranges from 72% the 86% with cecal intubation achieved in 95% patients [54]. Colonoscopy can reveal the bleeding lesion, such as colonic varices or PHC. Colonoscopic evaluation in inflammatory bowel disease often reveals edematous, friable and ulcerated mucosa. Differential diagnosis may therefore require careful interpretation of pathologic findings to obtain an accurate diagnosis. Unfortunately, colonoscopy for evaluation of LGIB may give erroneous results in some cases of vascular ectasia and PHC. Vascular ectasia may be confused with traumatic mucosal lesions from the procedure or may not be seen due to volume depletion or administration of meperidine for sedation, both of which can cause vascular spasm and poor filling of vascular lesions [17].

In patients with active LGIB when colonoscopy is not feasible due to massive bleeding or in some cases of occult bleeding, radionuclide imaging and CT angiography, MR angiography and formal abdominal angiography may be necessary. For visualizing the bleeding source, radionuclide imaging requires that the bleeding rate be 0.1 to 0.5 ml per min and is often erroneous. The various forms of abdominal angiography requires greater than 1 ml per min [55,56]. Accuracy rates for these procedures vary greatly. For example, the accuracy of radionuclide imaging is 24% to 78% and the accuracy of the various forms of abdominal angiography is 27% to 77% for bleeding localization, depending upon the series [9].

There are important considerations involving the evaluation of patients with LGIB and cirrhosis [57,58]. Patients with venous thrombosis or portal vein thrombosis may require hematology, interventional radiology and vascular surgery consultations [46,47]. Patients may have cardiovascular instability or cardiac pacemakers with or without defibrillators and may require cardiology consultation. The general dictum of pharmacology of starting with low doses of medication and slowly advancing to larger doses is all the more important in the sedation of the elderly patient or patient with hepatic encephalopathy during endoscopy. Midazolam and narcotics are generally safe.

However, initial dosages should be lower and titration should be more gradual [59]. Modified anesthesia care (MAC) IV sedation guided by ASA criteria and constant monitoring can be performed, especially in clinical settings when deeper sedation is required.

It is estimated that 5% patients with GI bleeding, whether occult or overt, will have a negative upper GI endoscopy and colonoscopy [8]. Other endoscopic methods are available for evaluation of patients with obscure bleeding [60]. These methods visualize the small intestine, which may be an important source of either overt or occult bleeding in these patients. Wireless capsule endoscopy has become an important tool for the diagnosis of obscure GI Bleeding, being able to non-invasively visualize the entire small intestine [61,62]. Push enteroscopy and balloon enteroscopy are modalities that provide for both the evaluation and treatment of obscure GI bleeding from the small intestine [63].

Treatment of LGIB (Table 4)

The principles of treatment of patients with cirrhosis and LGIB are similar to those with UGIB [10,11,32]. Colonoscopy provides the best method for controlling LGIB as it provides many methods for direct control of hemorrhage with a vast array of endoscopic devices for control of hemorrhage, such as clips, ligation devices, injection of epinephrine and sclerosing agents, heater probe or bipolar probe thermal coagulation, band ligation, argon plasma coagulation, and application of fibrous glue [10,11,16,32,64,65].

In cases when endoscopy cannot control hemorrhage, abdominal angiography not only permits the identification of the bleeding source, but offers the potential of treatment with intra-arterial infusion of vaso-constricting agents such as vasopressin and somatostatin or embolization of the bleeding vessel [62]. For persistent bleeding not amenable to control by colonoscopic methods, abdominal angiography with infusion of vasopressin or somatostatin or embolization is successful in about 90% of cases. The somatostatin analogue Octreotide is safe and effective for patients with LGIB, especially if the patient is not a candidate for TIPS. It can be administered for a 3-5 day infusion. Embolization with polyvinyl alcohol particles or microcoils provides a more definitive means of controlling hemorrhage. Although intra-arterial vasopressin infusion has been reported to be successful in controlling the bleeding in up to 90% of patients, intolerance to the cardiovascular complications of vasopressin is common. Mesenteric ischemia and intestinal infarction can occur in up in to 20% of patients treated with infusions and/or embolization. Additionally, bleeding recurrence can occur in up to 50% of patients with LGIB treated with these angiographic methods, depending upon the series.

Table 4. *Modalities for the treatment of LGIB.*

Medications	Endoscopic methods	Radiologic methods	Surgical methods
Beta-adrenergic blockade (prevention of further bleeding)	Thermal coagulation	Abdominal angiography	Resection
TIPS	Band ligation	Vasopressin infusion	Shunt surgery
Somatostatin analogue infusion	Metallic clips	Somatostatin analogues	Liver transplantation
Vasopressin infusion	Epinephrine injection	Embolization	
	Sclerosing agent injection	TIPS	
	Fbrous glue		

As in UGIB treatment attempts to reduce portal pressure to less than 12 mmHg in patients with severe bleeding from colorectal varices, portal vein thrombosis and PHC should be considered in patients with cirrhosis and active LGIB. Addition of a non-selective beta-adrenergic blocking agent, such as propranolol or nadolol should be considered if patients with PHC are hemodynamically stable for prevention of further bleeding. Transjugular intrahepatic portosystemic shunt (TIPS) can reduce portal pressure and reduce hemorrhage and should be considered if LGIB cannot be controlled by endoscopic or angiographic methods and the patient is an appropriate candidate for TIPS [10,11,66-70].

Other treatments of LGIB depend upon the cause of the bleeding. Treatment of mesenteric thrombosis and portal vein thrombosis may be challenging in patients with liver disease and coagulopathy and may require hematologic, radiologic and vascular surgery consultations for management. Thrombectomy by interventional radiology or surgery may be effective. Treatment of infectious colitis depends on the type of infection and the source of bleeding. Radiation proctitis can be treated with a variety of agents, including argon plasma coagulation, formalin application, sucralfate enemas and hyperbaric oxygen therapy. Comparative controlled data for patients with radiation proctitis are limited and it is unknown which therapy is most effective [64,71,72].

Patients who fail angiographic, endoscopic and portal pressure reducing therapy for control of LGIB require surgery [32]. Every effort should be made to identify the bleeding source prior to referral for surgery, which often requires segmental bowel resection. Surgery may be necessary in up to 24% of patients with massive LGIB from diverticular disease [73-75]. Colonic resection and/or transanal ligation may be required for treatment of massive LGIB due to ileal and colonrectal varices. Shunt surgical therapy to control hemorrhage from colorectal varices or PHC may be lifesaving when TIPS fails, but can be associated with worsening hepatic encephalopathy. Blind segmental resection is associated with a re-bleeding rate of 47% and morbidity and mortality rate of 83% and 57%, respectively. It should be reserved for the rare instance of exsanguinating hemorrhage when immediate life-saving surgery is required [27,32,67,73]. Localization of bleeding by a positive preoperative angiogram reduces the risk of rebleeding [69]. Liver transplantation may be the viable option for the prevention of recurrent bleeding and should be considered in selected cases [11,12].

In patients with cirrhosis and LGIB one must extrapolate from the limited studies in patients with cirrhosis and LGIB and studies in patients with cirrhosis and UGIB and the general population to define success rates of therapy. LGIB is controlled in the majority of patients with and without cirrhosis. Jensen and Machicado reported no rebleeding during a 30 month follow up after endoscopic therapy when compared to a 53% rebleeding rate in patients treated with conservative medical therapy alone [51,52]. Despite improvements in localization and treatments of LGIB, the mortality rate for severe LGIB varies from 5-10% [4,52]. Unfortunately, the true incidence, diagnoses, risks and results of treatment of LGIB in cirrhosis remain poorly defined, since there are no large epidemiologic studies available. Further investigations with large multicenter epidemiologic studies are warranted to assess the true magnitude and treatments of LGIB in patients with cirrhosis.

Conclusion

In conclusion, LGIB in patients with cirrhosis may be associated with life-threatening complications similar to those with UGIB. The true incidence, diagnoses, risks of bleeding and results of treatment remain poorly defined. The incidence and type of LGIB in patients with cirrhosis corresponds to the Child-Pugh class, the increase in portal hypertension, coagulopathy, age-specific diseases, co-morbid diseases and polypharmacy. Bleeding may be chronic and mild or severe and life threatening, requiring endoscopic, radiologic or surgical intervention. Since there are no large epidemiologic studies available, further investigations with large multicenter epidemiologic studies are warranted to assess the true magnitude and treatments of LGIB in patients with cirrhosis.

References

1. Kalafatelli M, Triantos CK, Nikolopoulou V, et al. Non-variceal gastrointestinal bleeding in patients with liver cirrhosis: A review. Dig Dis Sci. 2012;57:2743-54.

2. Misra SP, Dwivedi M, Misra V. Prevalence and factors influencing hemorrhoids, aanorectal varices and colopathy in patients with portal hypertension. Endoscopy. 1996;28(4):340-5.

3. Santoro GA, Aiello C, Galloro G, et al. Massive lower gastrointestinal hemorrhage in patients with portal hypertensive enteropathy: a report of 2 cases. Hepatogastroenterology. 1997;44(16):1029-32.

4. Strate LL. Lower GI bleeding: Epidemiology and diagnosis. Gastroenterol Clin North Am. 2005;34(4):643-64.

5. Bresci G, Parisi G, Capria A. Clinical relevance of colonic lesions in cirrhotic patients with portal hypertension. Endoscopy. 2006;38(8):830-5.

6. Bresci G, Gambardella L, Parisi G, et al. Colonic disease in cirrhotic patients with portal hypertension: An endoscopic and clinical evaluation. J Clin Gastroenterol. 1998;26(3):222-7.

7. Rockey DC. Occult gastrointestinal bleeding. N Engl J Med. 1999;341:38-46.

8. Mujica VR, Barkin JS. Occult gastrointestinal bleeding. General overview and approach. Gastrointest Endosc Clin North Am. 1996;6:833-45.

9. Rockey DC. Lower gastrointestinal bleeding. Gastroenterology. 2006;130:165-71.

10. Garcia-Tsao G, Lim JK. Management and treatment of patients with cirrhosis and portal hypertension: Recommendations from the Department of Veterans Affairs Hepatitis C Resource Center Program and the National Hepatitis C Program. Am J Gastroenterol. 2009;104(7):1802-29.

11. Garcia-Tsao G, Bosch J. Management of varices and variceal hemorrhage in cirrhosis. N Engl J Med. 2010;362:823-32.

12. Cello JP, Crass RA, Federle MP. Colonic varices: An

unusual source of lower gastrointestinal hemorrhage. West J Med. 1982;136(3):352-5.

13. Misra BV, Misra SP, Dwivedi RA, et al. Colonic mucosa in patients with portal hypertension. J Gastroenterol Hepatol. 2003;18(3):302-8.

14. Ito KR, Shiraki K, Sakai T, et al. Portal hypertensive colopathy in patients with liver cirrhosis. World J Gasstroenterol. 2005;11:3127-30.

15. Median C, Vilaseca J, Videla S, et al. Outcome of patients with ischemic colitis: Review of fifty-three cases. Dis Colon Rectum. 2004;47:180-4.

16. Zuckerman GR, Prakash C. Acute lower intestinal bleeding. Part II: Etiology, therapy and outcomes. Gastrointest Endosc. 1999;49(2):228-38.

17. Brandt LJ, Boley SJ, Mitsudo S. Clinical characteristics of and natural history of colitis in the elderly. Am J Gastroenterol. 1982;77:382-36.

18. Boley SJ, Sammartano R, Adams A, et al. On the nature and etiology of vascular ectasias of the colon. Degenerative lesions of aging. Gastroenterology. 1977;72:650-60

19. Foutch PG. Angiodysplasia of the gastrointestinal tract. Am J Gastroenterol. 1993;88:807-18.

20. Descamps C, Schmit A, Van Gosssum A. "Missed" upper gastrointestinal tract lesions may explain "occult" bleeding. Endoscopy. 1999;31:452-5.

21. Boley SJ, Sprayregen S, Sammartano RJ, et al. The pathophysiologic basis for the angiographic signs of vascular ectasias of the colon. Radiology. 1977;125:615-21.

22. Reinus GF, Brandt LJ. Vascular ectasias and diverticulosis. Common causes of lower intestinal bleeding. Gastroenterol Clin North Am. 1994;23:1-20.

23. Imperiale TF, Ransohoff DF. Aortic stenosis, idiopathic gastrointestinal bleeding and angiodysplasia: Is there an association? A methodologic critique of the literature. Gastroenterology. 1988;95:1670-6.

24. Reilly HF III, al-Kawas FH. Dieulafoy's lesion. Diagnosis and management. Dig Dis Sci. 1991;36:1702-7.

25. Stewart EB, Moore MT, Marks RG, et al. Correlates of constipation in an ambulatory elderly population. Am J Gastroenterol. 1992;87:859-64.

26. Tseng CA, Chen LT, Tsai KB, et al. Acute hemorrhagic rectal ulcer syndrome: A new clinical entity? Report of 19 cases and review of the literature. Dis Colon Rectum. 2004;47:895-903.

27. Bokhari M, Vernava AM. Diverticular hemorrhage in the elderly-is it well tolerated? Dis Colon Rectum. 1996;39:191-5.

28. Maguire HH Jr. Bleeding colonic diverticula: A reappraisal of natural history and management. Ann Surg. 1994;220:653-6.

29. Aldoori WH, Giovannucci EL, Rimm EB, et al. Use of acetaminophen and non-steroidal anti-inflammatory drugs:

A prospective study and the risk of symptomatic diverticular disease in men. Arch Fam Med. 1998;7:255-60.

30. Wilcox CM, Alexander L, Cotsonis GA, et al. Non-steroidal anti-inflammatory drugs are associated with both upper and lower gastrointestinal bleeding. Dig Dis Sci. 1997;42:990–7.

31. Stollman NH, Raskin JB. Diverticular disease of the colon. J Clin Gastroenterol. 1999;29:241-52.

32. Zuccaro G Jr. Management of the adult patient with acute lower gastrointestinal bleeding. American College of Gastroenterology. Practice Parameters Committee. Am J Gastroenterol. 1998;93:1202-8.

33. Bajaj JS, O'leary JG, Reddy KR, et al. Second infections independently increase mortality in in hospitalized patients with cirrhosis: The North American consortium for the study of end-stage liver disease (NACSELD) experience. Hepatology. 56:2328-35.

34. Lew JF, Glass RI, Gangarosa RE et al. Diarrheal deaths in the United States, 1979 through 1987: A special problem for the elderly. JAMA. 1991;265:3280-4.

35. Guerrant RL, Van Gilder T, Steiner PS, et al. Infectious Diseases Society of America. Practice guidelines for the management of infectious diarrhea. Clin Infect Dis. 2001;32:331-51.

36. Slotwiner-Nie PK, Brandt LJ. Infectious diarrhea in the elderly. Gastroenterol Clin North Am. 2001;30:625-35.

37. Raj V, Lichtenstrein DR. Hepatobiliary manifestations of inflammatory bowel disease. Gastroenterol Clin North Am. 1999;28:491-513.

38. Sorensen HT, Friis S, Olsen JH et al. Risk of liver and other types of cancer in patients with cirrhosis: A nationwide study in Denmark. Hepatology. 1998;28(4):921-5.

39. Robert JH, Sacher DB, Aufses AH, et al. Management of severe hemorrhage in ulcerative colitis. Am J Surg. 1990;159:550-5.

40. Farmer RG, Hawk WA, Turnbull RB. Clinical patterns in Crohn's diseases: A statistical study of 615 cases. Gastroenterology. 1975;68:627-35.

41. Peura DA, Lanza FL, Gostout CJ, et al. The American college of gastroenterology bleeding registry: Preliminary findings. Am J Gastroenterol. 1997;92:924-8.

42. Richter JM, Christiansen MR, Kaplan LM, et al. Effectiveness of current technology in the diagnosis and management of lower gastrointestinal hemorrhage. Gastrointest Endosc. 1995;41:93–8.

43. Kim HS, Kim WH, Kim YH, et al. Risk factors for immediate post-polypectomy bleeding of the colon: A multicenter study. Am J Gastroenterol. 2006;101:33-1341.

44. Muhldorfer SM, Kekos G, Hahn EG, et al. Complications of therapeutic gastrointestinal endoscopy. Endoscopy. 1992;24:276-83.

45. Rex DK, Lewis BS, Waye JD. Colonoscopy and endoscopic therapy for delayed post-polypectomy hemorrhage. Gastrointestinal Endoscopy. 1992;38:127-9.

46. Northrup PG, Caldwell SH. Coagulation in liver disease: A guide to the clinician. Clin Gastroenterol Hepatol. 2013;9:1064-74.

47. Tripodi A, Mannucci PM. The coagulopathy of chronic liver disease. N Engl J Med. 2011;365:147-56.

48. Hosking SW, Bird NC, Johnson AG, et al. Management of bleeding varices in the elderly. BMJ. 1989;298:152-3.

49. Hilton D, Iman N, Burke GJ, et al. Absence of abdominal pain in older persons with endoscopic ulcers: a prospective study. Am J Gastroenterol. 2001;96:380–4.

50. Informed consent for gastrointestinal endoscopy. Gastrointest Endosc. 1988;34:26S-7S.

51. Jensen DM, Machicado GA. The diagnosis and treatment of severe hematochezia. The role of urgent colonoscopy after purge. Gastroenterology. 1988;95:1569-74.

52. Jensen DM, Machicado GA, Jutabha R, et al. Urgent colonoscopy for the diagnosis and treatment of severe diverticular hemorrhage. N Engl J Med. 2000;342:78-82.

53. Elta GH. Urgent colonoscopy for acute lower GI bleeding. Gastrointest Endosc 2004;59:402-8.

54. Way JD, Bashkoff E. Total colonoscopy: Is it always possible? Gastrointest Endosc. 1991;37:152-4.

55. Zuckerman DA, Bocchini TP, Birnbaum EH. Massive hemorrhage in the lower gastrointestinal tract in adults: Diagnostic imaging and intervention. Am J Roentgenol. 1993;160:703–11.

56. Hammond KL, Beck DE, Hicks TC, et al. Implications of negative technetium 99m-labeled red blood cell scintigraphy in patients presenting with lower gastrointestinal bleeding. Am J Surg. 2007;193:404-7.

57. Zerey M, Paton BL, Khan PD, et al. Colonoscopy in the very elderly: A review of 157 cases. Surg Endosc. 2007;21:1806-9.

58. Qureshi WA, Zuckerman MJ, Adler DG, et al. Standards of Practice Committee, American Society for Gastrointestinal Endoscopy. ASGE Guideline: modifications in endoscopic practice for the elderly. Gastrointest Endosc 2006; 63:566-9.

59. Eisen GM, Chutkan R, Goldstein JL, et al. Modifications in endoscopic practice for the elderly. American Society for Gastrointestinal Endoscopy. Gastrointest Endosc 2000; 52:849-51.

60. Gralnek IM. Obscure-overt gastrointestinal bleeding. Gastroenterology. 2005;128:1424-30.

61. Neu B, Ell C, May A, et al. Capsule endoscopy versus standard tests influencing management of obscure digestive bleeding: Results from a German multicenter trial. Am J Gastroenterol. 2005;100:1736-42.

62. Sun B, Rajan E, Cheng S, et al. Diagnostic yield and therapeutic impact of double-balloon enteroscopy in a large cohort of patients with obscure gastrointestinal bleeding. Am J Gastroenterol. 2006;101:2011-5.

63. Saurin JC, Delvaux M, Vahedi K, et al. Clinical impact of capsule endoscopy: 1 year follow-up study. Endoscopy. 2005;37:318-23.

64. Kwan V, Bourke MJ, Williams SJ, et al. Argon plasma coagulation in the management of symptomatic gastrointestinal vascular lesions: experience in 100 consecutive patients with long-term follow-up. Am J Gastroenterol 2006; 101:58-63.

65. Yad YZ, Zeid AA. Portal hypertensive colopathy and haematochezia in cirrhotic patients:an endoscopic study. Arab J Gastroenterol. 2011;12(4):184-8.

66. Guy GE, Shetty PC, Sharma RP, et al. Acute lower gastrointestinal hemorrhage: treatment for super selective embolization with polyvinyl alcohol particles. Am J Roentgenol. 1992;159:521-6.

67. Browder W, Cerise EJ, Litwin MS. Impact of emergency angiography in massive lower gastrointestinal bleeding. Ann Surg. 1986;204:530-6.

68. Sherman LM, Shenoy SS, Cerra FB. Selective intra-arterial vasopressin: Clinical efficacy and complications. Ann Surg. 1979;189:298-302.

69. Parkes BM, Obeid FN, Sorensen VJ, et al. The management of massive lower gastrointestinal bleeding. Am Surg. 1993;59:676-8.

70. Yoshie K, Fujita Y, Moriya A, et al. Octreotide for severe bleeding from portal hypertensive colopathy: A case report. Eur J Gasstrenterol Hepatol. 2001;13:1111-3.

71. Vyas FL, Mathai V, Selvamani B, et al. Endoluminal formalin application for haemorrhagic radiation proctitis. Colorectal Dis. 2006;8:342-6.

72. Dall'Era MA, Hampson NB, Hsi RA, et al. Hyperbaric oxygen therapy for radiation induced proctopathy in men treated for prostate cancer. J Urol. 2006;176:87-90.

73. Stabile PE, Stamos MJ. Surgical management of gastrointestinal bleeding. Gastroenterol Clin North Am. 2000;29:189–222.

74. Setya V, Singer JA, Minken SL. Subtotal colectomy as a last resort for unrelenting, unlocalized, lower gastrointestinal hemorrhage: Experience with 12 cases. Am Surg. 1992;58:295-9.

75. Gianfrancisco JA, Abcarian H. Pitfalls in the treatment of massive lower gastrointestinal bleeding with "blind" subtotal colectomy. Dis Colon Rectum. 1982;25:441-5.

*Correspondence to:

Maxwell M Chait
The ColumbiaDoctors Medical Group
180 East Hartsdale Avenue, Hartsdale
New York
USA
Telephone: +1-914-725-2010
Fax: +1-914-725-6488
E-mail: maxwellchait@gmail.com