Surgical Options and Approaches for Lower Gastrointestinal Bleeding: When do we operate and what do we do?

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Abstract

Keywords

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- lower gastrointestinal hemorrhage
- CT angiography
- anticoagulation

Lower gastrointestinal bleeding (LGIB) is a common entity encountered by the surgeon. Though most LGIB stops on its own, familiarity with the diagnoses and their treatments is critical to optimal patient care. Even in 2016, surgery may be required. Advances in imaging have led to an enhanced ability to localize bleeding. Newer anticoagulants have developed which provide ease of use to the patient, but challenges to caregivers when bleeding arises.

The role of the surgical consultant with regard to lower gastrointestinal bleeding (LGIB) is one that requires knowledge of the burgeoning armamentarium of diagnostic and therapeutic modalities and understanding of the results of various surgical options. Confounding the care of these critically ill patients is the old age of studies which report surgical outcomes. Fortunately, the number of nonoperative options are growing and becoming both increasingly available and effective. Only a small percentage of patients with LGIB ultimately require surgery.

For this article, we will define LGIB as that from distal to the ligament of Treitz. Czymek et al¹ reported on 63 patients requiring surgery in a single university hospital in Germany. They found the source in these patients to be mentioned below:

- Diverticular (59%).
- Arteriovenous malformation/angiodysplasia (13%).
- Small intestine diverticulum (8%).
- Chronic inflammatory bowel disease (8%).
- Cancer (5%).
- Other (16%).

The surgeon caring for the bleeding patient needs to be cognizant of the possible sources and their likelihood to respond to nonoperative therapies. This chapter will review

both the common and the more rare indications. It is our goal to synthesize the variables into a guide for the surgeon. Further, we will review the growing number of anticoagulants and our approach to the anticoagulated patient.

Of predominant importance is diverticular bleeding, especially as patient's age increases. Diverticulosis is present in up to 30% of patients over 50 years of age. Of all LGIB episodes, 20 to 65% are due to diverticulosis. Significant bleeding occurs in 3 to 15% of patients with diverticula. Diverticular bleeding fortunately stops spontaneously in 75% of episodes. Rebleeding, after a single bout of diverticular bleeding, is frequent and ranging from 14 to 38%. After a second episode of bleeding, the risk of again bleeding is 21 to 50%.^{2,3}

Diagnosis of Lower Gastrointestinal Hemorrhage

Modalities preceding surgery are institution dependent but include the following:

Nasogastric tube placement with bile aspirate. It is important to exclude an upper GI source as they represent 15% fulminant of patients with hematochezia.

Digital rectal exam and rigid proctoscopy: Allows rapid evaluation of an anorectal source of bleeding.

CT angiography: this important noninvasive modality allows accurate identification of the bleeding site and as well as anatomic information.

Visceral angiography: it is an invasive modality that provides accurate localization and the opportunity for potential therapy through embolization.

Nuclear localization: it is a very sensitive means to identify low rate bleeding but suffers from a lack of specificity of bleeding origin.

Colonoscopy: it is a useful and widely available diagnostic and therapeutic modality. Accessing colonoscopy can be complicated via issues with staffing and bowel preparation.

The changing paradigm in patient evaluation is described clearly in a study from the University of Pennsylvania. These authors sought to optimize the nature and sequence of diagnostic imaging when managing LGI hemorrhage to reduce subsequent morbidity and mortality. Analysis was conducted of prospectively acquired data from an interventional radiology database and of individual electronic medical records from an academic tertiary medical center. On January 1, 2009, a new, evidence-based, institutional protocol that formally incorporated computed tomographic angiography (CTA) to manage acute LGI hemorrhage was launched after multidisciplinary consultation. All records of patients who underwent visceral angiography (VA) for acute LGI hemorrhage, from January 1, 2005 to December 31, 2012, were evaluated. A total of 161 angiographic procedures were performed during the study period (78 before and 83 after protocol implementation). The use of CTA increased from 3.8 to 56.6%, while the use of nuclear scintigraphy decreased from 83.3 to 50.6%. Nuclear scintigraphy and CTA had similar sensitivity and specificity; localization of hemorrhage site by CTA was more precise and consistent with angiography findings. Preceding visceral angiography with a diagnostic study improved positive localization of the site of LGI hemorrhage compared with visceral angiography alone. Increasing the use of CTA for preangiography appeared to increase positive yield at visceral angiography. The authors concluded that CTA can be used as part of a LGIB management algorithm and did not worsen renal function despite the additional contrast load.⁴

Management of Lower Gastrointestinal Hemorrhage

As we shall soon examine, surgery still has relevance despite the improvements in both localization and nonsurgical intervention by embolization. Köhler et al in 2014 addressed exactly this question. Their group performed a retrospective analysis of surgery after transarterial embolization between January 2009 and December 2012 at the Sisters of Charity Hospital in Linz. As seen from the diagram from their published work, 2 of 14 patients who had transarterial embolization of large bowel lesions required surgery for rebleeding and one of two required surgery after angioembolization was utilized in the rectum (►Fig. 1).⁵

The goal to prevent surgery is clearly always laudable. Super-selective embolization has been shown to control colonic hemorrhage with a low rate of postembolization ischemia.⁶ Of 27 patients initially controlled with arterial embolization at Hartford Hospital, six patients rebled and five required surgery.

Both studies thus reveal two important concepts that super-selective angioembolization is effective and that it does not eliminate the need for surgical intervention.

Surgical Management of LGI Hemorrhage

Delay in providing surgery for some patients with LGIB can be deadly. Though the study is from 1991 and involves small number of patients, one study from Wayne State clearly illustrates the morbidity and mortality of massive LGIB. In this study, from 1980 to 1986, 49 total abdominal colectomies were performed for LGIB. Among 33 emergent operations, 13 patients had less than 10 units of blood transfused, one (7%) died, and there was one complication. Twenty patients had 10 or more blood transfusions and nine (45%) died ($p = 0.05$ vs. former group). This latter group also had 16 major complications, including five anastomotic leaks, three intra-abdominal abscesses, and three myocardial infarctions (►Table 1).⁷

The decision with regard to operation type is dependent on successful localization. Farner et al from Baylor in 1999

Fig. 1 Transarterial embolization of large bowel lesions required surgery for re-bleeding (Köhler et al⁵). LGIB, lower gastrointestinal bleeding.

Table 1 Mortality in relation to units of packed red blood cells transfuse

Transfusion (units)	Mortality (%)
> 10	45
< 10	7

looked at 77 patients with an acute LGIB who required operation after 2 or more units of transfused packed red blood cells (PRBCs) between the years 1987 and 1997. Fifty limited colon resections and 27 total colectomies were performed during this 10-year period. They found recurrent bleeding was significantly more common in the limited colectomy group than in the total colectomy group (18 vs. 4%). Morbidity and mortality were not significantly different.⁸

The functional outcome after subtotal colectomy for bleeding has been compared to that of segmental colectomy. Preoperative localization of LGIB has been advocated on the presumption that lower morbidity and mortality are associated with limited colonic resection versus abdominal colectomy. Extensive preoperative evaluation, especially when repeatedly negative, may unnecessarily delay surgical therapy in the actively hemorrhaging patient. A group from St. Mary's Hospital in Grand Rapids Michigan looked at 61 patients admitted for massive LGIB who received greater than unit PRBCs transfused preoperatively over a 5-year period. More time elapsed before surgery in the limited colectomy (LIM) group (95.4 ± 13.0 hours) compared with the total abdominal colectomy (TAC) group (73.7 ± 22.2 hrs). There was no significant difference in Apache's score, age, or morbidity. Mortality rates were similar between the two groups (LIM = 15%, TAC = 6%). There was no instance of intractable diarrhea, postoperatively, in either group. These authors concluded that TAC is a safe method of treating massive LGI hemorrhage.⁹

The incidence of rebleeding also influences operation type. In a classic study from the Henry Ford Hospital, 31 patients who underwent colon resection for hemodynamic instability and/or the need for continued transfusions were investigated. In their work, segmental colectomy (21 patients), or subtotal colectomy (10 patients) was compared. Rebleeding rate (mean follow-up 1 year):

- Subtotal colectomy was 0%.
- Segmental resection with positive angiography was 14%.
- Segmental resection with negative angiography was 42%.

The complication rate including myocardial infarction, adult respiratory distress syndrome (ARDS), pneumonia, and renal failure was highest (83%) in those patients receiving segmental resection with a negative angiogram.

The mortality rate was also highest for segmental resection patients with negative angiography (57%) These authors suggest that segmental resection should be performed when the site of hemorrhage is identified angiographically. They reserved subtotal colectomy for massive bleeding with negative angiography.¹⁰

In currently unpublished data, Greco et al utilized the National Surgery Quality Improvement Program (NSQIP) database to better understand the modern surgical management of lower gastrointestinal hemorrhage. The authors identified all patients who underwent colorectal resection for bleeding in both the American College of Surgeons NSQIP (ACS NSQIP) participant use data file (PUF) and the procedure targeted PUF for colectomy for the years 2012 to 2013. The group compared patients who underwent partial colectomy to those who underwent total colectomy. Univariate analyses were used to compare the demographics, comorbidities and operative characteristics of both groups. They found that 427 patients underwent colorectal resection for the indication of LGI hemorrhage. Among them, 85.3% (n = 364) underwent a partial colectomy, and 14.7% (n = 63) underwent total colectomy. Patients who had total colectomy were more likely than those with partial colectomies to have received more than 4 units of blood prior to surgery (77.8 vs. 55.5%, *p* < 0.01). Patients who had partial colectomy were more likely to have undergone laparoscopic procedures (35.3 vs. 20.0%, *p* = 0.02) and to have a stoma created at the time of surgery (20.6 vs. 1.6%, *p* < 0.01). On univariate analysis, total colectomy was associated with an increased risk of postoperative ileus, cardiac, and renal complications, and mortality (all *p* < 0.05), but not with surgical site infection, anastomotic leak, return to the operating room or readmissions. On multivariate analysis, total colectomy was associated with increased risk of cardiac complications (odds ratio [OR] = 5.53, 95% confidence interval [CI]: 1.3–22.8) and renal complications (OR = 9.6, 95% CI: 2.2–43.0), but not with ileus (*p* = 0.21) or mortality (*p* = 0.10).¹¹ Thus, the most common procedure performed for LGI hemorrhage in a recent, national cohort was partial colectomy. The national predominance of segmental colectomy may be influenced by the increasing ability to accurately localize bleeding.

Special Cases of LGI Hemorrhage

Other less common causes of LGI hemorrhage include rectal varices and radiation proctitis. Radiation proctitis is a complication of direct beam radiation to the pelvis seen in 2 to 20% of patients with higher incidence in patients undergoing external beam radiation than those undergoing intensity-modulated radiation therapy or brachytherapy. Radiation proctitis can be classified as acute, which occurs immediately to 3 months after radiation or chronic, which occurs 3 months or more after radiation with mean onset of 8 to 12 months. Acute radiation proctitis is often self-limiting with discontinuation of radiation therapy and presents with diarrhea, nausea, tenesmus, cramping, and minor bleeding. Chronic radiation proctitis usually arises after the cessation of therapy and has the same symptoms of acute radiation proctitis but can also include severe bleeding, strictures, fistula, and perforation due to compromise of blood supply to the rectal wall as a consequence of radiation. Histologically, in acute radiation proctitis there is loss of microvilli with induration and hyperemia. Chronic radiation proctitis causes focal destruction of small arterioles and intimal fibrosis.¹²

Colonoscopy or sigmoidoscopy is commonly used to diagnose radiation proctitis. On colonoscopic evaluation, the rectal mucosa of patients with chronic radiation proctitis is pale, noncompliant, and friable with telangiectasias.

The majority of patients with rectal bleeding from radiation proctitis present with minimal hemorrhage that often self-resolves. As bleeding is not massive, topical approaches are employed first and most commonly. We personally have had success with dilute 0.4% topical formalin placed directly on the affected rectal mucosa via a large cotton applicator through a proctoscope. Patients with radiation proctitis also can be treated nonoperatively with NSAIDs, sucralfate, hyperbaric oxygen therapy, or short chain fatty acid enemas. Other more invasive techniques, such as thermal coagulation, radiofrequency ablation, or cryoablation can be used to control bleeding from telangiectasias. In patients who ultimately require surgery, microvascular damage to the rectal mucosa not only is the source of much of their symptomatology, but also can significantly impair healing, many studies report high mortality and complication rates postoperatively. An ostomy can be created to divert the flow of stool in patients suffering from strictures or fistulous disease and was found in one study to be effective in improving symptoms of bleeding caused by radiation proctitis.¹³ Severe and intractable bleeding in most cases is rarely controlled by fecal diversion and in those with severe symptoms of bleeding a proctectomy may be necessary.

Bleeding rectal varices are another uncommon etiology of LGI hemorrhage. Rectal varices are dilated veins that originate more than 4 cm from the anal verge that serve as a pathway for portal venous flow between the superior rectal veins and the middle inferior rectal veins.¹⁴ They present most commonly in patients with hepatic dysfunction, occurring in 38 to 94% of patients with portal hypertension. Rectal and colonic varices can also occur in patients with anomalies of portal venous outflow in the absence of hepatic dysfunction.¹⁵ Rectal varices can be diagnosed with colonoscopy, sigmoidoscopy, or endoscopic ultrasound. The same endoscopic grading system is used for evaluating rectal varices as is used for esophageal varices, grading form (F) from 0 to 3 on scale of size and caliber, color (C) of white or blue, and red color signs (RC) which indicate higher risk of bleeding (Japanese Research Committee on Portal Hypertension).

Though the incidence of rectal varices in patients with portal hypertension is relatively high, the incidence of bleeding from rectal varices is low, only 0.5 to 5% of patients with rectal varices will experience hemorrhage as a complication.¹⁶ Initial management of bleeding rectal varices includes resuscitation with fluid and blood products as needed. Active bleeding can be managed endoscopically, by interventional radiology, or surgically. Endoscopically, bleeding rectal varices can be managed using similar techniques to those used to manage bleeding esophageal varices including endoscopic injection sclerotherapy, endoscopic band ligation, or injection of cyanoacrylate. Transjugular intrahepatic portosystemic shunt (TIPS) is a procedure that is used to decrease portal hypertension by creating a communication between the portal vein and hepatic vein and has been shown in some

studies to be effective in managing active bleeding of rectal varices by decompression. In one study by Kochar et al, TIPS was shown to effectively control bleeding in 67% of cases.¹⁷ Bleeding rectal varices can also be managed surgically by methods, such as suture ligation, directly or with a circumferential stapling device, inferior mesenteric vein occlusion, and portocaval shunting. In patients who need surgery for bleeding rectal varices, mortality can be as high as 80% within 2 months of surgery,¹⁸ most likely because the patients who ultimately require surgical intervention are often high surgical risk because of concurrent liver failure.

Novel Anticoagulants

In recent years, new oral anticoagulants (NOAC) like dabigatran, rivaroxaban, and apixaban have been increasingly prescribed for stroke prevention in patients with atrial fibrillation. Advantages of these agents over traditional vitamin K antagonists, such as warfarin include predictable pharmacodynamics, thereby foregoing the need for frequent laboratory monitoring and fewer drug and dietary interactions. One of the major disadvantages of these agents was difficulty of reversal in the event of acute hemorrhage or emergency surgery. Until recently, no specific reversal agents were available for NOACs, making the management of bleeding patients a significant challenge for clinicians.

Dabigatran (Pradaxa; Boehringer Ingelheim) is the only oral direct thrombin inhibitor available in the U.S. It is approved for preventing embolic complications in patients with nonvalvular atrial fibrillation (NVAF), management of venous thromboembolism (VTE) in patients treated with parenteral anticoagulation for 5 to 10 days, reduce risk of recurrent VTE in previously treated patients, and for prophylaxis of VTE in patients who have undergone hip replacement surgery. Dabigatran has its peak effect in 0.5 to 2 hours and has a half-life of approximately 8 hours.¹⁹ It undergoes primarily renal excretion, and its half-life can be prolonged in patients with renal impairment.

Rivaroxaban (Xarelto; Janssen Pharmaceuticals) is a direct factor Xa inhibitor approved for stroke prevention in NVAF, treatment of deep venous thrombosis (DVT), and pulmonary embolism (PE), and reducing risk of recurrence in those previously treated, and prophylaxis for VTE in patients undergoing knee and hip replacement surgery. It has an onset of action of 2 to 4 hours and half-life ranges from 7 to 11 hours.¹⁹ It is eliminated by both renal and hepatic mechanisms.

Apixaban (Eliquis; Bristol-Myers Squibb) is also an oral direct factor Xa inhibitor. It is approved in the U.S. for prevention of embolic complications in patients with NVAF, treatment of and reduction of recurrence of DVT/PE, and DVT/PE prophylaxis following knee or hip replacement surgery. It has a peak onset of 1 to 3 hours and half-life of 12 hours. Apixaban is metabolized primarily by the liver and excreted in urine and feces.

Edoxaban (Savaysa; Daiichi Sankyo) is an Xa inhibitor approved for stroke risk reduction in NVAF and treatment of DVT/PE after 5 to 10 days of initial therapy with a parenteral anticoagulant. It reaches peak plasma concentration 1 to

2 hours after administration and has a 10 to 14 hours of half-life. It is excreted by both renal and hepatic pathways.

Noninferiority studies demonstrated that NOAC were not associated with higher overall bleeding risk. However, bleeding risk appears to be site-specific.^{20,21} The randomized evaluation of long-term anticoagulant therapy (RE-LY) trial found that while dabigatran and warfarin were associated with similar risks of all-site major bleeding, dabigatran was associated with more GI bleeding.²² The Rocket AF Trial (Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation) found rivaroxaban to be associated with more major and minor episodes of GI bleeding than warfarin, though the two groups had similar rates of major life-threatening bleeds.²³ NOACs have been hypothesized to confer risk of GI bleeding through both systemic and local, topical effects.²¹ Incomplete absorption of NOAC from the GI tract is suggested to contribute to higher risk of GI bleeding, while simultaneously demonstrating lower intracranial and all-site major bleeding compared to warfarin. Specifically, the bioavailability of the prodrug dabigatran is only 6%. Those of rivaroxaban and apixaban are higher, 60 to 80 and 50%, respectively. In all these cases, active drug can be recovered from the feces. Presence of active anticoagulant in the GI tract lumen after oral ingestion is thought to potentiate bleeding from vulnerable lesions.

In contrast to warfarin, there were no specific reversal agents for NOACs until recently. Furthermore, evidence-based guidelines for reversal of NOAC in emergent settings is still largely lacking, making management of patients taking NOAC who present with a major active bleed or require emergent procedures exceptionally challenging. As far as reversing the effects of NOACs, their characteristic short half-lives can be used to their advantage. Oftentimes by simply withholding the NOAC, hemostasis will normalize over 12 to 24 hours.²⁴ Unlike warfarin, in general there is no role of fresh frozen plasma (FFP) or vitamin K in the reversal of NOAC.²⁵

Nonspecific prohemostatic agents are available that can reverse the anticoagulant effects of NOACs. Three-factor prothrombin complex concentrate (PCC) contains factors II, IX, and X. Four-factor PCC also includes factor VII. Use of PCCs for the reversal of NOAC-associated bleeding is off-label. An activated PCC (FEIBA [anti-inhibitor coagulant complex, Takeda Pharmaceutical Company Ltd. Lexington, MA]) also exists and is approved by the Food and Drug Administration, (FDA) for use in bleeding episodes in patients with hemophilia A and B. Use of inactivated forms of PCC are preferred over FEIBA due to higher reported thrombotic complications with FEIBA.²⁵

Hemodialysis can be used to reverse the anticoagulant effects of dabigatran in patients presenting concurrently with renal failure. The direct Xa inhibitors (rivaroxaban, apixaban, and edoxaban) are highly protein bound and, therefore, cannot be cleared using hemodialysis.^{21,25}

Idaracizumab (Praxbind, Boehringer Ingelheim) was recently approved by the FDA for use in the reversal of dabigatran. It is a monoclonal antibody that specifically binds and neutralizes dabigatran.²⁶ Idarucizumab binds to dabigatran with 350-fold higher affinity than thrombin. Initial half-life of the idarucizumab–dabigatran complex is approximately 45 minutes, and 90% of the complex is cleared within 4 hours

of administration. Trials have demonstrated dose-dependent, immediate, and sustained inhibition of dabigatran.²⁷ No drug-related adverse events or thrombotic complications were reported in phase 1 and 2 studies.

Andexanet alfa is in development for reversal of direct factor Xa inhibitors (rivaroxaban, apixaban, and edoxaban). Andexanet alfa competitively binds to and inhibits the circulating anticoagulants.²⁶ Studies have demonstrated reversal of the effects of rivaroxaban and apixaban with bolus dosing of andexanet alfa, and maintenance of reversal when the bolus is followed by infusion of the agent.²⁸ No serious adverse events or thrombotic complications have been reported.

Ciraparantag (PER977) is another drug in development which binds factor Xa inhibitors and dabigatran. Animal studies found the drug rapidly reversed the effects of NOACs. Early human studies found ciraparantag reversed the effects of edoxaban within 30 minutes of administration, and that its reversal effects were sustained for 24 hours.²⁶ No significant adverse events, or procoagulant effects, have been observed for ciraparantag.

The initial approach to managing the patient taking NOAC who presents with an acute bleed is similar to the management of any bleeding patient. Initial evaluation includes assessment of hemodynamic status, sending laboratory studies, in particular hemoglobin level, coagulation studies, and type and cross-match. As in LGIB bleeds in nonanticoagulated patients, the treatment will likely ultimately involve colonoscopy.²⁹

Minor bleeds can often be managed with observation and supportive measures alone. Temporarily withholding the NOAC is often adequate treatment.^{22,25} It is important to determine the timing of the last dose of NOAC. More significant bleeding, but without hemodynamic compromise, should also be managed by stopping NOACs. Resuscitation should be provided with fluid replacement or transfusions as necessary to maintain diuresis and, therefore, clearance of the NOAC. If the patient is stable endoscopic evaluation is preferably delayed for 12 to 24 hours until the NOAC has been cleared.²⁵

Management of major active bleeding with hemodynamic instability becomes more complicated. It is critical to know the exact timing of the last dose of NOAC as gastric lavage can be considered within 2 hours of ingestion to prevent further absorption of anticoagulant.^{22,25} The patient's hepatic and renal function should be assessed, as this will affect how long the anticoagulant effects of NOACs will be expected to last. Hemodialysis can be considered to clear dabigatran in those with renal failure. Nonspecific PCCs should be considered with continued active bleeding. Idaricizumab is a specific reversal agent to be considered for dabigatran. Andexanet alfa may be available in the near-future for direct Xa inhibitors. Clinicians should consider the source and hemodynamic significance of the bleed, the patient's individual stroke risk, the timing of the last dose of NOAC, and current coagulation studies when deciding whether to administer such reversal agents.²⁶

As in other LGIBs, in which anticoagulants are not involved, emergent colonoscopy should be considered in the hemodynamically unstable patient with continued active bleeding. Adjunctive studies, such as CT angiogram, nuclear

medicine studies, and formal angiography should also be employed as appropriate.²² Operative intervention for LGIB is often the final therapeutic intervention when all other measures have failed.

Conflict of Interest

None declared.

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