CME

Management of Patients With Acute Lower Gastrointestinal Bleeding: An Updated ACG Guideline

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Acute lower gastrointestinal bleeding (LGIB) is a common reason for hospitalization in the United States and is associated with significant utilization of hospital resources, as well as considerable morbidity and mortality. These revised guidelines implement the Grading of Recommendations, Assessment, Development, and Evaluation methodology to propose recommendations for the use of risk stratification tools, thresholds for red blood cell transfusion, reversal agents for patients on anticoagulants, diagnostic testing including colonoscopy and computed tomography angiography (CTA), endoscopic therapeutic options, and management of antithrombotic medications after hospital discharge. Important changes since the previous iteration of this guideline include recommendations for the use of risk stratification tools to identify patients with LGIB at low risk of a hospital-based intervention, the role for reversal agents in patients with life-threatening LGIB on vitamin K antagonists and direct oral anticoagulants, the increasing role for CTA in patients with severe LGIB, and the management of patients who have a positive CTA. We recommend that most patients requiring inpatient colonoscopy undergo a nonurgent colonoscopy because performing an urgent colonoscopy within 24 hours of presentation has not been shown to improve important clinical outcomes such as rebleeding. Finally, we provide updated recommendations regarding resumption of antiplatelet and anticoagulant medications after cessation of LGIB.

KEYWORDS: lower gastrointestinal bleeding, hematochezia, colonoscopy

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/AJG/C827, http://links.lww.com/AJG/C828

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INTRODUCTION

Acute lower gastrointestinal bleeding (LGIB) is one of the most common reasons for hospitalization in the United States due to a digestive disorder, accounting for over 100,000 admissions annually (1). Although historically LGIB has referred to a bleeding source originating distal to the ligament of Treitz, small bowel bleeding is considered a separate entity, with a distinct diagnostic and therapeutic algorithm (2). For the purposes of this clinical practice guideline, LGIB refers to hematochezia or bright red blood per rectum originating from a colorectal source.

The purpose of this document was to update the previously published 2016 American College of Gastroenterology (ACG) LGIB guideline (3). In this document, we will review the epidemiology and risk factors of onset of LGIB, initial assessment, and role of risk stratification tools to identify patients at low and high risk of complications. We will then review resuscitation strategies, reversal of coagulopathy and management of LGIB in patients on antithrombotics, diagnostic testing with a focus on colonoscopy and computed tomography angiography (CTA), and the data on urgent vs elective inpatient colonoscopy. We will conclude by reviewing endoscopic hemostatic options and risk and benefits of resumption of antithrombotic medications after cessation of bleeding. We will focus the discussion on updates to management since the previous guideline was published.

METHODS

The panel members formulated clinically pertinent questions related to the management of LGIB framed in the PICO (population, intervention, comparator, and outcome) format. With the assistance of 2 medical librarians, a systematic English-language literature search of bibliographic databases (including EMBASE, Ovid MEDLINE, and ISI Web of Science) was performed from March 2, 2015, through December 1, 2021, for each PICO question. March 2 was chosen as the beginning date because this was when the literature search ended for the previous guideline (3). The literature search was manually repeated on

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April 1, 2022, to capture additional citations relevant to the PICO questions. All citations for each PICO question were screened by the primary author, and the most relevant citations for each PICO question were reviewed by the panel. Preference was given to randomized controlled trials (RCTs) and meta-analyses when available. However, given the relatively limited evidence base in LGIB as compared with other conditions such as upper GI bleeding (UGIB) (4), observational studies were used when RCTs were unavailable or limited. In the setting of limited high-quality evidence for certain PICO questions, the authors purposefully chose to include recommendations given how frequently clinicians encounter LGIB in the hospital setting.

Each recommendation (Table 1) includes an assessment of the strength of the recommendation and the quality of evidence based on the GRADE methodology, followed by a summary of the evidence (5). The strength of a recommendation is graded as Strong when the evidence shows the benefit of the intervention or treatment clearly outweighs any risk. The strength is recommended as Conditional when there is uncertainty as to the risk-benefit ratio. The certainty of evidence is graded as high if further research is unlikely to change the confidence in the estimate of the effect, moderate if further research is likely to have an important impact and may change the estimate, and low if further research is very likely to change the estimate.

Key concepts are statements that are not amenable to the GRADE process because of the structure of the question and/or limited available evidence. Most key concepts represent expert opinion based on extrapolation of the available evidence. Table 2

Table 1. Summary and strength of recommendations

1. We suggest using risk stratification tools (e.g., Oakland score ≤8) to identify low-risk patients with LGIB who are appropriate for early discharge and outpatient diagnostic evaluation. Risk scores should be used to supplement but not replace clinician judgment. (Conditional recommendation, low-quality evidence)
2. We suggest a restrictive strategy of red blood cell transfusion (threshold for transfusion at a hemoglobin level of 7 g/dL) in hemodynamically stable patients with LGIB. (Conditional recommendation, low-quality evidence)
3. Although most patients with LGIB on vitamin K antagonists are unlikely to require reversal, we suggest reversal of patients who present with a life-threatening LGIB and have an INR substantially exceeding the therapeutic range. For patients on vitamin K antagonists to prevent stroke in nonvalvular atrial fibrillation who require reversal, 4-factor PCC is preferred to FFP because of the rapidity of INR reduction. (Conditional recommendation, very low-quality evidence)
4. For patients on direct oral anticoagulants, we suggest reversal for the small subset of patients who present with a life-threatening LGIB that does not respond to initial resuscitation and cessation of the anticoagulant alone. For patients requiring reversal, targeted reversal agents (idarucizumab for dabigatran and andexanet alfa for apixaban and rivaroxaban) should be used when available if the direct oral anticoagulant has been taken within the past 24 hr. (Conditional recommendation, very low-quality evidence)
5. We recommend against administration of antifibrinolytic agents such as tranexamic acid in LGIB. (Strong recommendation, moderate-quality evidence)
6a. We recommend performance of colonoscopy for most patients who are hospitalized with LGIB because of its value in detecting a source of bleeding. (Strong recommendation, low-quality evidence) 6b. However, colonoscopy may not be needed in patients where bleeding has subsided and the patient has had a high-quality colonoscopy within 12 mo with an adequate bowel preparation showing diverticulosis with no colorectal neoplasia. (Conditional recommendation, very low-quality evidence)
7. We suggest performing a CT angiography as the initial diagnostic test in patients with ongoing hemodynamically significant hematochezia. However, CT angiography is of low yield in patients with minor LGIB or those in whom bleeding has clinically subsided. (Conditional recommendation, low-quality evidence)
8. We recommend that patients who have a CT angiography demonstrating extravasation be promptly referred to interventional radiology for transcatheter arteriography and possible embolization. For specialized centers with experience performing endoscopic hemostasis, a colonoscopy can also be considered after a positive CT angiography. (Strong recommendation, moderate-quality evidence)
9. For patients hospitalized with LGIB requiring a colonoscopy, we recommend performing a nonemergent inpatient colonoscopy, as performing an urgent colonoscopy within 24 hours has not been shown to improve clinical outcomes such as rebleeding and mortality. (Strong recommendation, moderate-quality evidence)
10. When detected, we recommend treatment of diverticular stigmata of hemorrhage with through-the-scope clips, endoscopic band ligation, or coagulation. (Strong recommendation, moderate-quality evidence)
11a. We recommend discontinuing nonaspirin NSAIDs after hospitalization for diverticular hemorrhage. (Strong recommendation, low-quality evidence) 11b. We suggest discontinuing aspirin for primary cardiovascular prevention after hospitalization for diverticular hemorrhage given the risks of recurrent diverticular hemorrhage. (Conditional recommendation, low-quality evidence) 11c. We suggest continuing aspirin after hospitalization for diverticular hemorrhage for patients with an established history of cardiovascular disease given the benefits of reducing future ischemic events. (Conditional recommendation, low-quality evidence) 11d. We recommend that providers re-evaluate the risks vs benefits of continuing nonaspirin antiplatelets such as P2Y12 receptor antagonists in a multidisciplinary setting after hospitalization for diverticular hemorrhage given the demonstrated risk of recurrent diverticular hemorrhage. (Strong recommendation, low-quality evidence)
12. We recommend resuming anticoagulation after cessation of LGIB given that resumption of anticoagulation has been shown to decrease the risks of postbleeding thromboembolism and mortality. (Strong recommendation, moderate-quality evidence)

CT, computed tomography; FFP, fresh frozen plasma; INR, international normalized ratio; LGIB, lower gastrointestinal bleeding; NSAID, nonsteroidal anti-inflammatory drug; PCC, prothrombin complex concentrate; PRBC, packed red blood cell.

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Table 2. Key concepts

1. A focused history, physical examination, and laboratory evaluation should be obtained at the time of patient presentation to assess the severity of bleeding and its possible location and etiology. Initial patient assessment and hemodynamic resuscitation should be performed simultaneously.
2. Patients with hemodynamic instability and/or suspected ongoing bleeding should receive intravenous fluid resuscitation with the goal of optimization of blood pressure and heart rate before endoscopic evaluation/intervention.
3. Hematochezia associated with hemodynamic instability may be indicative of an UGIB source, and an upper endoscopy should be performed if the suspicion is high to exclude a proximal source of bleeding.
4. Endoscopic hemostasis can be considered safe and effective in patients who have an INR of 2.5 or less.
5. Platelets should be administered in the setting of severe LGIB to maintain a platelet count of $>30 \times 10^9$/L, and a higher threshold of $>50 \times 10^9$/L can be considered if endoscopic procedures are required. There is no benefit to routine platelet transfusion for patients on antiplatelets.
6. For patients with LGIB on cardiac aspirin for secondary prevention, aspirin should be continued during hospitalization if possible. Nonaspirin antiplatelets should be held initially for patients with severe hematochezia. However, for patients with recent cardiac stents within 1 yr, a multidisciplinary approach should be used to determine the safety of temporarily holding antiplatelets.
7. The colonic mucosa should be carefully inspected during insertion and withdrawal, with aggressive attempts to wash residual stool and blood to identify bleeding sites. The terminal ileum should be intubated to exclude proximal sources of bleeding when feasible if a colonic source of bleeding is not found. Use of a clear cap is recommended to assist in detection and treatment of bleeding.
8. In patients undergoing inpatient colonoscopy, administration of 4–6 L of PEG-based bowel preparation has historically been recommended; however, split-dose preparations and/or the use of low-volume preparations can also be considered. Unprepared evaluation or routine flexible sigmoidoscopy is not recommended, unless the source is known to be emanating from the anorectal area or distal colon.
9. Endoscopic therapy is recommended when finding active bleeding or stigmata of hemorrhage, irrespective of the etiology.
10. For patients experiencing rebleeding after initial hemostasis or cessation of bleeding, repeat colonoscopy can be considered depending on the patient's stability and likelihood of successful repeat endoscopic therapy. In patients with suspected recurrent diverticular bleeding with recent colonoscopy who are hemodynamically stable, observation can be considered.

INR, international normalized ratio; LGIB, lower gastrointestinal bleeding; PEG, polyethylene glycol; UGIB, upper gastrointestinal bleeding.

summarizes the key concepts in this guideline. Each PICO question, along with the specific literature search strategy and evidence tables, is provided in the Supplementary Material (http://links.lww.com/AJG/C827 and http://links.lww.com/AJG/C828).

These guidelines are established for clinical practice with the intent of suggesting preferable approaches to particular medical problems as established by interpretation and collation of scientific valid research, derived from extensive review of published literature. When exercising clinical judgment, healthcare providers should incorporate this guideline along with the patient's needs, desires, and their values to fully and appropriately care for patients with LGIB. This guideline is intended to be flexible, not necessarily indicating the only acceptable approach, and should be distinguished from standards of care that are inflexible and rarely violated.

EPIDEMIOLOGY AND RISK FACTORS

LGIB remains one of the most common reasons for hospitalization in the United States due to a digestive disorder. In 2018, there were 271,575 emergency department (ED) visits and 113,020 hospital admissions for LGIB listed as a primary diagnosis (1). Compared with previous years, management of patients who are hospitalized for LGIB is more complex, with increasing age and comorbidities, higher transfusion requirements, and longer lengths of hospital stay (6).

Epidemiologic studies indicate that the incidence of LGIB may be rising relative to the incidence of UGIB. In a Finnish population-based cohort study, the incidence rate of LGIB was significantly higher than that of UGIB (1.26 per 1,000 person-years; 95% confidence interval [CI] 1.15–1.38 compared with 0.94 per 1,000 person-years; 95% CI 0.85–1.04) (7). Similar findings were seen in a population-based cohort study from Hong Kong where the incidence of LGIB surpassed that of UGIB over time, and the incidence of LGIB seemed to be particularly increasing in patients older than 80 years (8). The overall incidence of LGIB is believed to range between 33 and 87 of 100,000; however, high-quality epidemiologic studies in LGIB are lacking (9–11). Possible reasons for the rising incidence of LGIB include an aging population and increasing antithrombotic use. Compared with patients presenting with UGIB, patients with LGIB tend to be older. In the 2 prospective national UK audits of patients with UGIB (12) and LGIB (13), patients with LGIB had a median age of 74 years (interquartile range [IQR] 57–83) compared with 68 years (IQR 49–81) for those with UGIB.

Risk factors of the onset of LGIB include antiplatelet use, including aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), and P2Y12 inhibitors such as clopidogrel. In a population-based study of nearly 200,000 new users of low-dose aspirin, the incidence of LGIB was 1.68 per 1,000 person-years and was higher than that of UGIB. Importantly, case-fatality rates were very low for LGIB (<1%), and the majority were managed as outpatients (14). In a systematic review of observational studies, the pooled relative risk (RR) of LGIB with the use of aspirin was 1.8 (1.1–3.0), although there was significant heterogeneity between studies (15). The risk of LGIB with low-dose aspirin was shown to be higher than nonusers of aspirin in a large Taiwanese population cohort. The use of both aspirin (hazard ratio [HR] 2.75, 95% CI 2.06–3.65) and NSAIDs (HR 8.61, 95% CI 3.28–22.6) was an independent risk factor of LGIB in this cohort (16). For new aspirin users, the risk of LGIB in a population database was shown to be higher than UGIB in patients who had *Helicobacter pylori* eradicated (17). Aspirin and nonaspirin NSAIDs have both been shown to increase the risk of diverticular bleeding (18–20), believed to be due to mucosal ulceration within the dome or neck of a diverticula, subsequently contributing to arterial rupture into the colon lumen (21). Other potential explanations for aspirin-induced LGIB include an increased risk of bleeding from

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colorectal polyps (22). Data are more limited predicting the risk of LGIB with the use of P2Y12 drugs such as clopidogrel; however, studies have shown an increased risk of diverticular bleeding and all-cause LGIB with nonaspirin antiplatelets such as clopidogrel (23,24).

There are less data establishing systemic oral anticoagulants as risk factors of LGIB. Vitamin K antagonists (VKAs) are known to increase the risk of all-cause GI bleeding (GIB) by 3-fold compared with placebo (25), likely by triggering bleeding from preexisting lesions in the GI tract. Direct oral anticoagulants (DOACs) have been shown to be associated with a similar risk of major GIB compared with traditional anticoagulation; however, dabigatran and rivaroxaban particularly have an increased risk of GIB compared with warfarin and other DOACs (26,27). However, there is no difference in the risk of LGIB between DOACs and conventional anticoagulants (odds ratio [OR] 0.88, 95% CI 0.67–1.15) (26). The overall risk of LGIB was also found to be similar between rivaroxaban and dabigatran when compared with warfarin (28). When comparing risk between individual DOACs, data suggest that rivaroxaban has a higher risk of LGIB compared with apixaban (HR 1.53, 95% CI 1.00–2.33) (27).

As compared with antiplatelet drugs, DOACs have not been shown to increase the risk of new-onset diverticular hemorrhage (29). However, patients who experience new-onset LGIB after initiation of oral anticoagulants may be more likely to be subsequently diagnosed with colorectal cancer (30,31), indicating the importance of ensuring that patients are up-to-date with colon cancer screening before initiation of these drugs or shortly after if it is not feasible to do this before initiation. Finally, combinations of antiplatelet and anticoagulant drugs are associated with an increased risk of LGIB with an overall incidence of 70 of 1,000 person-years; the greatest risk occurred in patients with combination anticoagulant/antiplatelet therapy and triple antithrombotic therapy (32).

For patients with known underlying diverticulosis, data are lacking regarding the risks of subsequently experiencing a diverticular hemorrhage. In a long-term Japanese cohort study of patients with colonoscopy-confirmed asymptomatic diverticulosis, the cumulative risks of new-onset diverticular hemorrhage was 0.21% at 1 year, 2.2% at 5 years, and 9.5% at 10 years, with an overall incidence rate of 0.46 per 1,000 patient-years. Variables that were predictive of new-onset diverticular bleeding included age older than 70 years and presence of right and left-sided diverticulosis (33). Unlike the development of diverticulitis, dietary factors have not been clearly implicated to increase the risk of diverticular hemorrhage (34,35).

ETIOLOGY OF LGIB

LGIB comprises a heterogeneous group of etiologies, each with a distinct pathophysiology and clinical course. Although diverticular bleeding is the most common cause of LGIB (36), the frequency of diverticular bleeding within LGIB cohorts ranges widely in published reports and depends largely on factors such as utilization and timing of colonoscopy as well as the definition of diverticular bleeding. Defining a source of LGIB as diverticular in the absence of stigmata of hemorrhage (SRH) can be challenging because there is significant variability between institutions in the extent of additional diagnostic workup performed to exclude an upper or small bowel source of bleeding. In the UK audit of patients presenting with LGIB, diverticular bleeding was the most common cause of LGIB, representing 26.4% of cases (13). However, in a large, multicenter Japanese cohort where inpatient colonoscopy was performed in 88% of patients, diverticular bleeding was responsible for 64% of all cases; this included patients with definitive diverticular hemorrhage where SRH was seen at a diverticula or presumed diverticular hemorrhage based on a colonoscopy demonstrating diverticulosis and no other source of bleeding being found (37). Other common etiologies of LGIB include ischemic colitis, hemorrhoids, angioectasias, colorectal neoplasia, postpolypectomy bleeding, colitis (inflammatory, infectious, or radiation-related), rectal/stercoral/NSAID-induced ulcers, and radiation proctopathy (36–38). Less common etiologies may include Dieulafoy lesion and colorectal varices. Depending on the timing and utilization of inpatient colonoscopy, no source of bleeding is often found for patients admitted with LGIB. In fact, 23% of patients with LGIB in the UK audit had no diagnosed etiology of bleeding (13). Importantly, the most frequent diagnostic study in this cohort was flexible sigmoidoscopy (21.5%) and colonoscopy was used only in 4% of the cohort, limiting the overall generalizability and reflecting wide variation in the approach to investigation and management between countries. In cohorts with high utilization of colonoscopy, the rates of undiagnosed bleeding are as low as 5% (37).

INITIAL MANAGEMENT

Initial triage/evaluation

Key concepts

1. A focused history, physical examination, and laboratory evaluation should be obtained at the time of patient presentation to assess the severity of bleeding and its possible location and etiology. Initial patient assessment and hemodynamic resuscitation should be performed simultaneously.

A thorough history and physical examination is needed to determine potential sources of bleeding and help identify patients at risk of severe bleeding and adverse outcomes such as rebleeding and mortality. Pertinent components of the history should include but not be limited to the presence of cardiovascular, oncologic, or renal comorbidities; prior GI surgeries; and associated symptoms such as abdominal pain, alteration in bowel habits, or unintentional weight loss. Physical examination should include careful attention to vital signs and assessment for signs of hypovolemia, which will help dictate resuscitation. Careful rectal examination can help determine whether a bleeding source may be emanating from the anorectal region or indicate the presence of melena, which may increase the likelihood of an UGIB. Medications should be reviewed to determine the presence of NSAIDs, antiplatelets, and anticoagulants. History and examination findings such as a preceding history of decompensated liver disease or prior peptic ulcer disease along with epigastric discomfort on examination or visible stigmata of advanced liver disease may indicate the possibility of an upper GI source of bleeding in a patient with severe hematochezia.

Risk assessment

Recommendations

1. We suggest using risk stratification tools (e.g., Oakland score ≤8) to identify low-risk patients with LGIB who are appropriate for early discharge and outpatient diagnostic evaluation. Risk scores should be used to supplement but not replace clinician judgment. (Conditional recommendation, low-quality evidence)

Initial risk assessment is increasingly important to identify patients who are at either low or high risk of requiring a hospital-

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based intervention. Patients identified as being low-risk for requiring a hospital-based intervention can be observed and managed conservatively and potentially be discharged from the hospital with early outpatient follow-up, thereby allowing for preservation of scarce resources and significant cost savings.

Low-risk clinical prediction tools are widely used in patients with UGIB. The Glasgow Blatchford Score (GBS) was derived and validated to identify patients with UGIB who would require a hospital-based intervention (39). Updated ACG guidelines for UGIB suggest that patients presenting to the ED with UGIB who have a GBS of 0 or 1 be discharged with outpatient follow-up, rather than be admitted (4). Data on similar clinical prediction tools in LGIB have been lacking until recently. Using data from the UK audit of patients admitted with LGIB, Oakland et al. derived and validated a clinical score to predict safe discharge, defined as the absence of rebleeding, blood transfusion, therapeutic intervention, or 28-day hospital readmission (Table 3). Investigators then externally validated this score in 288 additional patients with LGIB at 2 UK hospitals and found that age, sex, history of LGIB, rectal examination findings, heart rate, systolic blood pressure, and hemoglobin level strongly discriminated safe discharge in both derivation and validation cohorts. These components made up the Oakland score; a score of 8 or less predicted a 95% probability of safe discharge (40). The Oakland score was externally validated using data from a network of 140 hospitals across the United States; the area under the receiver-operating characteristic curve (AUROC) for safe discharge was 0.87, despite one of the 7 variables comprising the Oakland score (digital rectal examination) being unavailable in the data set. The investigators found that a score of 8 or less had a sensitivity of 98% for safe discharge, and extending the score to 10 points or lower maintained a sensitivity of 96% for safe discharge (41). Based on these data, the European Society for Gastrointestinal Endoscopy and the British Society of Gastroenterology strongly recommend that in patients with a self-limited lower bleed and no adverse clinical features, an Oakland score of ≤8 can be used to guide patients for outpatient evaluation (42,43). Hreinsson et al. derived the SHA_2PE score using a retrospective cohort of 581 patients with LGIB; independent predictors of low-risk patients who did not require a hospital-based intervention included systolic blood pressure ≥100 mm Hg, hemoglobin level >12 g/dL, nonuse of antiplatelets and anticoagulants, and pulse <100 (44). The AUROC of this score in identifying low-risk patients who did not require a hospital-based intervention was 0.83. However, an external validation study of 251 patients with LGIB showed that the SHA_2PE incorrectly classified 14 patients who required a hospital-based intervention as being low-risk (45).

Both of these tools are promising and may help identify patients who are low-risk for requiring a hospital-based intervention; patients identified as being low-risk who do not have ongoing bleeding and have had a recent, high-quality colonoscopy excluding etiologies such as colorectal neoplasia may be discharged early from the hospital with outpatient follow-up, thereby avoiding potentially unnecessary inpatient colonoscopy. At present, we lack prospective, multicenter studies demonstrating that using either the Oakland score or the SHA_2PE score in the ED is a safe and effective strategy to manage patients with LGIB in the outpatient setting. Before widespread implementation of this score, further multicenter data on utilization of Oakland score thresholds to guide early discharge are needed to demonstrate that rebleeding rates are low and outpatient follow-up is achievable with minimal loss to follow-up (46).

Table 3. Validated clinical prediction tools in LGIB to predict patients at low risk of hospital intervention

Oakland score	
Age, yr	
<40	0
40–69	1
>70	2
Sex	
Female	0
Male	1
Previous LGIB admission	
No	0
Yes	1
DRE findings	
No blood	0
Blood	1
Heart rate (bpm)	
<70	0
70–89	1
90–109	2
>110	3
Systolic blood pressure (mm Hg)	
50–89	5
90–119	4
120–129	3
130–159	2
>160	0
Hemoglobin (g/dL)	
3.6–6.9	22
7.0–8.9	17
9.0–10.9	13
11.0–12.9	8
13.0–15.9	4
>16.0	0
SHA_2PE score	
Systolic pressure <100 mm Hg	1
Hemoglobin (g/dL)	
<10.5	2
10.5–12.0	1
Antiplatelet therapy	1
Anticoagulant therapy	1
Pulse >100 bpm	1
Emergency department bleeding	1

bpm, beats per minute; DRE, digital rectal examination; LGIB, lower gastrointestinal bleeding.
Comments: Oakland score ≤8 predicted safe discharge. Safe discharge was defined as the absence of all of the following after presentation: rebleeding, defined as additional blood transfusion requirements or a further decrease in hematocrit concentration of 20% or more after 24 hours of clinical stability; red blood cell transfusion; therapeutic intervention to control bleeding, defined as endoscopic, radiologic, or surgical hemostasis; in-hospital death; and readmission with further lower gastrointestinal bleeding within 28 days. SHA_2PE score ≤1 indicates that hospital-based intervention is unlikely. Hospital-based intervention defined as requirement of red blood cell transfusion, endoscopic hemostatic therapy, arterial embolization, or surgery.

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Although several clinical prediction scores have been derived and validated to predict the risk of severe bleeding and adverse outcomes in LGIB, these tools are not widely used by clinicians. The NOBLADS score was derived and validated with the goal of predicting patients at increased risk of severe bleeding; this outcome was defined by continuous bleeding during the first 24 hours (transfusion of ≥2 units of packed red blood cells [PRBCs] and/or a decrease in hematocrit of ≥ 20% from baseline) and/or recurrent bleeding after initial colonoscopy. The NOBLADS score predicted severe bleeding with an AUROC of 0.77, and higher NOBLADS scores were associated with the need for PRBC transfusion, long hospital stay, and requirement of intervention (47). This score was externally validated in a retrospective Japanese cohort of 511 patients and found to predict severe bleeding with an AUROC of 0.74 (48). However, it is unclear whether patients identified as being high-risk for severe bleeding by the NOBLADS score leads to meaningful improved clinical outcomes through interventions such as transitioning to a higher level of care or earlier diagnostic testing with colonoscopy.

Several additional scores have been derived and validated to predict adverse outcomes in LGIB. The Birmingham Score, comprising sex and admission hemoglobin level, was found to predict a composite adverse outcomes in LGIB, including need for PRBC transfusion, endoscopic intervention, CTA, surgical intervention, rebleeding, and mortality (49). A single-center large retrospective database was used to derive and internally validate a score which predicted 30-day mortality in LGIB (50). Finally, investigators derived and validated the ABC score with the goal of accurately predicting mortality in an undifferentiated patient with GIB. This pre-endoscopic score consisting of variables such as age, blood urea level, albumin, creatinine, altered mental status, cirrhosis, disseminated malignancy, and American Society of Anesthesiologists score accurately predicted 30-day mortality in cohorts of patients with UGIB (AUROC 0.81, 95% CI 0.78–0.83) and LGIB (AUROC 0.84, 95% CI 0.79–0.89). Moreover, this score was superior to other established scores, which may be predictive of mortality in UGIB such as the AIMS65 and GBS scores (51).

At present, no score is widely used to predict adverse outcomes in LGIB. A prospective study of 170 patients with LGIB comparing a variety of pre-endoscopic scoring systems demonstrated that no score had an excellent predictive ability across all important outcomes in LGIB, including severe bleeding, need for PRBC transfusion, in-hospital recurrent bleeding, and need for endoscopic intervention (52). A few machine learning algorithms have been studied in small LGIB cohorts to accurately predict specific outcomes such as need for surgery and rebleeding (53,54); however, these algorithms have not been externally validated nor are they used clinically (55).

Risk prediction scores should not be used to replace clinical judgment and should likely be used as a supplemental tool in decision making. The likelihood is that clinical prediction scores are unlikely to be widely used unless they are automatically calculated in the electronic health record and then used to alert physicians as to the patient's individual risk (either low risk or high risk), thereby subsequently triggering specific pathways of management (56).

Hemodynamic resuscitation

Key concepts

2. Patients with hemodynamic instability and/or suspected ongoing bleeding should receive intravenous fluid resuscitation with the goal of optimization of blood pressure and heart rate before endoscopic evaluation/intervention.

Recommendations

2. We suggest a restrictive strategy of red blood cell transfusion (threshold for transfusion at a hemoglobin level of 7 g/dL) in hemodynamically stable patients with LGIB. (Conditional recommendation, low-quality evidence)

Patients who are hemodynamically unstable should receive intravenous fluid resuscitation with crystalloids with the goal of normalization of blood pressure and heart rate before any diagnostic or therapeutic intervention. In addition, patients with significant hematochezia with reduction in hemoglobin levels may require PRBC transfusion. Data on transfusion targets in LGIB are extrapolated from the UGIB literature. The benefit of a restrictive transfusion strategy was seen in a RCT of patients with UGIB; a restrictive transfusion strategy (hemoglobin threshold for transfusion of 7 g/dL) compared with a liberal transfusion strategy (hemoglobin threshold for transfusion of 9 g/dL) was associated with a significantly improved survival at 6 weeks, with a lower risk of further bleeding (57). In a meta-analysis of 5 RCTs comprising 1,965 patients with UGIB, a restrictive transfusion strategy was associated with a lower risk of all-cause mortality (RR 0.65, 95% CI 0.44–0.97) and rebleeding (RR 0.58, 95% CI 0.40–0.84) (58). A restrictive transfusion may not be applicable to patients presenting with hemorrhagic shock, given that these patients were largely excluded in the previous RCTs. Data are far more limited in a population restricted to patients with LGIB. In a post hoc analysis of the UK audit of LGIB, investigators looked at the relationships between a liberal transfusion strategy (defined as transfusion for ≥80 g/L [or ≥90 g/L] in patients with acute coronary syndrome) and a restrictive transfusion strategy. No difference was seen between a liberal and restrictive RBC transfusion strategy for odds of rebleeding (OR 0.89, 95% CI 0.6–1.22) or in-hospital mortality (OR 0.54, 95% CI 0.3–1.1) (59). Based on the available data, patients with LGIB who are hemodynamically stable without signs of shock should likely be managed with a restrictive transfusion strategy, although exceptions should be made in the setting of significant ongoing active bleeding and presence of shock. Previously published clinical guidelines have also recommended a higher threshold of 8 g/dL in stable patients with preexisting cardiovascular disease, despite the lack of supporting RCT evidence (60). A threshold of 8 g/dL can also be considered in patients with acute coronary syndrome and GIB; however, data are extremely limited on restrictive vs liberal thresholds in this population (4).

Exclusion of proximal source of bleeding

Key concepts

3. Hematochezia associated with hemodynamic instability may be indicative of an UGIB source, and an upper endoscopy should be performed if the suspicion is high to exclude a proximal source of bleeding.

For patients presenting with severe hematochezia, the possibility of a brisk, proximal source of bleeding should be considered, based on other clinical factors. In a study of 85 patients presenting with hematochezia and high-risk features who underwent esophagogastroduodenoscopy (EGD) before colonoscopy, 15% had a proximal source of bleeding (61). Ultimately, clinicians must rely on an individual's pretest probability for the patient having an upper source of bleeding. Important components of the

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history should be obtained, including a history of peptic ulcer disease or decompensated liver disease. Laboratory findings such as an elevated blood urea nitrogen (BUN)-to-creatinine (Cr) ratio may suggest an upper source of bleeding. A BUN-to-Cr ratio of >30 was found to have a likelihood ratio (LR) of 7.5 (95% CI 2.8–12.0) for UGIB, whereas the presence of blood clots in stool decreased the likelihood of a UGIB (LR 0.05, 95% CI 0.01–0.38) (62). In another diagnostic accuracy study of patients with GIB, the BUN-to-Cr ratio did not perform well in predicting an upper vs lower source of bleeding (AUROC 0.63), although a BUN-to-Cr cutoff of 35 had a specificity and positive predictive value of 90.1% and 89.1%, respectively, in predicting UGIB as compared with LGIB (63). Results of another study indicated that the BUN level alone was the strongest variable which predicted an upper vs lower source of bleeding; a threshold of 21 mg/dL predicted an UGIB vs LGIB source with a specificity of 93.0% (64).

Nasogastric aspirate has very poor sensitivity to establish an upper GI source of bleeding. In a retrospective cohort of patients with melena undergoing nasogastric aspirate, the sensitivity of nasogastric aspirate to establish an upper GI tract of bleeding was only 28%, and the negative predictive value was <1% (65). Finally, a systematic review was performed to assess the diagnostic precision of the BUN-to-Cr ratio and nasogastric aspiration in patients with GIB without hematemesis. Only 4 studies were identified, the sensitivity of both tests for a diagnosis of UGIB was very poor (negative LR of 0.6) (66). Based on the lack of data, routine placement of a nasogastric tube cannot be recommended. Because no head-to-head studies are available comparing initial EGD with initial colonoscopy or radiologic testing such as CTA in patients with severe hematochezia, clinicians ultimately should determine the pretest probability of an UGIB source based on clinical history and laboratory findings and perform an urgent EGD if the risk is considered high.

REVERSAL OF COAGULOPATHY AND MANAGEMENT OF ANTITHROMBOTICS

Management of patients on VKAs

Key concepts

4. Endoscopic hemostasis can be considered safe and effective in patients who have an international normalized ratio (INR) of 2.5 or less.

Recommendations

3. Although most patients with LGIB on VKAs are unlikely to require reversal, we suggest reversal of patients who present with a life-threatening LGIB and have an INR substantially exceeding the therapeutic range. For patients on VKAs to prevent stroke in nonvalvular atrial fibrillation who require reversal, 4-factor prothrombin complex concentrate (PCC) is preferred to fresh frozen plasma (FFP) because of the rapidity of INR reduction (Conditional recommendation, very low-quality evidence).

For patients presenting with LGIB on VKAs, the decision whether to reverse anticoagulation should be dependent on the patient's hemodynamic stability, severity of bleeding, and laboratory parameters including the INR level. In patients with minor bleeding who are unlikely to require a hospital-based intervention (e.g., Oakland score ≤8), oral anticoagulants may be continued if necessary. For patients with more significant bleeding requiring hospitalization, oral anticoagulants should be held at admission. In an analysis of 512 patients with GIB who were on warfarin or dabigatran in 5 phase III clinical trials, 26% were managed with discontinuation of the drug only (67). In another study of 133 patients with GIB while on warfarin in the ARISTOTLE trial, 76% had their drug interrupted during hospital admission (68).

For patients with hemodynamic instability and severe bleeding, reversal of anticoagulation may be warranted; options for reversal include vitamin K, FFP, and 4-factor PCC. European guidelines recommend administering vitamin K along with PCC (strong recommendation, low-quality evidence) or FFP if PCC is unavailable (weak recommendation, very low-quality evidence) for patients with hemodynamic instability (43,69). Recent joint ACG-Canadian Association of Gastroenterology guidelines on the management of antithrombotic agents in the setting of acute GIB suggest against the routine use of vitamin K and suggest PCC administration as compared with FFP administration for those patients who require reversal (conditional recommendation, very low certainty of evidence) (70).

Consideration should also be given to the degree of INR prolongation, severity of bleeding, as well as timing of any diagnostic and therapeutic procedures. Endoscopic therapy is effective even at moderately elevated INR levels (2.5 or less); however, reversal agents should be considered before endoscopy in patients with severe bleeding with hemodynamic instability and significant prolongation in INR substantially exceeding therapeutic levels. Importantly, INR at the onset of GIB or immediately before endoscopy has not been shown to be associated with rebleeding risk, and no significant difference in rebleeding has been seen between patients with an INR of <2.5 compared with >2.5 (71). In patients with a prolonged INR who do not have SRH and endoscopic therapy is not performed, anticoagulation can be continued.

Data are extremely limited in LGIB specifically on the use of PCC vs other strategies for anticoagulant reversal, despite reversal agents being used relatively commonly. In a multicenter, observational study of patients presenting with major bleeding on warfarin (52% of whom had GIB), 31% of patients received FFP compared with 23% of patients who received PCC (72). Treatment with PCC was shown to be noninferior to FFP in achieving effective hemostasis in one RCT including patients requiring urgent VKA reversal due to acute major bleeding (n = 202; 63% with GIB/nondefined nonvisible bleeding). Overall, 72.4% (n = 71/98) of patients who received PCC achieved effective hemostasis compared with 65.4% (n = 68/104) of patients who received FFP (73). In another RCT of PCC compared with FFP for rapid VKA reversal before urgent surgical or invasive interventions, PCC was found to be superior to FFP in effective hemostasis (90% vs 75%) and rapidity of INR reduction (55% in PCC group vs 10% in FFP group) while having a similar safety profile (74). In a post hoc analysis of these 2 RCTs limited to 42 patients with acute severe GIB, PCC administration compared with FFP was associated with a reduced time to the first endoscopic procedure. No difference was seen in hemostatic efficacy between the 2 groups (75). In another study of 40 patients on warfarin with mostly UGIB, PCC normalized INR levels more rapidly than FFP and was associated with less active bleeding on endoscopy compared with FFP (76). In a meta-analysis of PCC for reversal of VKA-associated bleeding, PCC was associated with a low risk of thromboembolic complications in comparison with FFP (77). In addition, PCC for VKA reversal as compared with FFP was associated with a reduction in all-cause mortality, more rapid INR reduction, and less volume overload (78).

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Data are clearly needed to help guide reversal strategies in LGIB-specific populations. However, based on its safety profile and the current available data, PCC should be considered as a first-line reversal option in unstable patients with severe, life-threatening LGIB despite resuscitation who have significant prolongation in their INR.

DOAC reversal

Recommendations

4. For patients on DOACs, we suggest reversal for the small subset of patients who present with a life-threatening LGIB that does not respond to initial resuscitation and cessation of the anticoagulant alone. For patients requiring reversal, targeted reversal agents (idarucizumab for dabigatran and andexanet alfa for apixaban and rivaroxaban) should be used when available if the DOAC has been taken within the past 24 hours (Conditional recommendation, very low-quality evidence).

Similar to the management of patients on VKA with LGIB, patients presenting with minor bleeding and who are at low risk of a hospital-based intervention on DOACs can likely have their medications continued. Patients with significant LGIB who are more likely to require an intervention should have their DOACs held at admission. Although data are lacking in the LGIB literature, it is likely that most patients with significant LGIB can likely be managed by holding the drug, adequate resuscitation, and waiting for the anticoagulant effect to dissipate.

Assessment of the anticoagulant effect on GIB using laboratory parameters such as prothrombin time and activated partial thromboplastin time should be considered, although interpretation of the levels and the need to obtain more specialized tests such as anti-factor Xa levels may depend on test availability and the specific clinical situation. Interpretation of prothrombin time and activated partial thromboplastin time may be limited because normal levels do not exclude clinically relevant levels of apixaban or rivaroxaban.

For patients with severe LGIB who have hemodynamic instability, there may be a role for reversal of the DOAC. There is limited benefit of vitamin K, FFP, or cryoprecipitate for the management of DOAC-related LGIB. However, targeted reversal agents are available at present, although data are lacking in patients with LGIB. The specific reversal agents idarucizumab and andexanet alfa have both been assessed in patients with DOAC-associated major bleeding (79,80). In a subanalysis of 137 patients in the RE-VERSE AD trial with GIB who received idarucizumab for reversal of dabigatran, 68.7% of evaluable patients experienced bleeding cessation within 24 hours, after a median duration of 2.4 hours. In this study, 43 of the 137 patients had a LGIB (81). Neither RE-VERSE AD nor ANNEXA-4 enrolled control groups because there was no accepted standard of care for DOAC reversal at the time of their design, and the use of a placebo was deemed unethical; it is therefore difficult to contextualize these results. In a nationwide analysis of 1,747 dabigatran users with GIB, administration of idarucizumab (compared with no administration) was also associated with an increased need for PRBC transfusion and an increase in overall costs of care, but was not associated with an altered risk of in-hospital mortality (82). In a small retrospective report of 21 patients receiving andexanet for factor Xa inhibitor-associated extracranial bleeding, effective hemostasis was only achieved in 48% of patients, and mortality and ischemic/thromboembolic complications were high (83). However, in a real-world, nationwide analysis of factor Xa inhibitor bleeding, those patients with GIB who received reversal with andexanet alfa only had an in-hospital mortality of 1% compared with 4% for those with GIB who received FFP or PCC for reversal (84). Further data are needed to determine the safety and efficacy of these 2 reversal agents in patients with severe LGIB and how these reversal strategies compare with withholding the DOAC alone.

At present, there is no definitive role for PCC in reversal of factor Xa inhibitors. In a systematic review and meta-analysis, 10 case series of 340 patients were identified who received PCC for reversal of the DOAC effect; the pooled proportion of effective hemostasis achieved was 69%. In addition, there was very little certainty based on single-arm case series, and it was impossible to determine whether PCC administration was superior to cessation of the factor Xa inhibitor alone (85).

Management of antiplatelets in an acute setting

Key concepts

5. Platelets should be administered in the setting of severe LGIB to maintain a platelet count of $>30 \times 10^9$/L, and a higher threshold of $>50 \times 10^9$/L can be considered if endoscopic procedures are required. There is no benefit to routine platelet transfusion for patients on antiplatelets.
6. For patients with LGIB on cardiac aspirin for secondary prevention, aspirin should be continued during hospitalization if possible. Nonaspirin antiplatelets should be held initially for patients with severe hematochezia. However, for patients with recent cardiac stents within 1 year, a multidisciplinary approach should be used to determine the safety of temporarily holding antiplatelets.

There are limited data on the management of antiplatelets in the acute setting of a patient presenting with significant LGIB. Empiric transfusion of platelets is not recommended for patients on antiplatelets. In a case-control study of patients with GIB on antiplatelet agents without thrombocytopenia, patients receiving platelet transfusion had no benefit in rebleeding and had higher mortality compared with controls with GIB who did not receive platelet transfusion (86). There are no data to guide specific transfusion thresholds in patients with LGIB with thrombocytopenia; however, transfusion of platelets in the setting of clinically significant bleeding to maintain a platelet count of $>30 \times 10^9$/L is recommended, and a higher threshold of $>50 \times 10^9$/L can be considered if an invasive procedure is required (87). Aspirin should be held and potentially permanently discontinued in patients who are on it for primary cardiovascular prevention. For patients on cardiac aspirin for secondary prevention, continuing aspirin during hospitalization is appropriate in most settings. However, temporary discontinuation should be considered in patients with severe and/or ongoing LGIB. If patients have high cardiovascular/thrombotic risk, then a decision to withhold antiplatelet therapy should be made in conjunction with a multidisciplinary approach. For patients on dual antiplatelet therapy, aspirin should be continued if possible while the P2Y12 receptor antagonist is held; however, in patients with previous stents within a year, the P2Y12 receptor antagonists should be resumed within a maximum of 5 days because of high risk of stent thrombosis (88).

Data on the safety and efficacy of endoscopic therapy on antiplatelets are sparse. In a multicenter study of patients with UGIB, patients on antithrombotics at the time of UGIB had similar rates of rebleeding after endoscopic intervention compared with those not on antithrombotics (89). In an analysis of

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patients admitted with LGIB in the UK audit of LGIB, patients on single and dual antiplatelet therapies had an increased risk of rebleeding, as compared with patients on anticoagulants (90). Most rebleeding events occurred within the first 5 days, and no difference was observed in in-hospital rebleeding between patients who had their antiplatelet continued throughout admission vs those who had the drug stopped for <5 days. Interestingly, the increased rate of rebleeding was not associated with an increase in the need for endoscopic intervention or mortality.

Role of antifibrinolytic agents

Recommendations

5. We recommend against the administration of antifibrinolytic agents such as tranexamic acid in LGIB. (Strong recommendation, moderate quality evidence)

To date, antifibrinolytic agents such as tranexamic acid have not been beneficial in the management of patients presenting with LGIB. In a randomized, double-blinded, placebo-controlled trial of 96 patients with LGIB, there was no significant difference between use of tranexamic acid and placebo for the primary outcome of reduction in hemoglobin levels and no difference in transfusion rates, transfusion volumes, intervention rates, or lengths of hospital stay (91). In a Japanese observational database study of patients admitted with diverticular hemorrhage, the use of tranexamic acid was not significantly associated with improved in-hospital mortality. Of note, the authors did find that tranexamic acid use was associated with lower blood transfusion needs, length of stay, and total hospitalization costs (92). Finally, in a large, international, randomized, placebo-controlled trial that included over 12,000 patients with significant GIB, tranexamic acid was not associated with a reduction in death from bleeding, all-cause bleeding, or mortality. Importantly, venous thromboembolic events were higher in patients receiving tranexamic acid as compared with placebo, as were seizures (93). On the basis of these studies, tranexamic acid does not have a benefit in LGIB and may be associated with an increased risk of harm.

DIAGNOSTIC TESTING

Role of colonoscopy

Key concepts

7. The colonic mucosa should be carefully inspected during insertion and withdrawal, with aggressive attempts to wash residual stool and blood to identify bleeding sites. The terminal ileum should be intubated to exclude proximal sources of bleeding when feasible if a colonic source of bleeding is not found. The use of a clear cap is recommended to assist in detection and treatment of bleeding.

Recommendations

6a. We recommend the performance of colonoscopy for most patients who are hospitalized with LGIB because of its value in detecting a source of bleeding (Strong recommendation, low-quality evidence).

6b. However, colonoscopy may not be needed in patients where bleeding has subsided, and the patient has had a high-quality colonoscopy within 12 months with an adequate bowel preparation showing diverticulosis with no colorectal neoplasia. (Conditional recommendation, very low-quality evidence)

Colonoscopy is considered the diagnostic test of choice for patients admitted with LGIB, given that it allows for the diagnosis of a specific etiology, mucosal tissue sampling, and possible therapeutic options for control of bleeding. The yield of colonoscopy in detecting the etiology of bleeding varies widely in the literature, depending on the location of the cohort and timing of colonoscopy performed. In a Japanese cohort where colonoscopy was performed in 88% of patients with LGIB, SRH was identified in 31% of cases who underwent endoscopy (37). In a European cohort of patients undergoing colonoscopy for LGIB, the overall diagnostic yield (both definitive and presumptive) was 79% (38). Endoscopic hemostasis rates in the cohort of patients undergoing colonoscopy within 24 hours were as high as 21%; however, endoscopic hemostasis was not associated with decreased mortality or rebleeding. In addition, there is a difference between diagnostic yield of colonoscopy and detecting SRH and/or active bleeding at the time of colonoscopy. In a cohort of patients undergoing colonoscopy for LGIB, the diagnostic yield was high at 68%; however, SRH was only seen in 15% of the colonoscopies performed and active bleeding only seen in 3.8% of cases (94).

Despite having a high diagnostic yield, the performance of endoscopic intervention may be relatively uncommon, particularly in Western cohorts. In a large insurance claims database of 16,640 patients undergoing colonoscopy for diverticular hemorrhage, endoscopic intervention defined using Current Procedural Terminology codes only occurred in 6% of patients. In addition, endoscopic intervention was not protective of 30-day rebleeding (95). In a large Western single-center retrospective study of patients undergoing colonoscopy for LGIB, endoscopic intervention during colonoscopy was only performed in 3% of patients; variables associated with the need for endoscopic intervention included age, early colonoscopy (<24 hours), and presence of colonic arteriovenous malformations (96). Using the Clinical Outcomes Research Initiative National Endoscopic Database, investigators showed that of 3,151 patients undergoing colonoscopy for LGIB, hemostasis was only performed in 144 patients (4.5%) (97).

Despite colonoscopy having relatively low rates of intervention, the value in detecting an etiology of bleeding is critical to determine subsequent management and triage of patients. Relatively rarer causes of LGIB include conditions such as ischemic colitis or colorectal cancer, which require close follow-up and specific management. The presence of malignant lesions in a cohort of patients undergoing colonoscopy for LGIB occurred in 2.5% of patients (94). For patients who are not up-to-date with colorectal cancer screening and present with hematochezia and other symptoms such as iron deficiency and/or weight loss, performing a colonoscopy has obvious value in detecting etiologies such as colorectal neoplasia.

Conversely, for patients who have had a recent colonoscopy within 12 months with an adequate bowel preparation and present with stable LGIB, patients can potentially be managed conservatively without performing a colonoscopy if their bleeding subsides while in the hospital. A similar conservative strategy is also reasonable in patients with an established history of recent diverticular bleeding presenting with recurrent stable LGIB. However, even if patients have had a recent colonoscopy within 12 months, a repeat inpatient colonoscopy may be required if there are new symptoms which could be suggestive of a different disease process such as inflammatory bowel disease or ischemic colitis.

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In addition to utilization of low-risk identification tools such as the Oakland score, further data on identifying who actually benefits from an inpatient colonoscopy is needed. Chung et al. conducted a retrospective analysis of patients with LGIB and derived a score which predicted patients who had potential bleeding sources requiring hemostasis, active bleeding on colonoscopy, or malignant-appearing lesions (94). Investigators have also shown that existing risk scores such as the NOBLADS score may predict finding SRH at the time of colonoscopy in patients with suspected diverticular hemorrhage (98). Other variables shown to be predictive of detecting SRH have included use of a cap, water-jet scope, performance by an expert colonoscopist, and performing an urgent colonoscopy (99).

The use of a transparent clear cap during colonoscopy has several potential benefits. It can help deflect mucosal folds and stabilize the tip of the endoscope, thereby improving mucosal visualization and potentially helping detect subtle sources of bleeding. Moreover, the clear cap can help facilitate endoscopic treatment by placing the target of therapy at an ideal and constant distance for delivering treatment while also aligning the target of therapy with the axis of the accessory channel (100). The terminal ileum should also be intubated when feasible to exclude a proximal source of bleeding if a colonic source of bleeding is not found. Patients who are extremely unlikely to either require hemostasis or have neoplastic lesions as the cause of their bleeding can potentially be followed as an outpatient without the need for a procedure.

Role of CTA

Recommendations

7. We suggest performing a CTA as the initial diagnostic test in patients with ongoing hemodynamically significant hematochezia. However, CTA is of low yield in patients with minor LGIB or those in whom bleeding has clinically subsided. (Conditional recommendation, low-quality evidence)

CTA has an increasing role in the diagnosis and management of LGIB because of the ability to rapidly obtain images without the need for a bowel preparation. In a meta-analysis of 14 observational studies, the sensitivity and specificity of CTA in the diagnosis of LGIB were 90% and 92%, respectively. However, the studies included in the meta-analysis were highly heterogeneous and varied as to whether colonoscopy was performed (101). CTA can precisely localize the source of arterial and venous GIB as well as delineate the vascular anatomy before embolization. In addition, multiphase CTA can be typically completed within minutes, even in hemodynamically unstable patients. Disadvantages of CTA include radiation dose and need for intravenous contrast. Moreover, negative results can occur if the patient is not actively bleeding (102). Patients with a negative CTA may benefit from a subsequent conservative strategy. In a retrospective study of patients undergoing CTA for LGIB, nearly 80% of patients with an initial negative CTA had no further clinical or radiologic evidence of rebleeding and settled spontaneously without the need for endoscopic or radiologic intervention (103). For patients with a negative CTA, there is limited role for immediate transcatheter angiography (TA); in a study of 14 patients with LGIB with a negative CTA subsequently undergoing TA, results of TA were negative in all cases (104).

Further data on risk factors to predict which patients with LGIB are likely to have a positive CTA are needed. In a retrospective analysis of 930 patients with LGIB, 10% of the population underwent initial CTA, and these patients were older and more likely to be hypotensive and receive PRBC transfusions. Only 9 of 93 patients had a positive CTA (105). In another larger retrospective cohort study of 854 patients undergoing CTA for LGIB, 20% of scans were positive. Factors associated with a positive CTA included recent bowel resection or endoscopic intervention, transfusion of more than 3 units of PRBC per day, use of antiplatelet agents, tachycardia, and hypotension (106). In addition, performance of CTA within 4 hours of hematochezia increases the likelihood of a positive test (107). A shock index (heart rate divided by systolic blood pressure) of ≥1 can also be used as a supplemental tool to predict active bleeding on CTA (108) but has not been shown to be strongly predictive of clinical outcomes in LGIB (42). Additional variables that may increase the probability of a positive CTA in patients with significant LGIB include recent use of NSAIDs or DOACs (109). In a large, multicenter Japanese cohort of patients admitted with LGIB, urgent CT within an hour was performed in 97.5% of the cohort, with 22.0% demonstrating extravasation on CT (37).

MANAGEMENT OF A POSITIVE CTA

Recommendations

8. We recommend that patients who have a CTA demonstrating extravasation be promptly referred to interventional radiology for transcatheter arteriography and possible embolization. For specialized centers with experience in performing endoscopic hemostasis, a colonoscopy can also be considered after a positive CTA. (Strong recommendation, moderate quality evidence)

Role of transcatheter arteriography. Patients who have a source identified at the time of CTA benefit from proceeding with a TA and potential mesenteric embolization if extravasation is seen on angiography. In a single-center study, preceding angiography with a diagnostic CTA was shown to improve localization of LGIB compared with TA alone (110). In addition, owing to the intermittent nature of LGIB and diverticular bleeding in particular, patients with a positive CTA likely have a short window of time where they benefit from proceeding to TA. In a single-center retrospective study of all patients who underwent angiography after a positive CTA for LGIB, invasive TA that was performed within 90 minutes after a positive CTA was 9 times more likely to detect extravasation (111). As such, angiography should be performed promptly after a positive CTA because the greater the time delay between CTA and TA, the weaker the correlation between a bleed observed between the 2 modalities (112). Depending on the institution, it may also be reasonable to provide the radiology service forewarning that a CTA is being ordered on a patient with unstable LGIB, to potentially allow for optimal coordination between services and timely performance of angiography. If CTA shows extravasation in the upper GI tract, then an urgent EGD should be performed.

To provide targeted therapy at the time of angiography, extravasation must be identified. The use of a microcatheter allows for superselective embolization of a single vasa recta at the site of bleeding. Embolization can typically be performed using microcoils, N-butyl cyanoacrylate (NBCA), or an ethylene-vinyl alcohol copolymer (113). Overall, efficacy rates are high and risks of ischemic complications are low if embolization can be limited to a distal site. In a meta-analysis of observational studies of patients

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receiving embolization with NBCA for LGIB, technical success was achieved in 98% of patients and major complications occurred in 4.6% of patients. The most common complication was the development of bowel infarction or development of an ulcer (114). In another systematic review and meta-analysis of 243 patients with LGIB undergoing TA with NBCA embolization, the technical success rate was 98.8%; however, 30-day rebleeding and mortality rate were 15.7% and 12.7%, respectively (115).

Role of colonoscopy after a positive CTA. Patients who have a positive CTA are more likely to have a source detected and treated at the time of a subsequent colonoscopy. In retrospective cohorts of patients with LGIB, the bleeding source was detected more frequently on colonoscopy when extravasation had been previously identified on CTA (107,116,117). Similarly, endoscopic intervention has been shown to be more common in patients undergoing early colonoscopy after urgent CT vs early colonoscopy alone (118). However, this strategy of routine CTA before colonoscopy (119) has not been shown to be beneficial to a strategy of either elective colonoscopy or TA after a positive CTA in reducing rebleeding or mortality. Nonetheless, in a study of 182 patients with LGIB undergoing CTA before colonoscopy, those who underwent colonoscopy after an urgent CT demonstrating extravasation (within 4 hours of presentation) were more likely to have SRH on colonoscopy, in addition to having reduced rebleeding within 30 days, compared with those who had a nonurgent CTA (120). A comparator group of patients who did not undergo CTA before colonoscopy was unavailable. Further data are needed on this approach, particularly in Western settings.

Comparing outcomes of angiography and colonoscopy. There are limited data comparing outcomes of patients who undergo CTA, have extravasation seen, and are subsequently treated by transarterial embolization with patients who are treated endoscopically by colonoscopy. In a retrospective cohort of patients with LGIB undergoing colonoscopy or angiography within 1 day of presentation, a higher percentage of the angiography group had a previous CTA and required intensive unit care, PRBC transfusion, or vasopressors. After propensity score matching between the 2 groups, there were no differences in mortality between the 2 groups; however, the angiography group was less likely to need emergency surgery within 1 day of admission compared with the colonoscopy group (121). Recently, investigators reported the outcomes of 71 patients who had a positive CTA for LGIB and underwent either colonoscopy (n = 27) or angiography (n = 44). Angiography had a higher yield of detecting active bleeding compared with colonoscopy (55% vs 26%, $P = 0.03$), but had similar rates of therapeutic intervention compared with colonoscopy (70% vs 56%, $P = 0.21$). Shorter time to procedure was the only significant predictor of confirmation of active bleeding and need for therapeutic intervention; rebleeding rates along with adverse events were not different between patients undergoing angiography or colonoscopy after a positive CTA (122).

In addition, there are limited available data comparing patients who undergo initial CTA vs initial colonoscopy as their first diagnostic test. In an observational study of 382 patients with LGIB, CTA was noninferior to colonoscopy in bleeding site detection (123). In another single-center, retrospective report of 183 patients with LGIB, 122 patients underwent colonoscopy as their first diagnostic test compared with 32 patients undergoing CTA. Time to first diagnostic examination was significantly reduced in the CTA group as compared with colonoscopy (3 vs 22 hours), and active bleeding was found significantly more frequently with CTA compared with colonoscopy (31% vs 15%, $P = 0.03$) (124). Finally, investigators published their experience on primary CTA vs colonoscopy in the setting of undifferentiated LGIB. Of 258 patients, 162 underwent initial elective colonoscopy compared with 96 patients who underwent CTA. When controlling for hypotension, PRBC transfusion, and time to intervention, colonoscopy was associated with a higher probability of source identification and hemostatic intervention; however, in the subgroup of patients with diverticular bleeding, CTA had higher rates of therapeutic intervention compared with colonoscopy (18% vs 3.8%) (125).

Although clinical data are limited on this topic, a survey study of radiologists indicated that for patients with hemodynamically significant LGIB, the first-line recommended diagnostic study was CTA, chosen in 62% compared with conventional angiography (19%), surgery (12%), or colonoscopy (4%). Conversely, in those with hemodynamically stable LGIB, the first-line recommended diagnostic study was inpatient colonoscopy (46%), followed by CTA (126). The decision on whether to perform initial CTA should ultimately be based on patient-level variables, including the severity of bleeding and likelihood of seeing extravasation, as well as system-level factors, such as the availability of interventional radiology and the institutional comfort and experience performing endoscopic hemostasis. Patients who are hemodynamically stable with resolution of active bleeding may benefit from initial colonoscopy because CTA is unlikely to be positive in the setting of cessation of bleeding. On the other hand, patients with severe ongoing active hematochezia may benefit from initial CTA because they may not be able to tolerate bowel preparation, and colonoscopy may fail to localize the precise source of bleeding because of a large amount of blood in the colon obscuring visualization.

Role of nuclear imaging. CTA is increasingly used for the diagnosis of LGIB compared with ^{99m}Technetium-labeled RBC scintigraphy; the latter study has significant limitations because of the relatively long duration of the study and the inability to precisely localize the site of bleeding. Owing to these limitations and the advantages of CTA, uptick of use of CTA increased from 3.8% to 57% at an academic medical center, whereas the use of nuclear bleeding scans decreased considerably over time (110). CTA was found to have a greater positive correlation with TA than RBC scintigraphy for assessing LGIB in active stable and hemodynamically unstable LGIB (127). In 2 retrospective studies of patients with LGIB receiving CTA as compared with RBC scintigraphy, CT was more accurate in detecting and localizing the source of LGIB (128,129). Given the widespread availability of CTA and the aforementioned disadvantages to nuclear imaging, RBC scintigraphy has a rapidly diminishing role in the diagnostic management of LGIB and should likely only be used in rare circumstances where CTA is unavailable or contraindicated because of a high concern for contrast-induced nephropathy.

TIMING OF COLONOSCOPY

Recommendations

9. For patients hospitalized with LGIB requiring a colonoscopy, we recommend performing a nonemergent inpatient colonoscopy because performing an urgent colonoscopy within 24 hours has not been shown to improve clinical outcomes such as rebleeding and mortality. (Strong recommendation, moderate-quality evidence)

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The optimal timing of inpatient colonoscopy for LGIB has been controversial. Prior guidelines had conditionally recommended performing a colonoscopy within 24 hours for patients with high-risk clinical features and signs or symptoms of ongoing bleeding. This recommendation had been partially based on a prior, nonrandomized, prospective study of 48 patients with severe diverticular bleeding who underwent colonoscopy within 12 hours and 73 historical controls who underwent colonoscopy within 12 hours but did not undergo endoscopic therapy. Endoscopic treatment significantly reduced the risks of rebleeding, need for emergency surgery, and hospital length of stay (130). Two RCTs published in the past 5 years have helped clarify the role of urgent colonoscopy. In a RCT of early colonoscopy (<24 hours) in LGIB compared with standard colonoscopy (within 24–72 hours), early colonoscopy (n = 79 patients) was associated with not only a reduced hospital length of stay (2 vs 3 days) but also an increased risk of recurrent bleeding (13% vs 3%) and hospital readmission (11% vs 3%) compared with patients undergoing elective colonoscopy (n = 80 patients) (131). No difference was seen in mortality, source of bleeding, or PRBC transfusion. In a second multicenter RCT of 170 patients comparing early colonoscopy (within 24 hours) to elective colonoscopy (24–96 hours), early colonoscopy was not associated with an increased rate of detecting SRH at colonoscopy or reduction in risk of rebleeding; moreover, there were no significant differences in successful endoscopic treatment, transfusion, or mortality (132).

Several meta-analyses comparing urgent or early colonoscopy with elective colonoscopy in LGIB have failed to confirm a clear benefit of urgent/early colonoscopy in important clinical outcomes (133–136). In a meta-analysis of 4 RCTs, urgent colonoscopy was not associated with a difference in therapeutic interventions, mortality, or rebleeding. When including observational studies, the standard colonoscopy group was associated with a higher rate of mortality in the standard group and a reduced length of stay in the urgent group (137). In a meta-analysis of 4 RCTs and 13 observational studies, no differences were seen between early and elective colonoscopy in rebleeding; similarly, a possible benefit of early colonoscopy was seen in mortality, surgery, and PRBC transfusion when including observational studies (138). Finally, in a meta-analysis restricted to 4 RCTs, early colonoscopy was not associated with a reduction in further bleeding, mortality, diagnostic yield, or need for endoscopic intervention (139). In summary, when limiting analysis to RCTs, there is no clinical benefit of urgent as opposed to elective colonoscopy in the setting of LGIB (Table 4).

Similarly, performing urgent colonoscopy as opposed to elective colonoscopy does not seem to have any sustained benefits after hospital discharge. In studies using large administrative data sets, patients undergoing urgent colonoscopy for LGIB had no benefits in post-hospital rebleeding or post-hospital readmissions (140) and may actually have worse outcomes in rebleeding, although this may be due to residual confounding (95). However, to minimize length of stay, if an inpatient colonoscopy is planned, it should be performed at the next available nonurgent opportunity.

Based on the available data demonstrating a lack of clear benefit in outcomes, urgent colonoscopy should likely only be performed in select, high-risk patients in situations where there is a high pretest probability of detecting SRH and performing endoscopic intervention (e.g., postpolypectomy bleeding). Moreover, this practice should ideally be performed by providers or bleeding teams who have expertise in endoscopic hemostasis in LGIB; however, consideration should be given as to whether there is local availability of CTA and interventional radiology. When urgent colonoscopy is performed, it should be performed with the assistance of a clear cap and water-jet to maximize the yield of finding SRH.

Conservative management of patients with LGIB. Further real-world data on conservative management of patients hospitalized with LGIB is needed given the high number of colonoscopies performed and the correspondingly low rate of endoscopic intervention. In a single-center, retrospective report of 142 consecutive patients with LGIB, conservative management, based on an elective colonoscopy within 2 weeks after spontaneous hemostasis in patients who had an initial negative CTA and did not present with shock, was an effective management strategy (141). In a retrospective cohort of 97 patients with stable LGIB, 38% of

Table 4. Meta-analyses comparing urgent (<24 hours) to elective (>24 hours) colonoscopy in LGIB

Study	No. in each arm (U vs E)	Diagnostic yield[a]	Rebleeding	LOS	PRBC	Endoscopic intervention	Mortality
Analysis limited to RCTs							
Kherad et al.	230/236	ND	ND	ND	ND	ND	ND
Anvari et al.	228/235	ND	ND	ND	ND	ND	ND
Tsay et al.	228/235	ND	ND			ND	ND
Combined analysis of observational studies and RCTs							
Anvari et al.	63,105/66,170	+U		+U	ND	ND	+U
Roshan Afshar et al.	9,889/14,630	+U	ND	+U	ND	+U	ND
Seth et al.	9,498/13,921	ND	ND	ND		ND	ND
Kouanda et al.	10,172/14,224	ND	ND	ND	ND	+U	ND
Sengupta et al.	422/479	+U	ND	ND	ND	+U	ND

E, elective; LGIB, lower gastrointestinal bleeding; LOS, length of stay; ND, no significant difference between groups; PRBC, packed red blood cell transfusion; RCT, randomized controlled trial; U, urgent.
Comments: +U indicates that the results favored urgent colonoscopy; ND indicates that there was no significant difference seen between groups.
[a]Diagnostic yield defined as definite or probable cause of acute LGIB.

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the cohort was discharged early from the ED with outpatient management; factors associated with early discharge included younger age, lack of antithrombotic medications, higher index hemoglobin and albumin, and lower BUN and creatinine scores. No significant difference was seen in 30-day rebleeding, readmission, or mortality between admitted or discharged patients (142). Finally, in another single-center study of 344 patients with LGIB, patients who were managed with supportive care only had no significant difference in mortality, 30-day readmissions, or inpatient rebleeding compared with patients who underwent diagnostic intervention (143).

BOWEL PREPARATION

Key concepts

8. In patients undergoing inpatient colonoscopy, administration of 4–6 L of polyethylene glycol (PEG)-based bowel preparation has historically been recommended; however, split-dose preparation and/or the use of low-volume preparations can also be considered. Unprepared evaluation or routine flexible sigmoidoscopy is not recommended, unless the source is known to be emanating from the anorectal area or distal colon.

Administration of bowel preparation is needed to visualize the colonic mucosa for potential sources of hemorrhage. Risks of bowel preparation in the setting of LGIB are generally low and have not been shown to be more common than bowel preparation for patients without LGIB (144). Unprepared evaluation may make it difficult for the endoscopist to successfully reach the cecum. In a small pilot study of 13 colonoscopies for LGIB by unprepared colonoscopy after tap-water enema was aided by water-jet pumps and mechanical suction devices, the cecum was successfully reached in 9 of 13 cases and endoscopic visualization was believed to be adequate in all cases (145). In another single-center experience of 33 unprepared colonoscopies for LGIB with the assistance of a PEG solution added to the water-jet tank, the cecum was reached successfully in every patient and a definitive source of bleeding was found in 91% of cases (146). Until further data demonstrates that this strategy is effective in larger studies of patients with LGIB, administration of bowel preparation is recommended.

The previous iteration of this guideline had recommended administration of 4–6 L of a PEG-based solution administered over 3–4 hours until the rectal effluent was clear of blood and stool. This recommendation was based on previous studies using large-volume, purge protocols with subsequent urgent colonoscopy (within 24 hours of presentation) demonstrating high rates of definitive diagnosis and hemostasis (3,130). However, more recent data have suggested that split-dose and/or smaller volume preparations may be preferred for inpatients because of higher efficacy and improved tolerability for patients. Owing to historically high inadequate bowel preparation rates at their institution, Yadlapati et al. designed and implemented an automated, split-dose bowel preparation order set for inpatients undergoing colonoscopy. Compared with a historical inpatient cohort receiving 4 L of PEG the evening beforehand, investigators noted a significant improvement in bowel preparation with the split-dose order set, with bowel preparation adequacy increasing from 43% to 86% after the intervention (147). In a single-center study evaluating the implementation of a split-dose bowel preparation order set in inpatients undergoing colonoscopy, patients receiving split-dose preparation experienced fewer procedural delays and decreased use of additional laxatives to ensure complete cleansing. In addition, 91% of patients receiving split-dose preparation favored split-dose administration for future bowel preparations suggesting excellent tolerability (148).

Recent data suggest that lower volume preparations may also be a reasonable alternative in patients undergoing inpatient colonoscopy. In a RCT of 44 inpatients, patients were randomized to same-day 1 L PEG vs split-dose 4 L PEG with a colonoscopy being performed within 4 hours of the last dose; patients with same-day 1 L bowel preparation had comparable bowel cleansing compared with the split-dose group (149). Rapid administration of the 1 L PEG solution has also been shown to be successful in case reports of patients with hematochezia requiring colonoscopy (150,151). In a pilot RCT of 25 patients randomized to a low-volume regimen (300 mL containing sodium sulfate, potassium sulfate, and magnesium sulfate), medium-volume regimen (2 L of PEG), or large-volume regimen (4 L of PEG), patients receiving a low-volume regimen had a slightly higher total Boston Bowel Preparation Scale compared with those receiving the high-volume regimen (7.4 vs 7.0), although the results were non-significant (152). Moreover, the low-volume group had excellent tolerability of the preparation, with a decreased perception of unpleasant taste of the preparation. Further head-to-head comparisons of low-volume preparations for inpatients undergoing colonoscopy are needed, but split-dose bowel preparation should be the default for patients undergoing elective (or next available) inpatient colonoscopy. For those patients in whom urgent colonoscopy is pursued, a regimen of 4–6 L of PEG administered over 3–4 hours until rectal effluent is clear is considered standard.

There are limited data on additional adjunctive techniques to improve tolerability of bowel preparation for patients undergoing inpatient colonoscopy, such as use of prokinetic or antiemetic drugs. In a RCT evaluating the efficacy of antiemetics before a split-dose 3 L PEG preparation, the use of supplemental domperidone and sulpiride was found to be associated with higher completion of PEG, reduced abdominal discomfort, and higher Boston Bowel Preparation Scale scores compared with the control group (153). Further data are needed, particularly because these medications are not routinely available or used in the United States.

Although placement of a nasogastric tube can be considered for patients who are unable to tolerate a bowel preparation before planned colonoscopy, this should be performed cautiously in patients with risk factors of aspiration. Of note, in previous studies of urgent colonoscopy after a rapid, large-volume preparation, a nasogastric tube was needed 33% of the time to facilitate administration of the preparation (130). In the future, owing to an increasing use of low-volume bowel preparations and more elective vs urgent colonoscopies, the practice of routine nasogastric tube placement for preparation administration should be re-examined and only be used when necessary.

LGIB PROTOCOLS

Institutional algorithms and protocols on the diagnosis and management of patients presenting with LGIB have been shown to be beneficial in improving certain in-hospital outcomes. Implementation of an institutional LGIB protocol prioritizing CTA for patients with active bleeding led to improvement in certain predefined process outcomes (increased use of the GI consultation service and increasing performance of CTA as opposed to tagged red blood cell scanning) and fewer transfusions

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(154). In another retrospective cohort analysis of patients with acute GIB, implementation of a multidisciplinary GIB protocol was able to successfully decrease PRBC transfusion, reduce hospital length of stay, and decrease hospital readmissions (155).

ENDOSCOPIC TREATMENT

Role of treatment of SRH

Key concepts

9. Endoscopic therapy is recommended when finding active bleeding or SRH, irrespective of the etiology.

When colonoscopy is performed for patients presenting with hematochezia, SRH should be treated endoscopically to reduce the risk of ongoing and recurrent bleeding. In a seminal study of patients with diverticular hemorrhage, endoscopic treatment of those with SRH was associated with a reduction in rebleeding and need for surgery compared with those patients treated medically (130). In an analysis of a multicenter Japanese cohort of patients with diverticular bleeding, treatment of definitive diverticular hemorrhage when SRH was identified during colonoscopy was associated with a significantly reduced risk of early and late rebleeding compared with those patients who had SRH and were treated conservatively. In this cohort, endoscopic treatment of SRH was also associated with reduced risk of rebleeding compared with patients with presumptive diverticular bleeding who were treated conservatively. Despite endoscopic treatment, however, early and late rebleeding rates remained high even in patients treated for definitive diverticular hemorrhage at 17.4% and 32.0%, highlighting the limitations of colonoscopy and endoscopic intervention for this condition (156).

Options for endoscopic treatment include injection of dilute epinephrine, through-the-scope or over-the-scope clips, endoscopic band ligation (EBL), contact thermal therapies including bipolar or multipolar coagulation, noncontact thermal therapy such as argon plasma coagulation (APC), and topical hemostatic therapy. Updates on endoscopic treatment options will be discussed in the context of diverticular hemorrhage, treatment of colonic angioectasias and vascular lesions, and postpolypectomy bleeding. We will not discuss management of bleeding from a hemorrhoidal source in this guideline.

Treatment of diverticular hemorrhage

Recommendations

10. When detected, we recommend treatment of diverticular SRH with through-the-scope clips, EBL, or coagulation. (Strong recommendation, moderate-quality evidence)

Diverticular bleeding typically presents with painless hematochezia, frequently large-volume in nature, because it is an arterial bleed occurring from the neck or dome of a diverticulum. When active bleeding (spurting or oozing) or SRH (nonbleeding visible vessel or adherent clot which cannot be removed with lavage) is seen, endoscopic treatments are effective in achieving initial hemostasis and reducing risks of recurrent bleeding. The most commonly used therapeutic options include through-the-scope clips, EBL, and bipolar coagulation. Endoscopic treatment using clips can be achieved successfully when direct clipping is performed onto a culprit vessel either at the diverticular neck or dome. Other options include indirect placement of clips around the neck or in a zipper fashion to close the diverticula; however, this may be associated with a higher risk of rebleeding compared with direct clipping (157). In a retrospective analysis of a large, multicenter Japanese cohort of patients with confirmed diverticular bleeding, direct clipping of a vessel on multivariable analysis was associated with a reduced risk of early and late rebleeding as well as blood transfusions, as compared with an indirect clipping technique (158). Finally, a distal attachment translucent cap can be used to invert and inspect the dome and place a clip at SRH (159). Endoscopic images and video depictions of direct clipping and subsequent endoscopic hemostasis for diverticular hemorrhage is available in recently published series (157,160).

EBL has been demonstrated to be safe and effective in several series (161) and has been shown to be performed by both experts and trainees with high efficacy and safety (162). To perform EBL, an endoscopic clip is used to mark SRH and the endoscope is withdrawn. The banding device is attached and the scope is reinserted to the marked diverticulum, whereupon the diverticulum is suctioned into the device and a band is deployed. This typically can be performed if the size of the diverticula is smaller than the diameter of the banding device. Marking the diverticula of interest with an adjacent tattoo before EBL has also been reported and may also be beneficial should endoscopic therapy fail and surgical management be needed (163). A new EBL device specific to colonic diverticular bleeding has been developed recently, which has a wider field of vision and seems to be equally effective in hemostasis; this device may also be associated with shorter procedure times compared with the conventional esophageal variceal ligation banding device placed on a gastroscope, which may limit therapeutic options to the left colon (164).

In a systematic review and meta-analysis of 16 studies and 384 patients with diverticular bleeding, bipolar coagulation, clipping, and EBL were all highly effective in initial hemostasis (99%–100%); however, EBL was more effective compared with clipping to avoid transarterial embolization or surgery (161). The use of multipolar coagulation also seems safe and effective for SRH located in the diverticular neck (165). Regarding rebleeding risk after endoscopic therapy, Nagata et al. conducted a meta-analysis of 16 studies of 780 patients demonstrating that pooled frequency of early rebleeding was significantly lower for EBL than clipping (8% vs 19%; $P = 0.012$), as was late rebleeding (9% vs 29%, $P = 0.02$) (166). In a retrospective analysis of a large multicenter Japanese cohort of 1,679 patients with diverticular hemorrhage, EBL compared with clipping was associated with reduced risk of early rebleeding (adjusted OR 0.46; $P < 0.001$) and late rebleeding (adjusted OR 0.62; $P < 0.001$), regardless of the timing of colonoscopy or presence of active bleeding at the time of colonoscopy (167). Perforation occurred in 2 patients (0.31%) undergoing EBL compared with no perforation in patients who got clips. Overall, these data suggest that both clipping and EBL are effective and durable options for initial treatment of diverticular hemorrhage; however, EBL may be preferable to clips for long-term rebleeding outcomes. Importantly, the preponderance of published data and experience on EBL is from Japanese cohorts where the presentation and initial evaluation of diverticular bleeding is considerably different from Western populations. Moreover, the prevalence of right-sided diverticulosis is higher in Japan, and optimal endoscopic management of diverticular bleeding may be different in Western populations where left-sided diverticulosis is more common (168).

Other techniques which have been described in case reports for effective management of refractory or recurrent diverticular

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bleeding include over-the-scope clips (169,170), topical hemostatic spray (171), and endoscopic detachable snare ligation therapy (172). The use of a Doppler ultrasound probe has also been described to help guide hemostasis in diverticular hemorrhage in single-center studies; however, further data are needed before widespread use (173,174).

Colonic angioectasias and vascular etiologies of bleeding

Colonic angioectasias typically present with occult blood loss with iron deficiency anemia, however, may also present with overt LGIB. Endoscopic therapy is indicated if there is evidence of acute or chronic blood loss. Advanced age and anticoagulant use may increase the risk of active bleeding from colonic angiodysplasias (175). There are limited data on outcomes of patients with colonic angioectasias and comparisons between treatment modalities. APC is an effective initial treatment modality (176). A flow rate of 0.8–1.0 L/min with a power of 20–40 W is typically used in the colon; however, newer electrosurgical generators have built-in settings for APC depending on the location of bleeding. Overall, the safety profile for APC in the treatment of angioectasias is excellent (177). For large angioectasias in the right colon, submucosal injection of fluid before APC can be considered to reduce the risk of perforation (178). Another technique which was shown to be safe and effective was submucosal injection below the arteriovenous malformation, followed by endoscopic resection and targeted coagulation therapy at the submucosal feeding vessel (179). Clipping can be another option for refractory bleeding due to angioectasias. Unfortunately, data on long-term risk of recurrence of colonic angioectasias are limited and challenging to interpret given the difficulty in distinguishing true recurrent bleeding from a previously treated lesion, vs new-onset bleeding from previously nonbleeding or new-onset angioectasias. In a meta-analysis of uncontrolled studies including patients with colonic and small bowel angiodysplasias, the pooled recurrence risk was 34% (180). Colonic Dieulafoy lesions (aberrant submucosal vessels leading to a minute defect in the colonic mucosa) are uncommon causes of LGIB, but can be successfully treated using combinations of epinephrine, clipping, and/or thermocoagulation (181).

Postpolypectomy bleeding

An extensive discussion on risk factors and prevention of postpolypectomy bleeding is beyond the scope of this guideline. However, when patients are hospitalized due to postpolypectomy bleeding, a colonoscopy is typically recommended for patients with ongoing bleeding and any hemodynamic compromise. Endoscopic therapy is indicated when active bleeding or SRH is seen at the polypectomy site. In a multicenter study of patients with postpolypectomy bleeding, 43% of the cohort did not require endoscopic hemostatic therapy; rebleeding and transfusion requirements were very low in those managed without intervention. Variables that were predictive of active bleeding at the time of colonoscopy included use of anticoagulants, left-sided polyps, prior use of electrocautery, and pedunculated polyp morphology (182).

Endoscopic management of postpolypectomy bleeding typically consists of through-the-scope clips, which are highly effective in initial treatment of bleeding (183). Additional options for treatment include direct thermal therapy, APC, and over-the-scope clips. Head-to-head comparisons for treatment are unavailable; thus, the decision for treatment technique should be made based on individual experience and preference as well as available equipment (184). Hemostatic powders have also shown excellent efficacy in initial hemostasis (97%, 95% CI 93%–100%) in the setting of postpolypectomy bleeding (185). In a multicenter study of 50 patients with LGIB (of which postpolypectomy bleeding was the most common etiology of bleeding), hemostatic powder, as monotherapy, part of combination therapy, or rescue therapy, was effective in achieving hemostasis in 98% of patients (186).

RECURRENT BLEEDING

Unfortunately, rebleeding is common for patients hospitalized with LGIB. In the UK audit of patients hospitalized with LGIB, rebleeding occurred in 13.6% of cases at a median of 3 days after presentation (13). Risk factors of recurrent bleeding have included older age (187,188), hemodynamic instability at presentation (38), and diverticular bleeding as the underlying etiology of bleeding (37). In cohorts of patients with diverticular bleeding, early rebleeding within 30 days of initial treatment has been reported to occur as frequently as 24% of the time (189). Unfortunately, there is no clear way to completely mitigate the risk of rebleeding, given that early rebleeding rates remain clinically significant despite endoscopic intervention. Regarding long-term risk of recurrent diverticular hemorrhage, the cumulative incidence of recurrent diverticular hemorrhage after an initial episode at 1, 2, and 5 years was shown to be 4.7%, 8.3%, and 15.7%, respectively. The median time between first and second episodes of diverticular hemorrhage was 1.2 years (190).

Role for repeat colonoscopy, angiography, and surgery

Key concepts

10. For patients experiencing rebleeding after initial hemostasis or cessation of bleeding, repeat colonoscopy can be considered depending on the patient's stability and likelihood of successful repeat endoscopic therapy. In patients with suspected recurrent diverticular bleeding with recent colonoscopy who are hemodynamically stable, observation can be considered.

For patients in whom a known source of bleeding is identified and treated endoscopically, but experience an episode of rebleeding, a repeat colonoscopy can be considered. However, there are limited comparative data on the benefit of repeat colonoscopy and attempt at endoscopic intervention vs proceeding to radiologic intervention in the setting of recurrent bleeding. In the setting of a known bleeding site and either recurrent or refractory bleeding despite endoscopic intervention, proceeding to TA with possible embolization is indicated. A previously placed endoclip can help perform a focused TA. A CTA can be considered if more precise localization is needed, followed by transcatheter arteriography (113).

Provocative angiography has been used in case series of patients with recurrent LGIB when conventional angiography does not determine active extravasation. In a case series of 12 patients with LGIB, provocative angiography (mainly using urokinase) was successful in identifying contrast extravasation in 50% of cases, subsequently allowing for embolization (191). In another report of 36 provocative angiographies using vasodilation using nitroglycerin, anticoagulation using heparin, and/or thrombolysis using a tissue plasminogen activator, 16 examinations (44%) were successful in identifying extravasation (192). Further data

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on long-term efficacy and safety of this approach are warranted before this technique can be routinely recommended for patients with recurrent LGIB.

There is a limited initial role for surgical evaluation in the setting of LGIB, and this option should only be considered after endoscopic or radiologic interventions have failed. In the UK audit of patients with LGIB, use of surgery was needed in 0.2% of all cases (13). In a retrospective comparison of patients managed with arteriography vs surgery after active LGIB was demonstrated by CTA, patients undergoing surgery had a 20% risk of major postoperative complications (193). Surgical resection may have a limited role in the setting of patients who experience recurrent significant LGIB after initial arteriography and embolization who either fail or are not candidates for repeat colonoscopy and cannot undergo recurrent embolization due to the presence of or concerns for ischemia. If surgery is deemed necessary, every attempt should be made to precisely localize the site of bleeding in the colon to allow for a limited, targeted resection. A nonlocalized hemicolectomy has a higher risk of recurrent bleeding compared with a localized source and subsequent targeted hemicolectomy. In an analysis of a National Surgical Quality Improvement Database, 85% of all colorectal resections performed in the setting of bleeding underwent partial colectomy and 15% underwent total colectomy; total colectomy was associated with an increased risk of cardiac and renal complications as well as postoperative ileus (194).

Resumption of antiplatelet medications and risk of recurrence

Recommendations

11a. We recommend discontinuing nonaspirin NSAIDs after hospitalization for diverticular hemorrhage. (Strong recommendation, low-quality evidence)

11b. We suggest discontinuing aspirin for primary cardiovascular prevention after hospitalization for diverticular hemorrhage given the risks of recurrent diverticular hemorrhage. (Conditional recommendation, low-quality evidence)

11c. We suggest continuing aspirin after hospitalization for diverticular hemorrhage for patients with an established history of cardiovascular disease given the benefits of reducing future ischemic events. (Conditional recommendation, low-quality evidence)

11d. We recommend that providers re-evaluate the risks vs benefits of continuing nonaspirin antiplatelets such as P2Y12 receptor antagonists in a multidisciplinary setting after hospitalization for diverticular hemorrhage given the demonstrated risks of recurrent diverticular hemorrhage. (Strong recommendation, low-quality evidence)

Discontinuation of NSAIDs after hospitalization for diverticular bleeding has been shown to significantly reduce rebleeding risk compared with those patients with ongoing NSAID use (195). The use of NSAIDs was associated with an increased risk of recurrent LGIB (HR 2.0, 95% 1.2–3.3) in a retrospective Japanese cohort of patients with acute LGIB (188).

Resumption and ongoing use of antiplatelet medications have been shown in multiple cohorts to be associated with an increased risk of recurrent diverticular hemorrhage. In a large retrospective analysis of a medical claims database, the use of platelet aggregation inhibitors (including clopidogrel, prasugrel, and ticagrelor) was significantly associated with an increased risk of second diverticular hemorrhage (HR 1.47, 95% CI 1.15–1.88) after an index episode of diverticular hemorrhage. The use of aspirin has also shown to potentially increase the risk of recurrent LGIB. In a retrospective analysis of 295 patients with LGIB on aspirin, continuation of aspirin was associated with a significantly increased risk of recurrent bleeding (HR 2.76, 95% CI 1.26–6.07) while also protective of serious cardiovascular events (HR 0.59, 95% CI 0.37–0.91) and death (HR 0.33, 95% CI 0.17–0.63) (196). Given that recurrent bleeding can be managed either conservatively or endoscopically, aspirin should be resumed after hospitalization for LGIB in patients with a history of cardiovascular disease to protect from future cardiovascular events.

Resumption of anticoagulants and risk of recurrence

Recommendations

12. We recommend resuming anticoagulation after cessation of LGIB given that resumption of anticoagulation has been shown to decrease the risks of postbleeding thromboembolism and mortality. (Strong recommendation, moderate-quality evidence)

The net benefit of resumption of anticoagulation after hospitalization for GIB is well-established. Several meta-analyses of observational studies have demonstrated that resumption of anticoagulation after hospitalization for GIB is associated with a reduction in thromboembolic events and mortality while also potentially increasing the risk of recurrent GIB (197–199). Regarding the benefits of resuming warfarin vs DOACs after hospitalization for GIB, a large insurance claims database showed that resumption of both warfarin and DOAC after GIB was associated with a decreased risk of thromboembolism; however, resumption of warfarin and rivaroxaban only was associated with an increased risk of recurrent GIB (200).

Data on anticoagulant resumption in LGIB-specific cohorts also indicate a potential benefit of anticoagulant resumption. In a large cohort of patients with an index episode of diverticular hemorrhage using the Optum database, discontinuing anticoagulation was associated with an increased risk of ischemic stroke (HR 1.93, 95% CI 1.17–3.19) at a median time of 115 days. Importantly, resumption of anticoagulation was not associated with an increased risk of recurrent diverticular hemorrhage (HR 0.98, 95% CI 0.79–1.22) (190). In an analysis of patients from the UK audit of LGIB on antithrombotic medications, the use of DOACs or warfarin was not associated with either in-hospital rebleeding or hospital readmission due to further bleeding (90). Finally, in an analysis of 150 patients with LGIB while on anticoagulants, resumption of anticoagulation was not associated with recurrent bleeding. When the cohort analysis was expanded to all patients with GIB, resumption of anticoagulation was associated with a reduced risk of follow-up ischemic events (201). The optimal time to resume anticoagulation after LGIB is not certain; however, resumption within 7 days of the bleeding event is typically recommended based on the net benefit of reduction in thromboembolic complications.

FUTURE RESEARCH PRIORITIES

Compared with other conditions in gastroenterology such as UGIB or inflammatory bowel disease, the lack of high-quality, randomized trial data to guide diagnosis and management in LGIB limits the strength of these recommendations. However,

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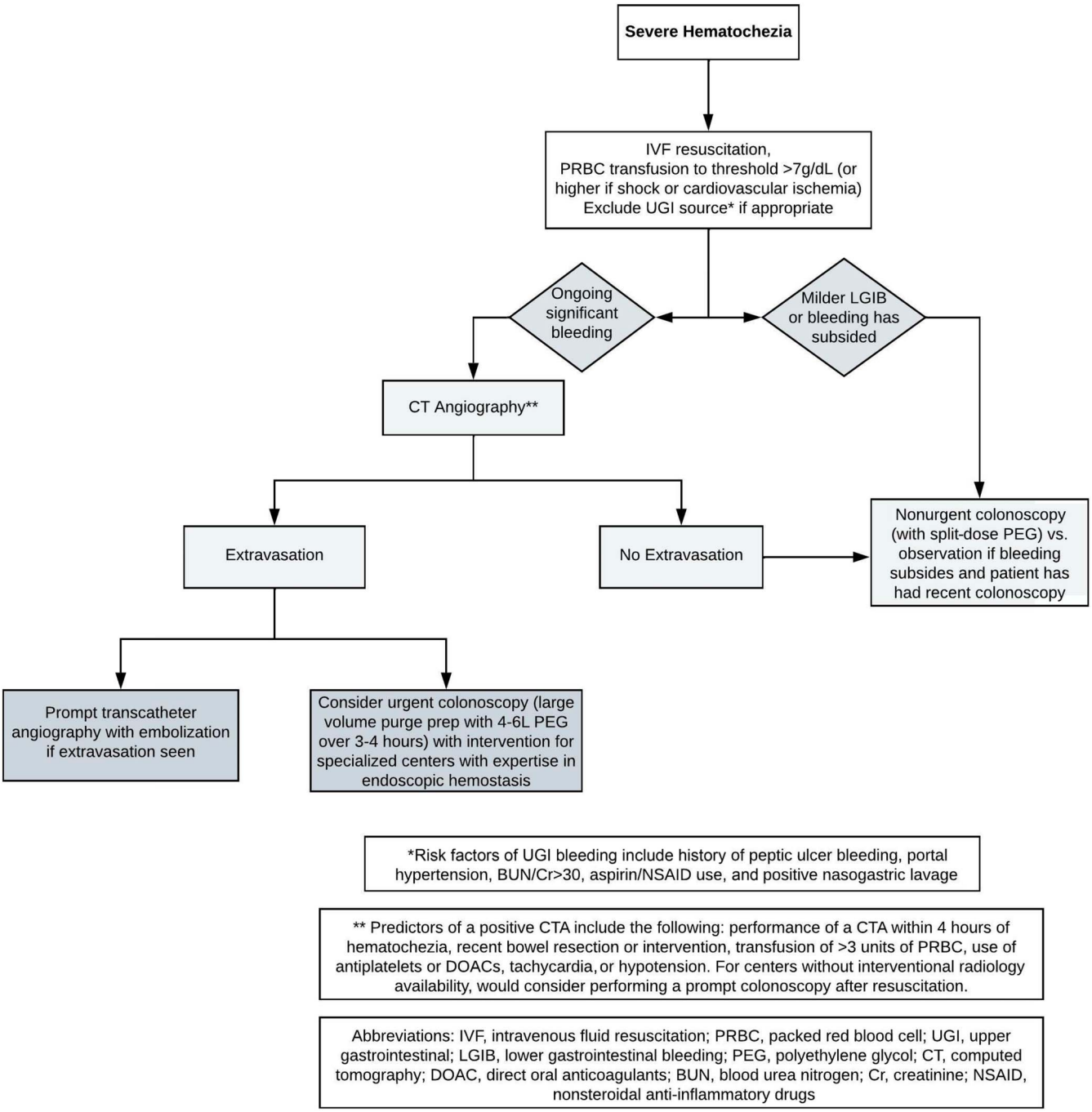

Figure 1. Suggested approach to the management of patients with severe hematochezia.

given how frequently clinicians manage patients who are hospitalized with LGIB and the overall high burden of colonoscopy performed for this condition, the panel wanted to provide guidance and evidence-based recommendations whenever possible. Future research in LGIB should be focused on a few key areas, in which further data are urgently needed.

First, additional validation of existing LGIB scores such as the Oakland score is needed to further identify low-risk patients with LGIB who are unlikely to require hospital-based intervention and can potentially be managed as an outpatient. This strategy needs to be proven safe with low risks of rebleeding and missed diagnoses such as colorectal cancer or inflammatory bowel disease before widespread implementation. When used, clinical prediction scores should be embedded into the electronic medical record and automatically trigger pathways and order sets to help guide clinicians. In addition, further clarity on whether a colonoscopy is needed in patients with hemodynamically stable, suspected diverticular bleeding in whom a recent colonoscopy has shown diverticulosis and excluded colorectal neoplasia. Conservative management may be a reasonable option for many of these patients, particularly given the low frequency of endoscopic intervention during colonoscopy

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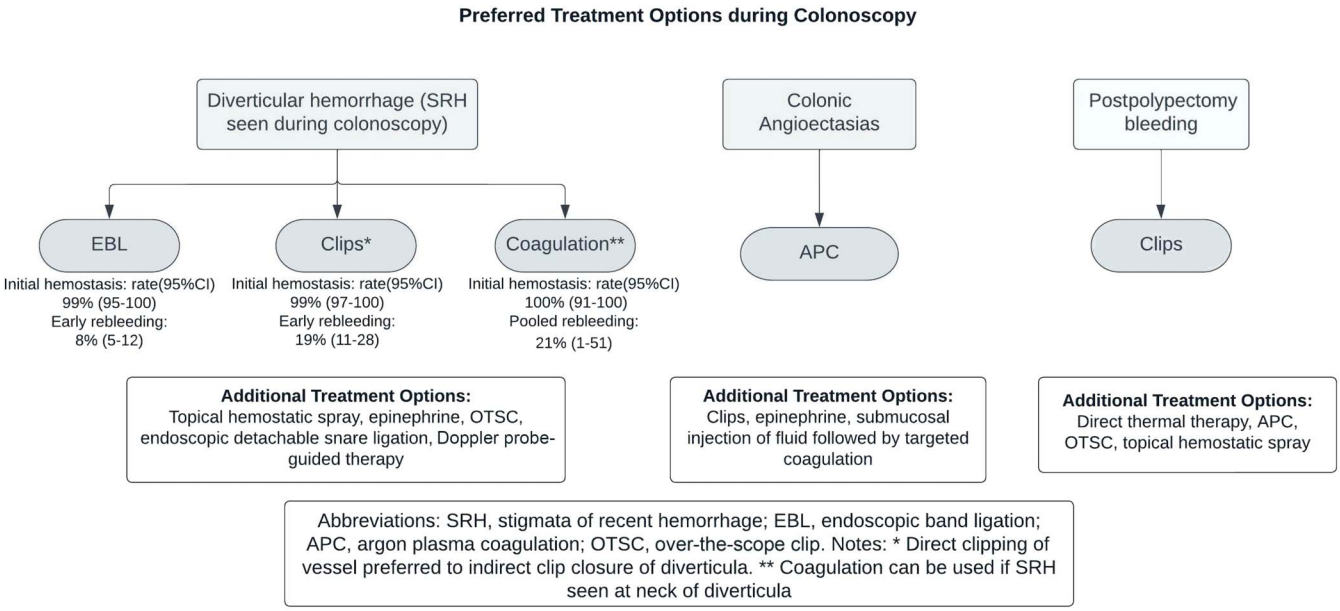

Figure 2. Endoscopic treatment based on etiology.

for LGIB in Western populations and the high rates of spontaneous hemostasis.

Second, further comparative data are needed between patients who undergo primary initial CTA vs primary colonoscopy for clinically significant LGIB. A validated clinical score predicting which patients have a high likelihood of having extravasation on a CTA would provide clarity in determining who benefits from an urgent CTA. Outcomes that should be captured include rates of diagnostic yield, rates of therapeutic intervention, lengths of stay, rebleeding risks, and complications. For patients who have a positive CTA, further data are needed on outcomes of patients treated by transcatheter arteriography and embolization vs patients undergoing urgent colonoscopy after a positive CTA.

Third, for patients presenting with severe LGIB while on anticoagulant medications, further data on the need and role for reversal agents are needed. Although most patients can likely be managed by withholding the anticoagulant drug, patients who are having severe hematochezia with signs of hemodynamic compromise may benefit from reversal agents before endoscopic intervention. Data on the use of reversal agents (such as PCC and targeted reversal agents) compared with withholding the drug alone are needed to determine the appropriate role for these drugs. Outcomes that should be captured should include time to endoscopy, endoscopic hemostasis, further bleeding, mortality, and thromboembolic complications. For future RCTs, investigators have proposed measuring a global end point

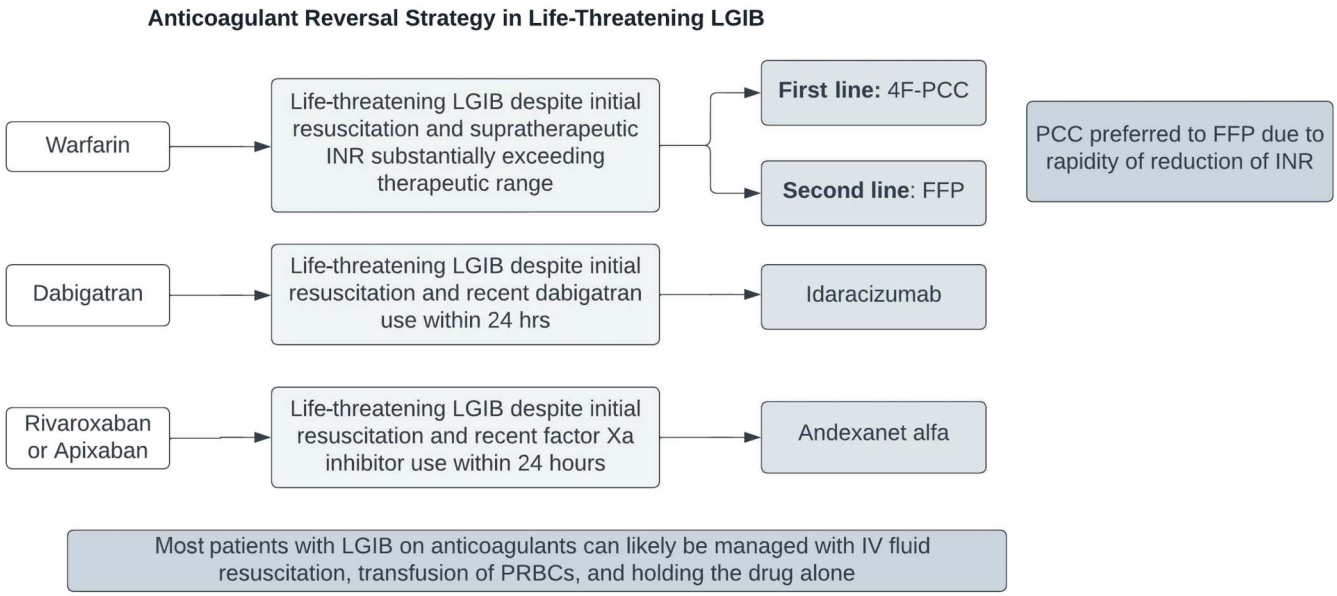

Figure 3. Anticoagulant reversal strategy based on life-threatening LGIB. 4F-PCC, 4-factor prothrombin complex concentrate; FFP, fresh frozen plasma; INR, international normalized ratio; IV, intravenous; LGIB, lower gastrointestinal bleeding; PRBC, packed red blood cell.

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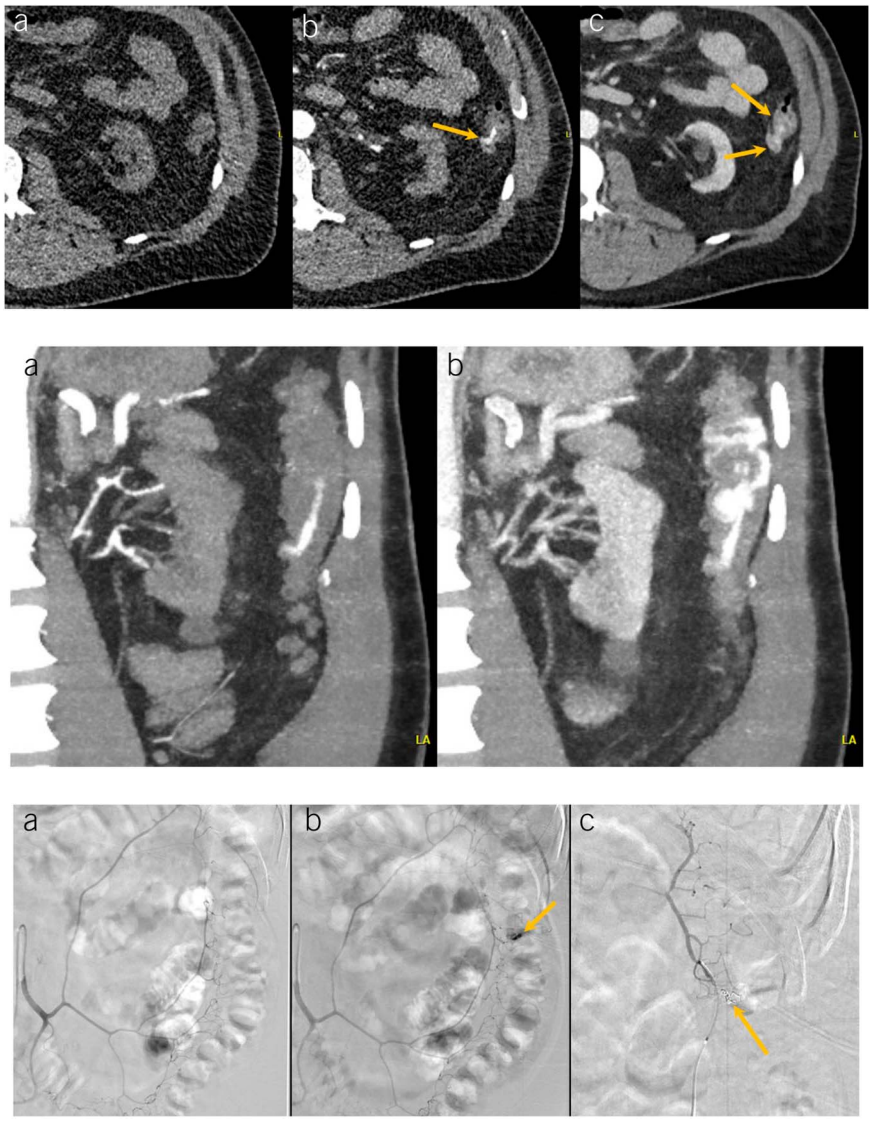

Figure 4. Panel 1: A 60-year-old man presenting to the emergency department with abrupt onset of painless hematochezia. The patient was found to be tachycardic and borderline hypertensive in the emergency department. The hemoglobin level was 7.6 g/dL. He was transfused 2 units of packed red blood cells and given 1 L of normal saline. After consultation with gastroenterology, a computed tomography angiography (CTA) was obtained. (**a**) Noncontrast CT series demonstrating no dense material in the left colon. (**b**) Arterial phase of CTA examination showing a linear accumulation of dense contrast within the colon (arrow), which can be seen to directly originate from a colonic diverticulum. This finding in combination with the noncontrast series is diagnostic of active bleeding. (**c**) Portal venous phase image of the CTA examination shows that the contrast has increased in volume and decreased in density (arrows). **Panel 2**: Coronal maximum intensity projection reformatted images from the same CTA scan demonstrating contrast accumulation within the colon. **Panel 3**: (**a**) Fluoroscopic inferior mesenteric artery angiogram. (**b**) Angiogram image obtained several seconds later shows contrast accumulation within the lumen of the descending colon (arrow). (**c**) Fluoroscopic image obtained showing embolization coils (arrows) within the artery supplying the bleeding diverticulum.

of further bleeding leading to blood transfusion, urgent interventions in the case of further bleeding or complications of initial intervention (repeat endoscopy, surgery, or interventional radiology), or death related to GIB (202).

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CONFLICTS OF INTEREST

Guarantor of the article: Neil Sengupta, MD.
Specific author contributions: N.S. was the primary author and wrote the initial draft of this guideline, as well as coordinated the literature search. J.D.F., V.J., A.K.S., L.L.S., and D.W. were involved in creation of the PICO questions, formulation of clinical questions, and edited the final draft. R.J.W. conducted the GRADE analysis.
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related to ergonomics. L.L.S. has written chapters for UpToDate. J.D.F., V.J., R.J.W., and D.W.: no relevant COI.

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