Diagnosis and management of acute lower gastrointestinal bleeding

Yotam Elimeleh[a] *and Ian M. Gralnek*[a,b]

Purpose of review
We review and summarize the most recent literature, including evidence-based guidelines, on the evaluation and management of acute lower gastrointestinal bleeding (LGIB).

Recent findings
LGIB primarily presents in the elderly, often on the background of comorbidities, and constitutes a significant healthcare and economic burden worldwide. Therefore, acute LGIB requires rapid evaluation, informed decision-making, and evidence-based management decisions. LGIB management involves withholding and possibly reversing precipitating medications and concurrently addressing risk factors, with definitive diagnosis and therapy for the source of bleeding usually performed by endoscopic or radiological means. Recent advancements in LGIB diagnosis and management, including risk stratification tools and novel endoscopic therapeutic techniques have improved LGIB management and patient outcomes. In recent years, the various society guidelines on acute lower gastrointestinal bleeding have been revised and updated accordingly.

Summary
By integrating the most recently published high-quality clinical studies and society guidelines, we provide clinicians with an up-to-date and comprehensive overview on acute LGIB diagnosis and management.

Keywords
colonoscopy, computed tomography angiography, endoscopic hemostasis, esophagogastroduodenoscopy, hematochezia, lower gastrointestinal bleeding, lower gastrointestinal hemorrhage, trans-arterial embolization

INTRODUCTION

Lower gastrointestinal bleeding (LGIB) is defined as bleeding originating from a colonic or rectal source distal to the ileocecal valve [1▪▪,2–4]. As reported by the United States (US) Centers for Disease Control, LGIB is among the most common gastroenterological causes for emergency department visits and hospital admissions, constituting approximately 30% of all GIB referrals, thereby rendering it a significant healthcare and economic burden [5▪]. In contrast to acute upper gastrointestinal bleeding (UGIB), high-level evidence from randomized controlled trials for providing guidance in diagnosing and managing acute LGIB are more limited. Thus, current guidelines for managing LGIB often rely on data derived from uncontrolled observational studies and/or expert opinion. In this review, we summarize the literature regarding the diagnosis and management of acute LGIB, emphasizing the most recently published evidence-based guidelines and data published in the previous 18 months.

PATIENT PRESENTATION

The most common clinical presentation of acute LGIB is hematochezia (fresh blood/maroon colored stools passed per rectum) [4] and/or rarely melena (black tarry stools) [1▪▪,2,3]. LGIB presents most commonly in the elderly on a background of significant comorbid illnesses, and often in patients being treated with antiplatelet or anticoagulant medications [4,6,7].

Colonic diverticular bleeding is consistently reported as being the most common cause of acute

[a]Ellen and Pinchas Mamber Institute of Gastroenterology and Hepatology, Emek Medical Center, Afula and [b]The Rappaport Faculty of Medicine Technion-Israel Institute of Technology, Haifa, Israel

Correspondence to Ian M. Gralnek, MD, MSHS, Institute of Gastroenterology and Hepatology, Emek Medical Center, Yitzhak Rabin Blvd 21, Afula 1834111, Israel. Tel: +972-4-6495545;
e-mail: ian_gr@clalit.org.il

Curr Opin Gastroenterol 2024, 40:34–42
DOI:10.1097/MOG.0000000000000984

KEY POINTS

- Acute LGIB requires prompt patient evaluation including risk stratification.
- In patients presenting with acute hematochezia and who are hemodynamically stable, colonoscopy should be the first diagnostic test of choice and may be performed sometime during the hospital stay.
- In patients presenting with acute hematochezia and hemodynamically unresponsive to fluid resuscitation or who are unable to receive preparation for colonoscopy, initial evaluation with CT angiography (CTA) is recommended.
- Endoscopic hemostasis treatment options include dilute epinephrine injection in combination with another hemostasis modality, mechanical therapy using through-the-scope (TTS) clips, cap-mounted clips or band ligation, contact thermal devices (bipolar or heater probe or coagulation forceps), noncontact thermal devices such as argon plasma coagulation (APC), and topical hemostatic agents.
- Radiological intervention for acute LGIB using trans-arterial catheter embolization (TAE) is indicated for patients not amenable or refractory to endoscopic hemostasis therapy.
- Surgical therapy has a very limited role in acute LGIB and is rarely indicated.

LGIB [1▪▪,2,3,8–10]. A recent multicenter, retrospective cohort identified diverticular bleeding as the definitive or presumptive source of hematochezia in nearly 64% of cases [4]. Other, less commonly identified causes of acute LGIB include ischemic colitis, delayed postprocedural bleeding (e.g. post polypectomy, endoscopic mucosal resection, or endoscopic submucosal dissection), inflammatory bowel disease, colorectal polyps and malignant neoplasms, rectal ulcer, hemorrhoids, drug-induced colopathy/ulcer, vascular malformations, and infectious/radiation colitis [2–4,9]. Table 1.

Reported risk factors for acute LGIB are gastrointestinal inflammatory conditions (e.g. ulcerative colitis and Crohn's disease), tumors or polyps, advanced age, major comorbidities including hypertension, diabetes mellitus, history of cerebrovascular and/or cardiovascular disease, renal or hepatic impairment, alcohol abuse, and use of antiplatelet agents and anticoagulants [4,6,11–13]. An increased LGIB risk has also been described in professional athletes, particularly endurance athletes, with proposed mechanisms including splanchnic hypoperfusion, frequent use of NSAIDs and mechanical trauma during intensive physical exertion [14].

Table 1. Potential causes of acute lower gastrointestinal bleeding

Benign	Hemorrhoids Anal fissure Solitary rectal ulcer Rectal prolapse Radiation proctopathy
	Angioectasias Dieulafoy's lesion Colonic or rectal varices
	Inflammatory bowel disease (ulcerative colitis, Crohn's disease) Ischemic colitis Infectious colitis
	Polyps (e.g. adenomas, hamartomas, juvenile type)
	Postendoscopic intervention (polypectomy, EMR, ESD) Postsurgical anastomotic ulcer
Malignant	Colorectal cancer Anal cancer Metastatic disease

EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection.

Despite their well known anti-inflammatory, analgesic and antipyretic effects, excessive NSAID use increases the risk of not only gastrointestinal bleeding, mainly upper, but also LGIB [15].

Reported in-hospital mortality rates for acute LGIB vary between 1 and 4%, with markedly higher mortality rates for 'in hospital bleeding' in patients admitted to hospital because of other medical causes with acute LGIB developing during hospitalization [4,6,7,16].

Initial assessment of patients with presumed acute lower gastrointestinal bleeding

Initial assessment of a patient presenting with signs/symptoms of acute LGIB (e.g. hematochezia) includes the measurement of vital signs to evaluate the patient's hemodynamic status and for risk stratification. A shock index greater than 1 (pulse divided by SBP at the time of patient presentation) can be used to define the patient as hemodynamically unstable [8].

It is important to obtain a history of the current gastrointestinal bleeding episode that includes time of onset, character of the bleeding (e.g. hematochezia, melena), any associated abdominal pain, and any previous similar bleeding events. In addition, it is important to attain the patient's past medical history, including identifying any comorbid medical conditions, prior intra-abdominal surgeries (e.g. vascular surgery/stenting), use of current medications, especially antithrombotic agents [9,15].

A focused physical examination should include cardiopulmonary examination and abdominal palpation in search of any focal tenderness, guarding, rebound, and/or mass. In addition, digital rectal examination should be performed, assessing for the presence of any anorectal lesions and for the presence of fresh blood or melena [1▪▪,3,9].

Initial laboratory evaluation should include complete blood count (CBC), serum electrolytes, including creatinine and blood urea nitrogen, albumin, international normalized ratio (INR), and blood type and cross match [3].

For hemodynamically unstable patients, immediate fluid resuscitation initially with crystalloids and possibly vasopressors is required until hemodynamic stability is achieved [1▪▪,3] (Fig. 1).

Risk stratification

Several preendoscopy risk stratification scores exist for acute LGIB. These scores may either aim to identify patients at high risk for clinical deterioration, re-bleeding and/or mortality, require inpatient evaluation, or aim to identify low-risk patients suitable for discharge from the emergency department with further evaluation in the outpatient setting. According to recent guidelines, risk scores are recommended to be used as adjunctive tools and should not replace clinical judgement [1▪▪,3,8].

The Oakland Score, derived and validated by Oakland *et al.* [17] in 2017, is a risk stratification score designed to identify 'lower risk' LGIB patients. The score integrates age, gender, history of LGIB, rectal examination findings, pulse, blood pressure, and hemoglobin levels to produce an overall risk score. An Oakland score 8 or less has been shown to be well tolerated for discharging 'low risk' patients with acute LGIB directly from the emergency department [16,17].

Another risk stratification score is the ABC score, designed for identification of patients with acute UGIB or LGIB at high risk for 30-day mortality (ABC score $\geq$8). The ABC score integrates age, laboratory parameters (urea, albumin, creatinine), comorbidities (altered mental status, cirrhosis, disseminated malignancy) and American Society of Anesthesiology (ASA) score at presentation [18].

Additional LGIB risk stratification scores developed in recent years include the Sengupta score for predicting 30-day mortality [19], NOBLADS score (NSAID use, No diarrhea, No abdominal tenderness, Blood pressure <100 mmHg, antiplatelet use, albumin <3.0 g/dl, Charlson co-morbidity index $\geq$2, and Syncope) [20] for prediction of severe bleeding, and the Strate score for identifying patients with acute severe LGIB [21].

Compared with other existing tools for LGIB risk-stratification, the Oakland score has been

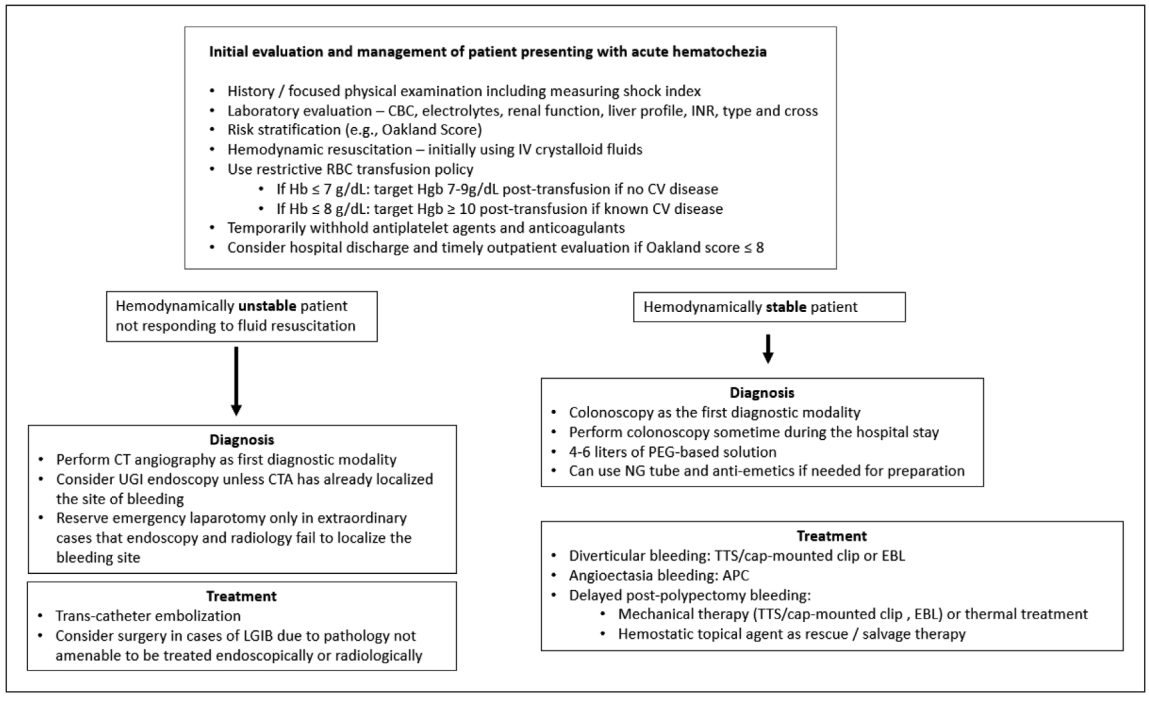

FIGURE 1. Management of acute lower gastrointestinal bleeding. CBC, complete blood count; CT, computed tomography; CTA, computed tomographic angiography; CV, cardiovascular; EBL, endoscopic band ligation; Hb/Hgb, hemoglobin; i.v., intravenous; LGIB, lower gastrointestinal bleeding; PEG, polyethylene glycol; TTS, through-the-scope; UGI, upper gastrointestinal.

shown to be the best predictor for severe bleeding [22], and in a recent meta-analysis comparing four validated LGIB risk-stratification scores, the Oakland score was reported to be the best predictor for safe patient discharge, major bleeding, and need for blood transfusion [23▪▪].

Recent guidelines on acute LGIB from the American College of Gastroenterology (ACG) [1▪▪], the European Society of Gastrointestinal Endoscopy (ESGE) [3], and the British Society of Gastroenterology (BSG) [8], recommend the Oakland score for risk stratifying patients presenting with acute LGIB.

Red blood cell transfusion strategy

Consensus exists amongst the latest ACG, ESGE, and BSG society guidelines regarding indications for RBC transfusion in acute LGIB, with a recommended restrictive transfusion strategy, and a threshold hemoglobin level of 7 g/dl for initiating RBC transfusion. In cases of active ischemia (especially acute coronary syndrome) or a history of cardiovascular disease, a more liberal blood transfusion hemoglobin threshold of 8–9 g/dl is recommended [1▪▪,3,8,24].

Furthermore, in a recent Cochrane systematic review examining various clinical conditions including GIB, a restrictive blood transfusion strategy with threshold hemoglobin level of 7–8 g/dl was shown to reduce RBC transfusion exposure by 41%, with no adverse impact on mortality, cardiovascular events, infections or thromboembolism [25].

Role of platelet transfusion

Routine platelet transfusion during LGIB is thought to be of no benefit and is not recommended for GIB patients without thrombocytopenia [26]. Current recommendation in the setting of significant LGIB is platelet transfusion to maintain a platelet count greater than 30 000/μl, or >50 000/μl if an invasive procedure is planned [1▪▪].

Antifibrinolytic agents

Accumulating high-quality evidence of recent years suggests no advantage in using antifibrinolytic agents such as tranexamic acid for GIB. This includes a recent international multicenter randomized, placebo-controlled trial (HALT-IT), in which no difference in mortality or arterial thromboembolic events was demonstrated for patients with acute UGIB or LGIB receiving tranexamic acid infusion. Moreover, there was a significantly higher rate of venous thromboembolic events demonstrated in the tranexamic acid group [27]. Therefore, antifibrinolytic agents such as tranexamic acid are not recommended as part of the treatment regimen in GIB [1▪▪,3,8].

Role of endoscopy

Patients presenting with hematochezia and hemodynamic instability, may have massive upper GIB as their source of bleeding [6,28]. Thus, current guidelines recommend for such patients to initially perform CT angiography (CTA). If CTA fails to demonstrate a lower gastrointestinal source of hemorrhage, esophagogastroduodenoscopy (EGD) should then be performed [1▪▪,3,8], as it may identify the source of bleeding in up to 15% of cases of severe hematochezia [1▪▪,4]. EGD may be performed with administration of intravenous erythromycin (250 mg intravenous 30–90 min before upper endoscopy) for improved endoscopic visualization [29].

In patients presenting with acute hematochezia and who are hemodynamically stable or are hemodynamically responsive to intravenous fluid resuscitation, colonoscopy should be the first diagnostic test of choice. Colonoscopy should preferentially be performed sometime during the hospital stay [1▪▪,3,8]. Traditionally, colonoscopy for acute LGIB was recommended to be performed within 24 h of patient presentation [2,30]. Several recent retrospective studies have failed to show any significant differences in mortality, rebleeding and re-hospitalization for early (<24 h) colonoscopy compared with delayed colonoscopy [31▪,32–34]. Furthermore, systematic reviews of RCTs have shown that colonoscopy performed within that early timeframe has not been shown to improve clinically relevant outcomes when compared with delayed (>24 h) colonoscopy [35,36]. Therefore, urgent colonoscopy within 24 h of patient presentation is no longer recommended and current guidelines recommend that the timing of colonoscopy be decided on a case-by-case basis [1▪▪,3,8].

Colonoscopy preparation is recommended using a poly-ethylene glycol (PEG)- based solution, and a recent RCT reported no significant difference in bowel preparation quality between high volume (4 l) and low volume (2 l) PEG-based solution in the setting of acute LGIB [37]. The diagnostic yield of colonoscopy in acute LGIB is variable ranging between 70 and 95%, mainly for identification of diverticulosis and 'suspected' diverticular hemorrhage [4,7,8].

Endoscopic hemostasis treatment options

Endoscopic hemostasis treatment options include dilute epinephrine injection in combination with another hemostasis modality, mechanical therapy

using through-the-scope (TTS), cap-mounted clips or band ligation, contact thermal devices (bipolar probe or hemostatic forceps), noncontact thermal devices such as argon plasma coagulation (APC), and topical hemostatic agents [1▪▪,3].

For colonic diverticular bleeding with high-risk stigmata of recent hemorrhage (e.g. active bleeding, nonbleeding visible vessel, adherent clot), mechanical therapy using TTS endoscopic clips is the recommended endoscopic therapy [1▪▪,3,8]. A recent multicenter retrospective study reported that direct clipping of the active bleeding site or the nonbleeding visible vessel, is superior to indirect clipping (i.e. zipper-like closure of the diverticulum) in preventing early (<30 day) and late (<1 year) re-bleeding, as well as in reducing RBC transfusion, with no significant difference in primary hemostasis [38]. Moreover, using this same dataset (CODE BLUE-J), Kobayashi *et al.* have recently reported that compared with endoscopic clipping (both TTS and over-the-scope clipping), endoscopic band ligation (EBL) as the primary treatment for diverticular bleeding was associated with significantly lower rates of early and late rebleeding, reduced need for interventional radiology and reduced length of hospital stay. Thus, EBL may be a promising technique for the treatment of acute diverticular hemorrhage, yet additional high level is needed [39].

The most common serious adverse event following polyp resection is postpolypectomy bleeding, occurring between 0.4 and 12.7% [40–43]. For prevention of postpolypectomy bleeding, current evidence suggests a significant benefit of prophylactic clipping following resection of large, right-sided, nonpedunculated polyps (≥2 cm) in patients receiving anticoagulation [40,44▪,45–50]. For EMR of large polyps (≥2 cm), a novel through-the-scope mucosal defect closure system was recently developed and in a multicenter prospective study was shown to have efficacy in closure of large post-EMR defects. The reported delayed postpolypectomy bleeding rate was 3.2% [51▪].

For large pedunculated polyps (≥1 cm), current data indicate that prophylactic clipping of the polyp stalk prior to hot snare resection is efficacious in preventing both immediate and delayed postpolypectomy bleeding and is thus recommended [52,53,54▪].

In case of immediate intraprocedural bleeding during polypectomy, ESGE guidelines recommend treatment with contact thermal coagulation (snare-tip soft coagulation or coagulation forceps), or TTS clipping, with or without dilute epinephrine injection [55▪].

For suspected delayed postpolypectomy bleeding, a conservative 'watchful waiting' approach may be initially attempted. If, however, bleeding is thought to be profuse and ongoing, repeat colonoscopy is indicated, and the recommended first-line endoscopic interventions includes clips (either through-the-scope or cap-mounted) or contact/noncontact thermal coagulation therapy, with or without dilute epinephrine injection. Topical hemostatic powders are recommended as second-line therapy if mechanical or thermal therapies fail [1▪▪,3,55▪].

APC is a relatively well tolerated, noncontact thermal hemostasis method used for tissue coagulation by discharging ionized argon gas (plasma) [56]. In the setting of acute LGIB, APC is recommended primarily for the treatment of superficial vascular lesions such as colorectal angioectasias [1▪▪]. In addition, APC has recently been shown to be effective in the treatment of bleeding secondary to portal hypertensive colopathy in cirrhotic patients [57].

Hemostatic powders are synthetic or biologically derived polymers that upon contact with moisture rapidly absorb water to form adhesive barriers and also locally promote coagulation cascade activation and platelet aggregation, thereby occluding the bleeding source [58▪]. These modalities have gained attention during recent years as simple, safe, and effective tools for primary, secondary, and bridging (e.g. before angiographic embolization) endoscopic treatment for a variety of GIB causes [58▪,59,60,61▪]. Topical hemostasis agents may be particularly effective for large and/or irregular bleeding surface areas such as colorectal tumors that are not amenable to other endoscopic hemostasis methods [59,60,61▪]. Topical hemostasis therapy may act as a bridge to definitive surgical resection of the tumor. A recent systematic review of randomized controlled trials showed no difference in primary hemostasis and a higher initial success rate for Hemospray compared with standard endoscopic therapy [62]. Hemostatic powders are currently recommended as second line or 'salvage' endoscopic therapy in acute LGIB [1▪▪,3,58▪].

The role of cross-sectional imaging

Owing to its high sensitivity and specificity in detecting bleeding extravasation rates as low as 0.3 ml/min, CT angiography is recommended as the initial diagnostic test for hemodynamically unstable LGIB patients presenting with acute hematochezia [1▪▪,3,8],

Role of interventional radiology and surgery

Radiological intervention for acute LGIB using trans-arterial catheter embolization (TAE) of the

involved vessel is indicated for patients with either a positive CT angiography, persistent LGIB nonresponsive to pharmacologic and endoscopic measures, or a significant LGIB with inability to achieve adequate bowel cleansing [1▪▪,3,8].

In a recent systematic review, Corrado *et al.* described empiric or blind TAE (i.e. for patients without extravasation on angiography but with indirect signs of bleeding such as aneurysm/pseudoaneurysm, vessel cut-off, or vascular irregularity/abnormality) performed for both LGIB and UGIB, a mean technical success rate of 97.7% (range 62–100%), a mean clinical success rate of 80% (range 51–100%), and a pooled adverse event incidence of nearly 10% [63]. Thus, empiric TAE may be considered as an alternative for surgery in such patients.

Surgical therapy has a very limited role in LGIB and is rarely indicated. Surgery may be indicated for LGIB not amenable or refractory to other interventional measures, including endoscopic and embolization therapy [1▪▪,3,8]. Moreover, in a recent nation-wide study in the United States involving over 364 000 LGIB cases, surgery carried a significant morbidity and in-hospital mortality risk [64].

Antiplatelets and anticoagulants

Management of antiplatelet medications during acute lower gastrointestinal bleeding

Antiplatelet medications used in clinical practice include aspirin and P2Y12 receptor inhibitors (e.g. Clopidogrel, Prasugrel, and Ticagrelor), all of which except Ticagrelor irreversibly inhibit platelet function for approximately 7–10 days [65▪▪].

Current LGIB guidelines recommend that aspirin given for primary cardiovascular prophylaxis (i.e. in patients with cardiovascular risk factors but without a previous cardiovascular event) should be withheld at the time of presentation [1▪▪,3,8], Moreover, in patients who do not meet appropriate indications for ongoing cardiovascular primary prophylaxis, permanent cessation of aspirin should be considered [3,8,66].

For patients with acute LGIB on aspirin monotherapy for secondary cardiovascular prophylaxis (i.e. patients who underwent a previous vascular event with or without intervention, following which aspirin therapy is prescribed indefinitely), guidelines recommend that aspirin should be continued without interruption, and if withheld at the time of patient presentation, aspirin should be re-started as soon as hemostasis is achieved (within 3–5 days) [1▪▪,3,8,66,67]. This owing to increased mortality and thrombotic events in GIB patients in whom aspirin was stopped and not restarted [68–70].

For patients presenting with acute LGIB on dual antiplatelet therapy (DAPT), management decisions should be taken embracing a multidisciplinary approach, and in consultation with cardiologists/neurologists. It is recommended to continue DAPT whenever possible if coronary stent(s) has been placed in the past 12 months because of the high risk of in-stent thrombosis. Alternatively, the P2Y12 receptor inhibitor should be temporarily withheld with aspirin continued. The P2Y12 inhibitor should then be re-started within 5 days [1▪▪,3,8,66,67].

These recommendations regarding resumption of antiplatelet therapy are further supported by the findings of a recent randomized trial showing a significantly lower incidence of cerebrovascular and cardiovascular events for GIB patients under aspirin monotherapy with early (<3 days) resumption of aspirin, and lower mortality for GIB patients under DAPT therapy in whom aspirin was continued and Clopidogrel was withheld and re-started within 7 days [71].

Management of oral anticoagulants during acute lower gastrointestinal bleeding

Oral anticoagulants (OAC) include direct oral anticoagulants (DOACs) and Vitamin K antagonists (VKAs) such as Warfarin.

DOACs include the direct thrombin inhibitor Dabigatran and the direct factor Xa inhibitors Rivaroxaban, Apixaban, and Edoxaban, all having a relatively short onset of action, reaching maximal effect within 3 h from administration, and short half-lives, with dissipation of their anticoagulant effect within less than 24 h [72]. Warfarin's onset of action and half-life are more prolonged, each taking several days, thereby delaying restoration of its anticoagulant effect following withdrawal [72].

Since their introduction, DOACs have been well studied and recent data suggest a favorable safety profile when compared with traditional VKA anticoagulants [73–75]. Compared with VKAs, DOACs generally are associated with lower mortality and lower rates of major bleeding and intracranial hemorrhage risk, with equivocal data in the literature regarding GIB risk under DOACs [11,72,74,76–79].

Management of oral anticoagulants during self-limited lower gastrointestinal bleeding

In patients who present with self-limited LGIB under oral anticoagulant therapy not requiring hospitalization (e.g. Oakland score ≤8) nor any invasive intervention, oral anticoagulants may be continued

without interruption, whereas in cases of a more significant LGIB, OAC should be withheld [1▪▪,3].

Major lower gastrointestinal bleeding during vitamin K antagonist treatment

For major LGIB with hemodynamic instability under VKA treatment, particularly if INR is above the therapeutic range, reversal of VKA is recommended preferentially using a four-factor prothrombin complex concentrate (PCC) rather than FFP [1▪▪,3,65▪▪,67]. This is because of the better efficacy of PCC and its more rapid reversal of VKA action [1▪▪,3,8,66,67]. Additionally, intravenous vitamin K administration is recommended by European and British guidelines [3,8,66].

Major lower gastrointestinal bleeding during direct oral anticoagulant treatment

For major LGIB while under DOAC therapy, withholding anticoagulation is the mainstay of treatment, with expected normalization of anticoagulant activity within 24 h [1▪▪,3,8,11]. Reversal agents specific for each DOAC are also available, namely Idarucizumab for Dabigatran and Andexanet alpha for Rivaroxaban, Apixaban, and Edoxaban [80].

According to recent guidelines, the use of DOAC reversal agents is recommended only in situations of life-threatening LGIB with persisting hemodynamic instability, and preferentially if the last DOAC dose was administered in the previous 24 h [1▪▪,3,8].

The joint American-Canadian guideline proposes to avoid using DOAC reversal agents because of a concern regarding their efficacy in hemostasis and in mortality prevention, as well as a potential prothrombotic effect [67].

Resumption of oral anticoagulants following lower gastrointestinal bleeding

For LGIB patients in whom oral anticoagulants are interrupted, treatment should be resumed after bleeding cessation and within 7 days or less from presentation for either VKAs or DOACs [1▪▪,3,8,66,67], with consideration for earlier ($\leq$72 h) anticoagulant resumption by bridging with unfractionated heparin (UFH) or low-molecular-weight heparin (LMWH) in patients estimated to be at high thrombotic risk [3,8,66].

Those considered to be at high thrombotic risk include those with a mechanical heart valve, a CHA2DS2-VASc score at least 4, patients with a recent (<3 months) cerebrovascular event or venous thromboembolism (VTE), with a history of recurrent/unprovoked VTE, VTE with active cancer, or those with prior thromboembolism with anticoagulant interruption [81].

When considering anticoagulation resumption in patients with both a high bleeding risk and a high thrombotic risk, alternatives to anticoagulants including left atrial appendage closure for atrial fibrillation or inferior vena cava filter for VTE should be considered, using a multidisciplinary approach in consultation with cardiologists and/or neurologists [66,81].

CONCLUSION

In this review article, we highlighted and summarized the most recent literature on LGIB, with an emphasis on clinical studies published in the past 18 months. This includes the latest American and European society guidelines and advancements in therapeutic options, thereby providing clinicians an up-to-date and comprehensive tool for LGIB diagnosis and management.

Acknowledgements

Guarantors of the article: I.M.G., Y.E.
Author contributions: Y.E. – writing the review; I.M.G. – critical review and editing of the review, finalizing of the review.

Financial support and sponsorship

None.

Conflicts of interest

Y.E,, none. I.M.G. is a consultant to Boston Scientific, Medtronic, Motus GI, and has received research funding from AstraZeneca and CheckCap.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:
- ▪ of special interest
- ▪▪ of outstanding interest

1. ▪▪ Sengupta N, Feuerstein JD, Jairath V, *et al.* Management of patients with acute lower gastrointestinal bleeding: an updated ACG Guideline. Am J Gastroenterol 2023; 118:208–231.
The latest and most up-to-date American society guideline for LGIB diagnosis and management.
2. Gralnek IM, Neeman Z, Strate LL. Acute Lower Gastrointestinal Bleeding. N Engl J Med 2017; 376:1054–1063.
3. Konstantinos T, Gkolfakis P, Gralnek IM, *et al.* diagnosis and management of acute lower gastrointestinal bleeding: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy 2021; 53:850–868.
4. Nagata N, Kobayashi K, Yamauchi A, *et al.* Identifying bleeding etiologies by endoscopy affected outcomes in 10,342 cases with hematochezia: CODE BLUE-J Study. Am J Gastroenterol 2021; 116:2222–2234.
5. ▪ Peery AF, Crockett SD, Murphy CC, *et al.* Burden and cost of gastrointestinal, liver, and pancreatic diseases in the United States: update 2021. Gastroenterology 2022; 162:621–644.
The latest and most up-to-date American epidemiological study covering the burden and costs of various gastrointestinal conditions.
6. Oakland K, Guy R, Uberoi R, *et al.,* UK Lower GI Bleeding Collaborative. Acute lower GI bleeding in the UK: patient characteristics, interventions and outcomes in the first nationwide audit. Gut 2018; 67:654–662.

7. Radaelli F, Frazzoni L, Repici A, *et al.* Clinical management and patient outcomes of acute lower gastrointestinal bleeding. A multicenter, prospective, cohort study. Dig Liver Dis 2021; 53:1141–1147.
8. Oakland K, Chadwick G, East JE, *et al.* Diagnosis and management of acute lower gastrointestinal bleeding: Guidelines from the British Society of Gastroenterology. Gut 2019; 776–789.
9. Kate V, Sureshkumar S, Gurushankari B, Kalayarasan R. Acute upper non-variceal and lower gastrointestinal bleeding. J Gastrointest Surg 2022; 26:932–949.
10. Oakland K, Guy R, Uberoi R, *et al.* Acute lower GI bleeding in the UK: patient characteristics, interventions and outcomes in the first nationwide audit. Gut 2017; 67:654–662.
11. Scridon A, Balan AI. Challenges of anticoagulant therapy in atrial fibrillation — focus on gastrointestinal bleeding. Int J Mol Sci 2023; 24:6879.
12. Vora P, Pietila A, Peltonen M, *et al.* Thirty-year incidence and mortality trends in upper and lower gastrointestinal bleeding in Finland. JAMA Netw Open 2020; 3:e2020172.
13. Mamas MA, Batson S, Pollock KG, *et al.* Meta-analysis comparing apixaban versus rivaroxaban for management of patients with nonvalvular atrial fibrillation. Am J Cardiol 2023; 166:58–64.
14. Papantonioua K, Michailidesa C, Balia M, *et al.* Gastrointestinal bleeding in athletes. Ann Gastroenterol 2023; 36:267–274.
15. Stiller CO, Hjemdahl P. Lessons from 20 years with COX-2 inhibitors: importance of dose–response considerations and fair play in comparative trials. J Intern Med 2022; 292:557–574.
16. Oakland K, Kothiwale S, Forehand T, *et al.* External validation of the Oakland score to assess safe hospital discharge among adult patients with acute lower gastrointestinal bleeding in the US. JAMA Netw open 2020; 3:e209630.
17. Oakland K, Jairath V, Uberoi R, *et al.* Derivation and validation of a novel risk score for safe discharge after acute lower gastrointestinal bleeding: a modelling study. Lancet Gastroenterol Hepatol 2017; 2:635–643.
18. Laursen SB, Oakland K, Laine L, *et al.* ABC score: a new risk score that accurately predicts mortality in acute upper and lower gastrointestinal bleeding: an international multicentre study. Gut 2021; 70:707–716.
19. Sengupta N, Tapper EB. Derivation and internal validation of a clinical prediction tool for 30-day mortality in lower gastrointestinal bleeding. Am J Med 2017; 130:601.e1–601.e8.
20. Aoki T, Nagata N, Shimbo T, *et al.* Development and validation of a risk scoring system for severe acute lower gastrointestinal bleeding. Clin Gastroenterol Hepatol 2016; 14:1562.e2–1570.e2.
21. Strate LL, Saltzman JR, Ookubo R, *et al.* Validation of a clinical prediction rule for severe acute lower intestinal bleeding. Am J Gastroenterol 2005; 100:1821–1827.
22. Tapaskar N, Jones B, Mei S, Sengupta N. Comparison of clinical prediction tools and identification of risk factors for adverse outcomes in acute lower GI bleeding. Gastrointest Endosc 2019; 89:1005.e2–1013.e2.
23. ■■ Almaghrabi M, Gandhi M, Guizzetti L, *et al.* Comparison of risk scores for lower gastrointestinal bleeding: a systematic review and meta-analysis. JAMA Netw Open 2022; 5:e2214253.

A systematic review and meta-analysis comparing the various LGIB risk-stratification tools.

24. Montoro M, Cucala M, Lanas Á, *et al.* Indications and hemoglobin thresholds for red blood cell transfusion and iron replacement in adults with gastrointestinal bleeding: an algorithm proposed by gastroenterologists and patient blood management experts. Front Med(Lausanne) 2022; 9:90379.
25. Carson JL, Stanworth SJ, Dennis JA, *et al.* Transfusion thresholds for guiding red blood cell transfusion. Cochrane Database Syst Rev 2021; 2021:; CD002042.
26. Zakko L, Rustagi T, Douglas M, Laine L. No benefit from platelet transfusion for gastrointestinal bleeding in patients taking antiplatelet agents. Clin Gastroenterol Hepatol 2017; 15:46–52.
27. HALT-IT Trial Collaborators. Effects of a high-dose 24-h infusion of tranexamic acid on death and thromboembolic events in patients with acute gastrointestinal bleeding (HALT-IT): an international randomised, double-blind, placebo-controlled trial. Lancet 2020; 395:1927–1936.
28. Nagata N, Kobayashi K, Yamauchi A, *et al.* Identifying Bleeding Etiologies by Endoscopy Affected Outcomes in 10,342 Cases With Hematochezia: CODE BLUE-J Study. Am J Gastroenterol 2021; 116:2222–2234.
29. Aziz M, Haghbin H, Gangwani MK, *et al.* Erythromycin improves the quality of esophagogastroduodenoscopy in upper gastrointestinal bleeding: a network meta-analysis. Dig Dis Sci 2023; 68:1435–1446.
30. Strate LL, Gralnek IM. ACG clinical guideline: management of patients with acute lower gastrointestinal bleeding. Am J Gastroenterol 2016; 111:459–474.
31. ■ Shiratori Y, Ishii N, Aoki T, *et al.* Timing of colonoscopy in acute lower GI bleeding: a multicenter retrospective cohort study. Gastrointest Endosc 2023; 97:89.e10–99.e10.

A retrospective study indicating that early colonoscopy in acute LGIB carries an increased rate of rebleeding and does not reduce mortality nor the rate of vascular interventions and embolization.

32. Lahat A, Klang E, Rahman N, *et al.* Utility of early colonoscopy for acute lower gastrointestinal bleeding: a retrospective cohort study. Therap Adv Gastroenterol 2023; 16:17562848221147756.
33. Sharma S, Sallout D, Acharya A, Adler DG. Early colonoscopy does not affect 30-day readmission after lower GI bleeding: insights from a nationwide analysis. Dig Dis Sci 2022; 67:3948–3954.
34. Ichita C, Nakajima M, Ohbe H, *et al.* Effectiveness of early colonoscopy in patients with colonic diverticular hemorrhage: nationwide inpatient analysis in Japan. Dig Endosc 2023; 35:520–528.
35. Anvari S, Lee Y, Yu J, *et al.* Urgent versus standard colonoscopy for management of acute lower gastrointestinal bleeding: a systematic review and meta-analysis of randomized controlled trials. J Clin Gastroenterol 2020; 54:493–502.
36. Tsay C, Shung D, Stemmer Frumento K, Laine L. Early colonoscopy does not improve outcomes of patients with lower gastrointestinal bleeding: systematic review of randomized trials. Clin Gastroenterol Hepatol 2020; 18:1696.e2–1703.e2.
37. Saviano A, Petruzziello C, Riccioni ME, *et al.* Lower gastrointestinal bleeding in the emergency department: high- volume vs. low-volume peg bowel preparation for colonoscopy: a randomized trial. Rev Recent Clin Trials 2023; 18:76–81.
38. Kishino T, Nagata N, Kobayashi K, *et al.* Endoscopic direct clipping versus indirect clipping for colonic diverticular bleeding: a large multicenter cohort study. United Eur Gastroenterol J 2022; 10:93–103.
39. Kobayashi K, Nagata N, Furumoto Y, *et al.,* CODE BLUE-J study collaborators. Effectiveness and adverse events of endoscopic clipping versus band ligation for colonic diverticular hemorrhage: a large-scale multicenter cohort study. Endoscopy 2021; 54:735–744.
40. Turan AS, Pohl H, Matsumoto M, *et al.* The role of clips in preventing delayed bleeding after colorectal polyp resection: an individual patient data. Clin Gastroenterol Hepatol 2023; 20:362.e23–371.e23.
41. Ouwehand RJ, Vleggaar FP, Vos WH De, Wolfhagen FHJ. Management of delayed bleeding after endoscopic mucosal resection of large colorectal polyps: a retrospective multicenter cohort study. Endosc Int Open 2020; 8:E1052–E1060.
42. Paszat LF, Sutradhar R, Luo J, *et al.* Perforation and postpolypectomy bleeding complicating colonoscopy in a population-based screening program. Endosc Int Open 2021; 09:E637–E645.
43. van der Star S, Moons LMG, Ter Borg F, *et al.* Management of delayed bleeding after endoscopic mucosal resection of large colorectal polyps: a retrospective multicenter cohort study. Endosc Int open 2020; 8:E1052–E1060.
44. ■ Bishay K, Meng ZW, Frehlich L, *et al.* Prophylactic clipping to prevent delayed colonic postpolypectomy bleeding: meta-analysis of randomized and observational studies. Surg Endosc 2022; 36:1251–1262.

A systematic review and meta- analysis, which demonstrated a significant benefit for postpolypectomy prophylactic clipping in polyps greater than 2 cm in diameter and located in the proximal colon.

45. Gweon T, Lee K, Lee S. Effect of prophylactic clip application for the prevention of postpolypectomy bleeding of large pedunculated colonic polyps: a randomized controlled trial. Gastrointest Endosc 2023; 94:148–154.
46. Chen B, Du L, Luo L, *et al.* Prophylactic clips to reduce delayed polypectomy bleeding after resection of large colorectal polyps: a systematic review and meta-analysis of randomized trials. Gastrointest Endosc 2021; 93:807–815.
47. Spadaccini M, Albéniz E, Pohl H, *et al.* Prophylactic clipping after colorectal endoscopic resection prevents bleeding of large, proximal polyps: meta-analysis of randomized trials. Gastroenterology 2020; 159:148.e11–158.e11.
48. Pohl H, Grimm IS, Moyer MT, *et al.* Clip closure prevents bleeding after endoscopic resection of large colon polyps in a randomized trial. Gastroenterology 2019; 157:977.e3–984.e3.
49. Ayoub F, Westerveld DR, Forde JJ, *et al.* Effect of prophylactic clip placement following endoscopic mucosal resection of large colorectal lesions on delayed polypectomy bleeding: a meta-analysis. World J Gastroenterol 2019; 25:2251–2263.
50. Yang T-C, Wu Y-H, Lee P-C, *et al.* Prophylactic clipping after endoscopic mucosal resection of large nonpedunculated colorectal lesions: a meta-analysis. J Gastroenterol Hepatol 2021; 36:1778–1787.
51. ■ Bi D, Zhang LY, Alqaisieh M, *et al.* Novel through-the-scope suture closure of colonic EMR defects (with video). Gastrointest Endosc 2023; 98:122–129.

A multicenter study that demonstrated high safety and efficacy level of a novel and unique suture device for closure of colonic mucosal defect.

52. Gweon TG, Lee KM, Lee SW, *et al.* Effect of prophylactic clip application for the prevention of postpolypectomy bleeding of large pedunculated colonic polyps: a randomized controlled trial. Gastrointest Endosc 2021; 94:148–154.
53. Soh JS, Seo M, Kim KJ. Prophylactic clip application for large pedunculated polyps before snare polypectomy may decrease immediate postpolypectomy bleeding. BMC Gastroenterol 2020; 20:68.
54. ■ Pattarajierapan S, Takamaru H, Khomvilai S. Difficult colorectal polypectomy: technical tips and recent advances. World J Gastroenterol 2023; 29:2600–2615.

A review article explaining and instructing endoscopists regarding the approach to resection of large and difficult polyps.

55. ■ Karstensen JG, Ebigbo A, Desalegn H, *et al.,* European Society of Gastrointestinal Endoscopy and World Endoscopy Organization. Colorectal polypectomy and endoscopic mucosal resection: European Society of Gastrointestinal Endoscopy Cascade Guideline. Endosc Int Open 2022; 10:E1427–E1433.

ESGE society guideline for performing colonic and rectal polyp resection and EMR

56. Xiao A, Liu D, He D, *et al.* Plasma scalpels: devices, diagnostics, and applications. Biomedicines 2022; 10:2967.

57. Demetiou G, Augoustaki A, Kalaitzakis E. Endoscopic management and outcome of nonvariceal bleeding in patients with liver cirrhosis: a systematic review. World J Gastrointest Endosc 2022; 14:163–176.

58. ■ Jiang SX, Chahal D, Ali-Mohamad N, *et al.* Hemostatic powders for gastrointestinal bleeding: a review of old, new, and emerging agents in a rapidly advancing field. Endosc Int Open 2022; 10:E1136–E1146.

A very recent review article overviewing current knowledge on each existing hemostatic powder preparation for endoscopic use.

59. Facciorusso A, Bertini M, Bertoni M, *et al.* Effectiveness of hemostatic powders in lower gastrointestinal bleeding: a systematic review and meta-analysis. Endosc Int Open 2021; 9:E1283–E1290.

60. Facciorusso A, Bertini M, Bertoni M, *et al.* Efficacy of hemostatic powders in lower gastrointestinal bleeding: clinical series and literature review. Dig Liver Dis 2021; 53:1327–1333.

61. ■ Pittayanon R, Khongka W, Linlawan S, *et al.* Hemostatic powder vs standard endoscopic treatment for gastrointestinal tumor bleeding: a multicenter randomized trial. Gastroenterology 2023; 165:762.e2–772.e2.

A recent multicenter randomized study that demonstrated a higher efficacy in immediate hemostasis and lower rates of 30-day rebleeding for hemostatic powders compared with standard endoscopic therapies in treatment of gastrointestinal tumor bleeding.

62. Deliwala SS, Chandan S, Mohan BP, *et al.* Hemostatic spray (TC-325) vs. standard endoscopic therapy for non-variceal gastrointestinal bleeding - a meta-analysis of randomized controlled trials. Endosc Int Open 2023; 24:288–295.

63. Ini C, Distefano G, Sanfilippo F, *et al.* Embolization for acute nonvariceal bleeding of upper and lower gastrointestinal tract: a systematic review. CVIR Endovasc 2023; 6:18.

64. Lee C, Orellana M, Benharash P, *et al.* The use of surgical intervention for lower gastrointestinal bleeding and its association with clinical outcomes and resource use. Surgery 2023; 173:1346–1351.

65. ■■ Abraham NS, Barkun AN, Sauer BG, *et al.* American College of Gastroenterology-Canadian Association of Gastroenterology Clinical Practice Guideline: management of anticoagulants and antiplatelets during acute gastrointestinal bleeding and the periendoscopic period. Am J Gastroenterol 2022; 117:542–558.

The latest and most up-to-date ACG/CAG society guidelines for management of antiplatelet and anticoagulant medications in acute gastrointestinal bleeding.

66. Veitch AM, Radaelli F, Alikhan R, *et al.* Endoscopy in patients on antiplatelet or anticoagulant therapy: British Society of Gastroenterology (BSG) and European Society of Gastrointestinal Endoscopy (ESGE) guideline update. Gut 2021; 70:1611–1628.

67. Barkun AN, Douketis J, Noseworthy PA, *et al.* Management of patients on anticoagulants and antiplatelets during acute gastrointestinal bleeding and the peri-endoscopic period: a clinical practice guideline dissemination tool. Am J Gastroenterol 2022; 117:513–519.

68. Sung JJY, Lau JYW, Ching JYL, *et al.* Continuation of low-dose aspirin therapy in peptic ulcer bleeding: a randomized trial. Ann Intern Med 2010; 152:1–9.

69. Chan FKL, Leung Ki E-L, Wong GLH, *et al.* Risks of bleeding recurrence and cardiovascular events with continued aspirin use after lower gastrointestinal hemorrhage. Gastroenterology 2016; 151:271–277.

70. Siau K, Hannah JL, Hodson J, *et al.* Stopping antithrombotic therapy after acute upper gastrointestinal bleeding is associated with reduced survival. Postgrad Med J 2018; 94:137–142.

71. Fan X, Meng X, Zhao L, Wang J. Time of resumption of antiplatelet drugs after upper gastrointestinal hemorrhage. Med Sci Monit 2022; 28:e936953.

72. Ferri N, Colombo E, Tenconi M, *et al.* Drug-drug interactions of direct oral anticoagulants (DOACs): from pharmacological to clinical practice. Pharmaceutics 2022; 14:1120.

73. Samaranayake CB, Anderson J, Upham JW, Keir G. Direct oral anticoagulants for cancer-associated venous thromboembolisms: a systematic review and network meta-analysis. Intern Med J 2022; 52:272–281.

74. Barbarawi M, Barbarawi O, Corcoran J, *et al.* Efficacy and safety of the non-vitamin K antagonist oral anticoagulant among patients with nonvalvular atrial fibrillation and cancer: a systematic review and network meta-analysis. Curr Probl Cardiol 2022; 47:101346.

75. Saviano A, Brigida M, Petruzziello C, *et al.* Gastrointestinal bleeding due to NOACs use: exploring the molecular mechanisms. Int J Mol Sci 2022; 23:13955.

76. Chen X, Wang L, Li H, *et al.* Comparative differences in the risk of major gastrointestinal bleeding among different direct oral anticoagulants: an updated traditional and Bayesian network meta-analysis. Front Pharmacol 2023; 13:1049283.

77. Cao Y, Zheng Y, Li S, *et al.* An updated meta-analysis of DOACs vs. VKAs in atrial fibrillation patients with bioprosthetic heart valve. Front Cardiovasc Med 2022; 9:899906.

78. Murphy AC, Koshy AN, Farouque O, *et al.* Factor Xa inhibition for the treatment of venous thromboembolism associated with cancer: a meta-analysis of the randomised controlled trials. Hear lung Circ 2023; 2022:716–725.

79. Hu J, Zhou Y, Cai Z. Outcome of novel oral anticoagulant versus warfarin in frail elderly patients with atrial fibrillation: a systematic review and meta-analysis of retrospective studies. Acta Clin Belg 2023; 367–377.

80. Connolly SJ, Crowther M, Eikelboom JW, *et al.,* ANNEXA-4 Investigators. Full study report of andexanet alfa for bleeding associated with factor Xa inhibitors. N Engl J Med 2019; 380:1326–1335.

81. Tomaselli GF, Mahaffey KW, Cuker A, *et al.* 2020 ACC Expert Consensus Decision Pathway on management of bleeding in patients on oral anticoagulants: a report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol 2020; 76:594–622.