Best Practice & Research Clinical Gastroenterology 42-43 (2019) 101615

Contents lists available at ScienceDirect

Best Practice & Research Clinical Gastroenterology

journal homepage: https://ees.elsevier.com/ybega/default.asp

The role of colonoscopy and endotherapy in the management of lower gastrointestinal bleeding

Neil Sengupta

Section of Gastroenterology, University of Chicago Medical Center 5841 S Maryland Avenue, MC 4076, Chicago, IL, 60637, USA

ARTICLE INFO

Article history:
Received 7 January 2019
Accepted 23 May 2019

Keywords:
Gastrointestinal hemorrhage
Colonoscopy

ABSTRACT

Colonoscopy is an integral diagnostic and therapeutic tool in the management of patients with lower gastrointestinal bleeding (LGIB). After resuscitation, reversal of coagulopathy, and exclusion of a proximal source of bleeding, colonoscopy should be performed in most patients with LGIB. Bowel preparation, typically with polyethylene glycol based solutions, is needed to closely inspect the colonic mucosa for bleeding sources. Colonoscopy within 24 h is recommended for high-risk patients with ongoing bleeding, although there is limited evidence that this strategy improves clinical outcomes. When active or stigmata of bleeding is detected, endoscopic intervention is indicated and can reduce future rebleeding. The most common options for endoscopic intervention include clipping, endoscopic band ligation, and coagulation, however rigorous head-to-head comparisons of different endoscopic tools are unavailable. Future research is needed to determine the optimal timing of colonoscopy, appropriate reversal strategies for patients on antithrombotics, and the most effective endoscopic hemostatic therapy.

Introduction

Acute lower gastrointestinal bleeding (LGIB) is a common reason for hospitalization across the world, and is a significant source of resource utilization and costs. With an aging population and widespread use of antithrombotic medications, hospitalization for LGIB will remain a common problem for clinicians. Although the majority of patients do well with resolution of bleeding, patients with severe comorbidities at the time of LGIB are at risk for post-discharge adverse outcomes[1–3]. Colonoscopy is the diagnostic and therapeutic test of choice in patients with LGIB, given its ability to provide a definitive diagnosis as well as therapeutic interventions. However, the optimal timing of inpatient colonoscopy remains controversial, and randomized trial data supporting the benefit of urgent colonoscopy is lacking in regards to its ability to improve meaningful clinical outcomes. Nonetheless, colonoscopy is recommended by societal guidelines given its favorable safety profile [2]. This review will cover the indications and role for colonoscopy in LGIB, bowel preparation prior to colonoscopy, timing of colonoscopy, and options for endotherapy.

Role of colonoscopy

Exclusion of proximal source

For patients with severe hematochezia or hemodynamic instability, colonoscopy should only be performed after exclusion of a proximal source of bleeding [2]. In a study of 85 patients presenting with hematochezia and high-risk features (tachycardia, hypotension, orthostasis, significant drop in hemoglobin, or blood transfusion requirement) who underwent urgent upper endoscopy prior to colonoscopy, 15% were found to have a proximal source of bleeding [4]. For those with a moderate suspicion of UGIB, a nasogastric lavage and aspirate can be considered prior to colonoscopy. Patients with severe hematochezia are higher risk for UGIB if they have a history of peptic ulcer disease, portal hypertension, significant non-steroidal anti-inflammatory drug use (NSAID) or antiplatelet use, or those with elevated blood urea nitrogen-to-creatinine ratio levels [5]. See Fig. 1 for a suggested approach to patients with LGIB.

Resuscitation

Patients should be adequately resuscitated with intravenous fluids with the goal of normalization of blood pressure and heart rate prior to performance of colonoscopy. Patients presenting with

E-mail address: nsengupta@medicine.bsd.uchicago.edu.

https://doi.org/10.1016/j.bpg.2019.05.002
1521-6918/

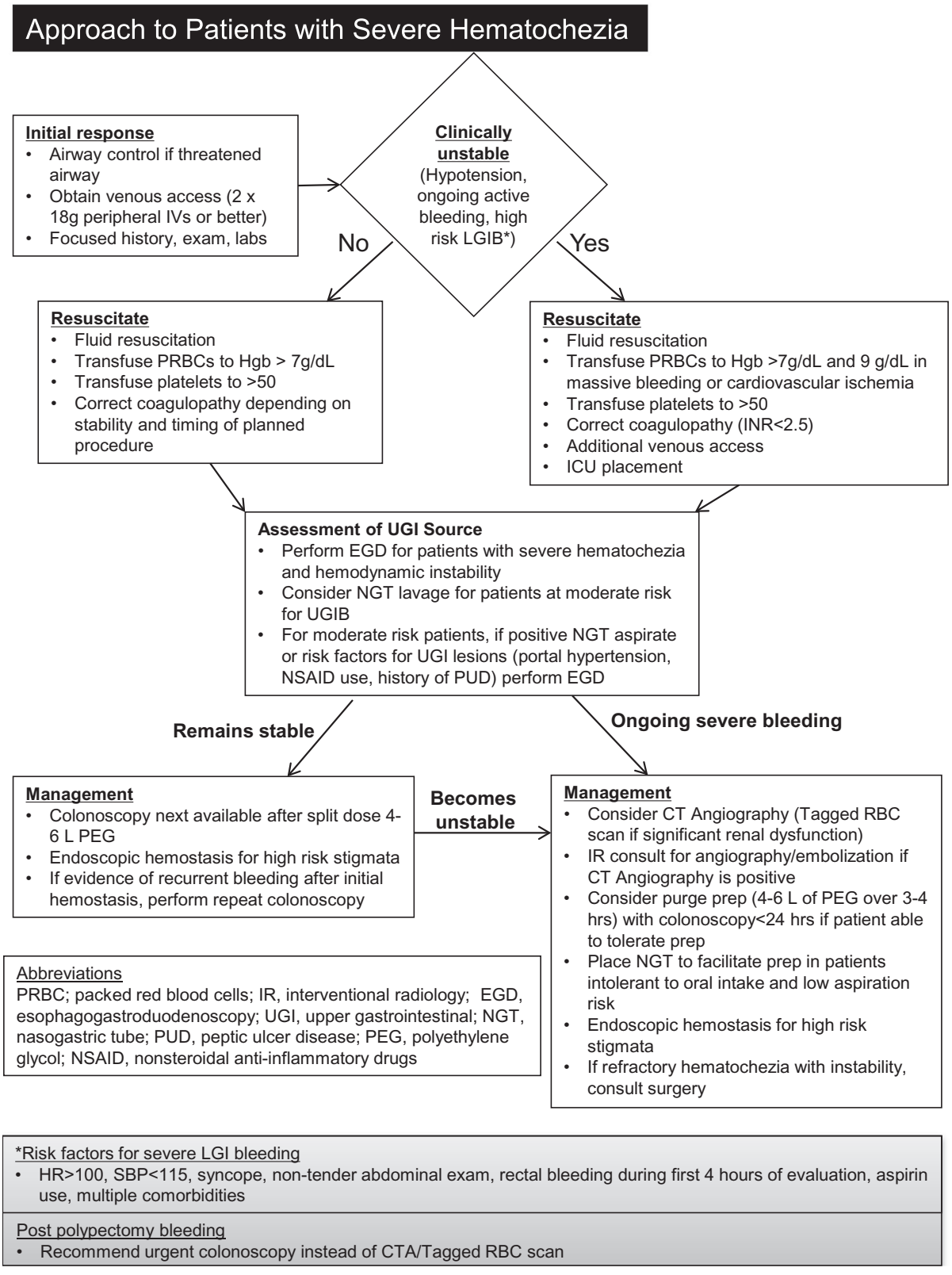

Fig. 1. Suggested algorithm for evaluation of severe hematochezia.

a significant drop in hemoglobin may require blood transfusions as part of their resuscitation. Transfusion protocols and cutoffs specific to LGIB have not been formally studied, and current societal recommendations are extrapolated from the UGIB literature. In a large randomized controlled trial (RCT) of patients with UGIB, patients assigned to a restrictive transfusion strategy (target over 7 g/dL) had a higher probability of 6-week survival, and a lower probability of rebleeding and adverse events compared to patients assigned to

a liberal transfusion strategy (target over 9 g/dL) [6]. Based largely on this study, clinical practice guidelines recommend transfusion to maintain hemoglobin levels above 7 g/dL, however more lenient cutoffs should be considered for patients with severe hematochezia or significant cardiovascular disease [7].

Reversal of coagulopathy

Data on reversal of coagulopathy prior to colonoscopy is extremely limited in LGIB, and recommendations are based on retrospective, observational studies of patients with UGIB. Patients with significant bleeding and coagulopathy should have their coagulation defects reversed prior to, or at the time of colonoscopy, in order to reduce active bleeding and maximize the success of endoscopic hemostasis. For patients with elevated INR levels above 2.5, reversal should depend on the patient's stability and intended timing of colonoscopy. Endoscopic hemostasis is considered safe and effective in patients with mild to moderate elevations in INR (1.5–2.5), although rigorous data demonstrating safety in LGIB is unavailable [2].

There is limited data to guide optimal platelet counts in patients with LGIB. Based on expert opinion statements, patients with thrombocytopenia and significant hematochezia should receive platelet transfusions to maintain a count of 50×10^9 prior to colonoscopy and therapeutic intervention [8].

Contraindications

Colonoscopy is a safe procedure, although there are rare risks detailed later in this review. Patients with ongoing severe hematochezia despite resuscitation are unlikely to tolerate bowel preparation and sedation required for a colonoscopy, and should be considered for radiographic interventions including computed tomography (CT) and angiography [9]. CT angiography is widely available with a high yield of diagnosis in those with ongoing bleeding, and is a first-line diagnostic test in patients with severe hematochezia who are unlikely to tolerate colonoscopy.

Other relative contraindications for colonoscopy include patients with toxic megacolon and suspected bleeding from fulminant colitis, where surgical management should be considered given the limited role for endoscopic therapy in these situations.

Practice points

- *For patients with hematochezia associated with hemodynamic instability, an upper endoscopy should be performed to exclude a proximal bleeding source.*
- *A restrictive transfusion strategy to maintain a hemoglobin level above* 7 g/dL *is recommended for most patients, although exceptions should be made for patients with massive bleeding.*
- *Endoscopic hemostasis is considered safe for patients with an INR of 2.5 or less.*

Diagnosis and yield of colonoscopy in LGIB

One of the main advantages to colonoscopy in the setting of LGIB is the ability to achieve a definitive or presumptive diagnosis of the source of bleeding. In prior studies, a definitive source of bleeding has been defined as a lesion visualized by colonoscopy or angiography which was actively bleeding or had clear stigmata of bleeding, including a non-bleeding visible vessel or adherent clot after irrigation. A presumptive source of bleeding included a lesion without active or stigmata of bleeding, and a subsequent thorough evaluation did not identify an additional potential bleeding site [10]. In previous RCTs comparing urgent colonoscopy to elective colonoscopy in LGIB, a definitive or presumptive diagnosis was achieved in 72–86% of all patients undergoing colonoscopy [4,10,11].

The most common source of LGIB identified by colonoscopy is diverticulosis (presumptive or definitive) occurring in 30–65% of cases, followed by hemorrhoidal bleeding, ischemic colitis, colonic angioectasias, and post-polypectomy bleeding [12]. Less common sources of bleeding include colorectal polyps/neoplasia, Dieulafoy's lesion, colitis/inflammatory bowel disease, radiation proctitis, and anorectal conditions [13,14].

In order to optimize the diagnostic yield of colonoscopy, the mucosa should be closely inspected using an adult or pediatric colonoscope as lesions may bleed intermittently and can be missed easily. Water-jet irrigation should be used to remove adherent stool or clot from the colonic mucosa. In addition, the terminal ileum should be intubated to exclude bleeding occurring from the small bowel.

Bowel preparation

Achieving an adequate bowel preparation is critical to successfully diagnose the source of LGIB and allow for effective therapeutic intervention. Unprepped endoscopy is not recommended, as thorough inspection of the colonic mucosa is required to localize subtle sources of bleeding, and presence of residual stool and blood can lead to poor visualization and theoretically increase the risk of perforation [2,15]. Repaka and colleagues performed a feasibility study of unprepped, hydroflush colonoscopy in patients with LGIB admitted to the intensive care unit using water enemas, followed by a colonoscopy with water-jet irrigation and a mechanical suction device. The cecum was reached in 9 of 13 patients, with adequate visualization of the mucosa in all patients [16]. However, this technique should only be considered a supplement to oral preparation until further data are available.

Direct comparisons of alternative bowel preparation agents in their success in achieving adequate visualization in the colon are unavailable. Prior trials utilized large volume (4–6 L), rapid purge protocols administered over a 3–4 h period using a polyethylene glycol based solution to successfully visualize the source of bleeding [10,17,18]. Because many patients with severe hematochezia are unable to tolerate large volume bowel preparation, a nasogastric tube (NGT) can be used to facilitate delivery of bowel preparation. In a RCT by Green et al. evaluating urgent colonoscopy, 50% of patients in the urgent colonoscopy arm required placement of a NGT due to the inability to tolerate the prep orally [10].

In a real world, non-trial setting, the rates of adequate inpatient bowel preparation are not ideal. In fact, hospitalized patients may independently be at risk for having an inadequate bowel preparation during colonoscopy [19]. In a recent study of 130 hospitalized patients undergoing colonoscopy, only 57% had an adequate bowel preparation, and afternoon procedures were a significant predictor for poor preparation [20]. Additional risk factors for poor preparation in inpatients are largely extrapolated from outpatients undergoing colonoscopy and include older age, higher body mass index, constipation, use of narcotics or tricyclic antidepressants, and neurologic conditions [21]. Importantly, inadequate inpatient bowel preparation has shown to be associated with increased length of stay (LOS) and hospital costs [22].

Although split dose bowel preparation is the standard of care for outpatients undergoing colonoscopy [23], there is less data supporting its use in hospitalized patients with LGIB. One reason for decreased widespread adoption of inpatient split dose bowel preparation is a concern for increased aspiration risk in the setting of recent fluid intake. However, in a recent prospective study of

inpatients undergoing colonoscopy, split dose preparation was not associated with increased gastric residual volume compared to overnight fasting [24]. Yadlapati and colleagues recently conducted a prospective study to develop an electronic order set integrating split dose bowel preparation, automated orders for rescue medications, and nursing bowel preparation checks. Following their intervention, the adequacy of inpatient bowel preparation increased from 42.5% to 85.7%, and hospital LOS following initiation of bowel preparation to discharge significantly decreased from 8.0 to 6.9 days, resulting in an estimated 1-year cost savings of $46,076 [25]. While further confirmatory data is needed, split dose preparation should be used in hospitalized patients with LGIB undergoing colonoscopy.

Providing hospitalized patients with an educational booklet on colonoscopy preparation and the use of a dedicated inpatient nurse facilitator also have been shown to be effective adjunctive tools to increase the quality of bowel preparation [26,27].

Overall, complications with use of polyethylene glycol based preparations are extremely rare. Volume overload was described after urgent bowel preparation in 4% of patients in an older study evaluating urgent colonoscopy in LGIB [17]. Severe vomiting after administration of polyethylene glycol via NGT leading to aspiration pneumonia has been described [28]. Other uncommon complications include vomiting induced esophageal perforation and Mallory-Weiss tears [29]. To reduce the risk of preparation related complications, aspiration precautions are recommended in older, debilitated patients, and NGT prep administration should be discouraged in patients at high baseline aspiration risk.

Practice points

- *Unprepped colonoscopy is not recommended, as close visualization of the mucosa is needed to detect sources of bleeding.*
- *Large volume, polyethylene glycol based preparation is the most studied inpatient bowel preparation, however data on the efficacy of different bowel preparations in the inpatient setting are lacking.*
- *Split dose bowel preparation should be used for hospitalized patients undergoing colonoscopy, as it does not increase gastric residual volume, and increases rates of adequate bowel preparation.*

Timing of colonoscopy

Randomized controlled trials

Urgent colonoscopy for LGIB was initially described as being safe and effective at both diagnosing and treating sources of LGIB in 1988 [17]. Subsequently, the CURE group conducted a prospective study of patients with diverticular hemorrhage who underwent colonoscopy and endoscopic intervention within 12 h, compared to historical controls who underwent urgent colonoscopy without endoscopic intervention. Patients who underwent endoscopic intervention had significantly lower rates of rebleeding (0% vs 53%), emergency hemicolectomy (0 vs. 35%), and LOS (2 days vs. 5 days) [18]. A subsequent RCT was done comparing urgent colonoscopy within 8 h to a standard care group where patients received angiographic intervention if there was ongoing bleeding, followed by elective colonoscopy. Patients randomized to the urgent group were more likely to have a definitive source of bleeding identified (42% vs. 22%), however there was no difference in mortality, LOS, transfusion, or rebleeding [10]. In another RCT of 72 patients randomized to urgent colonoscopy (<12 h) versus elective colonoscopy (36–60 h), there was no difference in rebleeding, blood transfusion, or therapeutic interventions [4]. Unfortunately, this trial was terminated prior to reaching the prespecified sample size. Most recently, investigators conducted the BLEED study, which was a nonblinded RCT of 132 patients undergoing urgent (<24 h) colonoscopy versus elective colonoscopy (1–3 days) [11]. The urgent group had a significantly lower LOS (2 days vs. 4 days), however this was balanced against a higher rate of recurrent bleeding and hospital readmissions. There was no significant difference in diagnosing a bleeding source or blood transfusions. To further explore the utility of urgent colonoscopy, a multicenter, RCT is underway in Japan to compare the efficacy of urgent colonoscopy (within 24 h) versus elective colonoscopy (24–96 h) in identifying stigmata of hemorrhage for patients with LGIB. Secondary outcomes will also include 30-day rebleeding rate, transfusion, LOS, and mortality [30].

Observational studies

As RCT data has been conflicting, observational studies have been used to guide expert recommendations for timing of colonoscopy in LGIB. A retrospective study by Strate and Syngal found that urgent colonoscopy (within 24 h) increases diagnostic yield, and decreases LOS [31]. Additional observational studies also demonstrated that colonoscopy within 24 h was associated with reduced LOS due likely to expedited discharge after a negative examination [32,33]. However, recent observational studies have questioned the benefit of urgent colonoscopy. In a retrospective, propensity-matched study of 163 pairs of patients with LGIB, early colonoscopy within 24 h led to higher rates of stigmata of hemorrhage, endoscopic therapy, and a shorter LOS [34]. However, there was no difference in mortality, transfusion, and the risk of rebleeding was higher (although not statistically significant). In another retrospective study of patients undergoing colonoscopy for LGIB, patients undergoing early colonoscopy (defined by day 2 of hospitalization) had shorter LOS, and more frequent endoscopic intervention, however there was no difference in 30-day mortality [35].

Meta-analyses

To date, four meta-analyses have been published on the utility of urgent colonoscopy in LGIB (Table 1). Seth and colleagues performed a meta-analysis of 6 studies (2 RCTs) and found that urgent colonoscopy was associated with increased identification of

Table 1
Pooled outcomes in meta-analyses comparing urgent to elective colonoscopy in LGIB.

Study	# in each arm (U vs. E)	Diagnostic Yield[a]	Rebleeding	LOS	PRBC	Endoscopic Intervention	Mortality
Seth [36]	9498/13921	ND	ND	ND	NR	ND	ND
Kouanda [37]	10172/14224	ND	ND	ND	ND	++ **with U**	ND
Sengupta [39]	422/479	++ **with U**	ND	ND	ND	++ **with U**	ND
Roshan Afshar [38]	9889/14630	++ **with U**	ND	**– with U**	ND	++ **with U**	ND

Abbreviations: LGIB, lower gastrointestinal bleeding; #, number; U, urgent colonoscopy; E, elective colonoscopy; LOS, length of stay; PRBC, packed red blood cell transfusion; ND, no difference; NR, not reported; ++, Increased; –, Decreased.

[a] Refers to overall diagnostic yield and rate of localization of LGIB.

stigmata of recent hemorrhage (pooled odds ratio [OR] 2.85), however there was no difference in surgery, LOS, or frequency of endoscopic intervention [36]. A meta-analysis by Kouanda and colleagues recently demonstrated similar findings [37]. Patients undergoing early colonoscopy (<24 h) had increased endoscopic interventions, but no difference in diagnostic yield. Importantly, there was no difference in LOS, rebleeding, transfusion, or mortality. In a third meta-analysis, early colonoscopy was associated with higher diagnostic yield, and shorter LOS, but was not associated with a difference in rebleeding or mortality [38]. Finally, our group published a meta-analysis of 6 studies, similarly demonstrating that early colonoscopy was associated with a higher diagnostic yield and endoscopic intervention, but no difference in rebleeding, LOS, or mortality [39]. See Table 1 for a summary of outcomes in the meta-analyses.

In summary, results from these meta-analyses indicate that though early colonoscopy may detect stigmata of bleeding and lead to more interventions (and potential earlier discharge), this intervention likely does not change the natural history of these patients or improve clinically relevant outcomes such as rebleeding or mortality.

Insurance claims studies

Recently, a large, retrospective cohort study of 20,010 patients with diverticular bleeding undergoing inpatient colonoscopy was published using insurance claims data. In the propensity-matched analysis, 8320 pairs of patients undergoing early colonoscopy (defined as occurring on the same day of hospitalization) were compared to those undergoing elective colonoscopy [40]. Patients in the early group received fewer endoscopic interventions (3% vs. 8%), and had a higher risk of 30-day rebleeding (OR 1.34, 95% CI 1.08−1.66). Although likely limited by residual confounding, this real-world, nationally representative data suggests that prior studies showing increased endoscopic interventions with early colonoscopy may have been biased as these studies were performed in tertiary-care, academic centers, often with specialized bleeding teams with greater expertise in treating acute LGIB. In real-world practice, early colonoscopy may also be performed at the expense of complete bowel preparation, thus leading to poor visualization and reduced interventions.

Summary

The American College of Gastroenterology conditionally recommends early colonoscopy (within 24 h) for patients with high-risk clinical features and signs of ongoing bleeding, although bases this recommendation based on low-quality evidence [2]. For patients without high-risk clinical features, significant comorbidities, or signs of ongoing bleeding, an elective colonoscopy can be performed. However, in light of results from recent meta-analyses and the insurance claims study, there is no clear evidence that urgent or early colonoscopy improves clinical outcomes such as rebleeding and mortality. Thus, further data is required (including the in-process RCT [30]) prior to widely advocating for early colonoscopy in patients with high-risk clinical features.

Practice points

- *Elective inpatient or next-available colonoscopy is recommended for patients without high-risk features or signs of ongoing bleeding*
- *Urgent colonoscopy within 24 h is recommended for high risk patients with ongoing bleeding and can more frequently detect stigmata of bleeding and lead to more endoscopic interventions, however there are no benefits in terms of rebleeding or mortality.*

Endoscopic hemostasis

The advantages of achieving endoscopic hemostasis during colonoscopy in both the control of active bleeding as well as the reduction of rebleeding through treatment of stigmata of hemorrhage have been well described [18,41]. In non-academic settings, however, the frequency of performing endoscopic hemostasis during colonoscopy for LGIB is low. In a population-based study using the Clinical Outcomes Research Initiative Database, less than 5% of patients presenting with hematochezia and undergoing inpatient colonoscopy received endoscopic hemostasis [14].

The optimal strategy for endoscopic hemostasis has yet to be defined, and is largely dependent on operator preference and experience. Data is limited on the efficacy of individual treatment modalities in LGIB, especially compared to the literature in UGIB.

Diverticular hemorrhage

Patients with diverticular hemorrhage typically present with large volume, painless hematochezia. Endoscopic intervention is recommended for patients with active bleeding from a diverticulum, presence of a non-bleeding visible vessel, or an adherent clot [2,18]. Endoscopic treatment is recommended for stigmata of hemorrhage as medical therapy alone is associated with an increased risk of rebleeding. In a recent study, patients with a visible vessel had a rebleeding rate of 60%, whereas patients with an adherent clot had a rebleeding rate of 42.9% [41]. Localization of stigmata of hemorrhage at a diverticulum requires careful endoscopic visualization with assistance of a water jet. Use of a clear plastic cap along with gentle suction can also aid in inverting the diverticulum to visualize stigmata present at the dome of a diverticulum [42].

Available techniques for endoscopic hemostasis include dilute epinephrine injection, bipolar electrocoagulation, through-the-scope clipping, endoscopic band ligation (EBL), and use of over-the-scope clips (OTSC). Bipolar electrocoagulation has been used in combination with epinephrine injection in case series[10, 18, 43, 44] with good rates of initial hemostasis (97%), but moderate rates of recurrent bleeding (24%).

Endoscopic clips are an option for hemostatic control, and are appealing given the avoidance of transmural injury and perforation, which can occur with thermal therapies. Techniques of clipping include the following: 1) direct placement over bleeding stigmata or a non-bleeding visible vessel; 2) clipping the mouth of the diverticulum closed in a zipper-like manner leading to tamponade; 3) Clipping from within a cap used to invert the diverticulum; 4) Use of epinephrine injection around the diverticulum to improve visibility along with clip placement [2,42]. See Fig. 2 for an example of clipping an actively bleeding diverticulum closed. In a retrospective study of 24 patients with active bleeding or stigmata of hemorrhage from diverticuli, clipping successfully treated 88% of patients without early rebleeding [45]. In a recent meta-analysis including additional case series utilizing clips as a treatment modality (with or without epinephrine), the pooled initial hemostasis rate was 99% and early rebleeding rate was 19% (Table 2) [46]. Diverticular hemorrhage in the right colon requiring endoscopic clipping (particularly indirect clipping of the diverticulum) was shown to predict recurrent bleeding [47]. In addition, OTSC have been used in small series with good safety and effect for diverticular hemorrhage [42].

EBL for diverticular hemorrhage is a technique that recently has become more popular. This technique includes identification of the culprit diverticulum, marking of the region using a clip or ink injection, and withdrawal of the scope. Subsequently, a band ligation device is attached to the colonoscope, the culprit lesion is suctioned

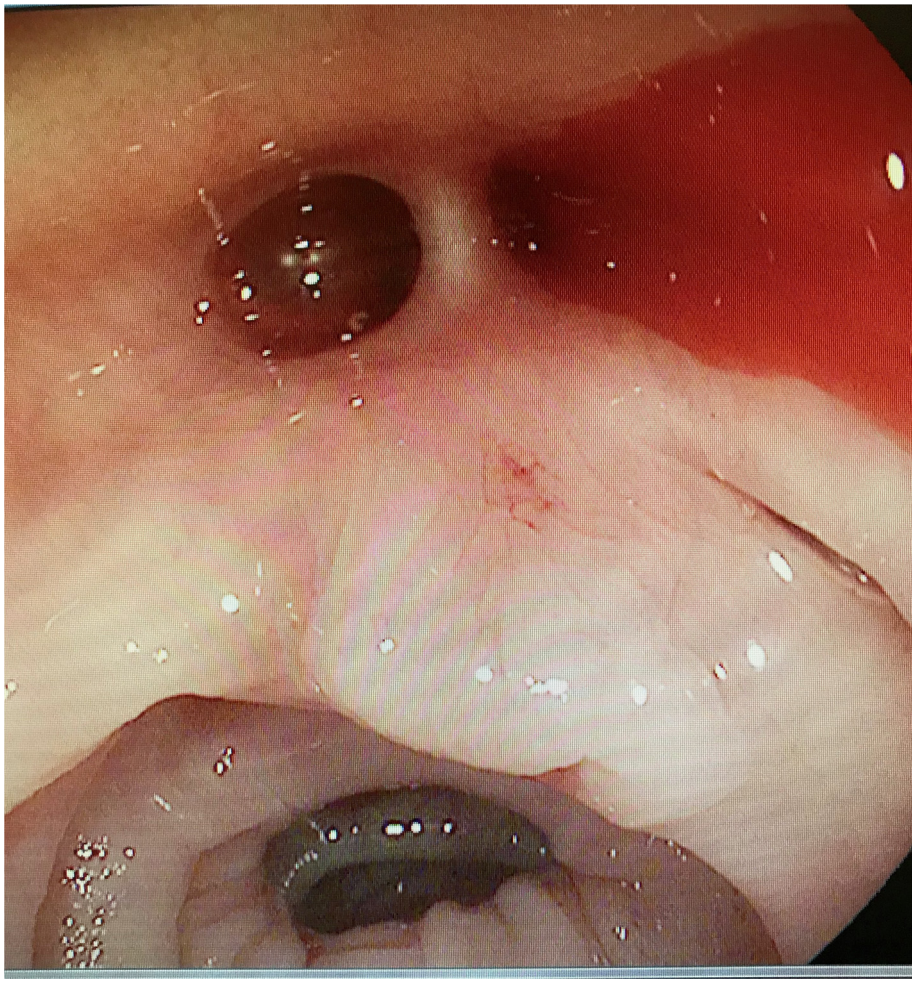

Fig. 2. a) Diverticulum with active bleeding; b) Clipping with zipper method to achieve hemostasis (*Images courtesy of Dr. Brian Riff*).

into the banding device, and the band is then deployed. In a pooled meta-analysis, the efficacy of band ligation in treating diverticular hemorrhage was 99%, and the early recurrent bleeding rate was 9% (See Table 2). [46] In this pooled analysis, EBL was more effective compared with clipping to avoid angiographic embolization or surgery. EBL was equivalent to bipolar coagulation and clipping for initial hemostasis and prevention of early rebleeding. Ikeya et al. published a retrospective study of 101 patients with definitive diverticular hemorrhage undergoing EBL. Early rebleeding occurred in 15% at a median of 5 days, and was managed conservatively in all but 1 case [48]. Risk factors for rebleeding included younger age, active bleeding at time of colonoscopy, and left sided colonic location. The probability of 1-year rebleeding was recently found to be 11.5% in patients undergoing EBL for diverticular hemorrhage versus 37.0% in patients undergoing clipping ($p = 0.018$), likely due to eradication of the culprit diverticulum in the EBL group. No patients in either group required surgery or had colonic perforation [49].

A newer technique for endoscopic hemostasis in diverticular hemorrhage is endoscopic detachable snare ligation (EDSL). This technique allows for insertion of the ligation snare through the forceps port without withdrawal of the scope. In a multicenter feasibility trial, bleeding diverticuli were detected in 123 patients, of whom 101 (82%) were successfully treated with EDSL. In the 22 patients who were not successfully treated, 20 were treated successfully with clipping. 8 patients (7.9%) experienced early recurrent bleeding, and 2 patients experienced mild adverse events [50].

Topical hemospray powder has demonstrated promise in management of UGIB, however data in terms of its efficacy in LGIB is limited. In a case series of 10 patients with diverticular hemorrhage, application of hemospray led to successful hemostasis in all cases [51].

An adjunctive technique to guide treatment for diverticular hemorrhage is Doppler ultrasound probe monitoring. In 46 patients with diverticular bleeding, 24 had major stigmata of hemorrhage at colonoscopy. Doppler ultrasound noted arterial flow in 92%, and no flow in patients without major stigmata. After endoscopic treatment, no patient had residual blood flow, and none of these patients experienced 30-day rebleeding [41]. A comparator arm without probe-guidance was unavailable, and thus future studies are needed to determine whether this technique should be widely used to guide efficacy of therapy.

Post-polypectomy bleeding

Post-polypectomy bleeding can occur immediately or can be delayed up to a few weeks following polypectomy. In a recent meta-analysis of population-based studies, the cumulative post-

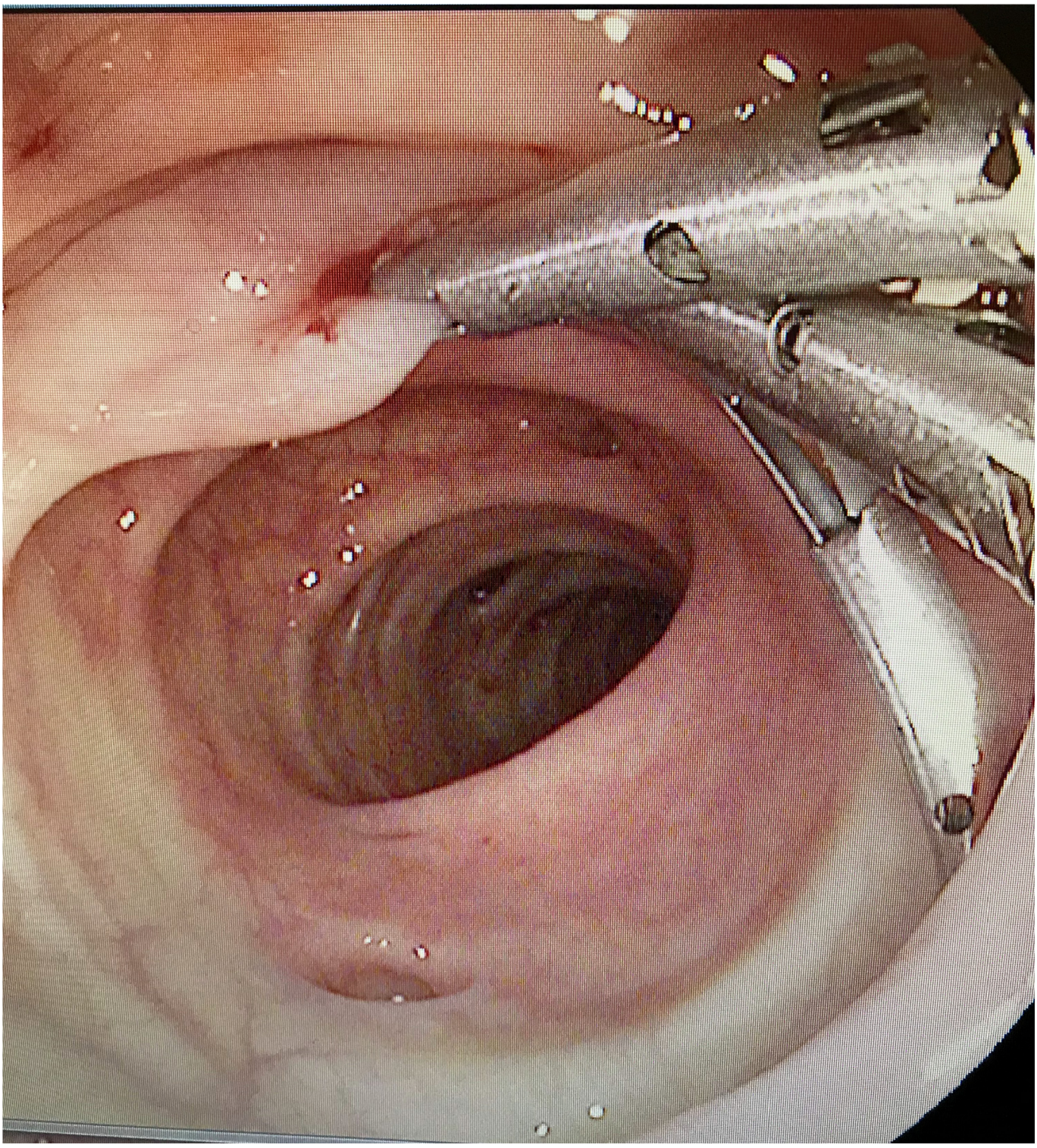

Fig. 2. (*continued*).

polypectomy bleeding rate was 9.8/1000 (95% CI 7.7–12.1) [52]. Major risk factors for post-polypectomy bleeding include large polyp size (>2 cm), thick stalk, right-sided colonic location, and use of antithrombotic therapy [2]. For a patient presenting with ongoing bleeding after polypectomy, repeat colonoscopy can identify stigmata of bleeding, which usually consists of a post-polypectomy ulcer with active bleeding, clot, or a red spot. Treatment options clipping, thermal therapy with or without use of epinephrine, and band ligation. Data is limited comparing endoscopic options for post-polypectomy bleeding, but endoscopic hemostasis and prevention of rebleeding is successful the majority of the time with clipping alone. Hemospray and OTSC have been used successfully as salvage treatments in cases of refractory post-polypectomy bleeding after failure of clipping [53,54].

Table 2
Estimates of Outcomes for Diverticular Hemorrhage Depending on Treatment Modality. ***Adapted from Ishii et al.*** [46].

Treatment Modality	Included Studies	Initial Hemostasis *(%, 95% CI)*	Early Rebleeding *(%, 95% CI)*	Need for IR/Surgery *(%, 95% CI)*[a]
Clips	8	0.99 (0.97–1.00)	0.19 (0.07–0.35)	0.08 (0.03–0.16)
Coagulation	4	1.00 (0.91–1.00)	0.21 (0.01–0.51)	0.18 (0.00–0.61)
EBL	5	0.99 (0.98–1.00)	0.09 (0.04–0.15)	0.00 (0.00–0.01)

Abbreviations: CI, confidence interval; IR, interventional radiology; EBL, endoscopic band ligation.
[a] Need for IR/surgery evaluated in 14/16 studies.

Colonic angioectasias

Colonic angioectasias are a common cause of LGIB in the elderly, who typically have right-sided lesions. Other predictors of blood loss from colonic angioectasias include increased comorbidities, more than 10 lesions in the colon, and ethnicity [55]. Endoscopic treatment is the first line option for patients with acute or chronic blood loss. The most commonly used therapy is argon plasma coagulation, which can improve hemoglobin levels, and reduce the frequency of blood transfusions [56]. For large colonic angioectasias located in the right colon, submucosal injection with saline prior to coagulation has been shown to be safe, potentially decreasing the risks of perforation [57]. Clipping is also an effective option for bleeding colonic angioectasias [42].

Miscellaneous sources of bleeding

Data on endoscopic therapies for additional sources of bleeding are sparse and limited to case series. Hemospray has been shown to effective in of patients with bleeding from colonic ulcers and neoplastic lesions [58]. Although bleeding from neoplasia or colitis is usually diffuse and self-limited, pinpoint bleeding from these lesions can typically be treated with clipping or argon plasma coagulation [42]. Although data is limited, hemospray will likely play a role in management of diffuse colonic bleeding from colitis or neoplasia in the future.

Practice points

- *Endoscopic intervention is recommended for active bleeding in the colon as well as stigmata of hemorrhage, as this can reduce rebleeding.*
- *Endoscopic clipping and endoscopic band ligation (EBL) are both effective endoscopic options for diverticular hemorrhage, and EBL may be associated with a reduced risk of recurrent bleeding.*

Complications

Overall, complications from colonoscopy in the setting of LGIB are relatively rare, reported to be between 0.3 and 1.3% for colonoscopy performed in the setting of LGIB [9]. In a single-center study of patients undergoing colonoscopy, adverse events were no more frequent in patients with LGIB undergoing colonoscopy than in patients without LGIB [59].

Specific risks include bowel perforation, volume overload secondary to bowel preparation, and aspiration pneumonia [60]. A recent meta-analysis of population-based studies demonstrated an overall perforation rate of 0.5/1000 (95% CI 0.4–0.7). Overall complication rates were higher for diagnostic examinations (including rectal bleeding) as compared to colon cancer screening examinations [52]. The risk of bowel perforation may theoretically be increased in the setting of suboptimal bowel preparation, given poor visualization. Patients over the age of 80 have been shown to be at higher risk for complications such as perforation during colonoscopy [61], and are a population who are overrepresented in those presenting with LGIB. Endoscopic hemostasis itself is safe, and does not lead to excess risk over the risks of baseline colonoscopy. The exception to this may be use of argon plasma coagulation for treatment of colonic angioectasias in the right colon, where the perforation rate has been reported to be up to 2.5% of cases [62].

Role of repeat colonoscopy and risk of rebleeding

For patients with clear evidence of recurrent bleeding after initial hemostasis, repeat colonoscopy should be considered, although there is limited data supporting this. In a small case series, the yield of repeat colonoscopy for early rebleeding from diverticulosis was 20% [2,63]. Risk factors for early rebleeding after colonoscopy are not well defined, but may include comorbid illness, NSAID or antiplatelet use, and presence of initial shock [64,65]. In a recent insurance claims study, risk factors for recurrent bleeding for patients hospitalized with diverticular hemorrhage included baseline chronic kidney disease, initial transfusion requirement, and performance of urgent colonoscopy [40].

Research agenda

- *Prospective studies utilizing risk prediction tools are needed to determine which select patients may benefit from urgent (<24 h) colonoscopy.*
- *Given increasing use of antithrombotics including direct oral anticoagulants, further data are needed on the optimal resuscitation strategy and role of reversal agents for these patients presenting with LGIB*
- *Head to head comparisons between inpatient bowel preparations are needed to determine which have the highest success rate in achieving adequate bowel preparation*

Summary

LGIB is a common reason for hospitalization, although the evidence base guiding diagnosis and management is significantly less compared to the UGIB literature. Exclusion of a proximal source of bleeding is required in patients with severe hematochezia, as up to 15% of patients may have a source of bleeding in the upper gastrointestinal tract. After resuscitation with fluids and blood transfusion if necessary, colonoscopy is recommended in order to detect a source of bleeding and potentially treat colonic lesions. Unprepped colonoscopy is not recommended as cecal intubation rates are low, and close visualization of the mucosa is needed to detect subtle bleeding sources. Prior studies in LGIB have used large volume, polyethylene glycol based preparations, often administered via NGT to good effect. In the real world setting, however, rates of adequate inpatient bowel preparations are suboptimal. Split dose preparation has been recently shown to increase quality of bowel preparation in the inpatient setting. Urgent colonoscopy (within 24 h of hospitalization) is recommended for patients with severe hematochezia and high-risk features as this has been

previously shown to be associated with increased diagnostic yield and a higher rate of therapeutic interventions. However, recent meta-analyses have shown that urgent colonoscopy is equivalent to elective colonoscopy in terms of important clinical outcomes. For active colonic bleeding or lesions with stigmata of hemorrhage, endoscopic hemostasis can reduce further rebleeding. Endoscopic clipping and band ligation are the most effective therapeutic options for diverticular hemorrhage, although rigorous head-to-head comparisons are unavailable.

Conflicts of interest

This author reports no financial or personal conflicts of interest in regards to this review paper.

Disclosures

None.

References

[1] Strate LL, Ayanian JZ, Kotler G, Syngal S. Risk factors for mortality in lower intestinal bleeding. Clin Gastroenterol Hepatol 2008;6(9):1004–10. quiz 955-.
[2] Strate LL, Gralnek IM. ACG clinical guideline: management of patients with acute lower gastrointestinal bleeding. Am J Gastroenterol 2016;111(4):459–74.
[3] Sengupta N, Tapper EB, Patwardhan VR, Ketwaroo GA, Thaker AM, Leffler DA, et al. Risk factors for adverse outcomes in patients hospitalized with lower gastrointestinal bleeding. Mayo Clin Proc 2015;90(8):1021–9.
[4] Laine L, Shah A. Randomized trial of urgent vs. elective colonoscopy in patients hospitalized with lower GI bleeding. Am J Gastroenterol 2010;105(12):2636–41. quiz 42.
[5] Srygley FD, Gerardo CJ, Tran T, Fisher DA. Does this patient have a severe upper gastrointestinal bleed? J Am Med Assoc 2012;307(10):1072–9.
[6] Villanueva C, Colomo A, Bosch A, Concepcion M, Hernandez-Gea V, Aracil C, et al. Transfusion strategies for acute upper gastrointestinal bleeding. N Engl J Med 2013;368(1):11–21.
[7] Laine L. Blood transfusion for gastrointestinal bleeding. N Engl J Med 2013;368(1):75–6.
[8] Razzaghi A, Barkun AN. Platelet transfusion threshold in patients with upper gastrointestinal bleeding: a systematic review. J Clin Gastroenterol 2012;46(6):482–6.
[9] Strate LL, Naumann CR. The role of colonoscopy and radiological procedures in the management of acute lower intestinal bleeding. Clin Gastroenterol Hepatol 2010;8(4):333–43. quiz e44.
[10] Green BT, Rockey DC, Portwood G, Tarnasky PR, Guarisco S, Branch MS, et al. Urgent colonoscopy for evaluation and management of acute lower gastrointestinal hemorrhage: a randomized controlled trial. Am J Gastroenterol 2005;100(11):2395–402.
[11] van Rongen I, Thomassen BJW, Perk LE. Early versus standard colonoscopy: a randomized controlled trial in patients with acute lower gastrointestinal bleeding: results of the bleed study. J Clin Gastroenterol 2018. https://doi.org/10.1097/MCG.0000000000001048. PMID: 29734211.
[12] Gralnek IM, Neeman Z, Strate LL. Acute lower gastrointestinal bleeding. N Engl J Med 2017;376(11):1054–63.
[13] Gralnek IM, Ron-Tal Fisher O, Holub JL, Eisen GM. The role of colonoscopy in evaluating hematochezia: a population-based study in a large consortium of endoscopy practices. Gastrointest Endosc 2013;77(3):410–8.
[14] Ron-Tal Fisher O, Gralnek IM, Eisen GM, Williams JL, Holub JL. Endoscopic hemostasis is rarely used for hematochezia: a population-based study from the clinical outcomes research initiative national endoscopic Database. Gastrointest Endosc 2014;79(2):317–25.
[15] ASoP Committee, Pasha SF, Shergill A, Acosta RD, Chandrasekhara V, Chathadi KV, et al. The role of endoscopy in the patient with lower GI bleeding. Gastrointest Endosc 2014;79(6):875–85.
[16] Repaka A, Atkinson MR, Faulx AL, Isenberg GA, Cooper GS, Chak A, et al. Immediate unprepared hydroflush colonoscopy for severe lower GI bleeding: a feasibility study. Gastrointest Endosc 2012;76(2):367–73.
[17] Jensen DM, Machicado GA. Diagnosis and treatment of severe hematochezia. The role of urgent colonoscopy after purge. Gastroenterology 1988;95(6):1569–74.
[18] Jensen DM, Machicado GA, Jutabha R, Kovacs TO. Urgent colonoscopy for the diagnosis and treatment of severe diverticular hemorrhage. N Engl J Med 2000;342(2):78–82.
[19] Ness RM, Manam R, Hoen H, Chalasani N. Predictors of inadequate bowel preparation for colonoscopy. Am J Gastroenterol 2001;96(6):1797–802.
[20] Jawa H, Mosli M, Alsamadani W, Saeed S, Alodaini R, Aljahdli E, et al. Predictors of inadequate bowel preparation for inpatient colonoscopy. Turk J Gastroenterol 2017;28(6):460–4.
[21] Beck KR, Shergill AK. Colonoscopy in acute lower gastrointestinal bleeding: diagnosis, timing, and bowel preparation. Gastrointest Endosc Clin N Am 2018;28(3):379–90.
[22] Yadlapati R, Johnston ER, Gregory DL, Ciolino JD, Cooper A, Keswani RN. Predictors of inadequate inpatient colonoscopy preparation and its association with hospital length of stay and costs. Dig Dis Sci 2015;60(11):3482–90.
[23] Rex DK, Boland CR, Dominitz JA, Giardiello FM, Johnson DA, Kaltenbach T, et al. Colorectal cancer screening: recommendations for physicians and patients from the U.S. Multi-society task force on colorectal cancer. Am J Gastroenterol 2017;112(7):1016–30.
[24] Agrawal D, Elsbernd B, Singal AG, Rockey D. Gastric residual volume after split-dose compared with evening-before polyethylene glycol bowel preparation. Gastrointest Endosc 2016;83(3):574–80.
[25] Yadlapati R, Johnston ER, Gluskin AB, Gregory DL, Cyrus R, Werth L, et al. An automated inpatient split-dose bowel preparation system improves colonoscopy quality and reduces repeat procedures. J Clin Gastroenterol 2018;52(8):709–14.
[26] Argyropoulos SK, Mahmood SK, Campbell EJ, Richter JM. Improving the quality of inpatient bowel preparation for colonoscopies. Dig Dis Sci 2018;63(2):338–44.
[27] Ergen WF, Pasricha T, Hubbard FJ, Higginbotham T, Givens T, Slaughter JC, et al. Providing hospitalized patients with an educational booklet increases the quality of colonoscopy bowel preparation. Clin Gastroenterol Hepatol 2016;14(6):858–64.
[28] Marschall HU, Bartels F. Life-threatening complications of nasogastric administration of polyethylene glycol-electrolyte solutions (Golytely) for bowel cleansing. Gastrointest Endosc 1998;47(5):408–10.
[29] Dominitz JA, Eisen GM, Baron TH, Goldstein JL, Hirota WK, Jacobson BC, et al. Complications of colonoscopy. Gastrointest Endosc 2003;57(4):441–5.
[30] Niikura R, Nagata N, Yamada A, Doyama H, Shiratori Y, Nishida T, et al. A multicenter, randomized controlled trial comparing the identification rate of stigmata of recent hemorrhage and rebleeding rate between early and elective colonoscopy in outpatient-onset acute lower gastrointestinal bleeding: study protocol for a randomized controlled trial. Trials 2018;19(1):214.
[31] Strate LL, Syngal S. Timing of colonoscopy: impact on length of hospital stay in patients with acute lower intestinal bleeding. Am J Gastroenterol 2003;98(2):317–22.
[32] Schmulewitz N, Fisher DA, Rockey DC. Early colonoscopy for acute lower GI bleeding predicts shorter hospital stay: a retrospective study of experience in a single center. Gastrointest Endosc 2003;58(6):841–6.
[33] Navaneethan U, Njei B, Venkatesh PG, Sanaka MR. Timing of colonoscopy and outcomes in patients with lower GI bleeding: a nationwide population-based study. Gastrointest Endosc 2014;79(2):297–306 e12.
[34] Nagata N, Niikura R, Sakurai T, Shimbo T, Aoki T, Moriyasu S, et al. Safety and effectiveness of early colonoscopy in management of acute lower gastrointestinal bleeding on the basis of propensity score matching analysis. Clin Gastroenterol Hepatol 2016;14(4):558–64.
[35] Nigam N, Patel P, Sengupta N. Outcomes of early versus delayed colonoscopy in lower gastrointestinal bleeding using a hospital administrative Database. J Clin Gastroenterol 2018;52(8):721–5.
[36] Seth A, Khan MA, Nollan R, Gupta D, Kamal S, Singh U, et al. Does urgent colonoscopy improve outcomes in the management of lower gastrointestinal bleeding? Am J Med Sci 2017;353(3):298–306.
[37] Kouanda AM, Somsouk M, Sewell JL, Day LW. Urgent colonoscopy in patients with lower GI bleeding: a systematic review and meta-analysis. Gastrointest Endosc 2017;86(1):107–117 e1.
[38] Roshan Afshar I, Sadr MS, Strate LL, Martel M, Menard C, Barkun AN. The role of early colonoscopy in patients presenting with acute lower gastrointestinal bleeding: a systematic review and meta-analysis. Therap Adv Gastroenterol 2018;11. 1756283X18757184.
[39] Sengupta N, Tapper EB, Feuerstein JD. Early versus delayed colonoscopy in hospitalized patients with lower gastrointestinal bleeding: a meta-analysis. J Clin Gastroenterol 2017;51(4):352–9.
[40] Nigam N, Ham SA, Sengupta N. Early colonoscopy for diverticular bleeding does not reduce risk of postdischarge recurrent bleeding: a propensity score-matching analysis. Clin Gastroenterol Hepatol 2019;17(6):1105–11.
[41] Jensen DM, Ohning GV, Kovacs TO, Jutabha R, Ghassemi K, Dulai GS, et al. Natural history of definitive diverticular hemorrhage based on stigmata of recent hemorrhage and colonoscopic Doppler blood flow monitoring for risk stratification and definitive hemostasis. Gastrointest Endosc 2016;83(2):416–23.
[42] Soetikno R, Ishii N, Kolb JM, Hammad H, Kaltenbach T. The role of endoscopic hemostasis therapy in acute lower gastrointestinal hemorrhage. Gastrointest Endosc Clin N Am 2018;28(3):391–408.
[43] Foutch PG, Zimmerman K. Diverticular bleeding and the pigmented protuberance (sentinel clot): clinical implications, histopathological correlation, and results of endoscopic intervention. Am J Gastroenterol 1996;91(12):2589–93.
[44] Bloomfeld RS, Rockey DC, Shetzline MA. Endoscopic therapy of acute diverticular hemorrhage. Am J Gastroenterol 2001;96(8):2367–72.
[45] Kaltenbach T, Watson R, Shah J, Friedland S, Sato T, Shergill A, et al. Colonoscopy with clipping is useful in the diagnosis and treatment of diverticular bleeding. Clin Gastroenterol Hepatol 2012;10(2):131–7.

[46] Ishii N, Omata F, Nagata N, Kaise M. Effectiveness of endoscopic treatments for colonic diverticular bleeding. Gastrointest Endosc 2018;87(1):58–66.
[47] Ishii N, Hirata N, Omata F, Itoh T, Uemura M, Matsuda M, et al. Location in the ascending colon is a predictor of refractory colonic diverticular hemorrhage after endoscopic clipping. Gastrointest Endosc 2012;76(6):1175–81.
[48] Ikeya T, Ishii N, Nakano K, Omata F, Shimamura Y, Ego M, et al. Risk factors for early rebleeding after endoscopic band ligation for colonic diverticular hemorrhage. Endosc Int Open 2015;3(5):E523–8.
[49] Nagata N, Ishii N, Kaise M, Shimbo T, Sakurai T, Akiyama J, et al. Long-term recurrent bleeding risk after endoscopic therapy for definitive colonic diverticular bleeding: band ligation versus clipping. Gastrointest Endosc 2018;88(5):841–853 e4.
[50] Akutsu D, Narasaka T, Kobayashi K, Matsuda K, Wakayama M, Hiroshima Y, et al. Newly developed endoscopic detachable snare ligation therapy for colonic diverticular hemorrhage: a multicenter phase II trial (with videos). Gastrointest Endosc 2018;88(2):370–7.
[51] Ng JL, Marican M, Mathew R. Topical haemostatic powder as a novel endoscopic therapy for severe colonic diverticular bleeding. ANZ J Surg 2019;89(3):E56–60.
[52] Reumkens A, Rondagh EJ, Bakker CM, Winkens B, Masclee AA, Sanduleanu S. Post-colonoscopy complications: a systematic review, time trends, and meta-analysis of population-based studies. Am J Gastroenterol 2016;111(8):1092–101.
[53] Ivekovic H, Bilic B, Markos P, Rustemovic N, Ostojic R, Monkemuller K. Successful use of Hemospray to control refractory post-polypectomy bleeding. Endoscopy 2015;47(Suppl 1 UCTN):E466–7.
[54] Alcaide N, Penas-Herrero I, Sancho-del-Val L, Ruiz-Zorrilla R, Barrio J, Perez-Miranda M. Ovesco system for treatment of postpolypectomy bleeding after failure of conventional treatment. Rev Esp Enferm Dig 2014;106(1):55–8.
[55] Diggs NG, Holub JL, Lieberman DA, Eisen GM, Strate LL. Factors that contribute to blood loss in patients with colonic angiodysplasia from a population-based study. Clin Gastroenterol Hepatol 2011;9(5):415–20. quiz e49.
[56] Olmos JA, Marcolongo M, Pogorelsky V, Herrera L, Tobal F, Davolos JR. Long-term outcome of argon plasma ablation therapy for bleeding in 100 consecutive patients with colonic angiodysplasia. Dis Colon Rectum 2006;49(10):1507–16.
[57] Suzuki N, Arebi N, Saunders BP. A novel method of treating colonic angiodysplasia. Gastrointest Endosc 2006;64(3):424–7.
[58] Holster IL, Brullet E, Kuipers EJ, Campo R, Fernandez-Atutxa A, Tjwa ET. Hemospray treatment is effective for lower gastrointestinal bleeding. Endoscopy 2014;46(1):75–8.
[59] Niikura R, Nagata N, Shimbo T, Sakurai T, Aoki T, Moriyasu S, et al. Adverse events during bowel preparation and colonoscopy in patients with acute lower gastrointestinal bleeding compared with elective non-gastrointestinal bleeding. PLoS One 2015;10(9):e0138000.
[60] Lhewa DY, Strate LL. Pros and cons of colonoscopy in management of acute lower gastrointestinal bleeding. World J Gastroenterol 2012;18(11):1185–90.
[61] Day LW, Kwon A, Inadomi JM, Walter LC, Somsouk M. Adverse events in older patients undergoing colonoscopy: a systematic review and meta-analysis. Gastrointest Endosc 2011;74(4):885–96.
[62] Foutch PG. Angiodysplasia of the gastrointestinal tract. Am J Gastroenterol 1993;88(6):807–18.
[63] Yen EF, Ladabaum U, Muthusamy VR, Cello JP, McQuaid KR, Shah JN. Colonoscopic treatment of acute diverticular hemorrhage using endoclips. Dig Dis Sci 2008;53(9):2480–5.
[64] Anthony T, Penta P, Todd RD, Sarosi GA, Nwariaku F, Rege RV. Rebleeding and survival after acute lower gastrointestinal bleeding. Am J Surg 2004;188(5):485–90.
[65] Fujino Y, Inoue Y, Onodera M, Kikuchi S, Endo S, Shozushima T, et al. Risk factors for early re-bleeding and associated hospitalization in patients with colonic diverticular bleeding. Colorectal Dis 2013;15(8):982–6.