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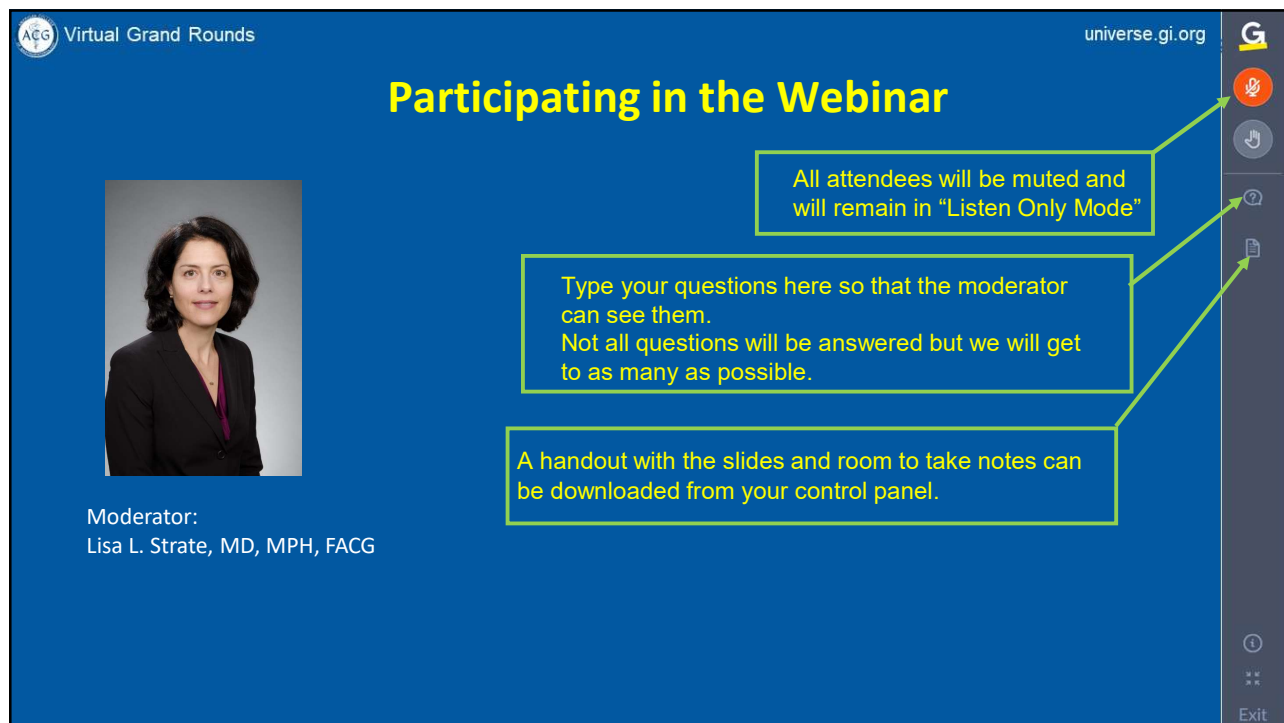
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Moderator:
Lisa L. Strate, MD, MPH, FACG

All attendees will be muted and will remain in "Listen Only Mode"

Type your questions here so that the moderator can see them.
Not all questions will be answered but we will get to as many as possible.

A handout with the slides and room to take notes can be downloaded from your control panel.

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ACG Virtual Grand Rounds

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 ACG Clinical Guideline: Diagnosis and Management of Biliary Strictures
 Faculty: Jennifer L. Maranki, MD, MSc
 Moderator: Anna Tavakkoli, MD
At Noon and 8pm Eastern




Week 36 – Thursday, September 7, 2023
 Food as Medicine for Inflammatory Bowel Disease
 Faculty: Jason K. Hou, MD, MS, FACP
 Moderator: Colleen Webb, MS, RD
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Neil Sengupta, MD
Dr. Sengupta has no relevant financial relationships with ineligible companies.



Lisa L. Strate, MD, MPH, FACP
Dr. Strate receives royalties from UpToDate.

**All of the relevant financial relationships listed for these individuals have been mitigated*

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Lower Gastrointestinal Bleeding – An Update



Neil Sengupta, MD

Associate Professor, Section of Gastroenterology



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The “Typical” Case

- 67yo F with CAD on ASA and OA on chronic NSAIDs presents with hematochezia
- Prior screening colonoscopy with good prep 3 years ago with left sided diverticulosis.
- Hospitalized 12 months ago with severe hematochezia, stabilized with resuscitation. At that admission, colonoscopy 24 hours after presentation and bowel preparation (4L PEG) showed left sided diverticulosis with blood throughout the colon without specific SRH, no intervention performed. Discharged on same regimen after cessation of bleeding
- At present, patient appears well, and is hemodynamically stable with 2gm drop in Hgb from baseline. + Bright red blood on DRE.

- Do we repeat a colonoscopy?
- If so, when should we perform a colonoscopy?
- If not, do we consider a CT Angiography or other diagnostic testing?
- Is no testing a reasonable option?
- How do we minimize risk of recurrence?

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- 1 | Epidemiology
- 2 | Risk stratification
- 3 | Initial assessment, antithrombotic reversal
- 4 | Yield and timing of colonoscopy vs. CTA
- 5 | Endoscopic hemostasis
- 6 | Minimizing risk of recurrence

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Lower Gastrointestinal Bleeding (LGIB)

- **Problem:** LGIB is a common reason for hospitalization leading to significant resource utilization

	Annual Admissions	Readmission rate	Deaths
LGIB	113,020	15.1%	0.5%

- **Outcome:** Most have good outcomes, however patients with significant comorbidities are at risk of adverse outcomes
- **Diagnostic Test:** Colonoscopy is diagnostic test of choice
- Optimal timing controversial
- Inpatient colonoscopy utilization differs across world
- Endoscopic treatment is infrequent in the US

Peery AF et al. Gastroenterology 2021

14

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Causes of Acute LGIB in Adults

Cause	Percentage of Cases
Diverticulosis	30-65
Ischemic colitis	5-20
Hemorrhoids	5-20
Colorectal polyps or neoplasms	2-15
Angioectasias	5-10
Postpolypectomy bleeding	2-7
Inflammatory bowel disease	3-5
Infectious colitis	2-5
Stercoral ulceration	0-5
Colorectal varices	0-3
Radiation proctopathy	0-2
NSAID-induced colopathy	0-2
Dieulafoy's lesion	Rare



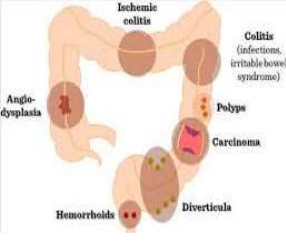

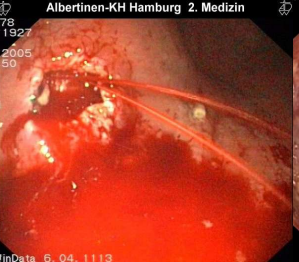
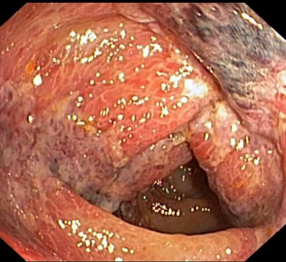




Figure 7 Diverticular bleeding.

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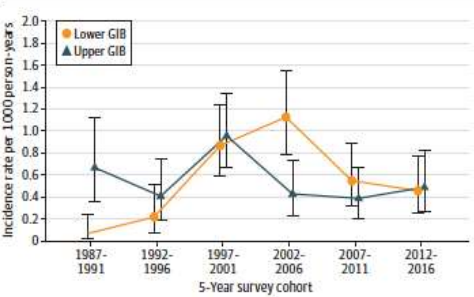
Gralnek IM et al. NEJM 2017

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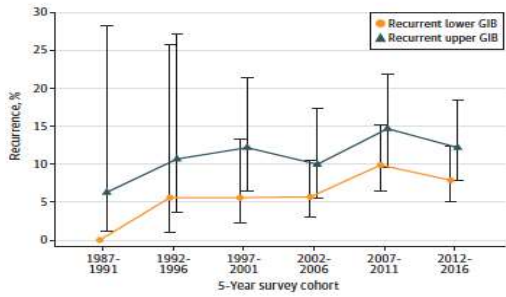
Epidemiology and Trends

Figure 1. Incidence Rate Trends in Major Upper and Lower Gastrointestinal Bleeding (GIB) for 5-Year Cohorts



Error bars indicate 95% CIs.

Figure 2. Recurrent Major Upper and Lower Gastrointestinal Bleeding (GIB) for 5-Year Cohorts

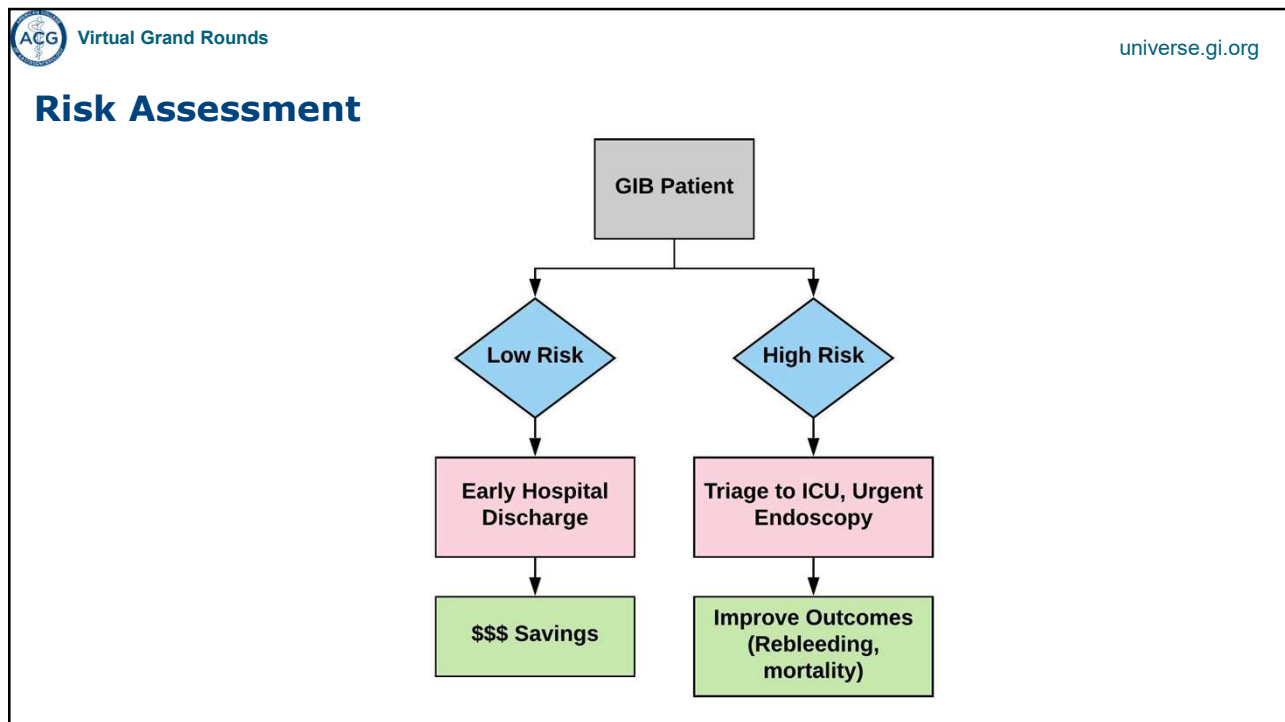


Error bars indicate 95% CIs.

- Incidence rates for major LGIB are stable and similar to UGIB
- Recurrence rate for major LGIB trending upwards
- Case fatality relatively low for LGIB (0.4%)

Vora P et al. JAMA Netw Open 2020 16

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Oakland Score for LGIB Assessment

GBS ≤ 1

→ Early discharge with outpatient f/u

GBS ≥ 7

→ High risk for endoscopic therapy

Oakland ≤ 8

→ Early discharge with outpatient f/u

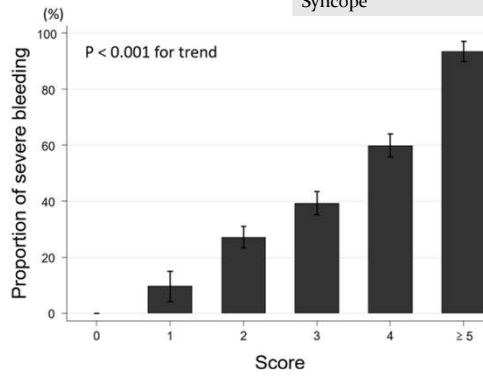
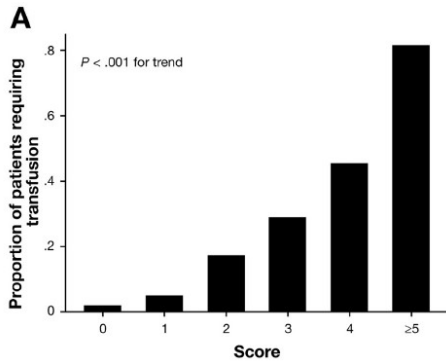
Predictor	Score component value
Age	
<40	0
40–69	1
≥ 70	2
Gender	
Female	0
Male	1
Previous LGIB admission	
No	0
Yes	1
DRE findings	
No blood	0
Blood	1
Heart rate	
<70	0
70–89	1
90–109	2
Systolic blood pressure	
<90	5
90–119	4
120–129	3
130–159	2
≥ 160	0
Haemoglobin (g/L)	
<70	22
70–89	17
90–109	13
110–129	8
130–159	4
≥ 160	0

Oakland et al. Lancet Gastroenterol Hepatol 2017

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Predicting Severe LGIB

Risk factor	Adjusted OR
NSAIDS	2.50 (1.28-4.90)
No diarrhea	2.24 (1.13-4.42)
No abdominal tenderness	2.97 (1.55-5.67)
BP <100 mm Hg	2.34 (1.26-4.35)
Antiplatelet (non-ASA)	1.97 (1.06-3.66)
Albumin <3.0 g/dL	2.94 (1.57-5.49)
Disease score ≥ 2	1.70 (1.04-2.78)
Syncope	2.49 (1.11-5.56)



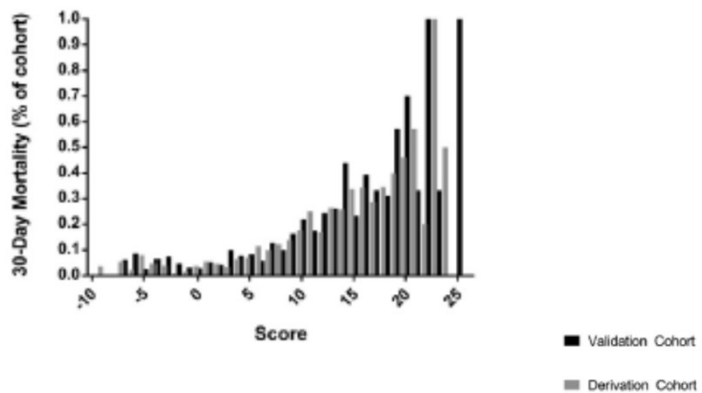
Aoki T et al. Clin Gastroenterol Hepatol 2016 19

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Predicting 30-day Mortality in LGIB

Variable	Categories	Points
Age	<30	-2
	30-39	-1
	40-49	0
	50-59	1
	60-69	2
	70-79	3
	80-90	4
Dementia	No	0
	Yes	5
Chronic kidney disease	No	0
	Yes	2
Metastatic cancer	No	0
	Yes	5
Systemic anticoagulant use	No	0
	Yes	1
Chronic pulmonary disease	No	0
	Yes	2
Admission hematocrit	<20	3
	20-29	1
	30-39	0
Admission albumin	>40	-1
	<2	13
	2-2.9	7
	3-3.9	0
	>4	-7

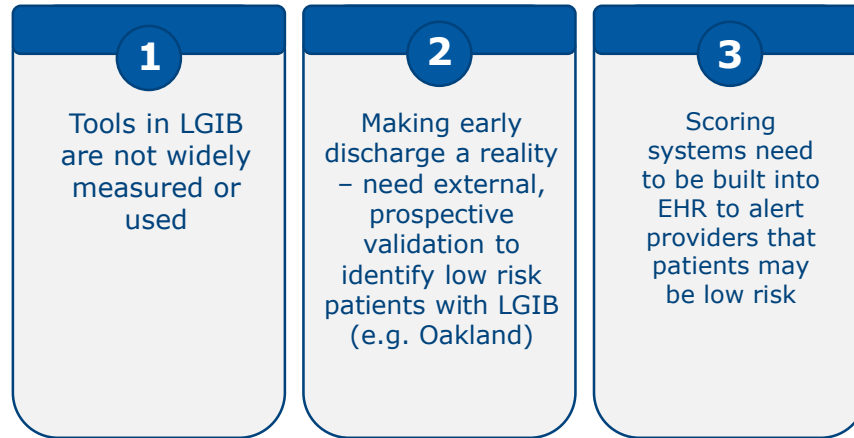
Total score range: -10 to 36.



Sengupta N. Am J Medicine 2017 20

20

Risk Stratification – Unmet needs and priorities



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Initial Management

Exclusion of Upper Source	Hematochezia with hemodynamic instability may be indicative of an UGIB source, and an EGD should be performed if suspicion is high
Transfusion	Restrictive transfusion strategy to maintain Hgb > 7g/dL recommended for most patients, some exceptions should be made for massive bleeding /cardiovascular ischemia (limited data in LGIB)
Coagulopathy	Endoscopic hemostasis is considered safe for patients with an INR < 2.5
Platelets	Patients with significant thrombocytopenia and significant hematochezia should receive platelets to maintain count > 30 (> 50 if colonoscopy planned)

Villanueva et al. NEJM 2013

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LGIB on Antithrombotics – General Principles

Resuscitation	<ul style="list-style-type: none"> • Stabilization with IVF and PRBC to support renal excretion of drug • Antifibrinolytic agents (tranexamic acid) not recommended
No benefit to routine platelet transfusion	<ul style="list-style-type: none"> • Study of patients on antiplatelets admitted with GIB receiving platelet transfusion: • Cases had more severe bleeding, higher risk of death, no decreased risk of recurrent bleeding (Zakko et al. CGH 2017) • Consider transfusion to maintain Plt>50 in severe bleeding and those requiring endoscopic hemostasis
Discontinue thienopyridine in acute setting	<ul style="list-style-type: none"> • Maintain ASA monotherapy (DAPT effect lasts 5-7 days) • Avoid <1yr post DES; <30 days post-BMS; <90 days post-ACS

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LGIB on Vitamin K Antagonists

Reversal agents in nonvalvular heart disease

- 4-factor prothrombin complex (PCC) preferred for reversal (factors II, VII, IX, and X)
- Vitamin K -> not recommended
- FFP not recommended as first line
 - Large volumes required and transfusion is slow
 - Transfusion associated pulmonary edema

Normalizing INR does not reduce rebleeding but delays endoscopy

Endoscopic therapy is safe on anticoagulation!

- Endoscopic therapy effective with moderately elevated INR (2.5)
- Reversal agents should be considered before endoscopy in patients with INR>2.5

Abraham N et al. Am J Gastroenterol 2022

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4FPCC vs. Plasma for VKA Reversal

	4F-PCC (n=87)	Plasma (n=81)	p value
Effective haemostasis (primary endpoint)	78 (90%)	61 (75%)	0.0142
Rapid INR reduction (co-primary endpoint)	48 (55%)	8 (10%)	<0.0001

Goldstein J et al. Lancet 2015 25

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Anticoagulant Reversal Strategy in Life Threatening LGIB

Warfarin → Life threatening LGIB despite initial resuscitation and supratherapeutic INR substantially exceeding therapeutic range

Dabigatran → Life threatening LGIB despite initial resuscitation and recent dabigatran use within 24 hrs

Rivaroxaban or Apixaban → Life threatening LGIB despite initial resuscitation and recent factor Xa inhibitor use within 24 hours

First-line: 4F-PCC

Second line: FFP

Idaracizumab

Andexanet alfa

PCC preferred to FFP due to rapidity of reduction of INR

The majority of patients with LGIB on anticoagulants can likely be managed with IV fluid resuscitation, transfusion of PRBCs, and holding the drug alone



Sengupta N. Am J Gastroenterol 2023

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Initial Diagnostic Testing - Colonoscopy

- Recommend for most patients with LGIB given value in detecting source of bleeding.
- May not be required if bleeding has subsided and patient has had a recent colonoscopy excluding colorectal neoplasia

 Pros	 Cons
High value in detecting etiology of bleeding, excluding neoplasia, and potentially providing treatment	Unclear value in patients with suspected diverticular bleeding with recent colonoscopy, low rates of intervention in Western cohorts



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Initial Diagnostic Testing (cont.)

CT Angiography

 Pros	 Cons
Ability to rapidly obtain images without need for prep	Unlikely to be positive unless patients have clinically significant hematochezia, pure diagnostic test which needs to be followed by angiography or colonoscopy

Angiography – Not used as initial test except in rare circumstances where precise source of bleeding is known

Tagged RBC study - Out of favor given long duration, and inability to precisely localize bleeding source

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Role of CT Angiography

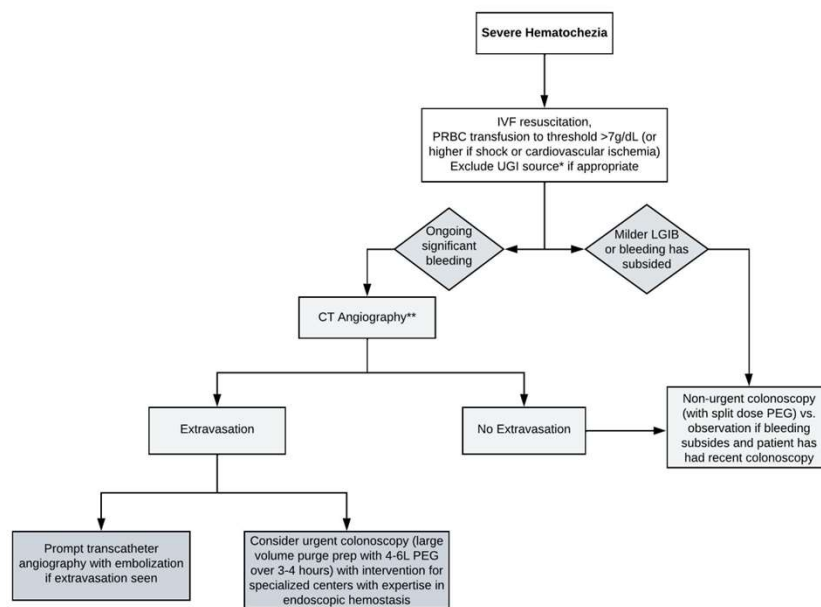
American College of Gastroenterology 2023

- Suggest performing a CTA as initial diagnostic test in patients with ongoing hemodynamically significant hematochezia.
- CTA is low yield in patients with minor LGIB or those in whom bleeding has clinically subsided.
- Patients with a CTA demonstrating extravasation be promptly referred to IR for a transcatheter angiography
- For specialized centers with experience in endoscopic hemostasis, a colonoscopy can also be considered after a positive CTA

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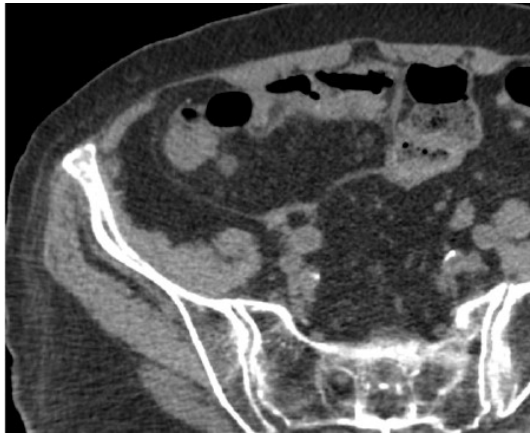


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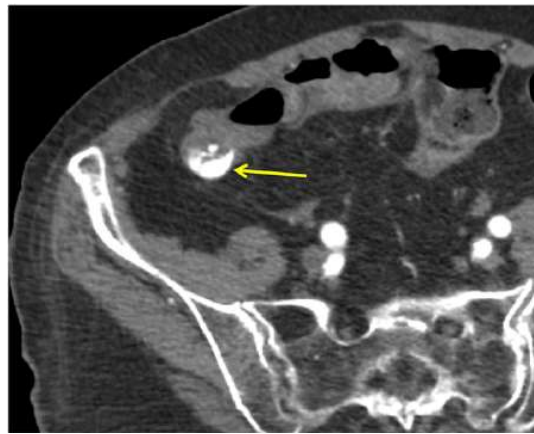
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CT Angiography for LGIB



Non-contrast, no hyperattenuating material in bowel lumen



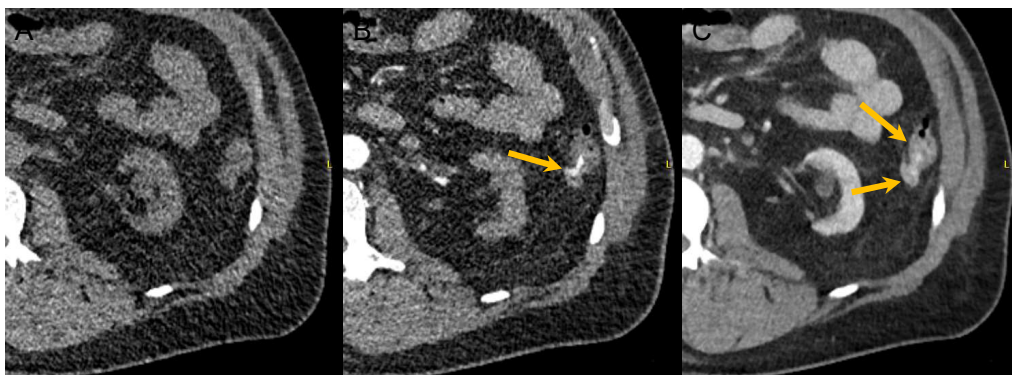
Active extravasation of contrast into the lumen of the colon on arterial phase image

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CT Angiography for LGIB



a) Non-contrast CT series demonstrating no dense material in the left colon

b) Arterial phase of CTA examination showing a linear accumulation of dense contrast within the colon (arrow), which can be seen to directly originate from a colonic diverticulum.

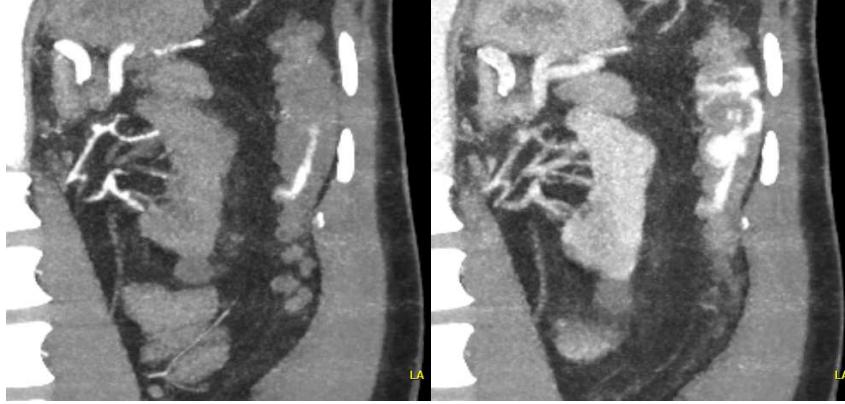
c) Portal venous phase image of the CTA examination shows that the contrast has increased in volume and decreased in density (arrows).

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CT Angiography for LGIB



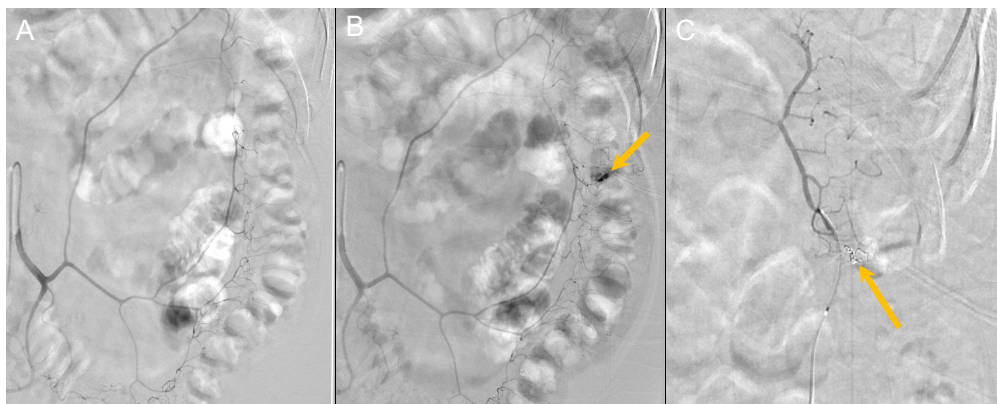
Coronal maximum intensity projection reformatted images from the same CTA scan demonstrating contrast accumulation within the colon.

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Angiography after Positive CTA



- Fluoroscopic inferior mesenteric artery angiogram.
- Angiogram image obtained several seconds later shows contrast accumulation within the lumen of the descending colon (arrow)
- Fluoroscopic image obtained showing embolization coils (arrows) within the artery supplying the bleeding diverticulum

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Predictors of a Positive CTA in LGIB

- Performance within 4 hours of hematochezia
- Recent bowel resection or endoscopic intervention
- Transfusion of >3U PRBC
- Use of antiplatelets or DOACs
- Tachycardia and hypotension

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Bowel Preparation for Colonoscopy

- **Unprepped colonoscopy is not recommended**, as close visualization of mucosa is recommended to detect sources of bleeding
- Historically, 4-6 L of PEG administered over 3-4 hours until rectal effluent clear
- Split dose bowel preparations preferred for inpatients
 - Improved frequency of adequate bowel preparation
 - Improved patient tolerability
- Low volume preparations may be alternative to traditional 4L PEG

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Inadequate Prep Rates



Risk Factors for Poor Preparation

- Older age
- Higher BMI
- Chronic constipation
- Use of narcotics/TCA
- Afternoon procedures



Interventions to Improve Preparation

- Split dose prep
- Electronic order sets
- Educational booklets
- Inpatient nurse facilitators
- Supplemental devices (Pure-Vu)

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Yield of Colonoscopy for LGIB

Sources of Bleeding	%
Definitive diverticular	23.1%
Presumptive diverticular	40.5%
Ischemic colitis	9.1%
Post procedure bleeding	4.5%
Rectal ulcer	2.5%
IBD	2.0%
Hemorrhoids	1.8%
Colorectal neoplasia	1.9%
Colorectal angioectasias	1.3%

Clinical Outcomes	%
Initial colonoscopy	88%
Time to colonoscopy	16h
Endoscopic therapy	31%
Successful therapy	96%
Surgery	1%
In-hospital rebleeding	15%
Post-dc rebleeding	26%
Mortality	0.9%

Nagata et al. Am J Gastroenterol 2021 38

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Endoscopic Intervention in US Population is Infrequent!

```

graph TD
    A["76,928 (9.1%)  
Individuals who underwent colonoscopy for the lone indication 'hematochezia'"] --> B["3,151 (4.1%)  
Individuals who underwent in-patient colonoscopy and had a colonoscopic diagnosis of bleed source other than or in addition to hemorrhoids"]
    A --> C["73,777 (95.9%)  
Individuals who underwent in-patient colonoscopy and had no colonoscopic diagnosis of bleed source or only likely bleed source was thought to be hemorrhoids"]
    B --> D["144 (4.6%)  
Received endoscopic hemostasis"]
    B --> E["3,007 (95.4%)  
Did not receive endoscopic hemostasis"]
    
```

- Less frequent in real-world, western institutions
 - Lack of inpatient bleed teams
 - Not practical/possible to perform urgent colonoscopy
 - Large volume purge prep not done
- **Less than 5%** of patients presenting with severe hematochezia undergoing inpatient colonoscopy received endoscopic hemostasis
- Those receiving hemostasis more likely to have AVMs or solitary ulcer

Ron-Tal Fischer et al. Gastrointest Endosc 2014 39

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Timing of Colonoscopy

- Non-emergent inpatient colonoscopy recommended for most patients hospitalized with LGIB
- Urgent colonoscopy within 24 hours has not been shown to improve rebleeding or mortality

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

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

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

Sengupta N. Am J Gastroenterol 2023 40

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Timing of Colonoscopy

	Early Colonoscopy (n=79), n(%)	Elective colonoscopy (n=80), n(%)	P-value
<i>Identification of SRH</i>	20 (25.3)	21 (26.3)	.89
<i>30-day rebleeding</i>	11 (15.3)	5 (6.7)	.09
<i>Transfusion</i>	30 (38)	26 (32.5)	.47
<i>Length of stay</i>	7.1	7.6	.11
<i>30-day mortality</i>	0	0	n/a

• No benefit seen to urgent/early colonoscopy in this RCT

Niikura R et al. *Gastroenterology* 2020

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Preferred Treatment Options during Colonoscopy

```

graph TD
    A[Diverticular hemorrhage (SRH seen during colonoscopy)] --> B(EBL)
    A --> C(Clips*)
    A --> D(Coagulation**)
    E[Colonic Angioectasias] --> F(APC)
    G[Post-polypectomy bleeding] --> H(Clips)
  
```

EBL
Initial hemostasis: rate(95%CI) 99% (95-100)
Early rebleeding: 8% (5-12)

Clips*
Initial hemostasis: rate(95%CI) 99% (97-100)
Early rebleeding: 19% (11-28)

Coagulation**
Initial hemostasis: rate(95%CI) 100% (91-100)
Pooled rebleeding: 21% (1-51)

APC

Clips

Additional Treatment Options:
Topical hemostatic spray, epinephrine, OTSC, endoscopic detachable snare ligation, doppler probe guided therapy

Additional Treatment Options:
Clips, epinephrine, submucosal injection of fluid followed by targeted coagulation

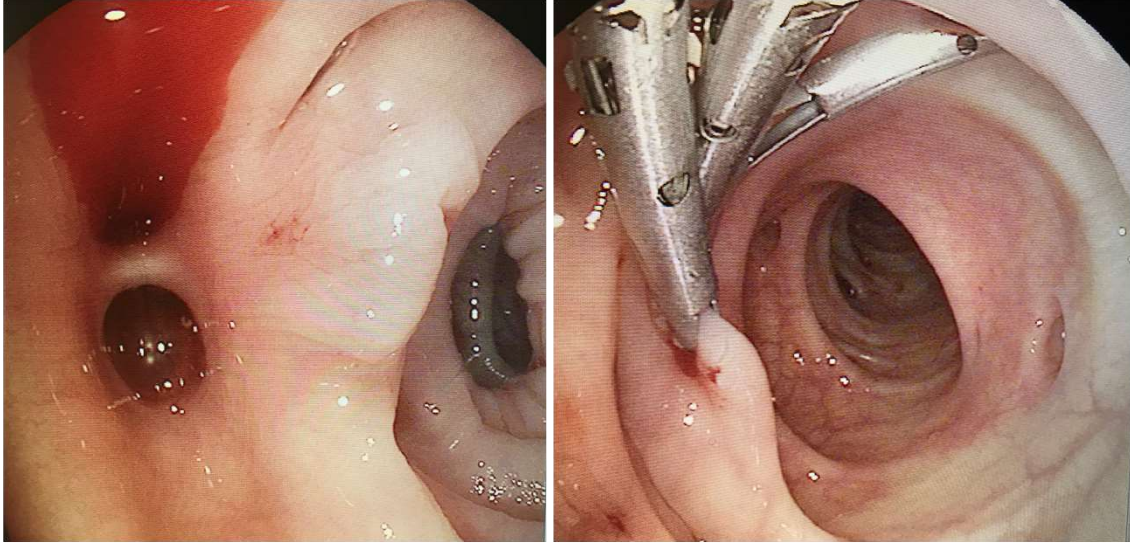
Additional Treatment Options:
Direct thermal therapy, APC, OTSC, topical hemostatic spray

Abbreviations: SRH, stigmata of recent hemorrhage; EBL, endoscopic band ligation; APC, argon plasma coagulation; OTSC, over the scope clips. Notes: * Direct clipping of vessel preferred to indirect clip closure of diverticula. ** Coagulation can be used if SRH seen at neck of diverticula

Sengupta N. *Am J Gastroenterol* 2023

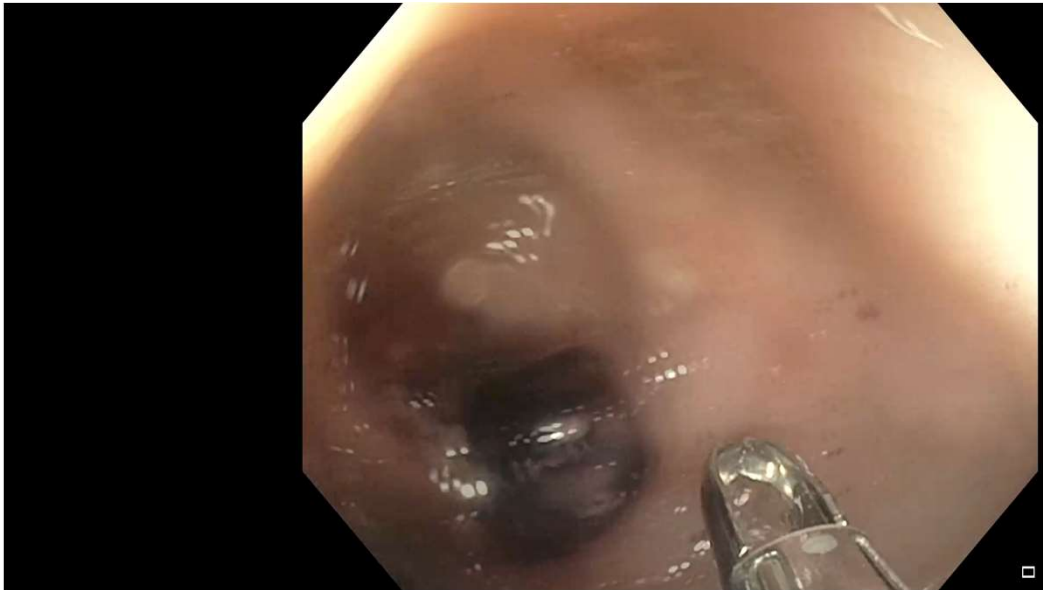
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Endoscopic Clipping of Diverticular Bleeding

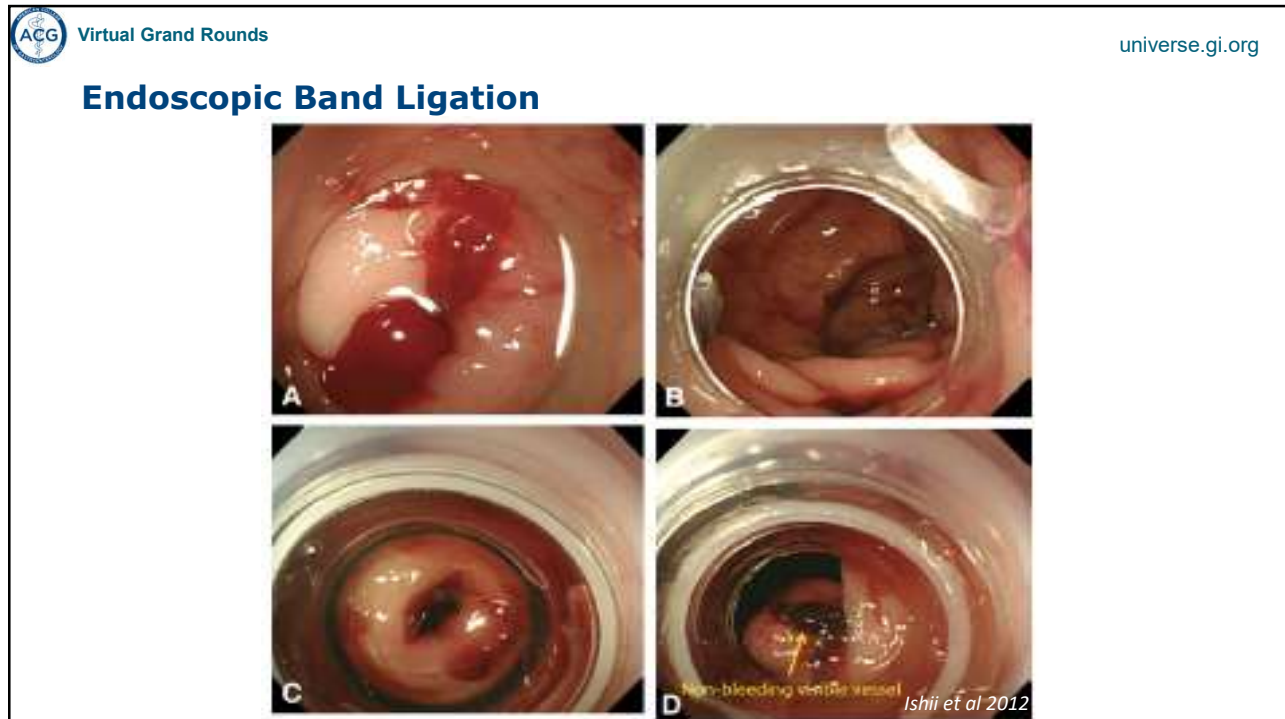


Courtesy: Dr. Brian Riff @ocgastro

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Prevention of Recurrent LGIB

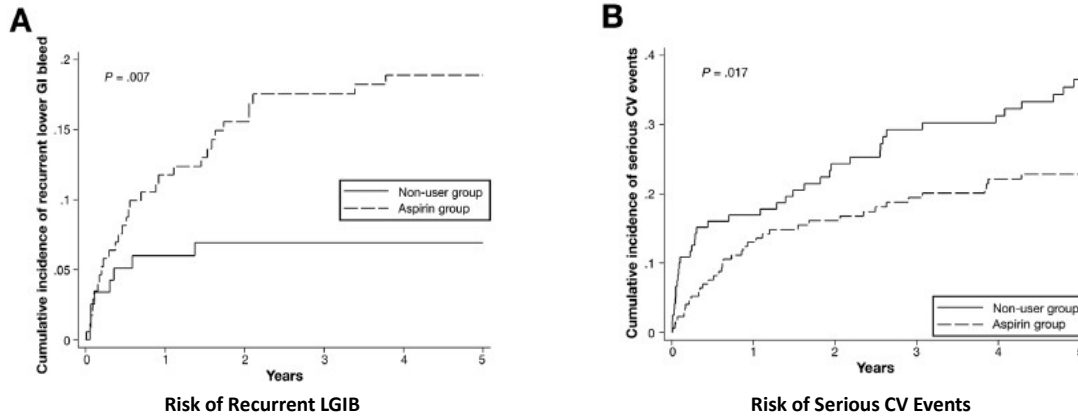
- 
 Avoid non-ASA NSAIDs in patients with a h/o LGIB secondary to diverticulosis or AVMs
- 
 Platelet aggregate inhibitors (but not anticoagulants) associated with recurrent diverticular hemorrhage
- 
 Discontinue aspirin for primary cardiovascular prevention
- 
 Continue aspirin for patients with history of cardiovascular disease

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Vajravelu R et al. *Gastroenterology* 2018

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Benefits of Resuming Antiplatelets in LGIB



- ASA use associated with higher rate of recurrent LGIB
- ASA use protective of future cardiovascular complications/death

Chan FK et al Gastroenterology 2016

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The Typical Case

- 67yo F with CAD on ASA and OA on chronic NSAIDs presents with stable BRBPR.
- Prior screening colonoscopy with good preparation 2 years ago with left sided diverticulosis.
- Hospitalized 6 months ago with severe hematochezia, stabilized with resuscitation. At that admission, colonoscopy 24 hours after presentation and bowel preparation (4L PEG) showed left sided diverticulosis with blood throughout the colon with specific SRH, no intervention performed.
- Discharged on same regimen after spontaneous cessation of bleeding. At present, patient appears well, and is hemodynamically stable with 2gm drop in Hgb from baseline.

- Do we repeat a colonoscopy?
- If so, when should we perform a colonoscopy?
- If not, do we consider a CT Angiography or other diagnostic testing?
- Is no testing a reasonable option?
- How do we minimize risk of recurrence?

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The “Typical” Case Diverticular Bleeding

- ***Do we repeat a colonoscopy?***
 - If bleeding has subsided, then I suspect there is limited benefit to doing a colonoscopy
- ***If so, when should we perform the colonoscopy?***
 - No benefit to urgent colonoscopy in terms of clinical outcomes, potential benefit to doing an elective colonoscopy in order to confirm a diagnosis
- ***If not, do we consider a CT Angiography or other diagnostic testing?***
 - Consider CTA for patients with severe hematochezia in order to locate site of extravasation. Unlikely to be useful when bleeding has subsided already.
- ***Is no testing a reasonable option?***
 - Yes! Especially, when other etiologies have been excluded with a recent colonoscopy
- ***How do we minimize risk of recurrence?***
 - Discontinue NSAIDs and antiplatelets when possible

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Future Research Agenda



- 1 Use risk assessment tools in prospective studies to determine who can be discharged early with outpatient colonoscopy (or no colonoscopy)
- 2 Identify which patients benefit from early colonoscopy vs. CTA
- 3 Gather more data on optimal resuscitation strategy and role of reversal agents for patients on DOACs
- 4 Need additional comparison between inpatient bowel preparations

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**All of the relevant financial relationships listed for these individuals have been mitigated*

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