



SMALL BOWEL BLEEDING

SIMON VEENSTRA 8 JULY 2024





- Definitions
- Epidemiology and risk factors
- Approach
- Investigations
- Causes
- Conclusion





Traditional Definitions



- Obscure GI bleeding → <u>traditionally</u> defined as GI bleeding of uncertain cause after non-diagnostic EGD and colonoscopy and
 - Term often used for small bowel bleed
- Obscure overt → visible GI bleeding (haematochezia, melaena, maroon stool) but no obvious cause on above investigations
- Obscure occult → positive FOBT usually in association with unexplained iron deficiency



Current Definitions



- Small bowel bleeding → AGA Guidelines 2015 proposed name change due to improved technology and detection rates of small bowel lesions¹
- Potential/Suspected small bowel bleeding bleeding, overt or occult, with negative bi-directional endoscopy
- Obscure GI bleeding reserved for bleeding where no source is identified despite the latest imaging modalities/dedicated small bowel evaluation



Anatomic Definitions

- Upper GI bleeding up to ligament of Treitz
- Lower GI bleeding below ligament of Treitz
- Mid-GI bleeding ampulla of Vater to IC valve¹
 - Upper GI to ampulla of Vater
 - Lower GI from ICV







Epidemiology



- Upper and lower GI source account for 90% of GI bleeds
- Small bowel source of bleeding occur in 5-10% of all GI bleeds
- Accounted for up to 75% of OGIB
- Risk factors



of sub Saharan Africa

Table 2 Risk factors for small bowel bleeding

From: Bleeding Lesion of the Small Bowel: an Extensive Update Leaving No Stone Unturned

Risk factors for SB bleeding	Predictor of:	OR, [95% confidence interval], P value	
Age > 60 [13]	Overt bleeding, vascular lesions [‡]		
Need of blood transfusion [12]	Overt bleeding, vascular lesions [‡]		
Hypertension [<u>12</u> ···]	Overt bleeding, vascular lesions [‡]		
Diabetes mellitus [<u>13</u>]	Overt bleeding, vascular lesions [‡]		
Hematologic disease [<u>13</u>]	Overt bleeding, vascular lesions [‡]		
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Anticoagulants usage [<u>13</u> , <u>14</u>]	Overt bleeding, vascular lesions [‡] [<u>13</u>]	4.30 [1.20–15.40], <i>P</i> = 0.028 [<u>14</u>]	
	Overt bleeding, vascular lesions ^{‡,*} [<u>14</u>]		
Prostaglandin analogue usage [<u>13</u>]	Overt bleeding, vascular lesions [‡]		
CKD≥4[<u>12</u> ··]	Overt bleeding, vascular lesions ^{‡,*}	4.03 [1.45–11.10], <i>P</i> = 0.007	
Hemodialysis [<u>13</u>]	Overt bleeding, vascular lesions ^{‡,*}	3.71 [1.32–10.47], <i>P</i> = 0.013	
Liver cirrhosis [<u>13</u>]	Overt bleeding, vascular lesions ^{‡,*}	4.90 [2.10–11.44], <i>P</i> < 0.001	
Thienopyridines [<u>14</u>]	Overt bleeding, vascular lesions ^{‡,*}	3.20 [1.30-8.40], <i>P</i> = 0.015	
NSAID use [<u>12</u> , <u>13</u> , <u>14</u>]	Overt bleeding, ulcerative lesions ^{‡,*}	4.73 [1.47–15.2], P = 0.009 [<u>12</u> ···]	
		2.97[1.52–5.81], <i>P</i> = 0.001[<u>13</u>]	
		2.50 [1.20-5.30], <i>P</i> = 0.018 [<u>14</u>]	
PPI use [<u>14</u>]	Overt bleeding, ulcerative lesions ^{‡,*}	2.00 [1.10-3.60], <i>P</i> = 0.021	
Low Hb level [<u>13</u>]	Occult bleeding, vascular lesions ^{‡,*}	0.63 [0.42–0.95], <i>P</i> = 0.028	
Hematologic disease [<u>13</u>]	Occult bleeding, vascular lesions ^{‡,*}	8.58 [1.08-68.31], <i>P</i> = 0.042	
Liver cirrhosis [<u>13</u>]	Occult bleeding, vascular lesions ^{‡,*}	7.45 [1.21–45.77], P = 0.013	
PPI use [<u>12</u> ••]	Occult bleeding, ulcerative lesions ^{‡,*}	3.18 [1.02–9.92], <i>P</i> = 0.05	
Low-dose aspirin [<u>12</u> …]	Occult bleeding, ulcerative lesions ^{‡,*}	3.57[1.21–10.50], <i>P</i> = 0.02	
Tobacco use [<u>12</u> ···]	Occult bleeding, ulcerative lesions [‡]		
Alcohol abuse [<u>12</u> ••]	Occult bleeding, ulcerative lesions [‡]		
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OR odds ratio, SB small bowel, CKD chronic kidney disease, NSAID nonsteroidal anti-inflammatory drugs, PPI proton-pump inhibitors, Hb hemoglobin

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Approach

ACG Clinical Guideline: Diagnosis and Management of Small Bowel Bleeding

Lauren B. Gerson, MD, MSc, FACG¹, Jeff L. Fidler, MD², David R. Cave, MD, PhD, FACG³ and Jonathan A. Leighton, MD, FACG⁴



PRACTICE GUIDELINES



Figure 1. Algorithm for suspected small bowel bleeding. CTE, computed tomographic enterography; MRE, magnetic resonance enterography; VCE, video capsule endoscopy.

1. Am J Gastroenterol 2015; 110:1265–1287

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PRACTICE GUIDELINES



Figure 2. Algorithm for brisk or massive suspected small bowel bleeding. CT, computed tomography.

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Approach

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PRACTICE GUIDELINES

CME

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Figure 3. Algorithm for sub-acute ongoing suspected small bowel bleeding. CTE, computed tomographic enterography; RBC, red blood cell; VCE, video capsule endoscopy.

Guidelines

🖗 Thieme

Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small-bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) Guideline – Update 2022

ESGE

Fig.1 Recommended approaches for diagnosis and treatment of suspected small-bowel bleeding (SSBB). a In patients with overt SSBB, small-bowel capsule endoscopy (SBCE) should be performed as soon as possible after the bleeding episode, ideally within 48 hours. **b** When SBCE is contraindicated or unavailable, device-assisted enteroscopy (DAE) and/or dedicated small-bowel (SB) cross-sectional imaging may be considered for SB evaluation, depending on availability, expertise, and clinical suspicion. c DAE can also be considered as alternative first-line examination in selected cases, depending on the clinical scenario and local availability, and should be performed optimally within 48-72 hours after the bleeding episode. **d** In patients with significant active bleeding and unsuitable for flexible endoscopy, computed tomography (CT) angiography or angiography may be considered. e Upper and/or lower gastrointestinal endoscopy may also be considered on a case-by-case basis to identify lesions overlooked at baseline endoscopy. CTE, computed tomography enterography.







Gastroenterology Foundation

? Second-look endoscopy ?



- and adaption address

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Study	Non-small bowel source in reach of EGD	Modality
Kitiyakara <i>et al.</i> 2005	2.8% (4/140)	VCE
Sidhu <i>et al.</i> 2006	4.7% (6/128)	VCE
Zamon <i>et al. 1998</i>	26% (25/95)	Push enteroscopy
Fry <i>et al.</i> 2009	13.1% (14/107)	DAE
Innocenti <i>et al. 2021</i>	10.7% (31/290) → Upper GI only 7.6% (22/290) → SB + upper GI	VCE
Clere-Jehl <i>et al.</i> 2016 (age > 65 with ongoing IDA)	64% (29/45)	VCE
Riccioni <i>et al.</i>	21%	VCE

- 1. Gastrointest Endosc. 2005; 62: 234-238
- 2. J Gastrointestin Liver Dis. 2006; 15: 375-377
- 3. Gastrointest Endosc. 1998; **47**: 372-376
- 4. Gastrointest Endosc. 1998; **47**: 372-376

- 5. Clin Res Hepatol Gastroenterol 2021; 45:101409
- 6. Medicine (Baltimore)2016; 95:e5339
- 7. Scand J Gastroenterol 2014; 49: 1020-1026



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- Video capsule endoscopy
 - Diagnostic yield 55-62%
 - Consistently superior to push-enteroscopy, CT enterography, CT angiography, and intraoperative enteroscopy
 - As good as DAE in evaluating and finding bleeding source
 - Yield is highest if performed early preferably within 48-72hrs but up to 14 days
 - Other factors increasing yield: history of overt bleed, use of antithrombotic agents, inpatient status, male, older age, liver and renal comorbidities, high transfusion requirements & use of antiplatelet/anticoagulants
- Excellent safety profile capsule retention rate of 1.2-2.1%



VCE





- 1st line examination for suspected small bowel bleeding given excellent safety profile, tolerability, and potential to visualize the small bowel mucosa. Strong recommendation, moderate quality evidence
- Recommended for overt SSBB as soon as possible after bleeding episode (ideally within 48 hours) to maximize diagnostic and subsequent therapeutic yield. Strong recommendation, high quality evidence



- VCE
 - Limitations:
 - Purely diagnostic
 - Difficulty localizing lesions
 - Small bowel transit time = first duodenal image to first caecal image
 - Anterograde approach if lesion falls within first 2/3
 - Retrograde approach if lesion falls within final 1/3
 - Al
 - OdoCapsule
 - Rapid transit through the proximal GI tract









- Device assisted enteroscopy
 - Double balloon enteroscopy, single balloon enteroscopy, spiral enteroscopy.
 - Advantages: diagnostic and therapeutic
 - Lower rate of complete examination, more invasive, time consuming
 - Diagnostic yield improves from 56% to 75% if preceded by positive VCE (can also guide decision on initial DAE approach: antero- vs retrograde)
 - DBE enteroscopy has higher rates of total enteroscopy compared to to SBE but diagnostic and therapeutic yield is similar





- Push enteroscopy
 - If lesions suspected to be very proximal (mean depth 80cm vs 230cm for DBE)
- Intraoperative enteroscopy
 - Rarely indicated
 - Consider in recurrent bleeding, where other modalities have failed to detect a source or where DAE cannot be performed without adhesiolysis
 - Good diagnostic yield but high morbidity rate (18%) and mortality (5%)



• DAE

Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small-bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) Guideline – Update 2022





- Alternative 1st line test in select cases depending on clinical scenario and local availability. Weak recommendation, low quality of evidence
- in patients with overt SSBB, DAE to be performed within 48-72 hours after the bleeding episode. Strong recommendation, high quality of evidence
- Consideration of DAE and/or dedicated small bowel cross sectional imaging as 1st diagnostic test in patients with SSBB depending on availability, expertise and clinical suspicion when VCE is not available or contraindicated. Weak recommendation, low quality of evidence





- Imaging
 - Barium studies not recommended low yield 3-17%
 - CT
 - enterography requires ingestion of large volume of contrast
 - enteroclysis contrast administered via nasoenteric tube
 - Overt bleeding can be detected without above techniques (i.e. CTA)
 - CTE lower yield than VCE (40% vs 53%)
 - VCE higher yields for vascular and inflammatory lesions however CTE may outperform with mass lesions
 - MR enterography
 - Not routinely used for evaluation of small bowel bleeding
 - Only small studies comparing CT and MRI
 - Can be considered in young patients because of lower radiation exposure





- Imaging
 - CT angiography
 - Usually performed to detect site of active bleeding in cases of acute overt bleeding
 - Can detect bleeding rates as slow as 0.3mls/min compared to conventional angiography (0.5ml-1.0ml/min) and 0.2 ml/min for ^{99m}Tc tagged RBC scintigraphy
 - Pooled sensitivity of 89% and specificity of 85% in acute GI bleeding through the GI tract
 - Advantages: widely available, performed rapidly, extraluminal pathology
 - Disadvantages: needs to be actively bleeding to detect extravasation, contrast and renal failure

Recommendations

- 1. In acute overt massive GI bleeding, conventional angiography should be performed emergently for hemodynamically unstable patients (strong recommendation, low level of evidence).
- 2. In hemodynamically stable patients with evidence of active bleeding, multiphasic CT (CTA) can be performed to identify the site of bleeding and guide further management (strong recommendation, low level of evidence).





- Imaging
 - Conventional angiography
 - Diagnostic and therapeutic options, diagnostic yield of 2-77%
 - Predictors of positive test: haemodynamic instability, >4u PRBC, minimal delay from presentation
 - Requires higher rate of bleeding 0.5-1.0ml/min
 - Risk of complications 10%
 - Renal failure
 - Thromboembolic events
 - Catheter site infections
 - Mesenteric ischaemia in up to 4%
 - Patients with a negative CTA or RBC scan are unlikely to have a positive angiogram
 - Good therapeutic options
 - Systematic review of 15 studies (309 patients)¹ included lesions outside the small bowel)
 - Clinical success rate of 95% and 30 day success rate of 76%
 - 12% rebleed rate





- Imaging
 - Scintigraphy
 - ^{99m}Tc-labeled RBC scintigraphy able to detect slower rates of bleeding
 - Wide range of diagnostic yields across studies (26-87%)
 - Limitations include localization accuracy (particularly in foregut and small bowel)
 - Meckel's scan (99mTc-pertecnetate scan)
 - Affinity for gastric mucosa (up to 50-60% of Meckel's diverticulum)
 - Highest diagnostic yield in children
 - False positives may occur in other conditions (ulcerative lesions, inflammatory lesions, AV malformations, obstruction, intussusception, other ectopic gastric mucosa (duplication cysts)





Angiographic

Conservative / Medical





HO Causes



Common causes		Rare causes		
Under age 40 years	Over age 40 years			
Inflammatory bowel disease	Angioectasia	Henoch-Schönlein purpura		
Dieulafoy's lesion	Dieulafoy's lesion	Small bowel varices and/or portal hypertensive enteropathy		
Neoplasia	Neoplasia	Amyloidosis		
Meckel's diverticulum	NSAID ulcers	Blue rubber bleb nevus syndrome		
Polyposis syndromes		Pseudoxanthoma elasticum		
		Osler-Weber-Rendu syndrome		
		Kaposi's sarcoma with AIDS		
		Plummer-Vinson syndrome		
		Ehlers-Danlos syndrome		
		Inherited polyposis syndromes (FAP, Peutz-Jeghers)		
		Malignant atrophic papulosis		
		Hematobilia		
		Aorto-enteric fistula		
		Hemosuccus entericus		



HO Causes



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HO Causes



Table 4 Causes of small bowel bleeding in the American College of Gastroenterology clinical guideline 2015			
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Under age 40 years	Over age 40 years		
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- Angiodysplasia
 - Generally found in elderly > 65
 - Several associations
 - Heyde's Syndrome
 - Ao Stenosis and angiodysplasia
 - high stress in AS causes shear-dependent cleavage of high molecular weight multimers of von Willebrand's factor (vWF)
 → acquired vWF deficiency
 - Ao valve replacement
 - Renal failure, haemodialysis
 - Uraemic platelet dysfunction
 - Management
 - Endoscopic
 - Medical: Supportive, Octreotide, thalidomide





RESEA	RCH SUMMARY	(
Thalidomide fo Due to Small-Inte	r Recurren estinal Ang	t Bleedin giodyspla	g sia	
Chen H et al. DC	DI: 10.1056/NEJMo	a2303706		
NUCLE PROTEIN glodpyplasia is the most common cause of small-intes- al bleeding. Treatments include angiographic emboli- tion and local abutton, but recurrent bleeding is com- on and may result in severe complications. There is an ente need for sale and effective or alt treatments for re- rerent bleeding in these patients.	Small-intestinal angiodysplasia	100-mg Thalidomide Group (N=51) Thulidomide	50-mg Thalidomide Group (N=49) Thalidomide	Placebo Group (N=50) Placebo
INICAL TRIAL sign: In a multicenter, double-blind, randomized, pla- bo-controlled trial in China, the efficacy and safety of	a4 bleeding episodes during previous year		Daily for 4 mo	
alidomide were evaluated for the treatment of recurrent reeding due to small-intestinal angiodysplasia (SIA).	Effective Response 250% reduction in bleeding episodes			

Octreotide vs Standard of care in Angiodysplasia-related bleeding: OCEAN study





- Hereditary Haemorrhagic Telangiectasia (HHT)/(Osler-Weber-Rendu Syndrome)
 - Autosomal dominant, high penetrance, 1:5000-8000
 - Mutations in the endoglin (HHT1) and ALK1 (HHT2) genes, and SMAD4 (JPHT overlap)
 - Majority of patients have history of prior recurrent epistaxis
 - tends to predate the development of cutaneous or visceral telangiectasias by a decade or more.
 - GI bleeding develops in the fourth or fifth decade of life
 - Take a history of spontaneous recurrent nosebleeds and family history
 - Physical examination: minute telangiectasia on the lips, nasal mucosa, tongue, palms, and palate.























- Hereditary Haemorrhagic Telangiectasia (HHT)/(Osler-Weber-Rendu Syndrome)
 - Diagnosis (Curacao Diagnostic Criteria)
 - Spontaneous and recurrent epistaxis
 - Multiple mucocutaneous telangiectasia at characteristic sites
 - Visceral involvement (e.g., gastrointestinal telangiectasia; pulmonary, cerebral, or hepatic arteriovenous malformations [AVMs])
 - A first-degree relative with HHT
- Management
 - Monitoring of Hb
 - Symptomatic treatment as required (iron supplementation/blood transfusions)
 - Endoscopic treatment
 - Angiography
 - Specific systemic therapy
 - Bevacizumab (VEGF-inhibitor, off-label)
 - Octreotide (reduces blood transfusion and endoscopic treatments, VERY EXPENSIVE)
 - Thalidomide/Pomalidomide (anti-angiogenesis properties)
 - Soy
 - Low dose tacrolimus (small numbers in trial)



- Dieulafoy lesions
 - Tortuous artery protruding into the mucosa from the submucosa,
 - Rare cause of GI bleed, but can be lifethreatening
 - Most commonly occur in stomach (lesser curvature)
 - Easily missed
 - Small bowel relatively uncommon site (2-10%) ^{1,2,3}
 - Diagnosis and management
 - Endoscopic
 - CTA
 - Surgical





1. Gastrointest Endosc, 2011, vol. 74 (pg. 573-80)

- 2. Gastrointest Endosc, 1999, vol. 50 (pg. 762-67)
- *3. Gastrointest Endosc*, 2003, vol. 58 (pg. 236-43)



- Blue rubber bleb nevus syndrome
 - Rare only 200 cases reported in literature
 - Venous malformations of the skin, soft tissues and GI tract
 - Bleeding usually occurs in childhood
 - Chronic iron deficiency
 - Endoscopic appearance: protuberant large polypoid blue venous blebs
 - Occur particularly in small bowel and colon
 - Management:
 - Band ligation
 - Surgical resection







- Small intestine tumours
 - Tumours of small intestine account for 5-7% of GI tumours overall
 - Common cause of small bowel bleeding in <50 age group
 - Types of 1° tumours:
 - Adenocarcinoma is the most common primary malignancy of the small bowel (accounting for 35– 50% of small bowel tumours)
 - Carcinoid tumours account for 20–40%
 - Lymphomas 14%
 - Sarcomas 11–13%





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- intestine account for 5-7% of all
- of small bowel bleeding in <50

urs:

- a is the most common primary e small bowel (accounting for 35wel tumours)
- irs account for 20–40%
- 6
- 3%



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- Gastrointestinal Stromal Tumours
 - Originate from interstitial cells of Cajal
 - Stomach most common origin but 30-35% in small bowel
 - GI bleeding caused by the compression, ischaemia and infiltration of overlying mucosa
 - Management
 - Surgical resection









- Small bowel ulcers
 - NASID-related
 - Can occur in 25-55% of patients who take full dose non-selective NSAIDs
 - Crohn's disease
 - Tuberculosis







on-selective NSAIDs





- Meckels diverticulum
 - Incomplete obliteration of the vitelline duct
 - Ectopic gastric mucosa >50% (& pancreatic occasionally)
 - Relatively common in the general population, but mostly asymptomatic, male predominance 1.5-4:1
 - Disease of the young: most common age of presentation is Between 10-30 years
 - Common symptoms
 - Bleeding (ectopic gastric mucosa)
 - Diverticulitis
 - Obstruction
 - Diagnosis Meckel's scan, superior mesenteric artery angiography, DBE, CE
 - Management \rightarrow surgery







Meckel's diverticulum – Rule of Twos

"occurs in 2% of the population; 2% are symptomatic, children are usually less than 2 years, affects males twice as often as females, is located 2 feet proximal to the ileocecal valve, is 2 inches long or less, and can have 2 types of the mucosal lining"



SUMMARY

- Guidelines
 - AGA
 - ESGE
- Causes
 - Not an exclusive list
- Therapeutics
- Approach







Take home points



- Proper evaluation of bleeding characteristics guides diagnostic/treatment algorithm
- VCE generally the preferred first line modality after a negative bidirectional endoscopy
- DAE offers both diagnostic and therapeutic options and may be of greatest benefit when guided by VCE findings
- Management of small bowel bleeding is difficult and each case should be managed on individual merits