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Multimodal Diagnostic and Therapeutic Strategies in Vascular Small Bowel Bleeding: Integrating Endoscopy, Imaging, and Pharmacologic Advances

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ABSTRACT

Background:
Vascular minor bowel bleeding (VSBB) constitutes a diagnostically challenging and clinically significant subset of gastrointestinal hemorrhage, especially in elderly and comorbid populations. Angiodysplasia, Dieulafoy lesions, ectopic varices, and hereditary hemorrhagic telangiectasia (HHT) are primary vascular causes. Recent advancements in endoscopic, radiologic, and pharmacologic technologies have dramatically improved the diagnostic yield and therapeutic precision in managing these lesions. **Objective:**
This comprehensive review aims to synthesise current evidence regarding the pathogenesis, diagnostic pathways, and therapeutic strategies for VSBB, while emphasising the integration of emerging tools such as artificial intelligence (AI), genetic testing, and angiogenic profiling. **Methods:**
An extensive review of published clinical guidelines, systematic reviews, randomised trials, and observational studies was conducted. Diagnostic algorithms and therapeutic options, including endoscopic therapies (e.g., argon plasma coagulation, sclerotherapy), radiologic interventions, pharmacologic agents (octreotide, thalidomide, bevacizumab), and surgical approaches, were critically evaluated. Special considerations for high-risk populations, including those with chronic kidney disease, HHT, and anticoagulant use, were explored. **Results:**
Video capsule endoscopy and device-assisted enteroscopy have emerged as cornerstones for diagnosis, with computed tomography angiography offering essential support in unstable patients. Endoscopic modalities remain first-line for most lesions, while pharmacologic therapy is crucial for diffuse or recurrent bleeding. Surgical interventions, including intraoperative enteroscopy and valve replacement in Heyde's syndrome, serve as definitive options in select patients. AI and molecular diagnostics offer transformative potential for early detection and personalized treatment. **Conclusion:**
VSBB requires a patient-specific, algorithmic management strategy combining clinical, endoscopic, radiologic, and pharmacologic insights. Continuous innovation, interdisciplinary collaboration, and the integration of AI and genomics will be vital to advancing precision medicine in this domain.

Keywords:
Vascular Small Bowel Bleeding, Angiodysplasia, Capsule Endoscopy, Deep Enteroscopy, CT Angiography, Argon Plasma Coagulation, Octreotide, Bevacizumab, Artificial Intelligence, Hereditary Hemorrhagic Telangiectasia.

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1. Introduction

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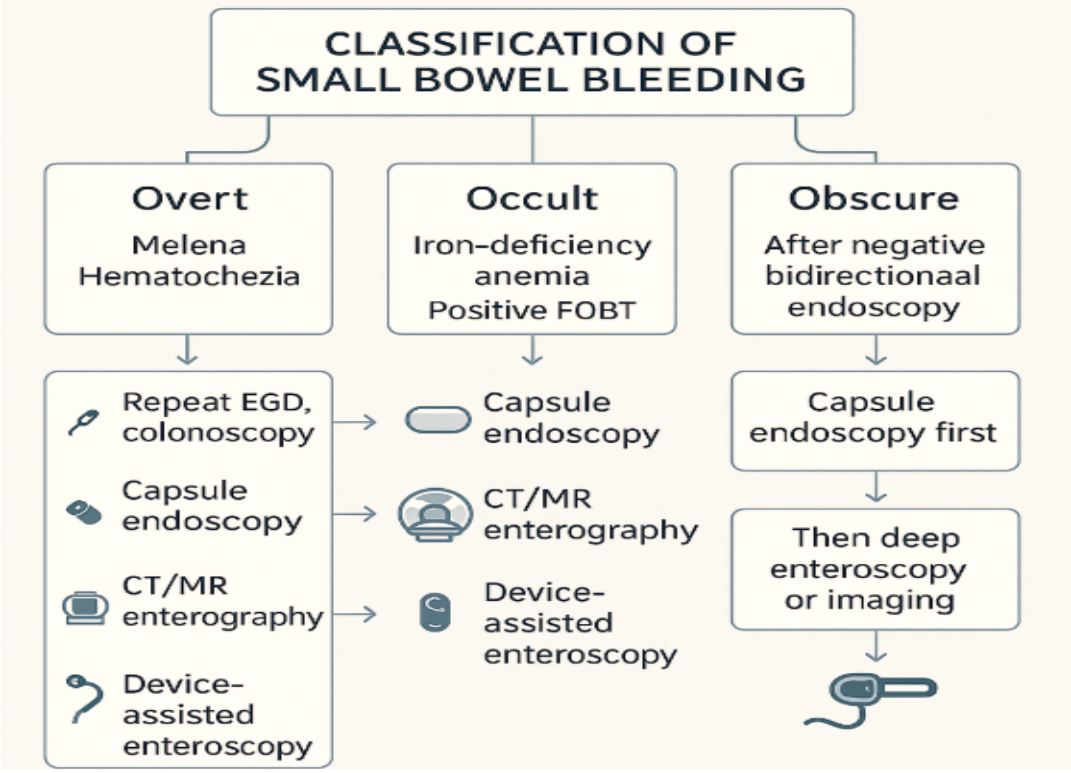
Small bowel bleeding (SBB), a subset of gastrointestinal (GI) hemorrhage, refers to bleeding originating from the small intestine, specifically the segment extending from the ligament of Treitz to the ileocecal valve. It constitutes approximately 5% of all GI bleeding cases, making it a relatively rare yet diagnostically challenging entity. SBB is primarily classified into three categories based on clinical presentation and diagnostic clarity: overt, occult, and obscure bleeding.[1-5]

Overt small bowel bleeding manifests with visible signs such as melena or hematochezia and is often easier to recognize clinically. **Occult bleeding** refers to bleeding not apparent to the naked eye but inferred through laboratory findings, such as iron-deficiency anemia or a positive fecal occult blood test. **Obscure bleeding**, historically a broader term, is now reserved for instances where GI bleeding persists despite negative findings on bidirectional endoscopy (esophagogastroduodenoscopy and colonoscopy), including advanced evaluations such as capsule endoscopy or deep enteroscopy.[5-10]

Figure 1: Classification of Small Bowel Bleeding illustrates these categories along with diagnostic approaches typically pursued in each case.



Recent years have witnessed a paradigm shift in both terminology and diagnostic strategies. The term "obscure GI bleeding" has become more restrictive, as advancements in imaging and endoscopic techniques have greatly enhanced our ability to localize bleeding sources within the small bowel. Technologies such as video capsule endoscopy (VCE), device-assisted enteroscopy (DAE), and computed tomography angiography (CTA) have significantly reduced the proportion of truly obscure cases.Given this evolving landscape, the clinical community has gravitated toward a more precise lexicon and classification system that better aligns with technological capabilities. As a result, contemporary gastroenterological literature now emphasizes the use of "small bowel bleeding" over the historically vague term "obscure GI bleeding."Among the myriad causes of SBB, **vascular lesions** are the most common, especially in elderly and comorbid populations. These include angiodysplasia, Dieulafoy lesions, varices, and hereditary hemorrhagic telangiectasia (HHT). These vascular sources of bleeding are uniquely suited to be identified and treated using the full spectrum of modern diagnostic and therapeutic modalities.[11-20]

Table 1: Vascular Causes of Small Bowel Bleeding

Lesion Type	Pathogenesis	Common Risk Factors	Clinical Features	Reference
Angiodysplasia	Dilated, thin-walled vessels due to chronic ischemia	Age > 50, vWD, CKD, LVAD	Intermittent occult/overt bleeding	21
Dieulafoy Lesion	Large-caliber artery erosion through mucosa	NSAID use, ischemia	Brisk, recurrent bleeding	22
Ectopic Varices	Portosystemic collaterals in portal hypertension	Cirrhosis, prior abdominal surgery	Life-threatening hemorrhage	23
Telangiectasias (HHT)	Genetic AVMs due to TGF-\u03b2 signaling defects	Autosomal dominant inheritance	Bleeding after age 50, anemia	24

The present review aims to synthesize current evidence and clinical practice guidelines surrounding the pathogenesis, diagnostic evaluation, and management of vascular SBB. The goal is to offer a comprehensive, algorithmic approach that integrates endoscopic, radiologic, and pharmacologic strategies, thereby enabling clinicians to optimize care for this complex yet increasingly manageable condition.[25-26]

Table 2: Classification and Diagnostic Pathways for Small Bowel Bleeding

Type of Bleeding	Clinical Manifestation	Initial Workup	Further Evaluation	Reference
Overt	Melena, hematochezia	EGD, colonoscopy	VCE, DAE, CTA	27
Occult	Iron-deficiency anemia, FOBT+	EGD, colonoscopy, labs	VCE, CTE/MRE, RBC scan	28
Obscure	Persistent bleeding, no source found	Repeat endoscopy, VCE, enteroscopy	Intraoperative enteroscopy, surgery	29

2. Epidemiology and Clinical Burden

Vascular small bowel bleeding (VSBB) accounts for the majority of clinically significant SBB cases, particularly in older adults and patients with systemic comorbidities. Epidemiological data suggest a marked age-related increase in the incidence of vascular lesions, particularly **angiodysplasia**, which is the most frequent cause of VSBB. In patients over the age of 50, angiodysplasia is responsible for up to 50% of small bowel bleeding cases, whereas in younger populations, tumors and inflammatory conditions are more commonly implicated.[30-32]

Angiodysplasia is most prevalent in elderly individuals, with studies estimating its detection in up to 2.9% of asymptomatic individuals undergoing endoscopy. The incidence further increases in populations with comorbid conditions such as chronic kidney disease, aortic stenosis, and those supported by left ventricular assist devices (LVADs). In contrast, **Dieulafoy lesions** are rare (comprising <2% of GI bleeding cases overall) but are capable of causing massive hemorrhage in middle-aged or elderly patients, often without warning signs.[33-35]

Varices and **telangiectasias** represent smaller yet clinically significant portions of VSBB. Varices, particularly ectopic varices in the small intestine, occur in the setting of portal hypertension and can be found in up to 21% of such patients. Telangiectasias, notably in hereditary hemorrhagic telangiectasia (HHT), occur in 80-90% of genetically confirmed cases and contribute to GI bleeding in approximately one-third of these individuals, primarily after the age of 50.From a health economics perspective, VSBB imposes a considerable burden on healthcare systems. Recurrent hospitalizations, frequent transfusion requirements, repeated endoscopic interventions, and prolonged diagnostic workups contribute significantly to both direct and indirect healthcare costs. For instance, patients with chronic bleeding from angiodysplasia may require multiple hospital admissions annually, with substantial utilization of blood products and endoscopic services. Moreover, ongoing bleeding is associated with decreased quality of life, increased morbidity, and the risk of unnecessary surgical intervention when bleeding remains undiagnosed.[36-40]

Figure 2 : demonstrates the age-related distribution of vascular lesions in SBB, illustrating the predominance of angiodysplasia in older adults compared to other vascular lesions.

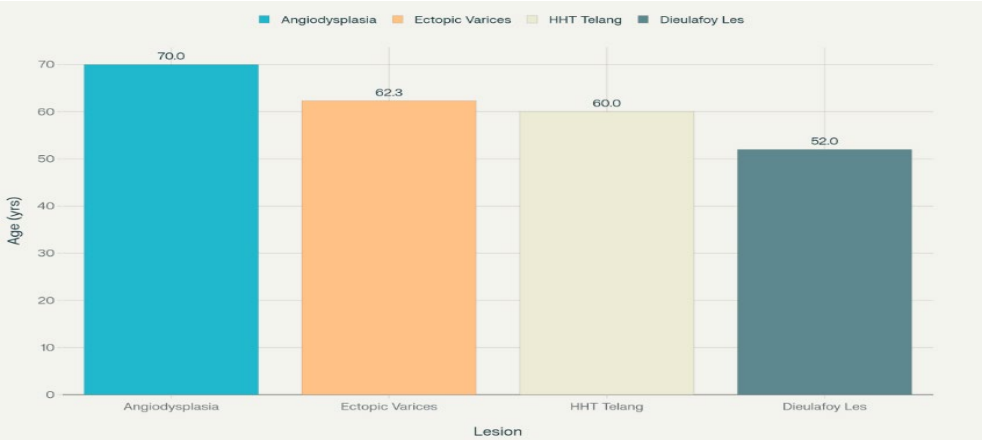


Table 3: Age-Related Distribution of Vascular Lesions in Small Bowel Bleeding

Age Group	Angiodysplasia	Dieulafoy Lesion	Ectopic Varices	Telangiectasias (HHT)	**Reference**
<30 years	Rare	Very rare	Rare	HHT onset possible	41
30-50 years	Occasional	Rare	Moderate (in cirrhotics)	Early HHT presentation	42
>50 years	Common	Moderate	Common	Predominant age of symptoms	43

3. Pathophysiology of Vascular Lesions in the Small Bowel

The pathogenesis of vascular lesions in the small bowel is complex, multifactorial, and often influenced by systemic comorbidities. Understanding the underlying mechanisms is essential for optimizing diagnostic strategies and guiding effective treatment plans. The most prevalent vascular lesions associated with small bowel bleeding include angiodysplasia, Dieulafoy lesions, ectopic varices, and telangiectasias, particularly those associated with hereditary hemorrhagic telangiectasia (HHT).44-48

3.1 Angiodysplasia

Angiodysplasia represents the most frequent vascular lesion responsible for small bowel bleeding, particularly in older adults. Histologically, these lesions are characterized by dilated, thin-walled vessels in the mucosa and submucosa, often without muscular support. Several mechanisms contribute to the formation of these lesions:

- **Chronic Intermittent Ischemia:** Repeated episodes of transient low-grade ischemia due to inadequate perfusion lead to vascular dilation and remodeling. This process is believed to weaken the vessel walls over time, predisposing them to rupture.

- **Increased Pro-Angiogenic Factors:** Elevated levels of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) have been demonstrated in patients with angiodysplasia, suggesting a role for aberrant angiogenesis in lesion development.
- **Von Willebrand Disease (vWD) and Acquired vWF Deficiency:** vWF is essential for platelet adhesion and aggregation. In conditions such as aortic stenosis or in patients with LVADs, increased shear stress leads to proteolysis of vWF multimers, resulting in an acquired form of vWD. This deficiency impairs hemostasis and contributes to recurrent bleeding from angiodysplastic lesions. This mechanism underlies **Heyde's Syndrome**, the co-occurrence of aortic stenosis and GI bleeding from angiodysplasia.[49-55]

3.2 Dieulafoy Lesions

Dieulafoy lesions are characterized by an abnormally large submucosal artery that protrudes through a small mucosal defect without evidence of ulceration or surrounding inflammation. These arteries are typically 1–3 mm in diameter substantially larger than normal mucosal capillaries and can rupture spontaneously, leading to brisk hemorrhage.

- **Pulsatile Erosion Mechanism:** The underlying hypothesis is that mechanical pulsation of the artery erodes the overlying mucosa, eventually exposing the vessel to the lumen. The exposed vessel can rupture and lead to sudden and severe bleeding.
- **Role of NSAIDs and Ischemia:** Chronic NSAID use may contribute to mucosal injury, promoting erosion over these anomalous vessels. Hypoperfusion and localized ischemia may further compromise mucosal integrity.[56-60]

3.3 Ectopic Varices

Ectopic varices are portosystemic collateral vessels that develop in atypical locations, including the small bowel, in response to elevated portal venous pressure. These vessels are prone to rupture, especially in the setting of cirrhosis or portal vein thrombosis.

- **Portal Hypertension-Driven Remodeling:** Elevated portal pressures lead to the formation of collateral channels that bypass the liver. In the small bowel, these manifest as tortuous, fragile varices within the submucosa.
- **Post-Surgical Factors:** Adhesions from prior abdominal surgeries can localize increased pressures to certain areas, predisposing specific bowel segments to ectopic varix formation.[60-65]

3.4 Telangiectasias and Hereditary Hemorrhagic Telangiectasia (HHT)

HHT is a genetic disorder caused by mutations affecting TGF-β signaling pathways, particularly in genes such as ENG, ACVRL1 (ALK1), and SMAD4. These mutations impair vascular development and integrity.

- **Arteriovenous Malformations (AVMs):** The hallmark of HHT is the formation of fragile AVMs throughout mucocutaneous and visceral tissues, including the GI tract. These lesions lack normal capillary beds, resulting in direct high-flow connections between arteries and veins that are susceptible to rupture.
- **Age-Related Progression:** Gastrointestinal telangiectasias in HHT typically develop later in life and are often silent until patients present with iron-deficiency anemia or overt bleeding after age 50.

3.5 Role of Comorbidities

Multiple systemic conditions contribute to the pathogenesis and persistence of vascular small bowel lesions:

- **Chronic Kidney Disease (CKD):** CKD is strongly associated with angiodysplasia. Proposed mechanisms include uremia-induced platelet dysfunction, altered intestinal perfusion, and increased vascular fragility. Studies indicate that up to 32% of patients with CKD have angiodysplastic lesions.
- **Aortic Stenosis:** As mentioned earlier, shear forces from a stenotic aortic valve can degrade vWF multimers, leading to a bleeding diathesis in patients with angiodysplasia.
- **Left Ventricular Assist Devices (LVADs):** Continuous-flow LVADs replicate the vWF-degrading effects of aortic stenosis, resulting in a similar acquired vWD. The non-pulsatile flow also promotes mucosal ischemia, compounding the bleeding risk.[65-70]

Figure 3 :provides a schematic overview of the pathophysiologic mechanisms associated with the major vascular lesions discussed in this section.

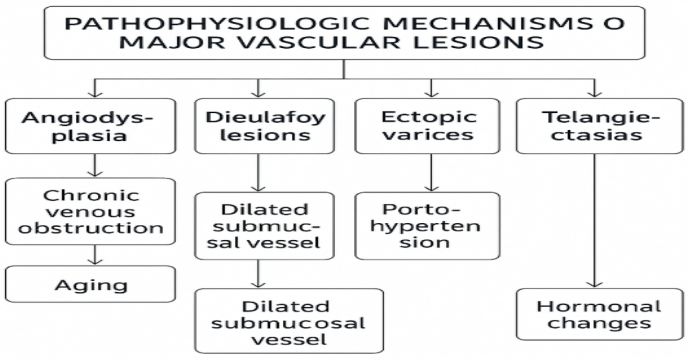


Table 4: Pathophysiological Mechanisms in Vascular Small Bowel Lesions

Lesion Type	Primary Mechanism	Contributing Factors	Reference
Angiodysplasia	Chronic ischemia, VEGF overexpression	CKD, aortic stenosis, LVAD, vWD	71
Dieulafoy Lesion	Arterial pulsation with mucosal erosion	NSAID use, local ischemia	72
Ectopic Varices	Portal hypertension-induced collaterals	Cirrhosis, portal vein thrombosis, abdominal surgery	73
Telangiectasias	Genetic AVMs via TGF-β pathway disruption	HHT (ENG, ALK1, SMAD4 mutations)	74

4. Diagnostic Approaches

The accurate diagnosis of vascular small bowel bleeding (VSBB) necessitates a stepwise, multimodal approach incorporating endoscopic, radiologic, and emerging advanced imaging techniques. The optimal strategy depends on clinical presentation, hemodynamic stability, and prior investigations.

4.1 First-line Endoscopic Workup

The initial evaluation of suspected VSBB begins with a repeat bidirectional endoscopy (esophagogastroduodenoscopy and colonoscopy), especially in patients presenting with overt bleeding. Despite previous negative results, a repeat examination can reveal missed lesions, particularly if performed during active bleeding episodes. Repeat endoscopy is recommended within 24 hours for hemodynamically unstable patients to maximize diagnostic yield.

Push enteroscopy, which allows direct visualization of the proximal jejunum, serves as a valuable early diagnostic tool, particularly when upper endoscopy is inconclusive. It enables both diagnostic assessment and therapeutic intervention (e.g., argon plasma coagulation or clipping) in cases of proximal vascular lesions.[75-80]

4.2 Capsule Endoscopy (CE)

Capsule endoscopy (CE) has revolutionized the evaluation of small bowel pathology and is considered the first-line investigation for stable patients with obscure gastrointestinal bleeding (OGIB), especially when initial endoscopies are non-diagnostic.

- **Diagnostic Yield:** CE demonstrates a diagnostic yield of approximately 50–70% for VSBB, with higher rates during active bleeding. Predictors of improved diagnostic

success include ongoing bleeding, lower hemoglobin levels, and shorter time intervals from bleeding onset to capsule ingestion.

- **Safety and Retention Risk:** While CE is minimally invasive and generally well-tolerated, the risk of capsule retention exists particularly in patients with suspected strictures, Crohn's disease, or prior abdominal surgeries. In such cases, a patency capsule is advised beforehand.

4.3 Device-Assisted Enteroscopy (DAE)

DAE techniques enable direct visualization, biopsy, and therapeutic intervention in deeper segments of the small intestine. Available technologies include:

- **Double-Balloon Enteroscopy (DBE):** Uses alternating inflation/deflation of balloons to pleat the bowel over the scope, allowing extensive traversal.
- **Single-Balloon Enteroscopy (SBE):** Similar to DBE but with one balloon; slightly lower depth of insertion but less technically demanding.
- **Motorized Spiral Enteroscopy (MSE):** Utilizes a rotating spiral segment to advance the scope; reduces procedure time and increases accessibility.

Each technique has strengths and limitations. DBE is considered the gold standard for deep enteroscopy with the highest diagnostic and therapeutic yield (up to 80% in some series), but it is more resource-intensive and operator-dependent. SBE offers a balance between accessibility and efficacy. MSE is promising but less widely available.

DAE is typically indicated when CE identifies a lesion requiring intervention, when CE is inconclusive but suspicion remains high, or in cases of massive bleeding requiring urgent intervention.

4.4 Radiologic Imaging

Radiologic modalities complement endoscopic techniques, especially in the context of active or recurrent bleeding:

- **CT Angiography (CTA):** Offers rapid, noninvasive visualization of active bleeding with sensitivity rates of ~70–80% for bleeding rates as low as 0.3–0.5 mL/min. It is most useful in hemodynamically unstable patients with overt bleeding.
- **CT Enterography (CTE):** Provides detailed mucosal and mural assessment of the small bowel, making it superior for detecting vascular malformations and tumors in stable patients with occult bleeding.

- **RBC Scintigraphy:** While sensitive for detecting bleeding rates as low as 0.1 mL/min, this nuclear scan has limited spatial resolution, making lesion localization imprecise. It is best utilized when CTA is unavailable or inconclusive.[80-90]

4.5 Diagnostic Algorithm Proposal

A tailored diagnostic strategy is crucial, and should be guided by the patient's hemodynamic status, bleeding pattern (overt vs. occult), and previous workup.[91]

Figure 4: illustrates a diagnostic algorithm based on acuity and prior evaluations

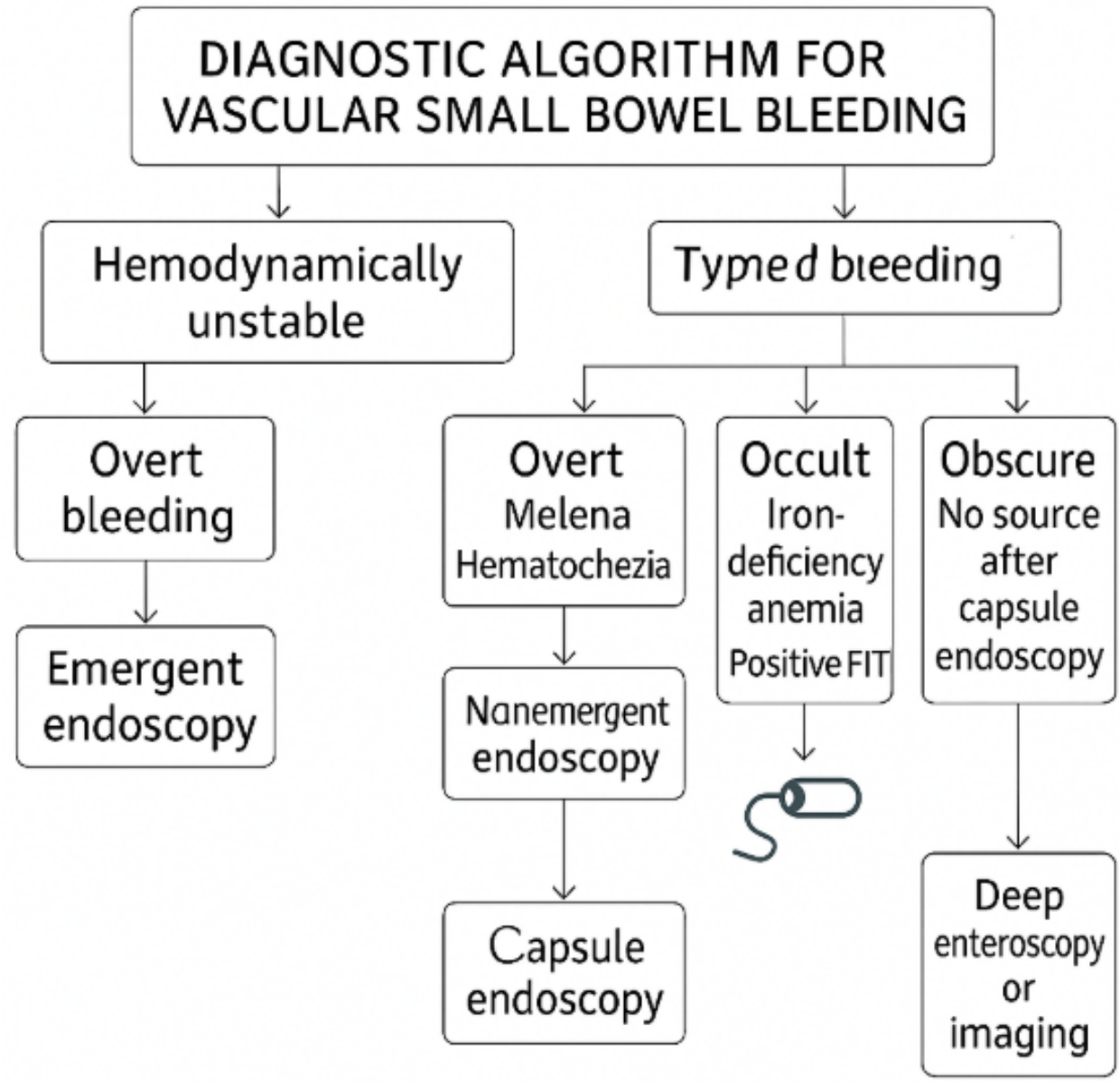


Table 5: Diagnostic Algorithm for Vascular Small Bowel Bleeding

Clinical Scenario	Initial Step	Secondary Investigations	Intervention Pathways	Reference
Overt, active bleeding (unstable)	Urgent EGD/colonoscopy ± CTA	DAE if source localized	Endotherapy, embolization, or surgery	92
Overt, active bleeding (stable)	Repeat EGD/colonoscopy	Capsule endoscopy → DAE	Endoscopic therapy or radiologic intervention	92
Occult bleeding with anemia	EGD + colonoscopy	CE ± CTE → DAE if needed	Iron therapy ± endotherapy if lesion found	93
Inconclusive prior workup	Repeat CE or DAE	Intraoperative enteroscopy	Segmental resection if localized	94

5. Management Strategies

Effective management of vascular small bowel bleeding (VSBB) requires a multidisciplinary approach that integrates endoscopic therapy, interventional radiology, medical treatment, and, in selected cases, surgery. Treatment should be individualized based on bleeding severity, lesion type, comorbid conditions, and prior treatment responses.[95]

5.1 Endoscopic Therapies

Endoscopic intervention remains the cornerstone of VSBB management. Various modalities are selected based on lesion characteristics, location, and availability:

- **Argon Plasma Coagulation (APC):** This non-contact thermal method is widely used for angiodysplasia. APC uses ionized argon gas to deliver monopolar electrical energy to coagulate superficial mucosal vessels. It is safe, effective, and particularly suitable for treating multiple, small, flat vascular lesions.
- **Electrocoagulation:** Includes bipolar and heater probe techniques for achieving thermal coagulation. Though slightly less precise than APC, it is useful in treating focal lesions or those not amenable to APC due to accessibility.
- **Mechanical Hemostasis (Clips):** Endoscopic clips provide mechanical compression and are preferred in managing actively bleeding Dieulafoy lesions. They offer immediate hemostasis and can be used in conjunction with injection therapy or APC.
- **Sclerotherapy:** Particularly effective for ectopic varices, this technique involves injecting sclerosants (e.g., ethanolamine oleate) into or adjacent to the varix to induce thrombosis and vessel obliteration. Though less commonly used in the small bowel, it can be life-saving when variceal sources are confirmed.[96-100]

5.2 Interventional Radiology

Angiographic embolization is a critical option for patients in whom endoscopic therapy fails or is unfeasible:

- **Embolization Approaches:** Superselective catheterization of the bleeding vessel is followed by delivery of embolic agents such as coils, polyvinyl alcohol particles, or gelfoam to arrest hemorrhage. Embolization is effective in 60–90% of cases, particularly in overt, ongoing bleeding where localization is achievable.
- **Risks and Limitations:** Embolization carries risks including bowel ischemia, infarction, and inadvertent non-target embolization. Its success heavily relies on real-time identification of active bleeding during angiography, which may not always be possible in intermittent bleeding scenarios.

5.3 Medical Management

For patients with diffuse angiodysplasia or recurrent bleeding despite intervention, pharmacologic therapy plays a vital role:

- **Octreotide:** A somatostatin analogue with vasoconstrictive and antiangiogenic properties. The OCEAN study and other RCTs have shown that long-acting octreotide significantly reduces transfusion requirements and bleeding recurrence in patients with GI angiodysplasia. It can be administered subcutaneously (daily) or intramuscularly (monthly depot).
- **Thalidomide:** Exerts antiangiogenic effects via downregulation of VEGF and bFGF. Clinical studies demonstrate a reduction in bleeding episodes; however, its use is limited by teratogenicity, peripheral neuropathy, and fatigue. It is often reserved for refractory cases.
- **Bevacizumab:** A monoclonal antibody targeting VEGF, with anecdotal evidence and small case series supporting its use in refractory GI angiodysplasia, especially in patients with concurrent malignancies or those intolerant to thalidomide. Its use is off-label and requires careful patient selection.[101-105]

5.4 Surgical Options

Surgery is a last-resort intervention, typically considered when bleeding is refractory to all other treatments or when the source is well-localized but inaccessible endoscopically:

- **Intraoperative Enteroscopy (IOE):** Conducted during laparotomy, this technique allows real-time enteroscopic evaluation and therapeutic intervention throughout the

small bowel. It is highly effective but invasive, requiring surgical and endoscopic expertise.

- **Segmental Resection:** If the bleeding source is localized and focal, resection of the involved bowel segment offers definitive management. However, its use must be balanced against the risks of anesthesia and postoperative complications, particularly in older patients.
- **Valve Replacement in Heyde's Syndrome:** In patients with aortic stenosis-associated angiodysplasia and acquired vWD, aortic valve replacement can resolve the bleeding diathesis. Both surgical and transcatheter aortic valve replacement (TAVR) approaches have been shown to normalize vWF multimers and reduce GI bleeding recurrence.[106-110]

Table 6: Therapeutic Options for Vascular Small Bowel Bleeding

Modality	Indications	Mechanism/Approach	Advantages	Limitations/Risks	Reference
Argon Plasma Coagulation	Angiodysplasia, superficial lesions	Non-contact thermal coagulation	Effective, widely available	Limited depth, not for large vessels	111
Clipping	Dieulafoy lesions, active bleeding	Mechanical compression	Immediate hemostasis	May dislodge; technical precision needed	112
Sclerotherapy	Ectopic varices	Chemical-induced thrombosis	Useful for variceal bleeding	Risk of perforation, less common usage	113
Embolization	Refractory bleeding, unstable patient	Catheter-directed vessel occlusion	Minimally invasive, high success rate	Risk of ischemia, needs active bleeding	114
Octreotide	Diffuse angiodysplasia	Antiangiogenic, splanchnic vasoconstriction	Reduces recurrence and transfusions	Requires long-term use	115
Thalidomide	Refractory angiodysplasia	VEGF inhibition	Oral agent, effective in trials	Teratogenic, neuropathy	116
Bevacizumab	Off-label, selected refractory cases	VEGF neutralization	Potent antiangiogenic action	Expensive, off-label, limited evidence	117
IOE + Resection	Localized source, failed other modes	Surgical and intraoperative endoscopy	Definitive treatment	Invasive, operative risk	118
Valve Replacement	Heyde's syndrome	Restores vWF multimers	Treats underlying cause	Cardiac procedure risks	119

6. Special Populations

Management of vascular small bowel bleeding (VSBB) must be tailored for specific patient populations that carry unique risks and therapeutic considerations. Among these, patients with chronic kidney disease (CKD), hereditary hemorrhagic telangiectasia (HHT), and those on anticoagulants or antiplatelet agents require specialized diagnostic and treatment strategies.[120]

6.1 Management in Chronic Kidney Disease (CKD)

Patients with CKD are particularly prone to bleeding from angiodysplasia due to several interrelated pathophysiological mechanisms:

- **Uremic Platelet Dysfunction:** Impaired platelet aggregation and adhesion due to uremic toxins lead to increased mucosal bleeding risk.
- **Vascular Fragility and Anemia:** Chronic anemia and endothelial dysfunction in CKD contribute to submucosal vessel rupture and persistent oozing.
- **Comorbidities:** Many CKD patients also suffer from diabetes, hypertension, and cardiovascular disease, compounding bleeding risk and complicating treatment.[121-125]

Management Strategies:

- First-line treatment includes endoscopic modalities such as APC.
- Long-acting octreotide is often effective for recurrent bleeding and may reduce transfusion requirements.
- Thalidomide can be considered in refractory cases but must be used cautiously due to nephrotoxicity and systemic side effects.
- Dialysis patients benefit from careful volume and blood pressure management to reduce mucosal ischemia.[126-130]

6.2 HHT Patients: Screening and Follow-up

Hereditary hemorrhagic telangiectasia (HHT) is a genetic condition associated with widespread mucocutaneous and visceral telangiectasias, including in the GI tract:

- **Screening:** All patients with HHT should undergo baseline screening with video capsule endoscopy (VCE) by age 50 or earlier if symptomatic. Repeated assessments every 2–3 years are advised if anemia persists without another identifiable cause.
- **Management:** Endoscopic ablation (APC or laser therapy) is first-line. Refractory bleeding can be addressed with medical therapy (octreotide or bevacizumab). Iron supplementation and transfusions are often needed.
- **Multidisciplinary Care:** Genetic counseling, coordination with hepatologists and pulmonologists (for AVMs in liver and lung), and periodic hemoglobin monitoring are critical.[131-140]

6.3 Patients on Anticoagulants or Antiplatelets

The widespread use of anticoagulants (e.g., warfarin, DOACs) and antiplatelet agents (e.g., aspirin, clopidogrel) has increased the prevalence and severity of GI bleeding, including from vascular lesions:

- **Risk Amplification:** These agents exacerbate bleeding from even minor vascular abnormalities, particularly angiodysplasia and Dieulafoy lesions.
- **Peri-Endoscopic Management:**
  - Temporary discontinuation of anticoagulants may be necessary in acute bleeding episodes, with bridging therapy considered for high-risk thrombotic patients.
  - Direct oral anticoagulants (DOACs) can be resumed 48–72 hours post-endoscopic intervention once hemostasis is secured.
- **Secondary Prevention:** If long-term anticoagulation is unavoidable, concurrent use of proton pump inhibitors and iron supplementation may help mitigate complications. Some patients may benefit from long-acting somatostatin analogues to reduce recurrence.[141-150]

Table 7: Management Strategies in Special Populations with Vascular Small Bowel Bleeding

Population	Risk Factors	Interventions	Monitoring/Follow-up	Reference
CKD	Platelet dysfunction, anemia, uremia	APC, octreotide, thalidomide	Hemoglobin, dialysis optimization	151
HHT	Genetic AVMs, mucosal fragility	VCE, APC, bevacizumab, iron therapy	VCE every 2–3 yrs, genetic screening	152
Anticoagulant/Antiplatelet users	Drug-induced bleeding potentiation	Hold meds temporarily, endoscopic therapy	Restart anticoagulation after 48–72 hrs	153

7. Future Directions and Research Gaps

As diagnostic and therapeutic technologies continue to evolve, several emerging directions promise to transform the management of vascular small bowel bleeding (VSBB). These innovations aim to improve early detection, personalize therapy, and reduce recurrence and healthcare burden.

7.1 AI-Based Bleeding Detection in Capsule Endoscopy

Artificial intelligence (AI) and machine learning (ML) algorithms are increasingly being integrated into gastrointestinal diagnostics. One promising application is the automated detection of bleeding lesions in video capsule endoscopy (VCE).

- **Benefits:** AI can significantly reduce the time required to review capsule images, increase diagnostic yield, and minimize interobserver variability.
- **Current Progress:** Several AI models have demonstrated over 90% sensitivity in detecting bleeding and vascular lesions in retrospective datasets. Ongoing trials are validating these algorithms in real-time clinical practice.
- **Challenges:** Integration with existing endoscopy software, standardization across platforms, and clinician training remain key hurdles.[154-160]

7.2 Genetic Testing in Unexplained or Recurrent VSBB

In patients with recurrent bleeding without an identifiable source, especially younger individuals or those with family history, genetic testing is emerging as a valuable tool.

- **Applications:** Identification of mutations in genes such as ENG, ACVRL1 (associated with HHT), or other angiogenesis-related genes may reveal occult hereditary vascular syndromes.
- **Clinical Utility:** Genetic insights can guide long-term screening protocols, risk stratification, and even therapeutic decisions.

7.3 Personalized Therapy Based on Angiogenic Profiles

Advancements in molecular diagnostics have enabled profiling of angiogenic biomarkers such as VEGF, angiopoietin, and bFGF in patients with VSBB.

- **Tailored Treatment:** Patients with elevated VEGF levels may benefit more from anti-angiogenic therapies like octreotide, thalidomide, or bevacizumab.
- **Future Potential:** Development of blood-based assays to assess angiogenic status in real time could lead to point-of-care decision-making and improved therapeutic efficacy.[161-170]

7.4 Development of Novel Biologics and Minimally Invasive Tools

Ongoing innovation is focused on enhancing therapeutic options with increased efficacy and safety:

- **Next-Generation Biologics:** Monoclonal antibodies and small molecule inhibitors with improved specificity for aberrant vascular pathways are under development.
- **Endoscopic Advancements:** Robotic-assisted enteroscopy, ultra-thin scopes, and magnetically guided capsule endoscopy are being explored to enhance reach, maneuverability, and therapeutic precision.
- **Minimally Invasive Imaging:** Integration of real-time fluorescent markers or contrast-enhanced capsule technologies may soon allow active bleeding and lesion characterization in a single procedure.[171-180]

Table 8: Future Directions in the Management of Vascular Small Bowel Bleeding

Innovation Area	Description	Clinical Impact	Reference
AI in Capsule Endoscopy	Automated bleeding detection, lesion classification	Reduced review time, improved accuracy	181
Genetic Testing	Identification of inherited vascular syndromes	Personalized screening and long-term care	182
Angiogenic Biomarker Profiling	VEGF, bFGF assays to guide therapy	Precision medicine, improved drug response	183
Novel Biologics	New antiangiogenic drugs (e.g., VEGF inhibitors)	Targeted therapy with fewer side effects	184
Advanced Endoscopic Tools	Robotic scopes, magnetic capsules	Deeper access and less invasive intervention	185

8. Discussion

Vascular small bowel bleeding (VSBB) represents a diagnostically complex yet increasingly manageable subset of gastrointestinal (GI) bleeding. The convergence of endoscopic innovation, high-resolution imaging, and pharmacologic advancements has transformed the diagnostic and therapeutic landscape. This review underscores the importance of integrating these modalities in a patient-specific, algorithm-driven framework.The predominance of angiodysplasia as the leading cause of VSBB particularly in the elderly and those with systemic comorbidities highlights the aging population's vulnerability. Risk factors such as chronic kidney disease (CKD), aortic stenosis, and left ventricular assist devices (LVADs) contribute to both lesion development and bleeding recurrence. Notably, acquired von Willebrand disease in these populations exacerbates the hemorrhagic risk, suggesting that a pathophysiologic understanding is essential for targeted therapy.[186-190]

Dieulafoy lesions and ectopic varices, although less common, present with life-threatening hemorrhage, necessitating rapid localization and intervention. The emergence of video capsule endoscopy (VCE) as a frontline diagnostic modality has drastically improved lesion detection, especially when performed early during active bleeding. However, its diagnostic yield is offset

by retention risks in patients with suspected strictures indicating a need for pre-procedural patency assessment.Device-assisted enteroscopy (DAE), particularly double-balloon enteroscopy (DBE), has emerged as the most definitive diagnostic and therapeutic tool for deep small bowel lesions. Yet, accessibility, procedural complexity, and operator dependence limit its widespread application. In this context, newer modalities like motorized spiral enteroscopy (MSE) and robotic-assisted scopes show promise in increasing procedural efficiency and reach.Radiologic tools such as CT angiography (CTA) and CT enterography (CTE) remain indispensable, particularly for hemodynamically unstable patients or those with occult bleeding. However, the spatial and temporal limitations of nuclear scintigraphy and the requirement for active bleeding during angiography necessitate a hybrid diagnostic approach.Therapeutically, argon plasma coagulation (APC) remains the mainstay for angiodysplasia, while clipping and sclerotherapy are reserved for focal or variceal lesions. Refractory or diffuse bleeding necessitates pharmacologic strategies most notably somatostatin analogues like octreotide, thalidomide, or even biologics such as bevacizumab. The clinical utility of these agents is increasingly being stratified by angiogenic profiles, marking a transition toward precision medicine.Surgical interventions, including intraoperative enteroscopy and segmental resection, remain pivotal for patients with localized, treatment-refractory lesions. Importantly, in patients with Heyde's syndrome, valve replacement not only addresses the cardiac etiology but also ameliorates the GI bleeding diathesis offering a curative pathway.Special populations such as CKD patients, HHT carriers, and those on antithrombotic agents present unique diagnostic and therapeutic challenges. In such cases, management must be nuanced balancing bleeding control with systemic disease burden and thrombotic risk.Emerging technologies offer considerable promise. Artificial intelligence (AI)-assisted capsule reading reduces interobserver variability and accelerates diagnostic timelines. Genetic testing and angiogenic biomarker profiling enable risk stratification and therapeutic targeting, while novel biologics and minimally invasive tools such as magnetically guided capsules and robotic enteroscopes enhance the safety and efficacy of intervention.Nonetheless, significant gaps remain. Prospective randomized controlled trials (RCTs) evaluating combination therapy, long-term efficacy of biologics, and cost-effectiveness of AI-guided diagnostics are urgently needed. Additionally, integration of genetic insights into clinical algorithms and real-time molecular diagnostics represents the next frontier in individualized care.191-200

9. Conclusion

Vascular small bowel bleeding (VSBB) remains a challenging clinical entity due to its diverse etiologies, intermittent presentation, and deep anatomical location. However, the integration of advanced endoscopic, radiologic, and pharmacologic modalities has significantly improved the diagnostic accuracy and therapeutic outcomes. Angiodysplasia, the most common cause of VSBB, particularly in the elderly and comorbid populations, necessitates a tailored, often multimodal management approach.Early use of video capsule endoscopy and device-assisted

enteroscopy alongside computed tomography angiography in unstable cases enables timely localization and intervention. Therapeutically, argon plasma coagulation, sclerotherapy, and endoscopic clipping form the first-line endoscopic arsenal, while pharmacologic agents such as octreotide, thalidomide, and bevacizumab offer promise in refractory or diffuse cases. Surgical approaches, including segmental resection and intraoperative enteroscopy, remain valuable in highly selected scenarios.Emerging innovations such as AI-assisted capsule reading, genetic testing, and biomarker-driven personalized therapies represent the future of precision medicine in VSBB. However, challenges persist in standardizing protocols, improving access to advanced technologies, and conducting high-quality clinical trials to validate novel interventions.Ultimately, the management of VSBB must evolve toward a patient-specific, algorithm-driven model that integrates clinical context, lesion type, and resource availability supported by continuous innovation and interdisciplinary collaboration.

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