

Small bowel intestinal bleeding

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Definitions

- Bleeding between the ampulla of Vater and the ileocecal valve
- Relatively uncommon

~5–10% of gastrointestinal bleeding

Definitions

- Potential small intestine bleeding
normal upper and lower endoscopy
- Overt small intestine bleeding
melaena or haematochezia with source identified in small intestine
- Occult small intestine bleeding
iron-deficiency anaemia with source identified in small intestine
- Obscure GI bleeding
no source of bleeding after upper and lower endoscopies, video capsule endoscopy and radiography

Rare causes

Henoch–Schoenlein purpura

Small bowel varices and/or portal hypertensive enteropathy

Amyloidosis

Blue rubber bleb nevus syndrome

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

Hemato-bilia

Aorto-enteric fistula

Hemosuccus entericus

Under 40 Years

Over 40 Years

Age 40
Threshold

Inflammatory
Bowel Disease

Meckel's
Diverticulum

Polyposis
syndromes

Shared Culprits

Dieulafoy's lesions
Neoplasia

Angioectasia

NSAID ulcers

Clues

- Angiodysplasia

Aortic stenosis (Heyde's Syndrome)

Left ventricular assist devices

- Over-the-counter NSAIDS
- Family or personal history of cancer
- Abdominal aortic aneurysm repair

Aorto-enteric fistula



Hereditary Haemorrhagic
Telangiectasia (HHT)

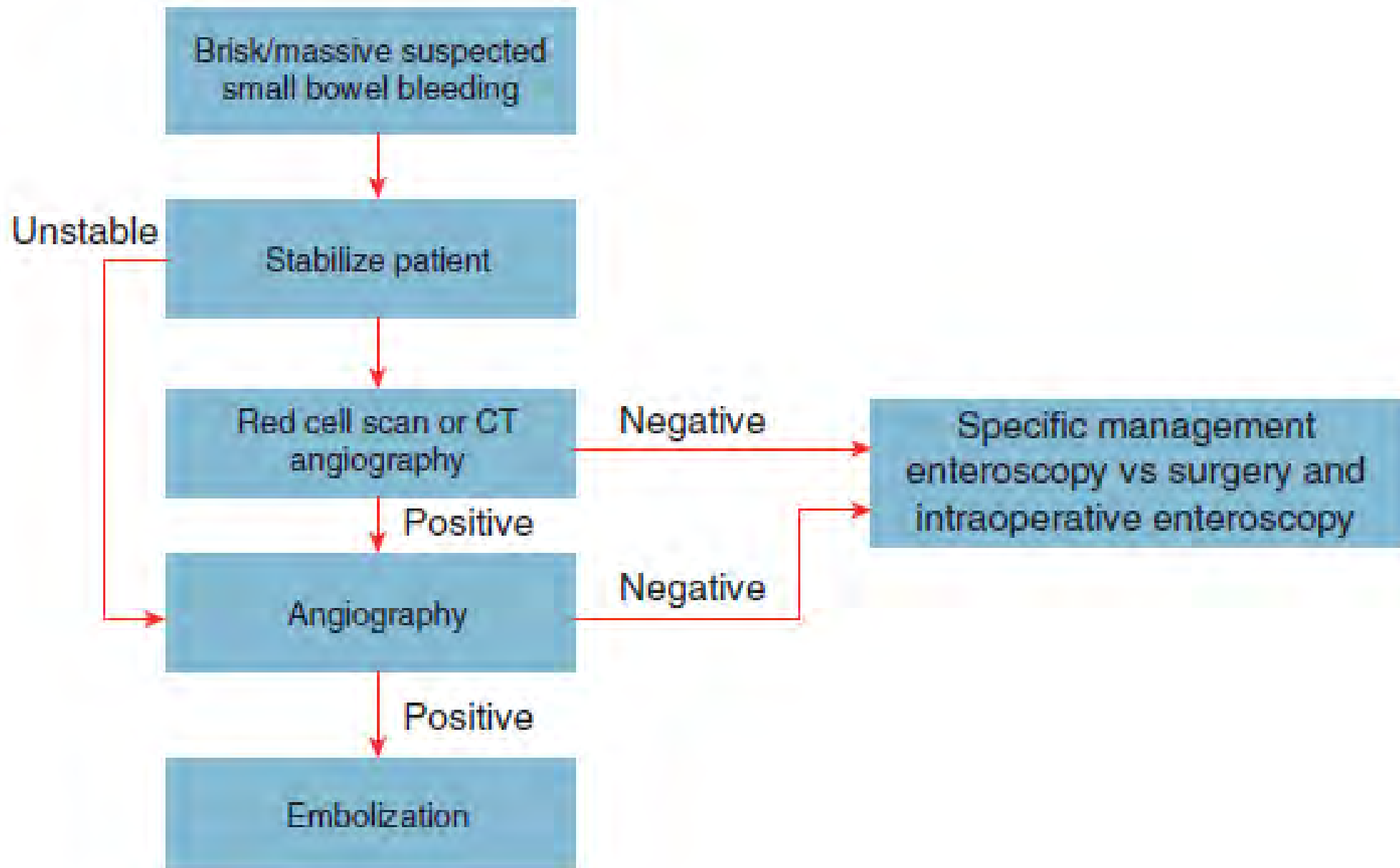


Peutz-Jeghers
Syndrome



Blue Rubber Bleb
Nevus Syndrome

Approach to work-up



Suspected small bowel bleeding

consider risks and benefits of investigations in those with major comorbidities and limited performance status

Up to 25% missed lesions

Video Capsule Endoscopy (VCE)

- First line evaluation of small bowel

potential to visualize entire small bowel

diagnostic yield up 62%

greatest yield within 48 hours

- Non-invasive, low complication rate

capsule retention (1.5% but up to 13% in Crohn's)

perforation (rare)

Limitations

- Limitations

lack of therapeutic capabilities

inability to control movement

difficulty in localizing the lesion

transit times useful in guiding the optimal route of device assisted endoscopy i.e. oral vs rectal

Time to lesion/time to caecum

<75% = oral

>75% = rectal



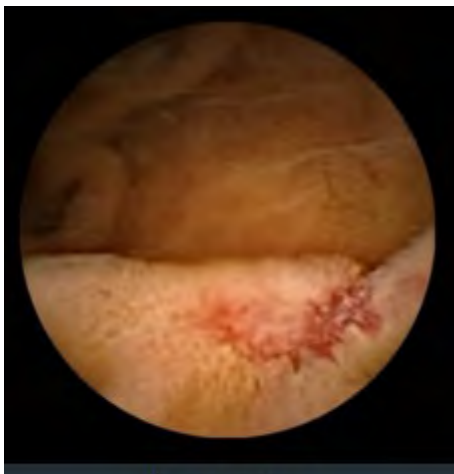
Feature	PillCam SB3	MiroCam MC2000	CapsoCam Plus	OMOM HD	EndoCapsule
Company	Medtronic	IntroMedic	CapsoVision	Jinshan Science and Technology	Olympus
Size (mm)	11.4×26.2	10.8×30	11×31	11×25	11×26
Weight (g)	3	3.25–4.70	3.8	4.5	3.3
No. of cameras	1	2 (dual-headed)	4 (side of capsule)	1	1
Field of view (°)	156	170 (×2)	360 (panoramic imaging)	172	160
Battery life (hr)	8–15	12	15	10	12
Transmission type	RF telemetry	Human body communication	N/A	RF telemetry	RF telemetry
Real-time viewing	Yes	Yes	No	Yes	Yes
Storage type	External receiver	External receiver	Onboard storage (capsule retrieval required)	External receiver	External receiver
Frame velocity (frames/s)	2–6	3 fps per camera, total 6 fps	12–20	2–6	2

RF, radio frequency; N/A, not available; fps, frames per second.

Best diagnostic yield (40% vs 35%) but longer reading time



Active Bleeding



Angiodysplasia



NSAID Enteropathy



Stenosis-NSAID Enteropathy



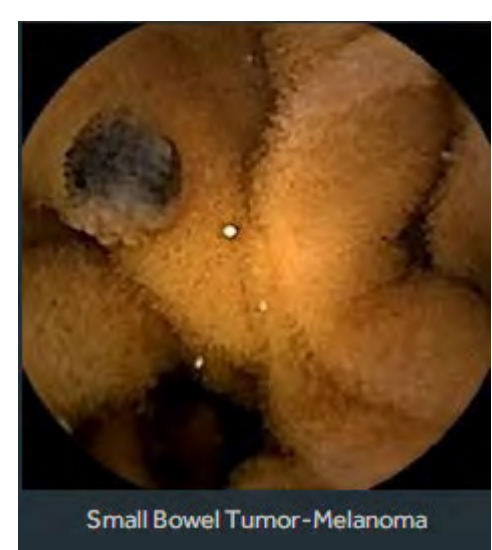
Small Bowel Varices



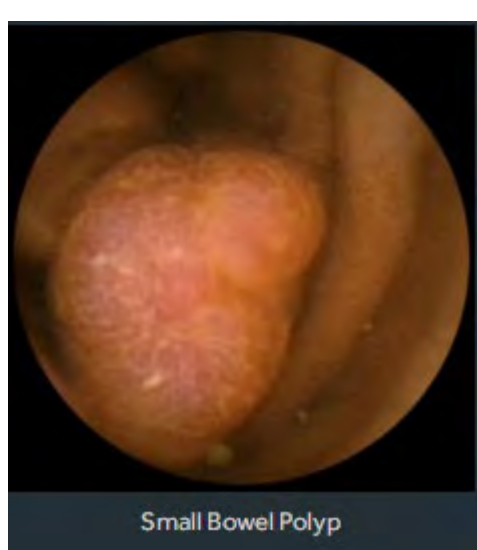
Angiodysplasia



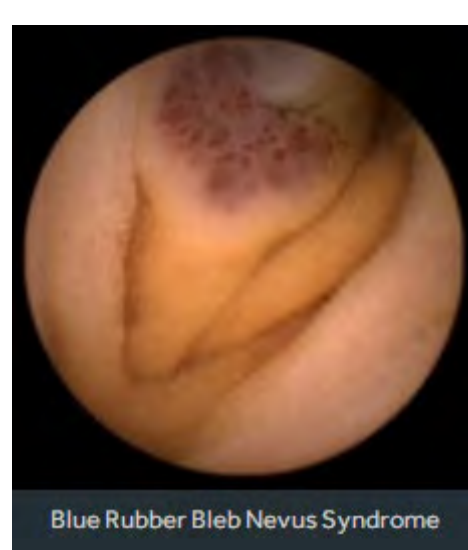
NSAID's Enteritis with Bleeding



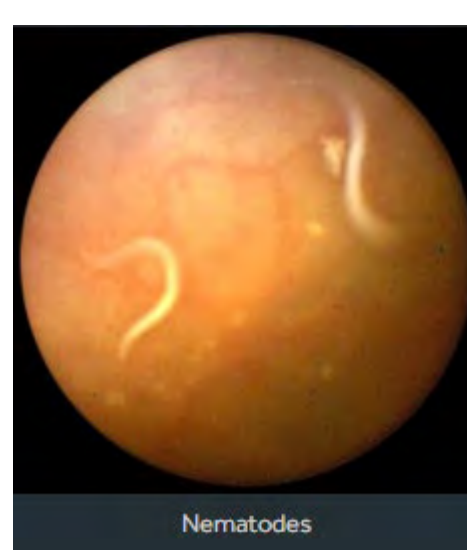
Small Bowel Tumor-Melanoma



Small Bowel Polyp



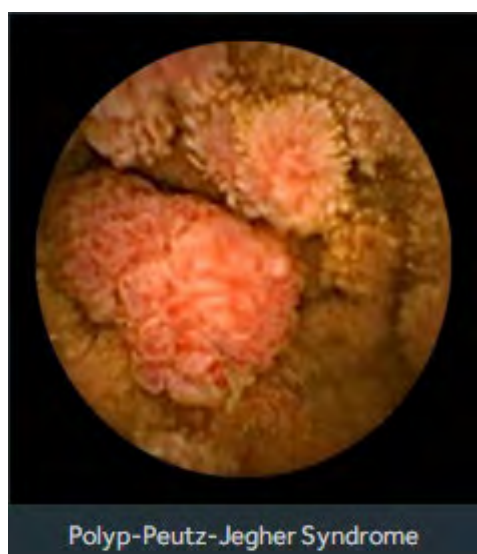
Blue Rubber Bleb Nevus Syndrome



Nematodes



Mass-Tumor



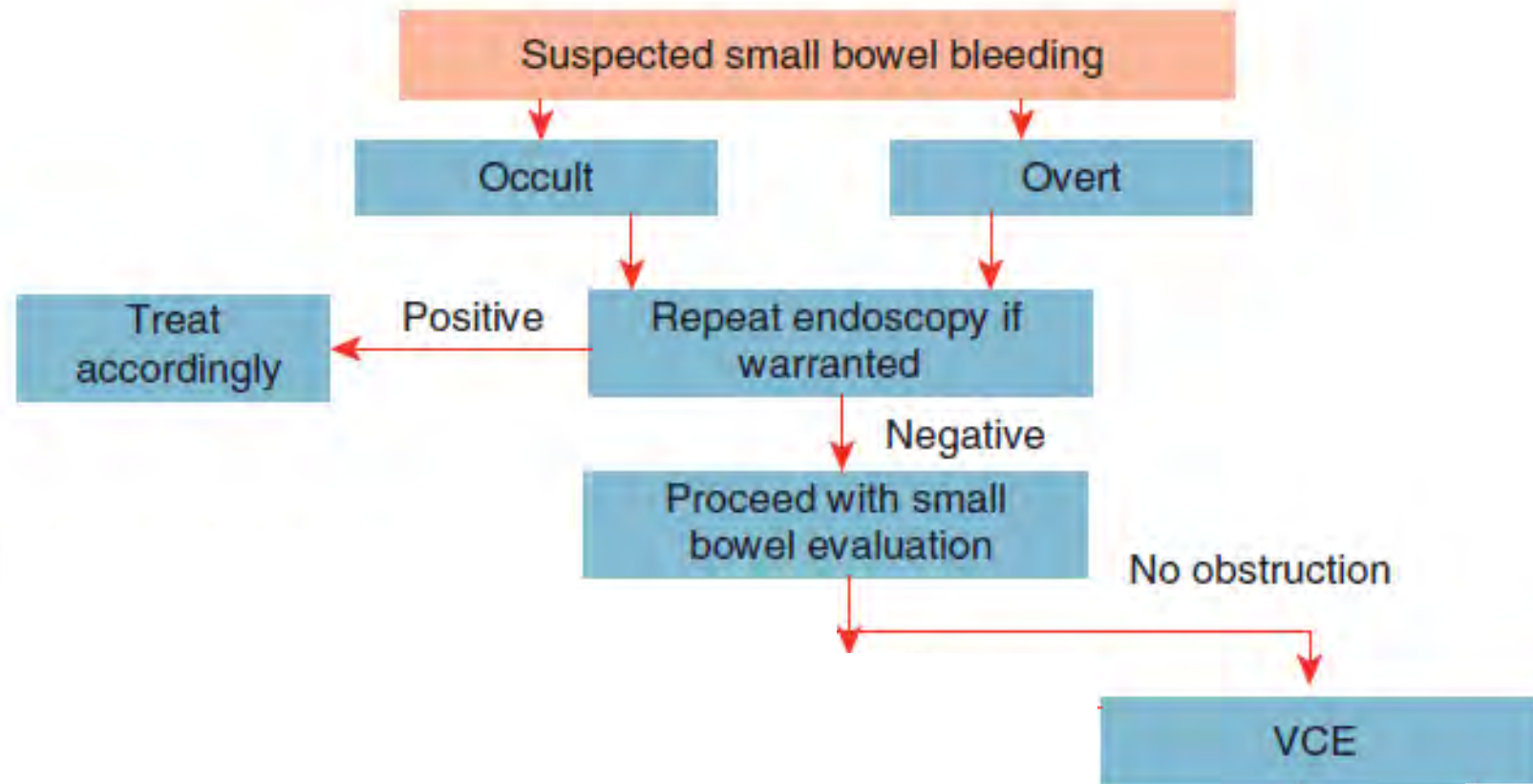
Polyp-Peutz-Jegher Syndrome



Venous Structure-Blue Rubber Bleb Nevus

New advances

- Flexible spectral imaging colour enhancement
- AI-assisted
 - higher sensitivity than human (99.9% vs 89%)
 - comparable specificity
 - reduced reading time (average 4.7 vs. 56.7 minutes)



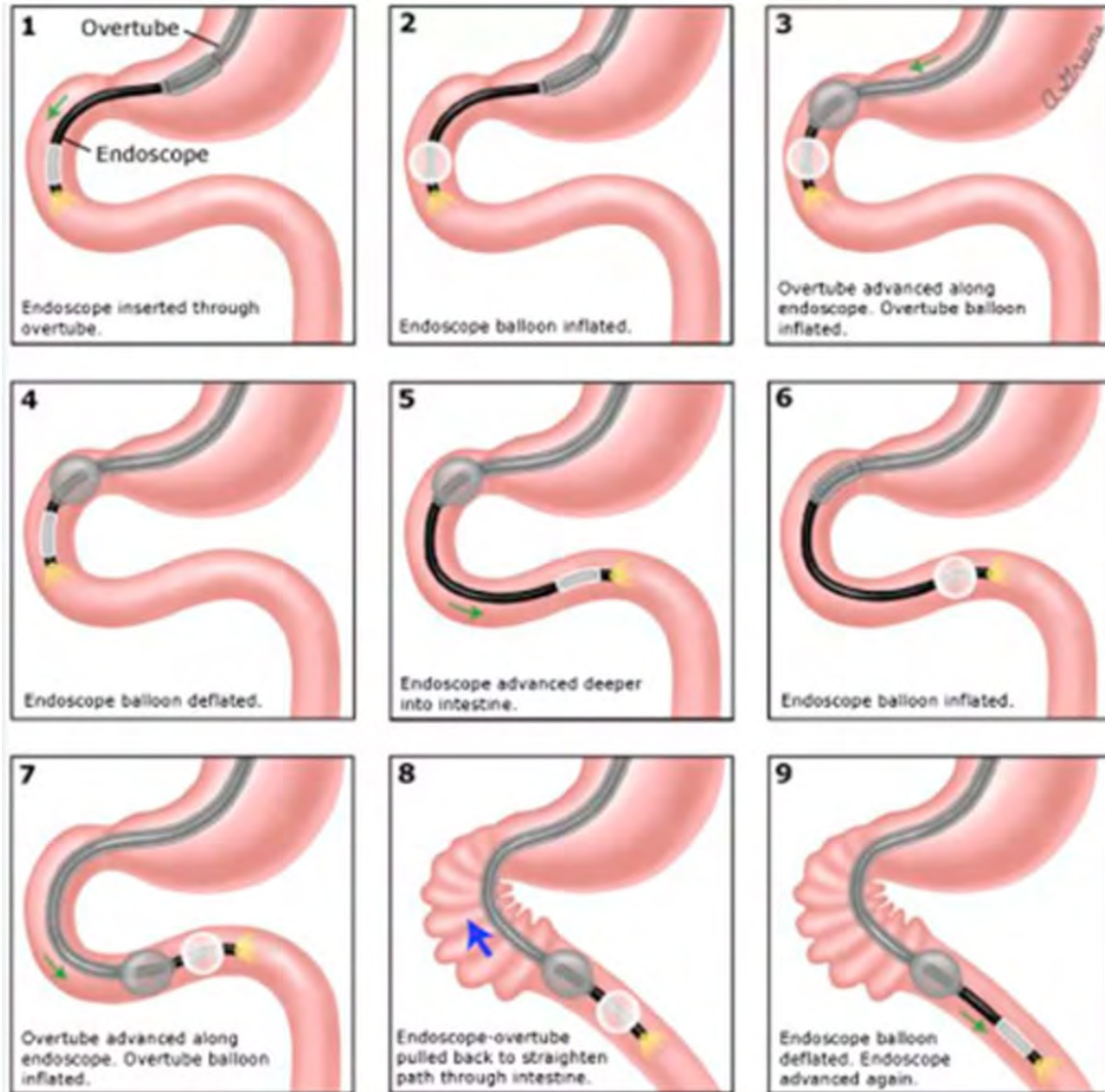
Deep enteroscopy

- Push enteroscopy
- Double ballon (DBE)
- Single ballon (SBE)
- Spiral (SE)

Push enteroscopy

- Enteroscopy past ligament of Treitz
- Up to 80 cm of jejunum

DBE



- Endoscope with overtube

Balloon on end of scope & overtube

Advancement cycles

Up to 360 cm beyond pylorus or 140 cm beyond ileocecal valve

- Diagnostic yield up to 80%

Higher if positive VCE

- Successful interventions up to 73%

- Latex

DBE

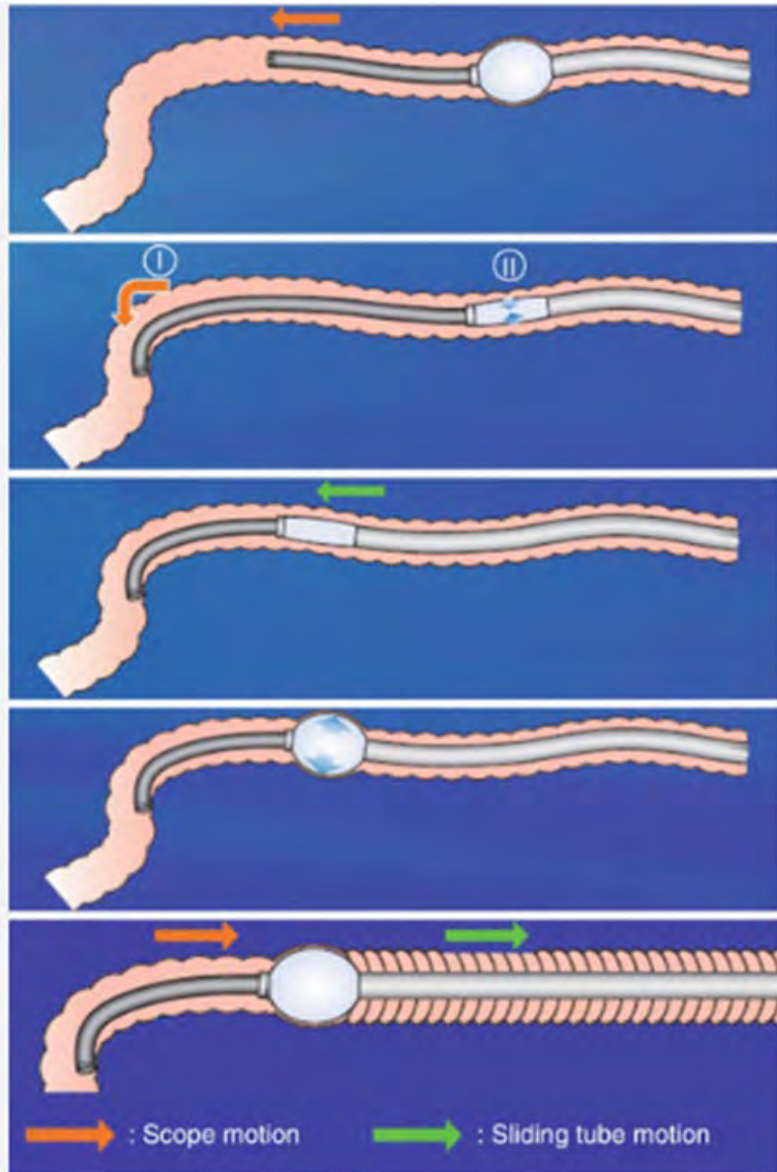
- Overall complication 1.2%

Pancreatitis

Ileus

Perforation

SBE



- Single balloon
- Tip of the scope as an anchor
- Advancement cycles
- Less depth than DBE
- Silicone

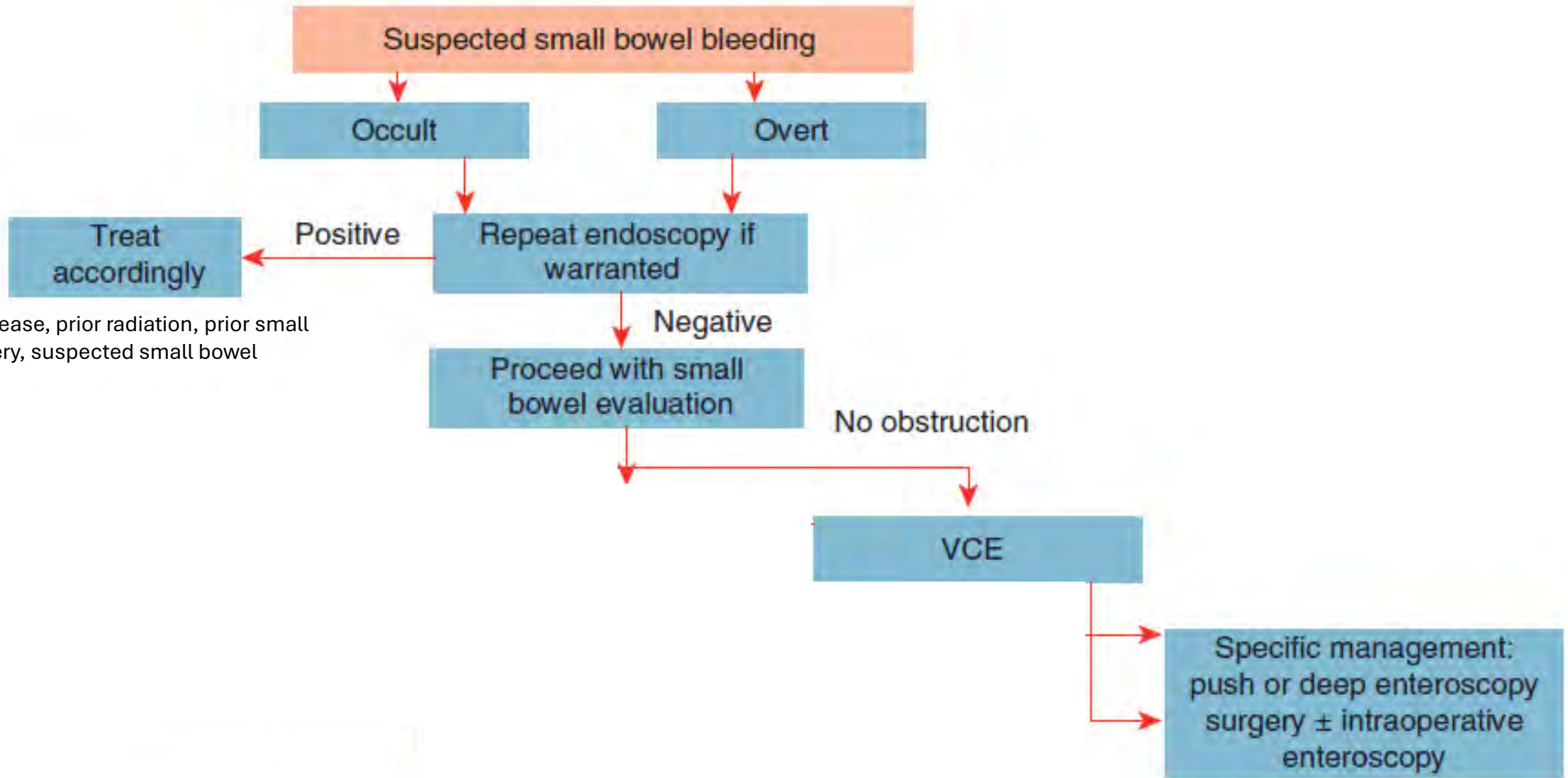
SE



- Overtube with an outer raised spiral ridge at its distal end
- Clockwise motion of the ridged overtube to draw the enteroscopy forward
- Faster than DBE and SBE but less depth
- Orally only

Intraoperative endoscopy

- Orally, rectally or via an enterotomy
- High complication rate

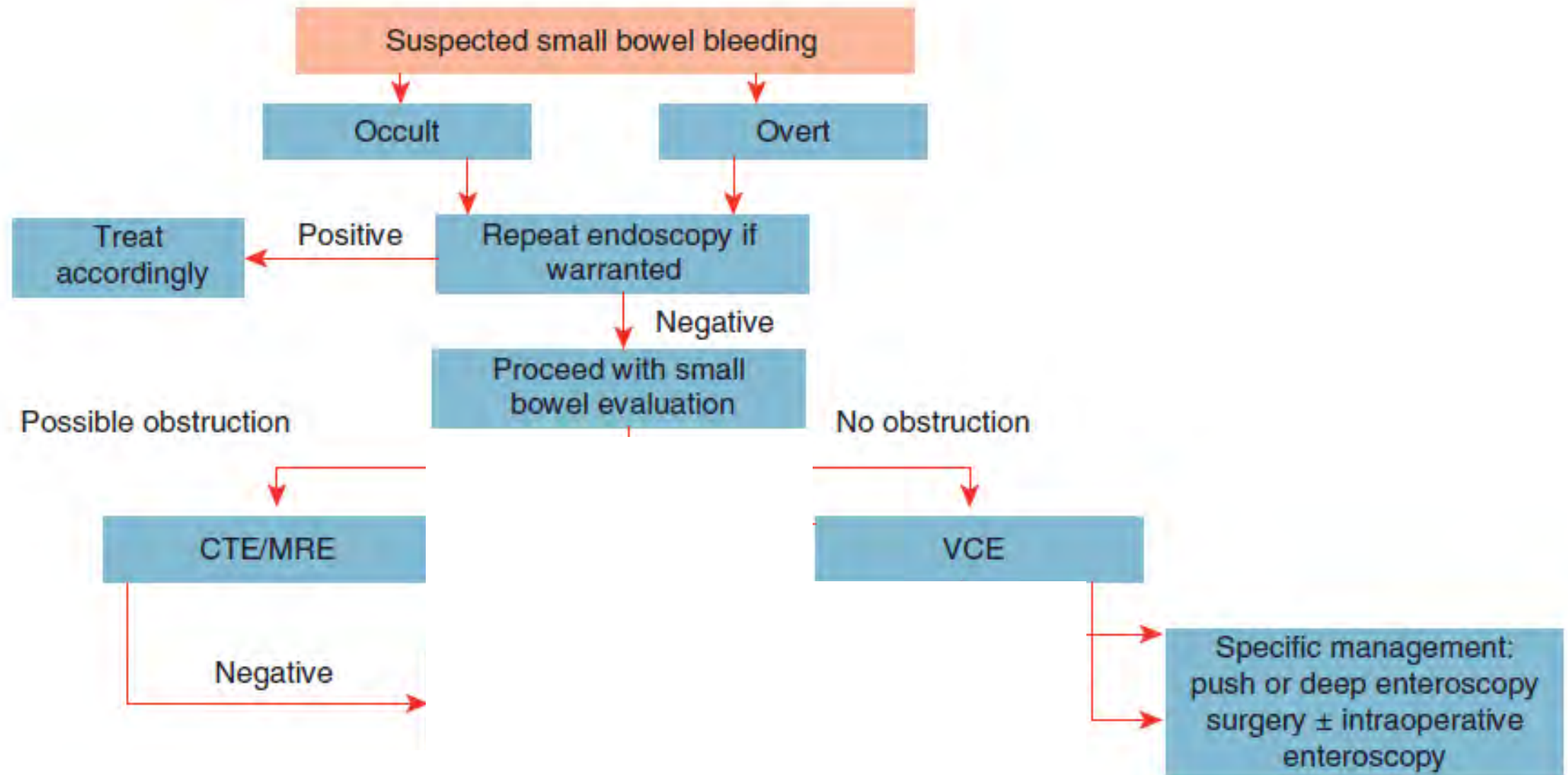


Crohn's Disease, prior radiation, prior small bowel surgery, suspected small bowel obstruction

Radiology

- Barium follow-through superseded
- CTE
- MRE

superior for detection of mural-based small bowel masses



Conservative management

- No source of bleeding found on VCE

Manage with iron

Wait and see

- Stop anticoagulation only if risk benefit ratio unfavourable

Angiodysplasia

- Small vascular lesions does not always need treatment

Treatment vs nontreatment ? difference

Up to 50% recurrence after treatment

Argon plasma coagulation treatment of choice

Angiodysplasia

- Hormonal therapy

No role

GI BLEEDING

Standard of Care Versus Octreotide in Angiodysplasia-Related Bleeding (the OCEAN Study): A Multicenter Randomized Controlled Trial



inhibition of angiogenesis
decrease in splanchnic flow
increase in vascular resistance
improved platelet aggregation

Variable	Octreotide	Standard of care	Difference	P value
	(n = 31)	(n = 31)		
Primary outcome^a				
Transfusion units	11.0 (5.5–16.5)	21.2 (15.7–26.7)	10.2 (2.4–18.1)	.012
RBC transfusion	8.2 (3.2–13.2)	16.8 (11.8–21.8)	8.6 (1.4–15.7)	
Intravenous iron infusions	2.8 (1.3–4.3)	4.6 (3.1–6.0)	1.8 (0.3–3.9)	
Treatment response				
Transfusion decrease \geq 50%	19/31 (61)	6/31 (19)	13/31 (42)	
Decrease 100%	5/19 (26)	1/6 (17)		
Concomitant care				
Required concomitant care	4/31 (13)	14/31 (45)		
Endoscopic APC	3/4 (75)	7/14 (50)	4/10 (40)	
Discontinue antithrombitics	1/4 (25)	4/14 (29)	3/10 (30)	
Start other treatment	0/4 (0)	7/14 (57)	7/10 (70)	
Endoscopic procedures¹				
Applied interventions	0.3 (-0.1 to 0.7)	1.2 (0.8–1.6)	0.9 (0.3–1.5)	
Applied interventions	0.1 (-0.1 to 0.4)	0.7 (0.4–0.9)	0.5 (0.2–0.9)	
Healthcare utilization²				
Bleeding episodes	5.3 (2.9–7.6)	8.5 (6.1–10.8)	3.2 (-0.2 to 6.6)	
Hospital admissions	0.5 (-0.2 to 1.1)	1.8 (1.2–2.5)	1.3 (0.4–2.3)	
Length of stay, <i>d</i>	2.3 (-0.4 to 5.0)	6.0 (3.3–8.7)	3.7 (-0.2 to 7.6)	
Emergency care	0.3 (-0.4 to 0.9)	1.6 (0.9–2.2)	1.3 (0.4–2.2)	
Ambulatory care	4.5 (2.5–6.5)	6.9 (4.9–8.9)	2.4 (-0.4 to 5.2)	
Biochemical analyses				
Hemoglobin, <i>mmol/L</i>	7.1 (6.6–7.6)	6.8 (6.3–7.2)	0.3 (-0.3 to 1.0)	
Ferritin, <i>ug/L</i>	199 (83–316)	180 (69–289)	20 (-140 to 180)	
Patient-reported outcome measures³				
Fatigue (MFI-20)	56.0 (49.3–62.8)	69.4 (63.0–75.8)	13.4 (4.1–22.6)	
Physical component score (SF-36) ^b	41.5 (37.6–65.3)	36.5 (32.8–40.2)	5.0 (-0.4 to 10.4)	
Physical functioning	58.4 (48.6–68.2)	39.2 (30.0–48.4)	19.2 (5.7–32.7)	
Role-physical	45.2 (30.1–60.4)	31.0 (16.6–45.4)	14.3 (-6.7 to 35.2)	
Bodily pain	69.9 (58.5–81.3)	62.3 (51.6–73.1)	7.6 (-8.1 to 23.3)	
General health	49.8 (41.1–58.6)	37.4 (29.1–45.6)	12.4 (0.4–24.5)	
Mental component score (SF-36) ^b	49.1 (44.6–53.6)	41.9 (37.6–46.2)	7.2 (1.0–13.4)	
Vitality	53.3 (44.7–62.0)	38.8 (30.6–47.0)	14.6 (2.6–26.5)	
Social functioning	73.5 (61.6–85.4)	57.7 (46.5–69.0)	15.8 (-0.7 to 32.2)	
Role-emotional	59.3 (43.5–75.1)	41.1 (26.1–56.1)	18.2 (-3.5 to 40.0)	
Mental health	75.8 (67.1–84.5)	62.2 (54.0–70.5)	13.6 (1.6–25.6)	
Adverse events				
Total number	22/31 (71)	21/31 (68)	1/31 (3)	
Drug-related	20/22 (91)	7/21 (33)		
Gastrointestinal	15/20 (75)	6/7 (86)		
Pain administration	9/20 (45)	0/7 (0)		
Glucose intolerance	3/20 (15)	2/7 (29)		
Anemia-related	12/22 (55)	20/21 (95)		
Other	6/22 (27)	2/21 (10)		

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Thalidomide for Recurrent Bleeding Due to Small-Intestinal
Angiodysplasia

Table 2. Primary and Secondary End Points.

End Point	100-mg Thalidomide Group (N=51)	50-mg Thalidomide Group (N=49)	Placebo Group (N=50)	Relative Risk, 100-mg Group vs. Placebo Group (95% CI)*	Relative Risk, 50-mg Group vs. Placebo Group (95% CI)*
Primary end point: effective response					
According to worst-case principle — no./total no. (%)†	35/51 (68.6)	25/49 (51.0)	8/50 (16.0)	4.29 (2.21 to 8.31)	3.19 (1.60 to 6.37)
Multiple imputation — (%)‡	75.5	55.9	14.0	5.42 (2.50 to 11.74)	4.02 (1.83 to 8.84)
Excluding occult bleeding episodes — no./total no. (%)	38/51 (74.5)	32/49 (65.3)	9/50 (18.0)	4.14 (2.24 to 7.64)	3.63 (1.94 to 6.78)
Including only bleeding episodes that resulted in blood transfusion or hospitalization — no./total no. (%)	43/49 (87.8)	35/44 (79.5)	16/44 (36.4)	2.41 (1.61 to 3.62)	2.19 (1.44 to 3.32)
Secondary end points					
Cessation of bleeding without rebleeding during the first follow-up period — no./total no. (%)	26/51 (51.0)	16/49 (32.7)	2/50 (4.0)	12.75 (3.19 to 50.88)	8.15 (1.98 to 33.64)
Receipt of a blood transfusion during the first follow-up period — no./total no. (%)	9/51 (17.6)	12/49 (24.5)	31/50 (62.0)	0.28 (0.15 to 0.54)	0.39 (0.23 to 0.68)
Hospitalization because of bleeding during the first follow-up period — no./total no. (%)	14/51 (27.5)	17/49 (34.7)	37/50 (74.0)	0.37 (0.23 to 0.60)	0.47 (0.31 to 0.71)
Median change in transfusion volume of red cells (IQR) — units§	-2.0 (-3.5 to -2.0)	-3.0 (-6.0 to -1.0)	0.0 (-2.0 to 1.0)	-2.43 (-3.49 to -1.37)	-3.32 (-4.92 to -1.72)
Median change in duration of bleeding (IQR) — days§	-3.8 (-5.2 to -1.3)	-2.4 (-5.3 to -0.5)	0.4 (-0.2 to 1.2)	-3.63 (-4.21 to -2.51)	-3.05 (-3.92 to -2.17)
Mean change in hemoglobin level (g per liter)¶	30.2±22.4	22.6±21.7	-3.8±9.5	34.05 (26.98 to 41.13)	26.38 (19.54 to 33.23)
Median change in no. of hospitalizations because of bleeding (IQR)§	-2.0 (-3.0 to -1.0)	-2.0 (-3.0 to -1.0)	0.0 (-1.0 to 1.0)	-1.74 (-2.26 to -1.21)	-1.72 (-2.34 to -1.10)
Median change in duration of hospital stays because of bleeding (IQR) — days§	-6.8 (-8.5 to -3.3)	-5.7 (-9.0 to -1.8)	-0.9 (-2.8 to 1.0)	-4.89 (-6.72 to -3.05)	-4.77 (-6.61 to -2.92)
Median change in no. of bleeding episodes (IQR)§	-5.0 (-6.0 to -3.0)	-3.0 (-4.0 to -1.5)	0.0 (-1.0 to 1.0)	-3.46 (-4.22 to -2.70)	-2.35 (-3.18 to -1.53)

* The widths of the confidence intervals have not been adjusted for multiplicity and cannot be used to infer treatment effects.

† P<0.001 by Fisher's exact test with 2 degrees of freedom, comparing all three groups.

‡ The logistic model — which included age (≥55 years), sex, body-mass index (≥24), and the presence of multiple small-intestinal angiodysplastic lesions — was used to impute missing values for fecal occult blood tests by means of the Mianalyze procedure (in SAS software, version 9.4).

§ This analysis compared the data from the first follow-up period (after the 4-month treatment period) with data from the observation period.

¶ This analysis included data from 47 patients in the 100-mg thalidomide group, 48 patients in the 50-mg thalidomide group, and 48 patients in the placebo group.

Reduction of at least 50% in the number of bleeding episodes

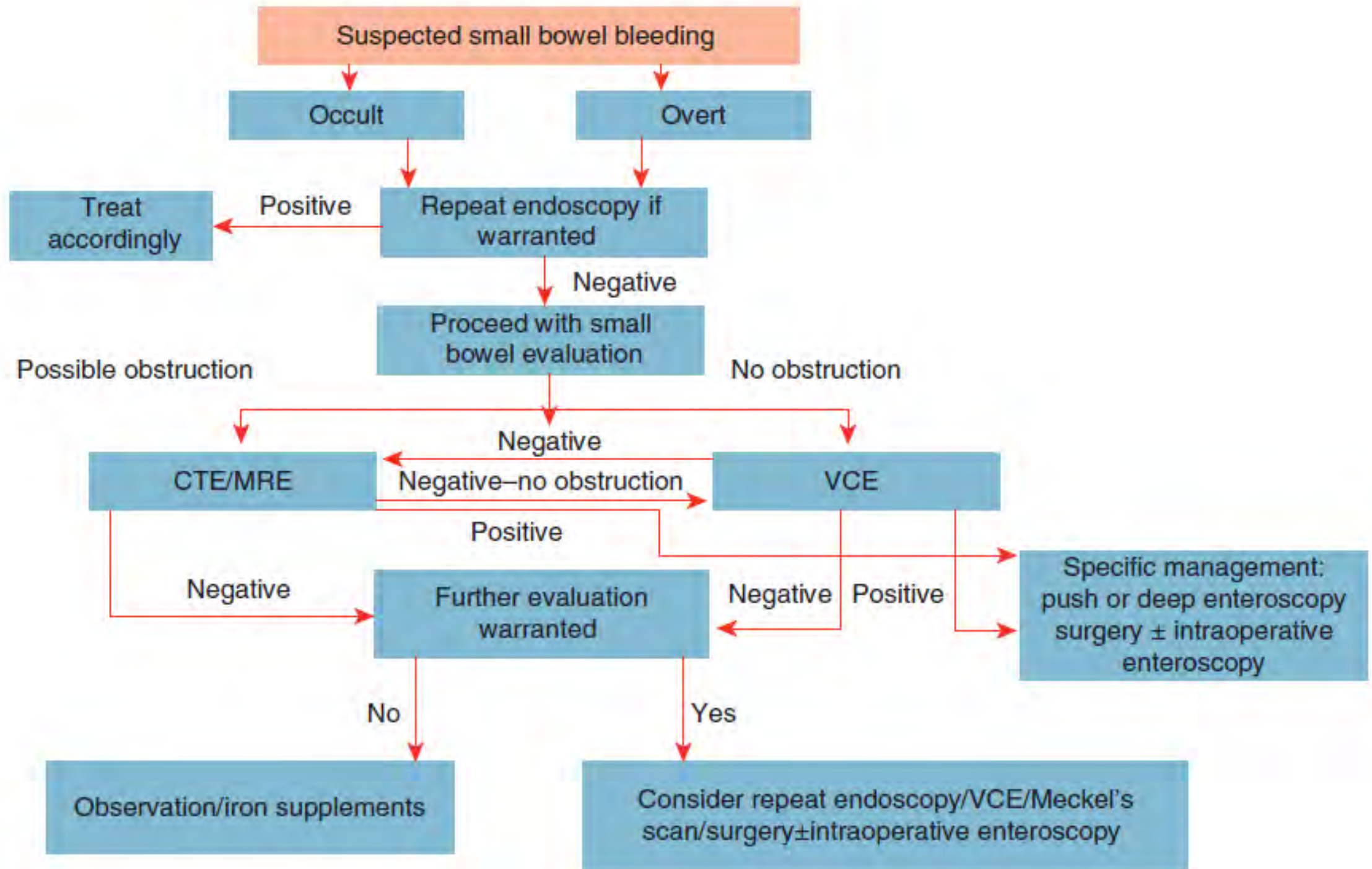
Table 3. Adverse Events.*

Event	100-mg Thalidomide Group (N=51)			50-mg Thalidomide Group (N=49)			Placebo Group (N=50)		
	Grade 1	Grade 2	Total	Grade 1	Grade 2	Total	Grade 1	Grade 2	Total
	<i>number of patients (percent)</i>								
Any adverse event	28 (54.9)	23 (45.1)	35 (68.6)	18 (36.7)	22 (44.9)	27 (55.1)	10 (20.0)	6 (12.0)	14 (28.0)
Cardiac disorders	0	0	0	1 (2.0)	1 (2.0)	2 (4.1)	1 (2.0)	0	1 (2.0)
Palpitation	0	0	0	1 (2.0)	0	1 (2.0)	1 (2.0)	0	1 (2.0)
Sinus bradycardia	0	0	0	0	1 (2.0)	1 (2.0)	0	0	0
Eye disorders	1 (2.0)	0	1 (2.0)	0	0	0	0	0	0
Dry eye	1 (2.0)	0	1 (2.0)	0	0	0	0	0	0
Gastrointestinal disorders	7 (13.7)	13 (25.5)	18 (35.3)	5 (10.2)	13 (26.5)	15 (30.6)	4 (8.0)	4 (8.0)	8 (16.0)
Constipation	1 (2.0)	12 (23.5)	13 (25.5)	1 (2.0)	10 (20.4)	11 (22.4)	0	2 (4.0)	2 (4.0)
Abdominal distention	3 (5.9)	2 (3.9)	5 (9.8)	3 (6.1)	1 (2.0)	4 (8.2)	1 (2.0)	2 (4.0)	3 (6.0)
Stomach upset	3 (5.9)	0	3 (5.9)	1 (2.0)	3 (6.1)	4 (8.2)	3 (6.0)	0	3 (6.0)
Dry mouth	2 (3.9)	0	2 (3.9)	2 (4.1)	0	2 (4.1)	0	0	0
General disorders and administration-site conditions	9 (17.6)	1 (2.0)	10 (19.6)	8 (16.3)	2 (4.1)	10 (20.4)	6 (12.0)	0	6 (12.0)
Fatigue	2 (3.9)	1 (2.0)	3 (5.9)	2 (4.1)	2 (4.1)	4 (8.2)	6 (12.0)	0	6 (12.0)
Peripheral edema	6 (11.8)	0	6 (11.8)	6 (12.2)	0	6 (12.2)	1 (2.0)	0	1 (2.0)
Chest congestion	1 (2.0)	0	1 (2.0)	0	0	0	0	0	0
Infections and infestations	0	0	0	1 (2.0)	1 (2.0)	2 (4.1)	0	0	0
Urinary tract infection	0	0	0	1 (2.0)	1 (2.0)	2 (4.1)	0	0	0
Investigations	0	2 (3.9)	2 (3.9)	1 (2.0)	5 (10.2)	6 (12.2)	0	2 (4.0)	2 (4.0)
Elevated liver-enzyme levels	0	1 (2.0)	1 (2.0)	1 (2.0)	3 (6.1)	4 (8.2)	0	1 (2.0)	1 (2.0)
Leukopenia	0	1 (2.0)	1 (2.0)	0	3 (6.1)	3 (6.1)	0	1 (2.0)	1 (2.0)
Nervous system disorders	15 (29.4)	9 (17.6)	23 (45.1)	7 (14.3)	9 (18.4)	14 (28.6)	4 (8.0)	0	4 (8.0)
Dizziness	8 (15.7)	2 (3.9)	10 (19.6)	3 (6.1)	2 (4.1)	5 (10.2)	4 (8.0)	0	4 (8.0)
Somnolence	9 (17.6)	0	9 (17.7)	4 (8.2)	1 (2.0)	5 (10.2)	1 (2.0)	0	1 (2.0)
Limb numbness	0	7 (13.7)	7 (13.7)	0	7 (14.3)	7 (14.3)	0	0	0
Skin and subcutaneous tissue disorders	1 (2.0)	2 (3.9)	3 (5.9)	0	2 (4.1)	2 (4.1)	0	0	0
Rash	0	2 (3.9)	2 (3.9)	0	2 (4.1)	2 (4.1)	0	0	0
Pruritus	1 (2.0)	0	1 (2.0)	0	0	0	0	0	0

* Adverse events were defined and graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 5.0) and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use E6 (R2) guideline. Events are summarized according to system organ class and preferred term. All adverse events were grade 1 or 2. Some patients had both grade 1 and grade 2 events.

Costs

- Octreotide 40mg R26000
- Thalidomide R2974
- Whole blood R1924 (2024)



Takeaway messages

- Structured diagnostic algorithm

Non-invasive VCE +/- radiography
targeted therapeutic endoscopy

- Tailor the treatment to the patient

Conservative vs endoscopic vs surgical

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