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Small Bowel Endoscopy

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Opinion statement

The small bowel is a challenging area for endoscopic evaluation and therapy due to its length and angulated configuration. A small lumen diameter and segmental peristalsis made it a perfect fit for examination by a novel ingestible wireless camera in a capsule. The development of capsule endoscopy changed the diagnosis and management of bleeding lesions, ulcers, and tumors deep in the small bowel, allowing earlier diagnosis with excellent patient acceptance. Device-assisted enteroscopy revolutionized small bowel therapy, particularly management of bleeding, Peutz-Jeghers polyposis, and tumor marking for minimally invasive surgery. Small bowel stricture dilation in select patients is safe and effective. Tools for a spectrum of small bowel therapies are available but remain suboptimal to tackle lesions on angulated folds deep in the small bowel. Universal terminology to describe the endoscopic appearance of vascular lesions will facilitate studies of endoscopic and medical therapy. The future holds improvements in imaging, easier advancement through the small bowel, and therapeutic capacity. This review focuses on methods of small bowel endoscopy, therapy, and outcomes.

Introduction

The small intestine is a relatively new territory for endoscopic diagnosis and treatment of disease. Over the past 15 years, advances in imaging and endoscopy have provided the practicing gastroenterologist new technologies to approach disease deep in the small bowel. The most common problems are gastrointestinal (GI) bleeding and ulcerating disease, which are more common and less well understood than previously thought. Early diagnosis and management of small bowel tumors and polyposis syndromes has revolutionized care. The main limitation to diagnosis and therapy in the small bowel remains its length (600 cm or longer in tall adults) and looped anatomy [1]. Fixed bowel due to previous surgery and altered anatomy further limit advancement in the small bowel. Evaluation of the small bowel with push enteroscopy allows diagnosis and therapy for

lesions in the very proximal jejunum (on average 80 cm beyond the ligament of Treitz) [2••]. Most lesions deeper in the small bowel are diagnosed and treated by capsule endoscopy (CE) in combination with device-assisted enteroscopy (DAE). Triple-phase computed tomography (CT) and magnetic resonance (MR) enterography as well as angiography are evolving in parallel and are combined with small bowel endoscopy for diagnosis and therapy. Intraoperative enteroscopy is now reserved for those with incomplete DAE and a high suspicion for a small bowel lesion or persistent bleeding with no lesion found. It has the advantage of both external and internal examinations of the entire small bowel and immediate lesion resection [3].

Capsule endoscopy and DAE have brought to the forefront the ability to visualize the entire small bowel for diagnostic and therapeutic purposes (Table 1). Previously, bleeding sources not identified by upper and lower endoscopy and radiographic evaluation of the small bowel were categorized into obscure overt and obscure occult bleeding based on the clinical presentation [4, 5]. Newer technologies have changed terminology from obscure gastrointestinal bleeding (OGIB) to small bowel bleeding in most cases [6••]. The term OGIB is now reserved for bleeding that is not identified within the GI tract, utilizing upper, lower, and small bowel endoscopy or radiographic evaluation [7] (Table 2). The future holds advancements in quality imaging and inspection, improved devices to access the small bowel, tools to advance therapy, and refinement in guidelines in the approach to GI bleeding. The management of small bowel disorders is an exciting and changing field. This article reviews recent advances in small bowel endoscopy with a focus on the methods, therapies, and outcomes.

Table 1. Small bowel endoscopy technologies available in the USA

Test	Pro	Con
Video capsule endoscopy	Excellent patient tolerance Best examination for flat mucosal lesions	Lack of tissue diagnosis Lack of therapy Poor localization Inability to size lesions Retention
PillCam (Given Imaging, Yokneam, Israel) EndoCapsule (Olympus America, Allentown, PA)	Radio-frequency transmission	Relative contraindication in cardiac devices
MiroCam (IntroMedic, Seoul, Korea)	Electric field body propagation Increased frames/second	Longer reading time ? Interacts with cardiac devices
Push enteroscopy	Widely available	Limited insertion depth Average insertion <100 cm
Device-assisted enteroscopy	Allows therapy Tissue sampling/marking	Incomplete exams Invasive Perforation, pancreatitis
Double balloon enteroscopy	Greatest depth of insertion	Time-consuming Limited tools Latex balloons
Single balloon enteroscopy	Shortest setup time	Low rate of complete enteroscopy Limited tools
Spiral enteroscopy	Shortest procedure time	Not available to new users
NaviAid AB device (SMART Medical Systems Ltd., Ra'anana, Israel)	Utilizes standard endoscopic equipment No specialized setup	Limited advancement No comparative studies

Table 2. Diagnostic yield of small bowel imaging modalities for GI bleeding

Test	Diagnostic yield (%)
Small bowel barium study [8•]	5
Push enteroscopy [8•]	30
Computed tomography enterography [9]	45
Video capsule endoscopy [8•, 10]	38–83
Device-assisted enteroscopy [11]	51–80
Intraoperative enteroscopy [6••]	58–88

Indications

The most common indication for evaluation of the small bowel is bleeding. Approximately 5 % of patients presenting with GI bleeding have no source found by upper endoscopy and colonoscopy [4, 12, 13]. In approximately 75 % of these patients, lesions can be identified in the small bowel using new endoscopic technologies [4]. The most common cause of small bowel bleeding is a vascular lesion. Angioectasias occur in association with disorders such as severe heart disease, chronic kidney disease, rheumatologic disorders, and cirrhosis [14, 15]. They most commonly present as occult bleeding or iron deficiency anemia in individuals over 60 years of age.

Alternative bleeding lesions in the small bowel include ulcers (mostly due to nonsteroidal anti-inflammatory drug (NSAID) use and Crohn's disease), tumors (gastrointestinal stromal tumor, carcinoid, lymphoma, and adenocarcinoma), polyps (hamartoma, granulation, and inflammatory), hemangiomas, and jejunal and Meckel's diverticulum. Less commonly, hemosuccus pancreaticus and aortoenteric fistulas cause small bowel bleeding [4]. Understanding the limitations of small bowel endoscopy for the detection of bleeding lesions is critical as both missed lesions and misinterpreted lesions can lead to clinical harm or overtreatment, respectively.

Other indications for evaluation of the small bowel include obstructive symptoms with abnormal imaging [Crohn's disease and other ulcerating/stenosing diseases (NSAID, radiation, ischemia, tuberculosis infection, nonspecific chronic ulcer, refractory celiac disease), tumor, lymphoma, polyposis syndromes] and chronic diarrhea when other symptoms/signs of disease are present. Small bowel lesion sampling and marking allows laparoscopic internal resection or mini-laparotomy, an advance over open laparotomy. Therapeutic indications include bleeding management, polypectomy, stricture dilation, direct percutaneous jejunostomy placement, stenting, and evaluation of the biliary system in patients with altered small bowel anatomy.

Capsule endoscopy

The development of wireless video CE in 1998 was a disruptive endoscopic technology. The first prototype transmitted vivid images of the small bowel

mucosa that allowed a rapid introduction for clinical use in 2001 [16, 17••]. Since then, other capsule devices (EndoCapsule, MiroCam) have been introduced to the USA with similar diagnostic yields [18, 19] (Table 1). Capsule endoscopy allows complete examination of the small bowel mucosa, is minimally invasive, is well tolerated by patients, and is the recommended next study for patients with GI bleeding when no source is found at upper and lower endoscopy [16]. Two randomized clinical trials have assessed the role of CE compared to push enteroscopy as a first-line study after a negative upper endoscopy and colonoscopy. Both studies show an increased diagnostic yield with CE when compared to push enteroscopy [20, 21]. A meta-analysis of 14 studies compared the diagnostic yield of CE to push enteroscopy demonstrating a higher diagnostic yield for CE (63 vs. 28 %, $P < 0.00001$) [8•]. In three studies comparing the yield of CE to small bowel barium radiography, the yield for any finding was even greater for CE (67 vs. 8 %, $P < 0.0001$) [8•]. Consideration should be taken for repeat standard endoscopy, and in those briskly bleeding, angiography or direct DAE is the best approach. In a retrospective study in OGIB using double balloon endoscopy (DBE), 24.3 % of patients had a definite source of bleeding outside of the small bowel [22].

In a large multi-center French study of OGIB, CE demonstrated a confirmed bleeding lesion in 56 % of patients, most in the small bowel. Primary small bowel findings included angioectasia (44 %), blood without a lesion (16 %), ulcers (19 %), and tumors (15 %) [23•]. Factors that are predictive of a positive CE include overt bleeding, male sex, age >60, and inpatient capsule study within 3 days of admission [23•, 24, 25]. Earlier performance of CE may be useful. In a small study of overt GI bleeding with a negative upper endoscopy, immediate capsule placement showed a positive finding in 75 % of patients, most in the small bowel [26•].

Other indications for CE include the evaluation of inflammatory bowel disease, refractory celiac disease [27], and diagnosis of polyposis syndromes (Peutz-Jeghers and familial adenomatous polyposis (FAP)) [16]. Small bowel ulcers in asymptomatic individuals are more common than previously thought. In the first clinical trial of CE to assess the effect of NSAIDs on the small bowel mucosa, 13.8 % of control subjects had small bowel mucosal breaks or ulcers at baseline [28]. Capsule endoscopy is more effective than barium studies in the evaluation for small bowel ulcers in Crohn's disease. There was a higher diagnostic yield with CE when compared to small bowel barium study (63 vs. 23 %, $P < 0.001$) and when compared to colonoscopy with ileoscopy (61 vs. 46 %, $P < 0.02$) [29].

Screening of the upper GI tract with a side-viewing endoscope for adenomas involving the ampulla is recommended in FAP beginning at the age of 25–30 years with an expectation that mortality can be improved [30]. The role of examination of the entire small bowel in FAP remains uncertain, although the performance of CE has been demonstrated to be safe and effective in polyp detection [31–33].

Improving diagnostic yield

The capsule endoscope travels through the small bowel propelled by peristalsis. Capsule movement is most rapid in the duodenum and tumbles in the small bowel with the possibility for missed lesions. Factors such as gastroparesis, bilious material/food residue, and impaired motility can limit complete examination of the small bowel and diagnostic yield [34]. In a large retrospective study, the capsule incompletion rate was 19 %. Factors associated with incomplete studies included inpatient hospitalization, previous small bowel surgery,

and moderate or poor bowel cleansing [35]. In a meta-analysis of 12 studies, purgative solutions compared to a clear liquid diet improved small bowel visualization and diagnostic yield [36]. In a subsequent meta-analysis of prokinetic agents and anti-foaming agents, simethicone improved visualization quality but capsule completion rate was not affected by promotility agents [37].

Interpretation and performance

With the capture of over 50,000 images utilizing a capture of 2 frames per second and an average reading time of 40–60 min [38], attempts to decrease the capsule reading time have been assessed using proprietary software and multi-view images. Removal of every other image and evaluation of a QuickView mode both resulted in decreased reading times, but with a diagnostic miss rate of 2 and 8 %, respectively [39]. The addition of an algorithmic suspected blood indicator (SBI) to QuickView mode resulted in 100 % sensitivity to identify active bleeding, although other small bowel lesions may have been missed [40].

Skilled CE reading is crucial to guide decision-making. Misinterpreted lesions are common and include red spots as vascular lesions; protrusions, pylorus, ampulla, and lymphangiectasias as mass lesions; air bubbles as polyps; and mucous or lens pressed against the mucosa as ulcers. Clinical guidelines recommend formal training as a part of a GI fellowship program or completion of a hands-on course with a review of the first ten capsule studies for credentialing. A more recent study utilizing a formalized assessment tool demonstrated improvement in CE interpretation among trainees completing more than 20 CE studies [41, 42]. The best way to improve CE interpretation is to perform DAE to correlate capsule findings.

To improve capsule completion rates, a longer duration of recording capsules to 12 h has been developed. Completion rates are increased when compared to 8-h capsule studies (88 vs. 79.5 %, $P = 0.03$) with an increased diagnostic yield (48.5 vs. 35 %, $P = 0.01$) [43]. To decrease the missed lesion rate, the capsule field of view has increased from 140° to 170° and a capsule with four cameras has been developed to allow a 360° view of the small bowel (CapsoCam, CapsoVision, Saratoga, CA). When compared to a standard capsule endoscope, the 360° viewing capsule had a similar diagnostic yield, but this identified significantly more small bowel lesions [44, 45]. Reading time was increased, and the capsule required retrieval from the body for data downloading that may impact on patient acceptance but is good for the environment.

CE complications

Capsule endoscopy has been reported to be safe with the implantable electromechanical cardiac devices studied but remains a relative contraindication to CE [46]. The primary complication of CE is capsule retention. Capsule retention is defined as the presence of the capsule within the digestive tract for at least 2 weeks after ingestion that requires further intervention [47]. In a single retrospective study of 5593 capsules, the retention rate was 0.3 % [48]. Higher rates have been reported in those with suspected Crohn's disease (1.6 %) or known Crohn's disease (13 %) [49]. Other factors associated with a retained capsule include diaphragm disease from NSAID use [50] and radiation therapy [51]. Small bowel

barium studies are of virtually no value in the prediction of capsule retention. Computed tomography and magnetic resonance enterography (MRE) improve the ability to detect small bowel wall thickening and helps identify those at risk for retention [10]. In small bowel Crohn's disease, capsule retention is associated with stricture length and the number of prestenotic dilations [52]. While capsule retention in the small bowel may warrant surgery, DAE is the primary method for retrieval [53]. A dissolvable patency capsule predicts capsule retention in Crohn's disease with known strictures that has led to safe performance of CE in patients with obstructive-type symptoms and prior passage of a patency capsule [54].

Device-assisted enteroscopy

In 2001, Yamamoto et al. reported on the use of DBE for total small bowel endoscopy that allowed tissue sampling and therapy [55••]. The technique was introduced in the USA in 2004. The DBE system utilizes a 200-cm enteroscope over which a 145-cm overtube is back-loaded. Latex balloons on the ends of both the enteroscope and overtube allow for forward advancement of the enteroscope with pleating of the examined portion of the small bowel onto the overtube in repetitive push-and-pull cycles [10]. In a prospective study of both push enteroscopy and DBE for suspected small bowel bleeding, DBE demonstrated a greater insertion depth (230 ± 100 vs. 80 ± 18 cm, $P < 0.0001$) and greater diagnostic yield (73 vs. 44 %). X-ray exposure and procedure time (68 ± 25 vs. 21 ± 10 min, $P < 0.0001$) were both greater for DBE [2••].

Other device-assisted technologies have since been developed. Most clinical data has been reported using the DBE technology. Single balloon endoscopy (SBE) uses the push-and-pull technique with a single balloon on the overtube. In a randomized prospective trial comparing SBE and DBE, rates of complete enteroscopy were higher for DBE when compared to SBE (66 vs. 22 %, $P < 0.0001$) but diagnostic yields were similar (52 vs. 42 %, $P = 0.42$) [56••]. A second randomized controlled trial was terminated when it was determined that the rate of total enteroscopy was significantly higher for DBE when compared to SBE (57 vs. 0 %, $P = 0.002$) [57•].

Spiral enteroscopy (SE) uses rotational energy to pleat the small bowel onto an overtube with a spiral-ridged tip using a pediatric colonoscope [58]. Once the overtube is rotated clockwise past the ligament of Treitz, further clockwise spinning allows for rapid pleating of the small bowel onto the overtube. In a US study, SE was performed with a mean procedure time of 41 ± 15 min and a diagnostic yield of 59 % with endoscopic therapies performed in 49 % [59]. When compared to SBE, the diagnostic yield of SE was not significantly different (59.6 vs. 43.4 %, $P = 0.12$) [7].

The newest device to assist enteroscopy is a novel through-the-scope balloon system using a standard endoscope. In one small study, both the antegrade and retrograde approaches into the small bowel were estimated to advance deeper than the standard push enteroscopy and ileoscopy. The diagnostic yield was 44 %, and the average advancement time was 15.5 min [60•]. When comparing the technologies, DBE has the advantage of deepest advancement in the small bowel, SBE has the fastest setup time, and SE is the quickest to perform.

Indications

The main indication for DAE is small bowel bleeding therapy. It is useful in the diagnosis and management of small bowel Crohn's disease, marking small bowel tumors for surgical resection, refractory celiac disease [61], small bowel lymphoma, enteroscopy-assisted endoscopic retrograde cholangiopancreatography (ERCP) in patients with Roux-en-Y anatomy [62], dilation of small bowel strictures [63], diagnosis of Meckel's diverticulum [64], and direct percutaneous endoscopic jejunostomy [65]. Double balloon enteroscopy has been reported to be safe and effective in children under 10 years of age [66].

Improving insertion depth

Total enteroscopy utilizing DBE has a steep learning curve (>150 cases) to increase success rates from 8 to 63 % [67]. Rarely can total enteroscopy be performed from one approach. Antegrade advancement into the small bowel has a short learning curve (10 procedures) to significantly decrease procedure time [68]. Retrograde advancement has a higher rate of failure and lower diagnostic yield when compared to antegrade advancement due to difficulty with stable intubation of the ileocecal valve for forward advancement [69]. Estimated 30–35 retrograde DBE procedures are required under supervision in order to achieve a technical success rate of 75 % [70].

Most of the small bowel has no distinguishing features other than a fold pattern in the proximal jejunum and distal ileum. A porcine simulation model to determine the distance reached in the small bowel using DBE has been validated by estimating the distance in centimeters of each push-and-pull advancement [71]. A second method of estimating insertion depth has been proposed, utilizing the insertion of the overtube that still requires validation [72]. Depth of insertion is improved by using carbon dioxide rather than air for insufflation (230 vs. 177 cm, $P = 0.008$). Carbon dioxide insufflation is also associated with decreased procedural abdominal pain [73].

Improving diagnostic yield

Device-assisted enteroscopy requires significant time and health-care resources. Clinical factors associated with improved diagnostic and therapeutic yield include time from the last episode of overt GI bleed [74], need for blood transfusion prior to DBE, and demonstration of ulcers or arteriovenous malformations on preceding endoscopy [75]. In the hospitalized setting, the need for pre-procedure blood transfusion was associated with an increased need for endoscopic therapy at DBE [76]. Artifacts reported at CE and incomplete enteroscopy contribute to the low diagnostic yields reported in DBE studies.

Therapy

Endoscopic therapy deep in the small bowel is challenging due to a torqued endoscope, poor tip position, and limited ability to position lesions. Available tools are also limited due to the length of the enteroscope and channel size. It is therefore important to have a team knowledgeable in DAE and to optimally position lesions before tool passage and therapy. Tools of 2.8 mm in diameter fit through the

enteroscope channel, but passage can be difficult or impossible when the tip of the enteroscope is flexed. The newer double balloon enteroscope with a 3.2-mm channel will circumvent some of these problems.

Bleeding vascular lesions are the most common reason for endoscopic therapy (Fig. 1). The pathogenesis of vascular lesions in the small bowel is poorly understood. Vascular lesions have been characterized according to their endoscopic appearance as angioectasia (red, flat, irregular venous lesion, 1 mm or larger), congenital arteriovenous malformation (arterial red protrusion with surrounding venous dilation), Dieulafoy's lesion (pulsatile arterial protrusion or pulsatile bleeding), and submucosal streaming vessels [77••]. Thermal therapy with argon plasma coagulation (APC) is very effective to treat small bowel angioectasias, but pulsatile or active bleeding lesions are better managed with hemostatic clips or bipolar coagulation. Placement of hemostatic clips and/or tattooing may be useful to identify the site in the event of rebleeding. With multiple angioectasias, hereditary hemorrhagic telangiectasia, or comorbidities that predispose to rebleeding after endoscopic therapy, medical therapy has been reported to be effective (octreotide, thalidomide, anti-vascular endothelial growth factors) [6••] (Fig. 2).

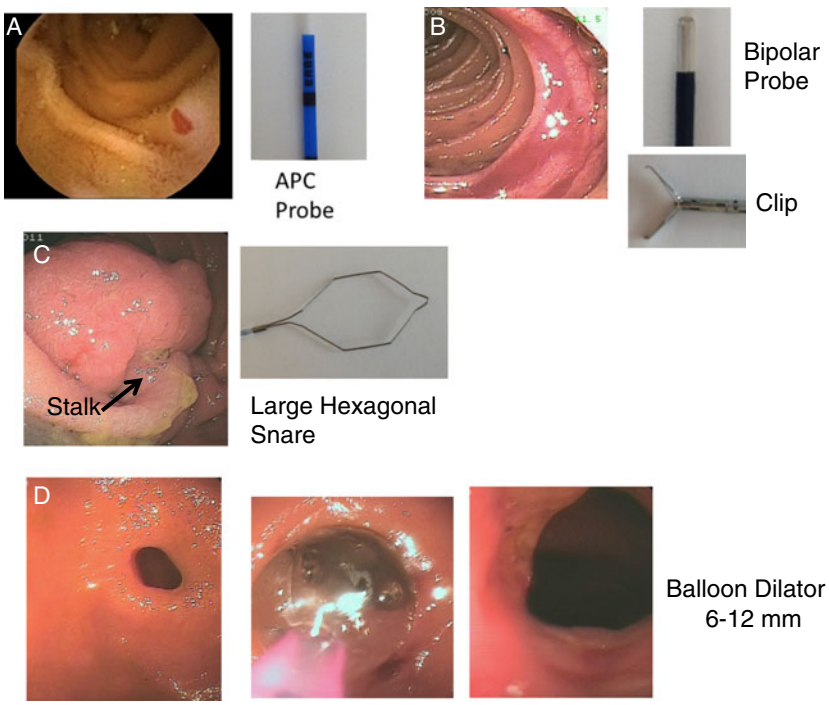

Fig. 1. Small bowel lesions amendable to endoscopic therapy and tools for therapy. **a** Angioectasia. Treated effectively with argon plasma coagulation (*APC*). **b** Submucosal streaming lesion. With washing, a stream of blood appears from beneath the mucosa. The entrance source of bleeding needs precise identification followed by either hemostatic clipping and/or bipolar thermal therapy. **c** Peutz-Jeghers large hamartoma with a long stalk (*arrow*) filling the lumen in the jejunum. A large hexagonal polypectomy snare allows maneuvering over the polyp head onto the stalk for hot snare resection. Injection of the stalk with ink may help identify the stalk during resection. **d** NSAID related, short (<1 cm), straight, bland stenosis, amendable to balloon dilation with relief of obstructive symptoms.

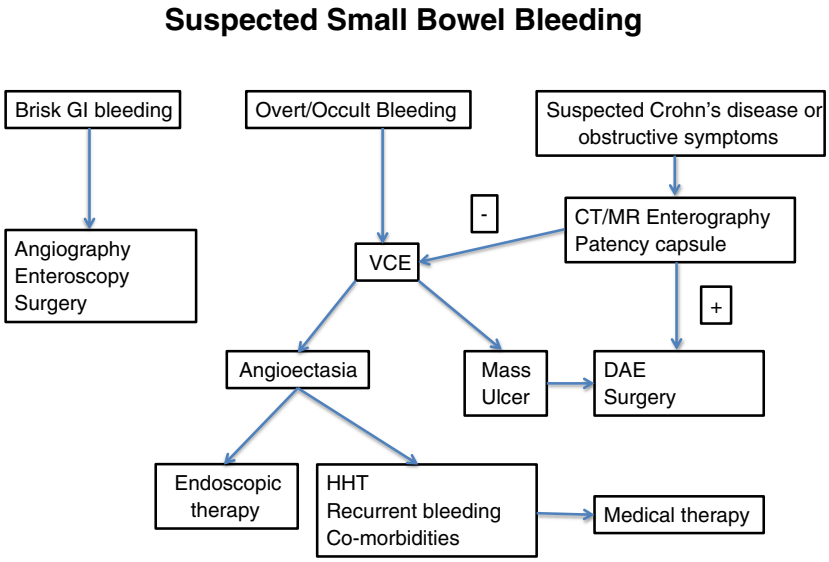

Fig. 2. Algorithm for the diagnosis and management of small bowel bleeding. *CT* computed tomography, *MR* magnetic resonance, *DAE* device-assisted enteroscopy, *HHT* hereditary hemorrhagic telangiectasia.

Polypectomy is another therapy performed in the small bowel. Peutz-Jeghers hamartomas may present with bleeding or obstructive symptoms. Device-assisted endoscopic resection of large polyps (>1 cm) particularly when started early in childhood has changed the management from surgical to endoscopic. Removing large polyps in the small bowel is challenging due to bowel angulations and small lumen size. Identification of the stalk is crucial, as piecemeal resection is associated with an increased risk of bleeding [78]. A large hexagonal snare and tattooing the polyp stalk can facilitate snare placement around the polyp head and onto the stalk (Fig. 1). A hemostatic clip at the cauterized stalk limits the rebleeding risk, particularly with resections deep in the small bowel that are difficult to reach. Other polypoid lesions that bleed (inflammatory/granulation/hyperplastic polyps, adenomas, hemangiomas) can be treated by snare polypectomy or thermal therapy. Without ultrasound knowledge of the depth of large hemangiomas and carcinoid tumors, caution should be taken due to a risk of perforation. When uncertain, tattoo placement for surgical resection should be performed. Two tattoos should be injected submucosally when possible to accurately mark a lesion site to allow laparoscopic resection.

Small bowel strictures are most often due to NSAIDs or Crohn's disease. Other causes include radiation, tumor, lymphoma, and surgical anastomosis [63, 79]. Small bowel strictures due to NSAIDs are notoriously missed on radiologic imaging studies and at laparoscopy for acute obstruction.

Indications for stricture dilation in Crohn's disease include short (<50 mm) fibrotic strictures with obstructive symptoms and no evidence of severe angulation or deep ulceration. Recommended balloon dilation is to a diameter of 12–15 mm to limit perforation risk (Table 3) [83].

Table 3. Stricture dilation in small bowel Crohn's disease (CD)

	Number of CD patients dilated	Perforation	Dilation mean diameter, mm (range)	Dilation number per patient	Success (%) (months of follow-up)
Fukumoto et al. [80]	23	0		1.6	74 (12)
Despott et al. [81]	9	1	15 (12–20)	2.3	89 (20)
Gill et al. [82]	10	2	13 (10–16.5)	1.7	70 (16)
Sunada et al. [83]	85	4	12 (8–20)	2.4	74 (60)

In the most recent study of DBE balloon stricture dilation in Crohn's disease, surgery-free rates were 87.3 % at 1 year, 78.1 % at 3 years, and 74.2 % at 5 years over a mean follow-up of 41.9 months [83].

Direct PEJ placement is safe and effective (93 %) with an average procedure duration of 33 min using the DBE technique [65]. Adhesions were the main cause of failed procedure. The most common complication was site ulcer/cellulitis. One major complication of gastric interposition required surgical management.

Balloon enteroscopy for ERCP in Roux-en-Y anatomy allows for successful advancement to the papilla and biliopancreatoenteric anastomoses. Utilizing SBE or DBE for advancement into the Roux limb allows for successful advancement to the papilla (93.5 %) and overall procedure success (88.1 %) [62]. Advanced techniques were at times required to cannulate a native papilla including withdrawal of the enteroscope with the overtube in place to allow for advancement of alternate endoscopes [62].

Complications

The complication rate of DBE is similar to that of standard endoscopy with the exception of pancreatitis. In the initial multi-continent study that included 2362 procedures, major complications included perforation (0.3 %), pancreatitis (0.3 %), and bleeding (0.8 %) with higher bleeding rates reported with large polyp resections (3 %) [78]. In a multi-center study in the USA that included 2478 DBE procedures, major complications included perforation (0.4 %), pancreatitis (0.2 %), and bleeding (0.2 %). There was a significantly higher risk of perforation in those with surgically altered anatomy undergoing retrograde DBE examinations [84•]. Recognized small bowel perforations at the time of the procedure may be successfully repaired with ligation clips (personal experience). Comparable risks of pancreatitis and procedural sedation have

been demonstrated in the performance of DBE in elderly patients with significant comorbidities [85].

CE with DAE: complementary technologies

Device-assisted enteroscopy is time-consuming and invasive and requires considerable resources. A meta-analysis of 11 studies compared the overall yield of CE with DBE with similar diagnostic yield (60 and 57 %, respectively). Given the comparable yields, less invasiveness, and better patient acceptance, CE has been recommended as the initial diagnostic test in suspected small bowel bleeding [86] (Fig. 2). In a cost-effective model for the diagnosis and management of OGIB, an initial anterograde DBE approach was the most cost-effective and resulted in a higher bleeding cessation rate compared to CE (86 vs. 76 %). However, when taking into account the higher complication rate for DBE, CE guiding DBE was the preferred approach [87].

High rates of rebleeding, similar to that of intraoperative enteroscopy or surgical resection, have been reported following therapeutic DBE, predominantly for small bowel vascular lesions. Rebleeding rates range from 23 to 46 % [88, 89, 90•]. In a pooled analysis of patients undergoing DBE for OGIB with a mean follow-up time of 26 ± 15 months, the rebleeding rate was 45 % [15]. Risk factors for rebleeding include cardiac disease, chronic renal failure, cirrhosis, anticoagulation, number of vascular lesions, and presentation with overt bleeding [89, 90•]. Multiple therapeutic procedures for vascular lesions with rebleeding may be required for improved long-term outcomes [91].

New technologies

Advances have been made in depth of field, optics, and compression of images to lessen the reading time for CE. New CE technology is aimed at real-time reading and a steerable capsule with sampling and therapeutic capabilities. Device-assisted enteroscopy technology is also marching on. A larger 3.2-mm channel double balloon enteroscope to improve therapeutic capacity is now available. A motorized spiral device to drive through the entire small bowel and allow therapy by a single operator is in development. Tools designed specifically for therapy deep in the small bowel are needed.

Conclusion

Over the past 15 years, significant advancements have been made in the field of small bowel enteroscopy that has dramatically improved the diagnosis and therapy of small bowel disease, particularly small bowel bleeding. Rebleeding in the small bowel remains a problem despite the ability to reach bleeding lesions and perform therapy, emphasizing the importance of comorbid diseases. Future prospective randomized studies that assess both medical and endoscopic therapies

are required to guide the approach to small bowel bleeding and rebleeding. Clinical parameters that predict rebleeding risk may be used to develop a risk score that would identify those that benefit from further endoscopic or medical therapy. Technology advances make it an exciting time for the diagnosis, management, and clinical research in small bowel disease.

Compliance with Ethical Standards

Conflict of Interest
Dejan Micic declares no conflict of interest.
Carol E. Semrad is a consultant for CapsoVision and Fujinon.

Human and Animal Rights and Informed Consent
This article does not contain any studies with human or animal subjects performed by any of the authors.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as
- • Of importance
- •• Of major importance

1. Buchman AL. Etiology and initial management of short bowel syndrome. Gastroenterology. 2006;130(2 Suppl 1):S5–s15.
2.•• May A, Nachbar L, Schneider M, Ell C. Prospective comparison of push enteroscopy and push-and-pull enteroscopy in patients with suspected small-bowel bleeding. Am J Gastroenterol. 2006;101(9):2016–24.

Parallel comparison of depth of insertion using push enteroscopy versus DBE.

3. Foutch PG, Sawyer R, Sanowski RA. Push-enteroscopy for diagnosis of patients with gastrointestinal bleeding of obscure origin. Gastrointest Endosc. 1990;36(4):337–41.
4. Raju GS, Gerson L, Das A, Lewis B. American Gastroenterological Association (AGA) institute technical review on obscure gastrointestinal bleeding. Gastroenterology. 2007;133(5):1697–717.
5. Gralnek IM. Obscure-overt gastrointestinal bleeding. Gastroenterology. 2005;128(5):1424–30.
6.•• Gerson LB, Fidler JL, Cave DR, Leighton JA. ACG clinical guideline: diagnosis and management of small bowel bleeding. Am J Gastroenterol. 2015;110(9):1265–87.

New clinical guideline for the management of small bowel bleeding supporting the definition "small bowel bleeding" and the redefining obscure gastrointestinal bleeding.

7. Khashab MA, Lennon AM, Dunbar KB, Singh VK, Chandrasekhara V, Giday S, et al. A comparative evaluation of single-balloon enteroscopy and spiral enteroscopy for patients with mid-gut disorders. Gastrointest Endosc. 2010;72(4):766–72.
8.• Triester SL, Leighton JA, Leontiadis GI, Fleischer DE, Hara AK, Heigh RI, et al. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with obscure gastrointestinal bleeding. Am J Gastroenterol. 2005;100(11):2407–18.

Strong meta-analysis comparing capsule to other small bowel imaging technologies.

9. Huprich JE, Fletcher JG, Alexander JA, Fidler JL, Burton SS, McCullough CH. Obscure gastrointestinal bleeding: evaluation with 64-section multiphase CT enterography—initial experience. Radiology. 2008;246(2):562–71.
10. Semrad CE. Small bowel enteroscopy: territory conquered, future horizons. Curr Opin Gastroenterol. 2009;25(2):110–5.
11. Leighton JA. The role of endoscopic imaging of the small bowel in clinical practice. Am J Gastroenterol. 2011;106(1):27–36. quiz 7.
12. Johnston SJ, Jones PF, Kyle J, Needham CD. Epidemiology and course of gastrointestinal haemorrhage in North-east Scotland. Br Med J. 1973;3(5882):655–60.
13. Spiller RC, Parkins RA. Recurrent gastrointestinal bleeding of obscure origin: report of 17 cases and a guide to logical management. Br J Surg. 1983;70(8):489–93.

14. Igawa A, Oka S, Tanaka S, Kunihara S, Nakano M, Aoyama T, et al. Major predictors and management of small-bowel angioectasia. BMC Gastroenterol. 2015;15:108.
15. Jackson CS, Gerson LB. Management of gastrointestinal angiodysplastic lesions (GIADs): a systematic review and meta-analysis. Am J Gastroenterol. 2014;109(4):474–83. quiz 84.
16. Gerson LB. Capsule endoscopy and deep enteroscopy: indications for the practicing clinician. Gastroenterology. 2009;137(4):1197–201.
17.•• Iddan G, Meron G, Glukhovsky A, Swain P. Wireless capsule endoscopy. Nature. 2000;405(6785):417.
A first report of a novel capsule endoscope.
18. Cave DR, Fleischer DE, Leighton JA, Faigel DO, Heigh RI, Sharma VK, et al. A multicenter randomized comparison of the Endocapsule and the Pillcam SB. Gastrointest Endosc. 2008;68(3):487–94.
19. Choi EH, Mergener K, Semrad C, Fisher L, Cave DR, Dodig M, et al. A multicenter, prospective, randomized comparison of a novel signal transmission capsule endoscope to an existing capsule endoscope. Gastrointest Endosc. 2013;78(2):325–32.
20. de Leusse A, Vahedi K, Edery J, Tiah D, Fery-Lemonnier E, Cellier C, et al. Capsule endoscopy or push enteroscopy for first-line exploration of obscure gastrointestinal bleeding? Gastroenterology. 2007;132(3):855–62. quiz 1164–5.
21. Segarajasingam DS, Hanley SC, Barkun AN, Waschke KA, Burtin P, Parent J, et al. Randomized controlled trial comparing outcomes of video capsule endoscopy with push enteroscopy in obscure gastrointestinal bleeding. Can J Gastroenterol Hepatol. 2015;29(2):85–90.
22. Fry LC, Bellutti M, Neumann H, Malfertheiner P, Monkemuller K. Incidence of bleeding lesions within reach of conventional upper and lower endoscopes in patients undergoing double-balloon enteroscopy for obscure gastrointestinal bleeding. Aliment Pharmacol Ther. 2009;29(3):342–9.
23.• Lepileur L, Dray X, Antonietti M, Iwanicki-Caron I, Grigioni S, Chaput U, et al. Factors associated with diagnosis of obscure gastrointestinal bleeding by video capsule enteroscopy. Clin Gastroenterol Hepatol: Off Clin Pract J Am Gastroenterol Assoc. 2012;10(12):1376–80.
A large multicenter cohort of patients undergoing capsule endoscopy with description of capsule findings and risk factors for obscure gastrointestinal bleeding.
24. Robinson CA, Jackson C, Condon D, Gerson LB. Impact of inpatient status and gender on small-bowel capsule endoscopy findings. Gastrointest Endosc. 2011;74(5):1061–6.
25. Singh A, Marshall C, Chaudhuri B, Okoli C, Foley A, Person SD, et al. Timing of video capsule endoscopy relative to overt obscure GI bleeding: implications from a retrospective study. Gastrointest Endosc. 2013;77(5):761–6.
26.• Schlag C, Menzel C, Nennstiel S, Neu B, Phillip V, Schuster T, et al. Emergency video capsule endoscopy in patients with acute severe GI bleeding and negative upper endoscopy results. Gastrointest Endosc. 2015;81(4):889–95.
A study that highlights the potential use of early capsule endoscopy in select patients with GI bleeding. This study bypasses the use of colonoscopy when upper gastrointestinal bleeding is suspected in favor of capsule endoscopy.
27. Van Weyenberg SJ, Smits F, Jacobs MA, Van Turenhout ST, Mulder CJ. Video capsule endoscopy in patients with nonresponsive celiac disease. J Clin Gastroenterol. 2013;47(5):393–9.
28. Goldstein JL, Eisen GM, Lewis B, Gralnek IM, Zlotnick S, Fort JG. Video capsule endoscopy to prospectively assess small bowel injury with celecoxib, naproxen plus omeprazole, and placebo. Clin Gastroenterol Hepatol: Off Clin Pract J Am Gastroenterol Assoc. 2005;3(2):133–41.
29. Triester SL, Leighton JA, Leontiadis GI, Gurudu SR, Fleischer DE, Hara AK, et al. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with non-stricturing small bowel Crohn's disease. Am J Gastroenterol. 2006;101(5):954–64.
30. Syngal S, Brand RE, Church JM, Giardiello FM, Hampel HL, Burt RW. ACG clinical guideline: genetic testing and management of hereditary gastrointestinal cancer syndromes. Am J Gastroenterol. 2015;110(2):223–62. quiz 63.
31. Iaquinto G, Fornasarig M, Quaia M, Giardullo N, D'Onofrio V, Iaquinto S, et al. Capsule endoscopy is useful and safe for small-bowel surveillance in familial adenomatous polyposis. Gastrointest Endosc. 2008;67(1):61–7.
32. Alderlieste YA, Rauws EA, Mathus-Vliegen EM, Fockens P, Dekker E. Prospective enteroscopic evaluation of jejunal polyposis in patients with familial adenomatous polyposis and advanced duodenal polyposis. Fam Cancer. 2013;12(1):51–6.
33. Yamada A, Watabe H, Iwama T, Obi S, Omata M, Koike K. The prevalence of small intestinal polyps in patients with familial adenomatous polyposis: a prospective capsule endoscopy study. Fam Cancer. 2014;13(1):23–8.
34. Triantafyllou K, Kalantzis C, Papadopoulos AA, Apostolopoulos P, Rokkas T, Kalantzis N, et al. Video-capsule endoscopy gastric and small bowel transit time and completeness of the examination in patients with diabetes mellitus. Dig Liver Dis: Off J Italian Soc Gastroenterol Italian Assoc Study Liver. 2007;39(6):575–80.
35. Westerhof J, Weersma RK, Koornstra JJ. Risk factors for incomplete small-bowel capsule endoscopy. Gastrointest Endosc. 2009;69(1):74–80.
36. Rokkas T, Papaxoinis K, Triantafyllou K, Pistiolas D, Ladas SD. Does purgative preparation influence the diagnostic yield of small bowel video capsule

endoscopy?: a meta-analysis. Am J Gastroenterol. 2009;104(1):219–27.
37. Kotwal VS, Attar BM, Gupta S, Agarwal R. Should bowel preparation, antifoaming agents, or prokinetics be used before video capsule endoscopy? A systematic review and meta-analysis. Eur J Gastroenterol Hepatol. 2014;26(2):137–45.
38. Delvaux M, Gerard G. Capsule endoscopy in 2005: facts and perspectives. Best Pract Res Clin Gastroenterol. 2006;20(1):23–39.
39. Westerhof J, Koornstra JJ, Weersma RK. Can we reduce capsule endoscopy reading times? Gastrointest Endosc. 2009;69(3 Pt 1):497–502.
40. Stein AC, Appannagari A, Habib I, Semrad CE, Rubin DT. A rapid and accurate method to detect active small bowel gastrointestinal bleeding on video capsule endoscopy. Dig Dis Sci. 2014;59(10):2503–7.
41. Faigel DO, Baron TH, Adler DG, Davila RE, Egan J, Hirota WK, et al. ASGE guideline: guidelines for credentialing and granting privileges for capsule endoscopy. Gastrointest Endosc. 2005;61(4):503–5.
42. Rajan E, Iyer PG, Oxentenko AS, Pardi DS, Alexander JA, Baron TH, et al. Training in small-bowel capsule endoscopy: assessing and defining competency. Gastrointest Endosc. 2013;78(4):617–22.
43. Rahman M, Akerman S, DeVito B, Miller L, Akerman M, Sultan K. Comparison of the diagnostic yield and outcomes between standard 8 h capsule endoscopy and the new 12 h capsule endoscopy for investigating small bowel pathology. World J Gastroenterol. 2015;21(18):5542–7.
44. Gerson LB. Capsule endoscopy and deep enteroscopy. Gastrointest Endosc. 2013;78(3):439–43.
45. Pioche M, Vanbiervliet G, Jacob P, Duburque C, Gincul R, Filoche B, et al. Prospective randomized comparison between axial- and lateral-viewing capsule endoscopy systems in patients with obscure digestive bleeding. Endoscopy. 2014;46(6):479–84.
46. Harris LA, Hansel SL, Rajan E, Srivathsan K, Rea R, Crowell MD, et al. Capsule endoscopy in patients with implantable electromedical devices is safe. Gastroenterol Res Pract. 2013;2013:959234.
47. Cave D, Legnani P, de Franchis R, Lewis BS. ICCE consensus for capsule retention. Endoscopy. 2005;37(10):1065–7.
48. Al-Bawardy B, Locke G, Huprich JE, Fletcher JG, Fidler JL, Barlow JM, et al. Retained capsule endoscopy in a large tertiary care academic practice and radiologic predictors of retention. Inflamm Bowel Dis. 2015;21(9):2158–64.
49. Cheifetz AS, Kornbluth AA, Legnani P, Schmelkin I, Brown A, Lichtiger S, et al. The risk of retention of the capsule endoscope in patients with known or suspected Crohn's disease. Am J Gastroenterol. 2006;101(10):2218–22.
50. Li F, Gurudu SR, De Petris G, Sharma VK, Shiff AD, Heigh RI, et al. Retention of the capsule endoscope: a single-center experience of 1000 capsule endoscopy procedures. Gastrointest Endosc. 2008;68(1):174–80.
51. Cheifetz AS, Lewis BS. Capsule endoscopy retention: is it a complication? J Clin Gastroenterol. 2006;40(8):688–91.
52. Rozendorn N, Klang E, Lahat A, Yablecovitch D, Kopylov U, Eliakim A, et al. Prediction of patency capsule retention in known Crohn's disease patients by using magnetic resonance imaging. Gastrointest Endosc. 2016;83(1):182–7.
53. Van Weyenberg SJ, Van Turenhout ST, Bouma G, Van Waesberghe JH, Van der Peet DL, Mulder CJ, et al. Double-balloon endoscopy as the primary method for small-bowel video capsule endoscope retrieval. Gastrointest Endosc. 2010;71(3):535–41.
54. Herrerias JM, Leighton JA, Costamagna G, Infantolino A, Eliakim R, Fischer D, et al. Agile patency system eliminates risk of capsule retention in patients with known intestinal strictures who undergo capsule endoscopy. Gastrointest Endosc. 2008;67(6):902–9.
55.•• Yamamoto H, Sekine Y, Sato Y, Higashizawa T, Miyata T, Iino S, et al. Total enteroscopy with a nonsurgical steerable double-balloon method. Gastrointest Endosc. 2001;53(2):216–20.
An initial description of the use of double balloon enteroscopy.
56.•• May A, Farber M, Aschmoneit I, Pohl J, Manner H, Lotterer E, et al. Prospective multicenter trial comparing push-and-pull enteroscopy with the single- and double-balloon techniques in patients with small-bowel disorders. Am J Gastroenterol. 2010;105(3):575–81.
A randomized comparison of DBE and SBE.
57.• Takano N, Yamada A, Watabe H, Togo G, Yamaji Y, Yoshida H, et al. Single-balloon versus double-balloon endoscopy for achieving total enteroscopy: a randomized, controlled trial. Gastrointest Endosc. 2011;73(4):734–9.
A second randomized comparison of DBE and SBE.
58. Akerman PA, Agrawal D, Chen W, Cantero D, Avila J, Pangtay J. Spiral enteroscopy: a novel method of enteroscopy by using the Endo-Ease Discovery SB overtube and a pediatric colonoscope. Gastrointest Endosc. 2009;69(2):327–32.
59. Judah JR, Draganov PV, Lam Y, Hou W, Buscaglia JM. Spiral enteroscopy is safe and effective for an elderly United States population of patients with numerous comorbidities. Clin Gastroenterol Hepatol: Off Clin Pract J Am Gastroenterol Assoc. 2010;8(7):572–6.
60.• Ali R, Wild D, Shieh F, Diehl DL, Fischer M, Tamura W, et al. Deep enteroscopy with a conventional colonoscope: initial multicenter study by using a through-the-scope balloon catheter system. Gastrointest Endosc. 2015;82(5):855–60.
A novel method for the utilization of a standard endoscope and a through-the-scope tool for advancement into the small bowel.
61. Hadithi M, Al-toma A, Oudejans J, van Bodegraven AA, Mulder CJ, Jacobs M. The value of double-balloon enteroscopy in patients with refractory celiac disease. Am J Gastroenterol. 2007;102(5):987–96.

62. Ishii K, Itoi T, Tonozuka R, Itokawa F, Sofuni A, Tsuchiya T, et al. Balloon enteroscopy-assisted ERCP in patients with Roux-en-Y gastrectomy and intact papillae (with videos). Gastrointest Endosc. 2015.
63. Kroner PT, Brahmbhatt BS, Bartel MJ, Stark ME, Lukens FJ. Yield of double-balloon enteroscopy in the diagnosis and treatment of small bowel strictures. Dig Liver Dis: Off J Italian Soc Gastroenterol Italian Assoc Study Liver. 2015.
64. Fukushima M, Kawanami C, Inoue S, Okada A, Imai Y, Inokuma T. A case series of Meckel's diverticulum: usefulness of double-balloon enteroscopy for diagnosis. BMC Gastroenterol. 2014;14:155.
65. Al-Bawardy B, Gorospe EC, Alexander JA, Bruining DH, Coelho-Prabhu N, Rajan E, et al. Outcomes of double-balloon enteroscopy-assisted direct percutaneous endoscopic jejunostomy tube placement. Endoscopy. 2016.
66. Yokoyama K, Yano T, Kumagai H, Mizuta K, Ono S, Imagawa T, et al. Double-balloon enteroscopy for pediatric patients: evaluation of safety and efficacy in 257 cases. Journal of Pediatric Gastroenterology and Nutrition. 2015.
67. Gross SA, Stark ME. Initial experience with double-balloon enteroscopy at a U.S. center. Gastrointest Endosc. 2008;67(6):890–7.
68. Mehdizadeh S, Ross A, Gerson L, Leighton J, Chen A, Schembre D, et al. What is the learning curve associated with double-balloon enteroscopy? Technical details and early experience in 6 U.S. tertiary care centers. Gastrointest Endosc. 2006;64(5):740–50.
69. Mehdizadeh S, Han NJ, Cheng DW, Chen GC, Lo SK. Success rate of retrograde double-balloon enteroscopy. Gastrointest Endosc. 2007;65(4):633–9.
70. Tee HP, How SH, Kaffes AJ. Learning curve for double-balloon enteroscopy: findings from an analysis of 282 procedures. World J Gastrointest Endosc. 2012;4(8):368–72.
71. Lopez Albors O, Soria F, Perez Cuadrado E, Morcillo E, Martin C, Carballo LF, et al. Validity of insertion depth measurement in double-balloon endoscopy. Endoscopy. 2012;44(11):1045–50.
72. Li XB, Dai J, Chen HM, Zhuang J, Song Y, Gao YJ, et al. A novel modality for the estimation of the enteroscope insertion depth during double-balloon enteroscopy. Gastrointest Endosc. 2010;72(5):999–1005.
73. Domagk D, Bretthauer M, Lenz P, Aabakken L, Ullerich H, Maaser C, et al. Carbon dioxide insufflation improves intubation depth in double-balloon enteroscopy: a randomized, controlled, double-blind trial. Endoscopy. 2007;39(12):1064–7.
74. Shinozaki S, Yamamoto H, Yano T, Sunada K, Miyata T, Hayashi Y, et al. Long-term outcome of patients with obscure gastrointestinal bleeding investigated by double-balloon endoscopy. Clin Gastroenterol Hepatol: Off Clin Pract J Am Gastroenterol Assoc. 2010;8(2):151–8.
75. Hussan H, Crews NR, Geremakis CM, Bahna S, LaBundy JL, Hachem C. Predictors of double balloon endoscopy outcomes in the evaluation of gastrointestinal bleeding. World J Gastrointest Endosc. 2014;6(6):248–53.
76. Kaffes AJ, Siah C, Koo JH. Clinical outcomes after double-balloon enteroscopy in patients with obscure GI bleeding and a positive capsule endoscopy. Gastrointest Endosc. 2007;66(2):304–9.
77.•• Yano T, Yamamoto H, Sunada K, Miyata T, Iwamoto M, Hayashi Y, et al. Endoscopic classification of vascular lesions of the small intestine (with videos). Gastrointest Endosc. 2008;67(1):169–72.
A classification system for small bowel vascular lesions to unify the terminology for clinical and research purposes.
78. Mensink PB, Haringsma J, Kucharzik T, Cellier C, Perez-Cuadrado E, Monkemuller K, et al. Complications of double balloon enteroscopy: a multicenter survey. Endoscopy. 2007;39(7):613–5.
79. Nishimura N, Yamamoto H, Yano T, Hayashi Y, Sato H, Miura Y, et al. Balloon dilation when using double-balloon enteroscopy for small-bowel strictures associated with ischemic enteritis. Gastrointest Endosc. 2011;74(5):1157–61.
80. Fukumoto A, Tanaka S, Yamamoto H, Yao T, Matsui T, Iida M, et al. Diagnosis and treatment of small-bowel stricture by double balloon endoscopy. Gastrointest Endosc. 2007;66(3 Suppl):S108–12.
81. Despott EJ, Gupta A, Burling D, Tripoli E, Konieczko K, Hart A, et al. Effective dilation of small-bowel strictures by double-balloon enteroscopy in patients with symptomatic Crohn's disease (with video). Gastrointest Endosc. 2009;70(5):1030–6.
82. Gill RS, Kaffes AJ. Small bowel stricture characterization and outcomes of dilatation by double-balloon enteroscopy: a single-centre experience. Ther Adv Gastroenterology. 2014;7(3):108–14.
83. Sunada K, Shinozaki S, Nagayama M, Yano T, Takezawa T, Ino Y, et al. Long-term outcomes in patients with small intestinal strictures secondary to Crohn's disease after double-balloon endoscopy-assisted balloon dilation. Inflamm Bowel Dis. 2016;22(2):380–6.
84.• Gerson LB, Tokar J, Chiorean M, Lo S, Decker GA, Cave D, et al. Complications associated with double balloon enteroscopy at nine US centers. Clin Gastroenterol Hepatol: Off Clin Pract J Am Gastroenterol Assoc. 2009;7(11):1177–82.
A multi-center US cohort reporting complications associated with double balloon enteroscopy.
85. Byeon JS, Mann NK, Jamil LH, Lo SK. Double balloon enteroscopy can be safely done in elderly patients with significant co-morbidities. J Gastroenterol Hepatol. 2012;27(12):1831–6.
86. Pasha SF, Leighton JA, Das A, Harrison ME, Decker GA, Fleischer DE, et al. Double-balloon enteroscopy and capsule endoscopy have comparable diagnostic yield in small-bowel disease: a meta-analysis. Clin Gastroenterol Hepatol: Off Clin Pract J Am Gastroenterol Assoc. 2008;6(6):671–6.

87. Gerson L, Kamal A. Cost-effectiveness analysis of management strategies for obscure GI bleeding. Gastrointest Endosc. 2008;68(5):920–36.
88. Gerson LB, Batenic MA, Newsom SL, Ross A, Semrad CE. Long-term outcomes after double-balloon enteroscopy for obscure gastrointestinal bleeding. Clin Gastroenterol Hepatol: Off Clin Pract J Am Gastroenterol Assoc. 2009;7(6):664–9.
89. Rahmi G, Samaha E, Vahedi K, Delvaux M, Gay G, Lamouliatte H, et al. Long-term follow-up of patients undergoing capsule and double-balloon enteroscopy for identification and treatment of small-bowel vascular lesions: a prospective, multicenter study. Endoscopy. 2014;46(7):591–7.
90.• Samaha E, Rahmi G, Landi B, Lorenceau-Savale C, Malamut G, Canard JM, et al. Long-term outcome of patients treated with double balloon enteroscopy for small bowel vascular lesions. Am J Gastroenterol. 2012;107(2):240–6.
A large study assessing the outcomes of double balloon enteroscopy with a focus on small bowel vascular lesions. Highlights rates of rebleeding and risk factors.
91. Shinozaki S, Yamamoto H, Yano T, Sunada K, Hayashi Y, Shinhata H, et al. Favorable long-term outcomes of repeat endotherapy for small-intestine vascular lesions by double-balloon endoscopy. Gastrointest Endosc. 2014;80(1):112–7.