Communication from the ASGE Standards of Practice Committee

GUIDELINE

The role of deep enteroscopy in the management of small-bowel disorders

Prepared by: ASGE STANDARDS OF PRACTICE COMMITTEE

Mouen A. Khashab, MD, Shabana F. Pasha, MD, V. Raman Muthusamy, MD, FASGE, Ruben D. Acosta, MD, David H. Bruining, MD, Vinay Chandrasekhara, MD, Krishnavel V. Chathadi, MD, Mohamad A. Eloubeidi, MD, MHS, FASGE, Robert D. Fanelli, MD, FACS, FASGE, SAGES Representative, Ashley L. Faulx, MD, FASGE, Lisa Fonkalsrud, BSN, RN, CGRN, SGNA Representative, Suryakanth R. Gurudu, MD, FASGE, Loralee R. Kelsey, BSN, RN, CGRN, SGNA Representative, Shivangi Kothari, MD, Jenifer R. Lightdale, MD, MPH, FASGE, NAPSGHAN Representative, John R. Saltzman, MD, FASGE, Aasma Shaukat, MD, MPH, FASGE, Amy Wang, MD, Julie Yang, MD, Brooks D. Cash, MD, FASGE, Previous Committee Chair, John M. DeWitt, MD, FASGE, Chair

This document was reviewed and approved by the Governing Board of the American Society for Gastrointestinal Endoscopy.

This is one of a series of position statements discussing the use of GI endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy (ASGE) prepared this text. In preparing this article, MEDLINE and PubMed databases were used to search for publications between January 1975 and December 2013 pertaining to this topic. The search was supplemented by accessing the "related articles" feature of PubMed, with articles identified on MEDLINE and PubMed as the references. Additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. When few or no data were available from well-designed prospective trials, emphasis was given to results from large series and reports from recognized experts. Weaker recommendations are indicated by phrases such as "We suggest…" whereas stronger recommendations are stated as "We recommend…." The strength of individual recommendations was based on both the aggregate evidence quality (Table 1)[1] and an assessment of the anticipated benefits and harms.

ASGE position statements for appropriate use of endoscopy are based on a critical review of the available data and expert consensus at the time that the documents are drafted. Further controlled clinical studies may be needed to clarify aspects of this document. This document may be revised as necessary to account for changes in technology, new data, or other aspects of clinical practice and is solely intended to be an educational device to provide information that may assist endoscopists in providing care to patients. This document is not a rule and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment. Clinical decisions in any particular case involve a complex analysis of the patient's condition and available courses of action. Therefore, clinical considerations may lead an endoscopist to take a course of action that varies from the recommendations and suggestions proposed in this document.

0016-5107/$36.00
http://dx.doi.org/10.1016/j.gie.2015.06.046

The diagnosis and treatment of small-bowel disorders is challenging because of the length of the small intestine, its anatomy, and the lack of appropriate tools. However, the introduction of video capsule endoscopy[2,3] (VCE) and deep enteroscopy[4] (DE) has changed the management of these patients. Although VCE can theoretically visualize the entire small intestine, it is unable to obtain biopsy specimens, cross altered anatomy, or perform therapeutic interventions. DE, on the other hand, has become the technique of choice for tissue acquisition or therapeutic intent within the GI tract between the ampulla of Vater and the ileocecal valve, a region referred to as the midgut.[5] DE techniques, which include double-balloon enteroscopy (DBE), single-balloon enteroscopy (SBE), and spiral enteroscopy (SE), have both diagnostic and therapeutic capabilities. DBE was first introduced by Yamamoto et al[4] in 2001 and is the most studied and established DE technique to date. Multiple studies have evaluated the usefulness of DBE for the diagnosis and management of different small-bowel conditions, particularly obscure GI bleeding (OGIB).[6-9] SBE and SE are more recent modalities in endoscopic evaluation of the small intestine. SBE was introduced to streamline the technique of push-and-pull enteroscopy.[10-12] The potential benefits of SBE over DBE include shorter set-up time, a 1-balloon cycle requirement

TABLE 1. GRADE system for the quality of evidence for guidelines

Quality of evidence	Definition	Symbol
High quality	Further research is very unlikely to change our confidence in the estimate of effect.	⊕⊕⊕⊕
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.	⊕⊕⊕◯
Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.	⊕⊕◯◯
Very low quality	Any estimate of effect is very uncertain.	⊕◯◯◯

GRADE, Grading of Recommendations Assessment, Development and Evaluation.
Adapted from Guyatt et al.[1]

TABLE 2. Technical specifications of enteroscopes

Endoscope make/model (manufacturer)	Type	Length, mm	Outer diameter, mm	Inner channel, mm	Field of view	Overtube required
EN-450T5 (Fujinon)	DBE scope	2300	9.4	2.8	140°	Yes
EN-450T5/W (Fujinon)	DBE scope	2300	9.4	2.8	140°	Yes
EN-450P5/20 (Fujinon)	DBE scope	2300	8.5	2.2	120°	Yes
EC-450BI5 (Fujinon)	DBE scope	1820	9.4	2.8	140°	Yes
SIF-Q180 (Olympus)	SBE scope	2000	9.2	2.8	140°	Yes
VSB-3430K (Pentax)	PE	2200	11.6	3.8	140°	No

DBE, Double-balloon enteroscopy; *PE,* push enteroscopy; *SBE,* single-balloon enteroscopy.

instead of 2, a less burdensome balloon control panel, and the use of a non-latex balloon.[13] SE permits evaluation of the small intestine by a rotate-to-advance technology. Its potential benefits include swift small-bowel examination, stability within the small bowel, and meticulous examination of the intestinal mucosa on both insertion and withdrawal of the enteroscope.[14-16] Techniques for DE are addressed in previous documents.[17] A new enteroscopy device (NaviAid; Smart Medical Systems, Ra'anana, Israel) has been designed to allow DE by using a standard adult colonoscope with the aid of a novel through-the-scope balloon.[18-20] Limited data regarding the use of this device for DE[18] and additional studies are needed before recommendations can be made.

DBE

The double-balloon enteroscope (Fujinon Inc, Tokyo, Japan) was introduced in 2001 as the first therapeutic DE tool. The DBE system comprises an enteroscope, an overtube, and a balloon-pump system. Three double-balloon enteroscopes currently are available and include the diagnostic (EN-450P5), therapeutic (EN-450T5), and short model (EC450-BI5) (Table 2).[21] The short model is mainly used for difficult ileocolonoscopies, ERCP in surgically altered anatomy, or proximal small-bowel endoscopy. Its main advantage is absence of the need for specially designed accessories because standard length endoscopic accessories can be used.[22] DBE may be performed in an antegrade or retrograde manner. Advancement through the small bowel is achieved with a series of cycles by using a push-and-pull technique.[17] By repeating this series of steps, a greater depth of small bowel can be intubated compared with push enteroscopy or ileoscopy.[7] General anesthesia often is used for antegrade procedures, whereas retrograde procedures usually are performed with patients under moderate sedation. The procedure requires additional personnel for handling of the overtube. The depth of intubation with DBE ranges from 240 cm to 360 cm past the ligament of Treitz with the antegrade approach and from 102 cm to 140 cm past the ileocecal valve with the retrograde approach.[7,8,23-26] The antegrade route typically is used for lesions located within the proximal two-thirds of the small bowel, whereas the retrograde route is used for lesions in the distal one third, based on capsule endoscopy transit times.[27] Interventions that may be performed during DBE include biopsies, mucosal injection, polypectomy, stricture dilation, hemostatic techniques (argon-plasma coagulation, electrocoagulation, and hemoclips), and retrieval of foreign bodies, including retained capsules.[28,29]

Total enteroscopy is defined as intubation of the entire small bowel by one or both routes. This approach is useful in patients with multiple small-bowel lesions, negative initial DBE, or high clinical suspicion for small-bowel pathology (ie, OGIB) after a nondiagnostic capsule endoscopy. The total enteroscopy rate for DBE ranges from 0% to 86% and is reportedly highest in the Asian population.[5,9] One systematic review of 66 published articles

TABLE 3. Technical specifications of enteroscope overtubes

Overtube make/model	Type	Length, mm	Outer diameter, mm	Inner diameter, mm	Balloon diameter or spiral height, mm	Scope compatibility
Fujinon						
TS-12140	DBE overtube	1450	12.2	10	40	EN-450P5/20
TS-13140	DBE overtube	1450	13.2	10.8	40	EN-450T5, EN-450T5/W
TS-13101	DBE overtube	1050	13.2	10.8	40	EC-450BI5
Olympus						
ST-SB1	SBE overtube	1320	13.2	11	40	SIF-Q180
Spirus Medical						
Endo-Ease Discovery, standard profile	Spiral enteroscopy	1180	14.5	9.8	5.5	SIF-Q180 EN-450T5 EN-450T5/W EN-450P5/20 EC-450BI5
Endo-Ease Discovery, low profile	Spiral enteroscopy	1180	14.5	9.8	4.5	SIF-Q180 EN-450T5 EN-450T5/W EN-450P5/20 EC-450BI5
Endo-Ease Vista, retrograde	Spiral enteroscopy	1000	17.4	13	5	Pediatric colonoscope

DBE, Double-balloon enteroscopy; *SBE,* single-balloon enteroscopy.

involving 12,823 DBE procedures reported an overall diagnostic yield of 68.1%, with vascular lesions (66%) as the most common finding. The pooled total enteroscopy rate was 44% by the combined (anterograde and retrograde) or antegrade-only approach. Pooled minor and major adverse event (eg, perforation, bleeding, pancreatitis, aspiration pneumonia) rates were 9.1% and 0.72%, respectively.[30]

Most of the data on adverse events from DE are for DBE, including the German DBE registry, with approximately 4000 DBE procedures, a U.S. data collection of about 2500 DBE procedures, and a European data collection of just under 2400 DBE procedures.[31-33] Based on these studies, the overall adverse event rate of DBE is approximately 1%. The most severe adverse event in diagnostic DBE is pancreatitis, which is reported in up to 0.3% of antegrade DBE procedures. The risk of severe adverse events is higher in therapeutic DBE and occurs in 3% to 4%.[32-34] Mortality related to DBE is rare and is reportedly 0.05%.[32]

SBE

The single-balloon enteroscope (Olympus, Tokyo, Japan) was introduced in 2007. In contrast to the DBE, this device has only 1 balloon (made of silicone)[21] at the distal end of the overtube (Table 2). Single-balloon enteroscopy also is performed by the push-and-pull technique.[17] The depth of intubation with SBE ranges from 133 cm to 256 cm past the ligament of Treitz with the antegrade approach and from 73 cm to 163 cm past the ileocecal valve with the retrograde approach.[12,35,36] The rate of total enteroscopy has been reported between 15% and 25%.[10,12] The diagnostic yield of SBE ranges from 47% to 60%, and the range of possible endoscopic therapeutics offered are similar to those of DBE.[12,36]

The overall adverse event rate from diagnostic SBE is approximately 1%,[37] which is equivalent to that of diagnostic DBE. The risk of deep mucosal tears or perforation of a diagnostic SBE examination might be higher if the endoscope tip is flexed during advancement of the overtube, which may occur in the presence of adhesions related to prior abdominal surgery or anastomotic strictures.[10-12,38] The technique of "power suction"[39] (continuous suction) might help to reduce the injuries caused by the inverted endoscope tip technique.

SE

The Endo-Ease Discovery SB (Spirus Medical, Stoughton, Mass) is a spiral overtube made of polyvinyl chloride (Table 3) that navigates the small bowel by using a rotational endoscopy technique. With the exception of 1 pilot study of 6 patients by using retrograde SE,[40] all studies have described SE by using the antegrade approach. The mean depth of intubation with SE ranges from 176 cm to 250 cm.[14,35,41] The main advantage of SE is the relative reduction of procedure time. However,

a major limitation is the very low rate of complete enteroscopies, mainly caused by difficult retrograde passage.[42] Adverse events with SE include minor mucosal tears, and perforation has been reported in 0.3% of patients.[43-45]

COMPARISON OF THE DIFFERENT DE TECHNIQUES

Multiple retrospective and prospective trials have compared the diagnostic yield, depth of maximal insertion allowed, efficacy, and adverse events of the 3 DE techniques. Four prospective randomized studies have compared technical aspects and therapeutic outcomes between DBE and SBE.[46-49] One prospective multicenter trial comparing the DBE and SBE techniques in 100 patients showed that the DBE technique yielded a higher rate of total enteroscopy and therapeutic yield compared with the SBE technique.[46] The rate of complete enteroscopy was 3 times higher in the DBE group compared with the SBE group (66% vs 22%; $P < .0001$). Therapeutic yield, defined as findings requiring treatment, was significantly higher in the DBE group (72% vs 48%; $P = .025$). These results are similar to those reported by a prospective single-center Japanese trial comparing DBE with SBE, which demonstrated a complete enteroscopy rate for DBE of 57% compared with 0% for SBE ($P = .002$).[47] In contrast, the third multicenter comparative trial found no differences between the 2 systems, but the rate of complete enteroscopy was lower than expected in the DBE group (18%).[48] The fourth study, from Australia, compared both techniques in a randomized trial of 116 patients and reported similar diagnostic and therapeutic yields, procedure times, and depth of maximal insertion between DBE and SBE.[49]

One prospective randomized trial comparing SE with DBE has been reported.[42] DBE was associated with longer procedure times; however, significantly deeper insertion and a higher rate of complete enteroscopy (92% vs 8%; $P = .002$) were achieved with DBE. Another multicenter prospective nonrandomized trial of 241 patients comparing DBE and SE found that diagnostic yield (70% vs 75%), therapeutic yield (66% vs 70%), procedure time (60 minutes vs 55 minutes), and depth of maximal insertion (200 cm vs 220 cm) were equivalent between both groups.[50]

Only 1 study to date has compared SBE and SE.[35] A total of 92 patients underwent 105 procedures (52 SBE, 53 SE). The most common indication for DE was OGIB (n = 42). The mean depth of maximal insertion for SE was significantly higher than that for SBE (301 cm vs 222 cm; $P = .001$). However, the diagnostic yield between SBE and SE (59.6% vs 43.4%; $P = .12$) and mean procedure times between SBE and SE (53 minutes vs 47 minutes; $P = .20$) were similar. Perforation occurred in 1 SBE procedure.

DE FOR OGIB

The most common indication for DE is OGIB. OGIB is defined as occult or overt bleeding of unknown origin that persists or reoccurs after an initial negative endoscopic evaluation including upper endoscopy and colonoscopy.[51] OGIB occurs in approximately 5% of all patients who present with GI hemorrhage.[52]

VCE is frequently the initial diagnostic test in patients with suspected OGIB, because it is minimally invasive and can visualize the entire small bowel. A secondary DE is indicated if either (1) VCE detects a lesion requiring biopsy or endoscopic intervention, or (2) a high suspicion of small-bowel bleeding remains despite a negative initial VCE.[53] This approach leads to a significant clinical improvement in over 75% of treated patients, including reduced transfusion and iron requirement needs.[54]

In multiple large studies of patients with OGIB, the diagnostic yield of DE ranged from 43% to 81%, with treatment success rates between 43% and 84%.[8,55-57] In 1 controlled, prospective trial of 52 patients with OGIB, DE was superior to push enteroscopy in length of small bowel visualized (230 cm vs 80 cm; $P < .0001$) and in diagnostic yield (63% vs 44%; $P < .0001$).[7]

A meta-analysis of 11 studies involving 375 patients, which compared VCE and DBE, reported similar diagnostic yields (60% vs 57%, respectively; $P = .42$) between the 2 tests. The pooled yield of both VCE and DE for angiectasias in the 350 patients with OGIB was identical at 24%.[58] A recent updated and revised meta-analysis of 10 studies involving 642 patients demonstrated that the pooled overall diagnostic yield for VCE and DBE was 62% and 56%, respectively ($P = .16$).[59] However, the diagnostic yield of DBE was significantly higher when performed after a positive VCE compared with negative VCE (75% vs 27.5%; $P = .02$).

SBE and SE also have been studied in patients with OGIB. A large single-center study used SBE to evaluate 161 patients with suspected small-bowel disorders, 59% of whom had OGIB. The diagnostic yield of SBE was 58%, and the most common findings were angiectasias. The concordance between VCE and SBE findings was 40%, and SBE detected new findings in 17%.[36]

Several studies have compared the cost effectiveness of different treatment strategies for patients with OGIB. Modeled cost-minimization analyses proposed DE as the most cost effective initial test after standard endoscopy for an endpoint of treatment or definitive diagnosis.[60,61] Another model suggested that initial DE was a cost-effective approach for patients with OGIB who likely have angiectasias in the small bowel (eg, patient aged >40 years) accessible with a single antegrade approach.[62] However, initial capsule endoscopy generally remains the preferred initial strategy because of its relative noninvasive nature and acceptable diagnostic yield in patients with

OGIB. Prior ASGE guidelines have advocated VCE as the primary diagnostic tool for small-bowel evaluation in patients presenting with OGIB; however, DE may be considered as the initial small-bowel diagnostic procedure in select circumstances (eg, where there is a high level of suspicion of small-bowel angiectasias or in patients with surgically altered anatomy).[53]

DE FOR SMALL-BOWEL TUMORS

Small-bowel tumors account for 3% to 6% of all GI neoplasms and 1% to 3% of GI malignancies.[63,64] After the advent of VCE and DE, the overall detection of small-bowel tumors has increased to 4% to 9%.[65,66] In patients with suspected small-bowel pathology, the diagnostic yield of DBE for small-bowel tumors is between 9% and 14%.[67-71] In a large multicenter Japanese study of patients undergoing DBE, small-bowel tumors were detected in 13.9% of 1035 patients. The most common indications for DBE in this study were suspected small-bowel tumors (42%) and OGIB (27%).[70] The majority of small-bowel tumors detected on DBE are adenocarcinomas, lymphomas, carcinoid tumors, and GI stromal tumors.[67,68,70]

A meta-analysis that compared VCE to DBE in patients with suspected small-bowel disorders found no difference in overall diagnostic yield or detection of small-bowel tumors.[58] These tests are therefore considered to be complementary in the evaluation of these patients. DE is useful for tissue diagnosis and therapeutic interventions in patients with small-bowel tumors detected on VCE or radiologic imaging. DE also is useful for detection of small-bowel tumors in patients in whom a high clinical suspicion for a tumor remains after negative VCE or other imaging. The miss rate of VCE for small-bowel tumors is reported as high as 18.9%,[72] and malignant small-bowel tumors missed on VCE may be detected on DE.[73,74] DE also may be useful for evaluating patients in whom VCE is contraindicated because of known or suspected small-bowel stenosis.[69]

DE permits performance of biopsies and tattoo placement for localization of small-bowel tumors during surgery. With the exception of GI stromal tumors, DE allows tissue diagnosis in the majority of patients with small-bowel tumors.[70] DE also allows other therapeutic interventions, including hemostasis, polypectomy, EMR, dilation, and palliative stenting.[70,71,75,76]

The majority of patients with polyposis syndromes now can be managed endoscopically with DE. This modality allows endoscopic resection of Peutz-Jeghers polyps (>1 cm).[77,78] In patients with a fixed small bowel related to prior resections and those with large polyps, laparoscopy-assisted DBE allows resection of multiple polyps in 1 session. This technique decreases the need for small-bowel resections and the risk for short bowel syndrome.[75,79] Intraoperative enteroscopy may be necessary for evaluation and management of patients in whom small-bowel tumors are beyond the depth of maximal insertion of DE.[71]

DE FOR CROHN'S DISEASE

The role of endoscopy in patients with inflammatory bowel disease is addressed in another ASGE guideline.[80] In general, DE has a limited role in the initial evaluation of patients with known or suspected Crohn's disease (CD), because of the high diagnostic yield of less-invasive modalities such as VCE and cross-sectional radiographic imaging (eg, Computed Tomography Enterography [CTE], Magnetic Resonance Enterography [MRE]). However, enteroscopy permits endoscopic and histologic evaluation and the potential for therapeutic interventions such as hemostasis, stricture dilation, or removal of a retained capsule. Therapeutic DE can delay or prevent surgery in patients with Crohn's disease and small-bowel strictures. In 2 small case series, patients with symptomatic small-bowel strictures from Crohn's disease were successfully dilated in 62% and 72% of cases, with surgery-free rates of 100% and 72%, respectively, during an average follow-up between 12 months and 20 months.[81,82]

In patients with suspected Crohn's disease, the overall yield of DE for small-bowel pathology ranges from 30% to 48%, with an adverse event rate of approximately 1% for diagnostic examinations.[83] A systematic review of diagnostic DBE for all indications found a pooled diagnostic yield of 63.4% (95% confidence interval, 42%-82.3%) for small-bowel pathology in patients with definite or suspected Crohn's disease, with a pooled minor and major adverse event rate for all indications of 9.1% and 0.72%, respectively.[30]

RECOMMENDATIONS

1. We recommend DE as an effective and safe technique for small-bowel examination. ⊕⊕⊕⊕
2. We recommend DBE as the most effective deep enteroscopy technique for achieving total enteroscopy. ⊕⊕⊕○
3. We suggest either DBE or SBE for retrograde enteroscopy. ⊕⊕○○
4. We recommend VCE as the first-line diagnostic tool for small-bowel evaluation in patients with OGIB. DE may be considered when positive findings are identified on VCE. ⊕○○○
5. We suggest that in select circumstances (eg, surgically altered anatomy or high suspicion for small-bowel angiectasias) DE may be considered as the initial small-bowel diagnostic procedure in patients with OGIB. ⊕⊕○○
6. We suggest that DE be used for tissue diagnosis and therapeutic interventions in patients with small-bowel tumors detected by other diagnostic tests (eg, VCE) or in those with high suspicion for tumors despite initial negative testing. ⊕⊕○○

7. We suggest that DE be considered in Crohn's disease patients with abnormalities seen on other imaging studies, if these abnormalities are within reach of the enteroscope. DE allows endoscopic and histologic evaluation and the potential for therapeutic interventions such as hemostasis, stricture dilation, or foreign body retrieval. ⊕⊕◯◯

DISCLOSURE

R. Fanelli disclosed financial relationships with New Wave Surgical Inc, Allurion Technologies Inc, Cook Surgical Inc, and Mosaic Medical Inc and is a consultant to Endogastric Solutions Inc. M. Khashab is a consultant to and member of the Medical Advisory Board for Boston Scientific and a consultant to Olympus and receives research support from Cook Medical. V. Chandrasekhara is a consultant to Boston Scientific. J. DeWitt is a consultant to and receives honoraria from Olympus America. R. Muthusamy is a consultant to Boston Scientific and Covidien GI Solutions and a stockholder in Capsovision Inc. S. Pasha provides research support for Given Imaging and Fujinon. K. Chathadi is a consultant to Boston Scientific. All other authors disclosed no relationships relevant to this publication.

Abbreviations: ASGE, American Society for Gastrointestinal Endoscopy; DBE, double-balloon enteroscopy; DE, deep enteroscopy; OGIB, obscure GI bleeding; SBE, single-balloon enteroscopy; SE, spiral enteroscopy; VCE, video capsule endoscopy.

REFERENCES

1. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924-6.
2. Iddan G, Meron G, Glukhovsky A, et al. Wireless capsule endoscopy. Nature 2000;405:417.
3. Meron GD. The development of the swallowable video capsule (M2A). Gastrointest Endosc 2000;52:817-9.
4. Yamamoto H, Sekine Y, Sato Y, et al. Total enteroscopy with a nonsurgical steerable double-balloon method. Gastrointest Endosc 2001;53:216-20.
5. Ell C, May A. Mid-gastrointestinal bleeding: capsule endoscopy and push-and-pull enteroscopy give rise to a new medical term. Endoscopy 2006;38:73-5.
6. Yamamoto H, Kita H, Sunada K, et al. Clinical outcomes of double-balloon endoscopy for the diagnosis and treatment of small-intestinal diseases. Clin Gastroenterol Hepatol 2004;2:1010-6.
7. May A, Nachbar L, Schneider M, et al. Prospective comparison of push enteroscopy and push-and-pull enteroscopy in patients with suspected small-bowel bleeding. Am J Gastroenterol 2006;101:2016-24.
8. Mehdizadeh S, Ross A, Gerson L, 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;64:740-50.
9. Khashab M, Helper DJ, Johnson CS, et al. Predictors of depth of maximal insertion at double-balloon enteroscopy. Dig Dis Sci 2010;55:1391-5.
10. Tsujikawa T, Saitoh Y, Andoh A, et al. Novel single-balloon enteroscopy for diagnosis and treatment of the small intestine: preliminary experiences. Endoscopy 2008;40:11-5.
11. Kawamura T, Yasuda K, Tanaka K, et al. Clinical evaluation of a newly developed single-balloon enteroscope. Gastrointest Endosc 2008;68:1112-6.
12. Ramchandani M, Reddy DN, Gupta R, et al. Diagnostic yield and therapeutic impact of single-balloon enteroscopy: series of 106 cases. J Gastroenterol Hepatol 2009;24:1631-8.
13. Upchurch BR, Vargo JJ. Single-balloon enteroscopy. Gastrointest Endosc Clin N Am 2009;19:335-47.
14. Akerman PA, Agrawal D, Chen W, et al. Spiral enteroscopy: a novel method of enteroscopy by using the Endo-Ease Discovery SB overtube and a pediatric colonoscope. Gastrointest Endosc 2009;69:327-32.
15. Akerman PA, Agrawal D, Cantero D, et al. Spiral enteroscopy with the new DSB overtube: a novel technique for deep peroral small-bowel intubation. Endoscopy 2008;40:974-8.
16. Buscaglia JM, Dunbar KB, Okolo PI 3rd, et al. The spiral enteroscopy training initiative: results of a prospective study evaluating the Discovery SB overtube device during small bowel enteroscopy (with video). Endoscopy 2009;41:194-9.
17. ASGE Technology Committee; DiSario JA, Petersen BT, Tierney WM, et al. Enteroscopes. Gastrointest Endosc 2007;66:872-80.
18. Kumbhari V, Storm AC, Khashab MA, et al. Deep enteroscopy with standard endoscopes using a novel through-the-scope balloon. Endoscopy 2014;46:685-9.
19. Kumbhari V, Storm AC, Okolo PI 3rd, et al. Efficient retrograde enteroscopy using a novel through-the-scope balloon. Surg Endosc 2014;28:2745-6.
20. Kumbhari V, Saxena P, Khashab MA. A new through-the-scope balloon-assisted deep enteroscopy platform. Gastrointest Endosc 2014;79:694.
21. Pasha SF, Leighton JA. Endoscopic techniques for small bowel imaging. Radiol Clin North Am 2013;51:177-87.
22. Khashab MA, Okolo PI 3rd. Accessing the pancreatobiliary limb and ERCP in the bariatric patient. Gastrointest Endosc Clin N Am 2011;21:305-13.
23. Gross SA, Stark ME. Initial experience with double-balloon enteroscopy at a U.S. center. Gastrointest Endosc 2008;67:890-7.
24. May A, Nachbar L, Ell C. Double-balloon enteroscopy (push-and-pull enteroscopy) of the small bowel: feasibility and diagnostic and therapeutic yield in patients with suspected small bowel disease. Gastrointest Endosc 2005;62:62-70.
25. Lenz P, Domagk D. Double- vs. single-balloon vs. spiral enteroscopy. Best Pract Res Clin Gastroenterol 2012;26:303-13.
26. Elena RM, Riccardo U, Rossella C, et al. Current status of device-assisted enteroscopy: Technical matters, indication, limits and complications. World J Gastrointest Endosc 2012;4:453-61.
27. Gay G, Delvaux M, Fassler I. Outcome of capsule endoscopy in determining indication and route for push-and-pull enteroscopy. Endoscopy 2006;38:49-58.
28. Di Caro S, May A, Heine DG, et al. The European experience with double-balloon enteroscopy: indications, methodology, safety, and clinical impact. Gastrointest Endosc 2005;62:545-50.
29. Flynn AD, Chiorean MV. Retrieval of a large foreign body from the ileum with double-balloon enteroscopy (with videos). Gastrointest Endosc 2014;79:519-20.
30. Xin L, Liao Z, Jiang YP, et al. Indications, detectability, positive findings, total enteroscopy, and complications of diagnostic double-balloon endoscopy: a systematic review of data over the first decade of use. Gastrointest Endosc 2011;74:563-70.
31. Gerson LB, Batenic MA, Newsom SL, et al. Long-term outcomes after double-balloon enteroscopy for obscure gastrointestinal bleeding. Clin Gastroenterol Hepatol 2009;7:664-9.
32. Moschler O, May AD, Muller MK, et al. Complications in double-balloon-enteroscopy: results of the German DBE register. Z Gastroenterol 2008;46:266-70.

33. Mensink PB, Haringsma J, Kucharzik T, et al. Complications of double balloon enteroscopy: a multicenter survey. Endoscopy 2007;39:613-5.
34. May A, Nachbar L, Pohl J, et al. Endoscopic interventions in the small bowel using double balloon enteroscopy: feasibility and limitations. Am J Gastroenterol 2007;102:527-35.
35. Khashab MA, Lennon AM, Dunbar KB, et al. A comparative evaluation of single-balloon enteroscopy and spiral enteroscopy for patients with mid-gut disorders. Gastrointest Endosc 2010;72:766-72.
36. Upchurch BR, Sanaka MR, Lopez AR, et al. The clinical utility of single-balloon enteroscopy: a single-center experience of 172 procedures. Gastrointest Endosc 2010;71:1218-23.
37. May A. Modern imaging techniques: which—when—why? Dig Dis 2013;31:63-8.
38. Tominaga K, Iida T, Nakamura Y, et al. Small intestinal perforation of endoscopically unrecognized lesions during peroral single-balloon enteroscopy. Endoscopy 2008;40(suppl 2):E213-4.
39. Kav T, Balaban Y, Bayraktar Y. The power suction maneuver in single-balloon enteroscopy. Endoscopy 2008;40:961-2; author reply 962.
40. Lara LF, Singh S, Sreenarasimhaiah J. Initial experience with retrograde overtube-assisted enteroscopy using a spiral tip overtube. Proc (Bayl Univ Med Cent) 2010;23:130-3.
41. Morgan D, Upchurch B, Draganov P, et al. Spiral enteroscopy: prospective U.S. multicenter study in patients with small-bowel disorders. Gastrointest Endosc 2010;72:992-8.
42. Messer I, May A, Manner H, et al. Prospective, randomized, single-center trial comparing double-balloon enteroscopy and spiral enteroscopy in patients with suspected small-bowel disorders. Gastrointest Endosc 2013;77:241-9.
43. Akerman PA, Haniff M. Spiral enteroscopy: prime time or for the happy few? Best Pract Res Clin Gastroenterol 2012;26:293-301.
44. Akerman PA, Cantero D. Spiral enteroscopy and push enteroscopy. Gastrointest Endosc Clin N Am 2009;19:357-69.
45. Judah JR, Draganov PV, Lam Y, et al. Spiral enteroscopy is safe and effective for an elderly United States population of patients with numerous comorbidities. Clin Gastroenterol Hepatol 2010;8:572-6.
46. May A, Farber M, Aschmoneit I, 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;105:575-81.
47. Takano N, Yamada A, Watabe H, et al. Single-balloon versus double-balloon endoscopy for achieving total enteroscopy: a randomized, controlled trial. Gastrointest Endosc 2011;73:734-9.
48. Domagk D, Mensink P, Aktas H, et al. Single- vs. double-balloon enteroscopy in small-bowel diagnostics: a randomized multicenter trial. Endoscopy 2011;43:472-6.
49. Efthymiou M, Desmond PV, Brown G, et al. SINGLE-01: a randomized, controlled trial comparing the efficacy and depth of insertion of single- and double-balloon enteroscopy by using a novel method to determine insertion depth. Gastrointest Endosc 2012;76:972-80.
50. Rahmi G, Samaha E, Vahedi K, et al. Multicenter comparison of double-balloon enteroscopy and spiral enteroscopy. J Gastroenterol Hepatol 2013;28:992-8.
51. Aktas H, Mensink PB. Small bowel diagnostics: current place of small bowel endoscopy. Best Pract Res Clin Gastroenterol 2012;26:209-20.
52. Gralnek IM. Obscure-overt gastrointestinal bleeding. Gastroenterology 2005;128:1424-30.
53. Fisher L, Lee Krinsky M, Anderson MA, et al. The role of endoscopy in the management of obscure GI bleeding. Gastrointest Endosc 2010;72:471-9.
54. 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;66:304-9.
55. Manabe N, Tanaka S, Fukumoto A, et al. Double-balloon enteroscopy in patients with GI bleeding of obscure origin. Gastrointest Endosc 2006;64:135-40.
56. Arakawa D, Ohmiya N, Nakamura M, et al. Outcome after enteroscopy for patients with obscure GI bleeding: diagnostic comparison between double-balloon endoscopy and videocapsule endoscopy. Gastrointest Endosc 2009;69:866-74.
57. Nakamura M, Niwa Y, Ohmiya N, et al. Preliminary comparison of capsule endoscopy and double-balloon enteroscopy in patients with suspected small-bowel bleeding. Endoscopy 2006;38:59-66.
58. Pasha SF, Leighton JA, Das A, et al. Double-balloon enteroscopy and capsule endoscopy have comparable diagnostic yield in small-bowel disease: a meta-analysis. Clin Gastroenterol Hepatol 2008;6:671-6.
59. Teshima CW, Kuipers EJ, van Zanten SV, et al. Double balloon enteroscopy and capsule endoscopy for obscure gastrointestinal bleeding: an updated meta-analysis. J Gastroenterol Hepatol 2011;26:796-801.
60. Albert JG, Nachtigall F, Wiedbrauck F, et al. Minimizing procedural cost in diagnosing small bowel bleeding: comparison of a strategy based on initial capsule endoscopy versus initial double-balloon enteroscopy. Eur J Gastroenterol Hepatol 2010;22:679-88.
61. Somsouk M, Gralnek IM, Inadomi JM. Management of obscure occult gastrointestinal bleeding: a cost-minimization analysis. Clin Gastroenterol Hepatol 2008;6:661-70.
62. Gerson L, Kamal A. Cost-effectiveness analysis of management strategies for obscure GI bleeding. Gastrointest Endosc 2008;68:920-36.
63. Schottenfeld D, Beebe-Dimmer JL, Vigneau FD. The epidemiology and pathogenesis of neoplasia in the small intestine. Ann Epidemiol 2009;19:58-69.
64. Jemal A, Thomas A, Murray T, et al. Cancer statistics, 2002. CA Cancer J Clin 2002;52:23-47.
65. Cheung DY, Choi MG. Current advance in small bowel tumors. Clin Endosc 2011;44:13-21.
66. Cobrin GM, Pittman RH, Lewis BS. Increased diagnostic yield of small bowel tumors with capsule endoscopy. Cancer 2006;107:22-7.
67. Cangemi DJ, Patel MK, Gomez V, et al. Small bowel tumors discovered during double-balloon enteroscopy: analysis of a large prospectively collected single-center database. J Clin Gastroenterol 2013;47:769-72.
68. Fry LC, Neumann H, Kuester D, et al. Small bowel polyps and tumours: endoscopic detection and treatment by double-balloon enteroscopy. Aliment Pharmacol Ther 2009;29:135-42.
69. Imaoka H, Higaki N, Kumagi T, et al. Characteristics of small bowel tumors detected by double balloon endoscopy. Dig Dis Sci 2011;56:2366-71.
70. Mitsui K, Tanaka S, Yamamoto H, et al. Role of double-balloon endoscopy in the diagnosis of small-bowel tumors: the first Japanese multicenter study. Gastrointest Endosc 2009;70:498-504.
71. Islam RS, Leighton JA, Pasha SF. Evaluation and management of small-bowel tumors in the era of deep enteroscopy. Gastrointest Endosc 2014;79:732-40.
72. Lewis BS, Eisen GM, Friedman S. A pooled analysis to evaluate results of capsule endoscopy trials. Endoscopy 2005;37:960-5.
73. Ross A, Mehdizadeh S, Tokar J, et al. Double balloon enteroscopy detects small bowel mass lesions missed by capsule endoscopy. Dig Dis Sci 2008;53:2140-3.
74. Chong AK, Chin BW, Meredith CG. Clinically significant small-bowel pathology identified by double-balloon enteroscopy but missed by capsule endoscopy. Gastrointest Endosc 2006;64:445-9.
75. Ross AS, Dye C, Prachand VN. Laparoscopic-assisted double-balloon enteroscopy for small-bowel polyp surveillance and treatment in patients with Peutz-Jeghers syndrome. Gastrointest Endosc 2006;64:984-8.
76. Ross AS, Semrad C, Waxman I, et al. Enteral stent placement by double balloon enteroscopy for palliation of malignant small bowel obstruction. Gastrointest Endosc 2006;64:835-7.
77. Kopacova M, Bures J, Ferko A, et al. Comparison of intraoperative enteroscopy and double-balloon enteroscopy for the diagnosis and treatment of Peutz-Jeghers syndrome. Surg Endosc 2010;24:1904-10.
78. Sakamoto H, Yamamoto H, Hayashi Y, et al. Nonsurgical management of small-bowel polyps in Peutz-Jeghers syndrome with extensive polypectomy by using double-balloon endoscopy. Gastrointest Endosc 2011;74:328-33.

79. Paski SC, Semrad CE. Small bowel tumors. Gastrointest Endosc Clin N Am 2009;19:461-79.
80. ASGE Standards of Practice Committee; Shergill A, Lightdale J, Bruining DH, et al. The role of endoscopy in inflammatory bowel disease. Gastrointest Endosc 2015;81:1101-21.
81. Hirai F, Beppu T, Sou S, et al. Endoscopic balloon dilatation using double-balloon endoscopy is a useful and safe treatment for small intestinal strictures in Crohn's disease. Dig Endosc 2010;22:200-4.
82. Despott EJ, Gupta A, Burling D, et al. Effective dilation of small-bowel strictures by double-balloon enteroscopy in patients with symptomatic Crohn's disease (with video). Gastrointest Endosc 2009;70:1030-6.
83. Bourreille A, Ignjatovic A, Aabakken L, et al. Role of small-bowel endoscopy in the management of patients with inflammatory bowel disease: an international OMED-ECCO consensus. Endoscopy 2009;41:618-37.