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

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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) 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.

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 (VCE) and deep enteroscopy (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 mid-gut. 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 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). 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.
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 DE18 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-450T5), therapeutic (EN-450T5/W), and short model (EC-450BI5) (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
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,

<table>
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<tr>
<th>Overtube make/model</th>
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<th>Length, mm</th>
<th>Outer diameter, mm</th>
<th>Inner diameter, mm</th>
<th>Balloon diameter or spiral height, mm</th>
<th>Scope compatibility</th>
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<tr>
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<td>12.2</td>
<td>10</td>
<td>40</td>
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<td>17.4</td>
<td>13</td>
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<td>Pediatric colonoscope</td>
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DBE, Double-balloon enteroscopy; SBE, single-balloon enteroscopy.
a major limitation is the very low rate of complete enteroscopies, mainly caused by difficult retrograde passage.\textsuperscript{42} Adverse events with SE include minor mucosal tears, and perforation has been reported in 0.3% of patients.\textsuperscript{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.\textsuperscript{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.\textsuperscript{46} The rate of complete enteroscopy was 3 times higher in the DBE group compared with the SBE group (66% vs 22%; \textit{P} < .0001). Therapeutic yield, defined as findings requiring treatment, was significantly higher in the DBE group (72% vs 48%; \textit{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 (\textit{P} = .002).\textsuperscript{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%).\textsuperscript{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.\textsuperscript{49}

One prospective randomized trial comparing SE with DBE has been reported.\textsuperscript{42} DBE was associated with longer procedure times; however, significantly deeper insertion and a higher rate of complete enteroscopy (92% vs 8%; \textit{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.\textsuperscript{50} Only 1 study to date has compared SBE and SE.\textsuperscript{55} A total of 92 patients underwent 105 procedures (52 SBE, 53 SE). The most common indication for DE was OGIB (\textit{n} = 42). The mean depth of maximal insertion for SE was significantly higher than that for SBE (301 cm vs 222 cm; \textit{P} = .001). However, the diagnostic yield between SBE and SE (59.6% vs 43.4%; \textit{P} = .12) and mean procedure times between SBE and SE (55 minutes vs 47 minutes; \textit{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.\textsuperscript{51} OGIB occurs in approximately 5% of all patients who present with GI hemorrhage.\textsuperscript{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.\textsuperscript{53} This approach leads to a significant clinical improvement in over 75% of treated patients, including reduced transfusion and iron requirement needs.\textsuperscript{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%.\textsuperscript{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; \textit{P} < .0001) and in diagnostic yield (63% vs 44%; \textit{P} < .0001).\textsuperscript{7}

A meta-analysis of 11 studies involving 375 patients, which compared VCE and DBE, reported similar diagnostic yields (60% vs 57%, respectively; \textit{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%.\textsuperscript{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 (\textit{P} = .16).\textsuperscript{59} However, the diagnostic yield of DE was significantly higher when performed after a positive VCE compared with negative VCE (75% vs 27.5%; \textit{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%.\textsuperscript{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.\textsuperscript{50,61} 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.\textsuperscript{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.57,66,70

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.59

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

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.57,79 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, endoscopy 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

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