Small bowel enteroscopy

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Over the past decade, the advent of capsule endoscopy and balloon-assisted enteroscopy has revolutionized the approach to small intestinal diseases. The small bowel is no longer out of reach, and has fallen within the diagnostic and therapeutic realm of the gastrointestinal endoscopist. Double-balloon enteroscopy was the first type of balloon-assisted endoscopy and is the method for which there are the most data. Single-balloon enteroscopy has since been introduced as an alternative balloon-assisted method, followed more recently by the development of spiral overtube-assisted enteroscopy. The purpose of the present article is to review these methods of small bowel enteroscopy and to discuss the latest developments. While the investigation of small bowel diseases cannot be addressed without considering the central role of capsule endoscopy, a detailed assessment is beyond the scope of the present article, and capsule endoscopy will only be discussed as it pertains to enteroscopy.

Key Words: Capsule endoscopy; Double-balloon enteroscopy; Single-balloon enteroscopy; Small bowel; Spiral enteroscopy

TECHNIQUE AND EQUIPMENT

By now, most readers have some familiarity with the basic concepts involved in double-balloon enteroscopy (DBE, Fujinon Inc, Japan). Briefly, DBE consists of a 200 cm endoscope and a 140 cm flexible, polyurethane overtube, both of which are fitted at the distal tip with an inflatable latex balloon (Figure 1A). The overtube balloon is inflated to grip the intestinal wall and hold it in place, preventing stretching of the intestine and enabling advancement of the endoscope without the formation of redundant loops of bowel. After advancement of the overtube to the distal tip of the endoscope, both balloons are simultaneously inflated while the endoscope and overtube are pulled back together in a shortening manoeuvre pleating the intestine back over the scope. This cycle is successively repeated as the endoscope is advanced through the small intestine. In contrast, single-balloon enteroscopy (SBE, Olympus Inc, Japan) (Figure 1B) is a latex-free system that has a balloon only on the overtube, meaning that endoscope tip deflection, usually together with suction, is required to ‘hook’ the bowel wall to enable shortening, whereas in DBE, this is accomplished directly by inflating the endoscope balloon. Both DBE and SBE may be performed via an anterograde approach through the mouth or via a retrograde approach through the anus. The techniques for performing DBE and SBE have been described in detail elsewhere (1-4). Spiral enteroscopy is a new and entirely different overtube-assisted method for which the earliest outcomes are just beginning to be reported (5,6). It uses a unique overtube called the Discovery SB (Spirus Medical Inc, USA), which has raised helices at its distal end, a locking device to fix the overtube to the endoscope and two foam handles at its proximal end to facilitate overtube rotation. Clockwise rotation of the spiral overtube acts in a similar manner to that of a screw, advancing the endoscope while pleating the bowel onto its surface. The spiral overtube can be used with either the Olympus SBE endoscope or the Fujinon DBE endoscope. However, this device is not approved for use in Canada, and the company does not intend to introduce it to the Canadian market in the near future.

Small bowel enteroscopy via the mouth can be performed without previous purgative bowel preparation after an overnight fast of 8 h to 10 h, although some centres prefer to use some form of bowel preparation. In contrast, retrograde balloon-assisted enteroscopy (BAE) requires full bowel preparation in the same manner as colonoscopy. While no specific regimen is recommended, it is essential to have a complete preparation because stool debris that accumulates between the endoscope and overtube creates friction that ultimately can impair ongoing advancement through the small bowel.

Fluoroscopy may be helpful when first learning BAE, but is generally not necessary once one is comfortable with the procedure; the exception is dilation of small bowel strictures, where fluoroscopy is important. It can also be useful when further insertion becomes limited and fluoroscopy may guide the repositioning of the endoscope to straighten any loops. Although we do not routinely use fluoroscopy, other centres continue to do so, with mean fluoroscopy times of 2 min at several American centres (7), and ranging from up to 5 min to 7 min in Japan (8).

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Cost may be a significant factor when considering investment in a small bowel endoscopy system (Table 1), particularly for existing Olympus endoscopy users who would need to purchase a dedicated Fujinon platform if they decided to adopt DBE rather than SBE. Thus, for those already using Olympus endoscopes, there may be an economic argument for choosing SBE. For both systems, the overtube is a disposable, single-use device that must be used fresh for each case. Standard colonoscope accessories, including biopsy forceps, polypectomy snare, injector needles, and 7 Fr argon plasma coagulation probes can be used with the SBE and therapeutic DBE (EN-450T5) endoscopes. Smaller, dedicated accessories are needed for the narrower channel in the pediatric DBE (EN-450P5) endoscope.

Training

BAE is a challenging procedure associated with a significant learning curve and must be performed frequently and on a consistent basis to master. This was illustrated by the DBE experience of the Mayo Jacksonville group (9), for whom the rate of complete enteroscopy was 8% and DBE was deemed to have a “helpful clinical impact” for 58% of the first 50 cases, whereas for cases 150 to 200, the rates of complete enteroscopy and clinical impact rose to 63% and 86%, respectively. Furthermore, in the first year of DBE performed at six tertiary referral centers in the United States (US) after experienced endoscopists had undergone a training course in Germany, stable insertion of the DBE endoscope through the ileocecal valve into the terminal ileum failed in 31% of cases (7). This steep learning curve has significant implications for training, meaning that BAE experience is likely best acquired during a dedicated endoscopy fellowship and not as part of a general gastroenterology residency. While there are no formal guidelines for the requisite training necessary to perform BAE, a recent American Society for Gastrointestinal Endoscopy (ASGE) technical review (10) suggests that advanced colonoscopy skill combined with dedicated and comprehensive training, preferably during a higher-tier advanced endoscopy fellowship, is necessary. The ASGE also contends that hands-on workshops alone cannot replace supervised training on human subjects. These recommendations have important implications for physicians in clinical practice interested in starting BAE because it implies the need to first devote time at another center with a small bowel endoscopist already experienced with the technique.

Approach to Gastrointestinal Bleeding

The indications for small bowel endoscopy are numerous and continue to expand (Table 2). However, the majority of patients are referred for the investigation of obscure gastrointestinal bleeding (OGBB) that remains unexplained after negative upper endoscopy and colonoscopy. In the past, such patients were evaluated with small bowel barium x-ray and push enteroscopy, but the evidence now clearly demonstrates that these tests are grossly inferior to capsule endoscopy (CE) (11,12) and to DBE (13), and that proceeding immediately to DBE may be the most cost-effective strategy (14,15). Nevertheless, the
general consensus is that most patients with OGIB should be evaluated first by CE, which can then select patients most likely to benefit from BAE or spiral enteroscopy. There are several reasons why the diagnostic strategy for OGIB in most cases should begin with CE:

- CE is relatively noninvasive and comfortable, whereas BAE procedures are very invasive and lengthy, typically lasting at least 100 min (7,9) and often associated with increased abdominal discomfort compared with conventional endoscopy (16).
- Patients may continue with their normal daily activities while undergoing CE, whereas BAE requires deep sedation, usually with propofol, but in some Canadian centres with general anesthesia.
- Meta-analysis data demonstrate that CE and DBE have similar diagnostic yields for identifying the sources of small bowel bleeding (17-19).
- CE can accurately select the correct route of insertion for BAE (oral versus anal) based on the relative location of abnormal CE findings in terms of small bowel transit time, thus making subsequent BAE more efficient (20,21).
- The diagnostic yield of DBE is significantly enhanced when performed after a previously positive CE (19).
- CE has a high negative predictive value, suggesting that most patients may be able to avoid undergoing BAE because the rebleeding rate after a negative CE study at 12 months follow-up is only 5% to 6% (22,23).

However, it must be remembered that CE can result in false-negative studies in which subsequent BAE may diagnose – and potentially treat – the bleeding etiology. In particular, concerns have been raised about a possible tendency for CE to miss small bowel mass lesions such as tumours (24). This was illustrated by a retrospective study of small bowel mass lesions involving 18 patients who were diagnosed using DBE (25). CE had been previously performed in 15 of these patients, but only detected the mass in five cases. Furthermore, CE visualizes the major papilla only 10% to 44% of the time, demonstrating how mass lesions have the potential to be missed (26,27). Finally, a recent meta-analysis that examined comparative studies of DBE and CE in patients with OGIB (19) found that 29% of patients with a negative CE had a bleeding source found with subsequent DBE. Therefore, when clinical suspicion is sufficiently high, or when patients have ongoing or recurrent evidence of bleeding after negative CE, further investigation with small bowel enteroscopy is clearly warranted.

Another important consideration when referring patients for small bowel investigations for presumed OGIB is whether a second ‘re-look’ gastroscopy and/or colonoscopy should be performed before referral for CE or BAE. Patients may continue with their normal daily activities while undergoing CE, whereas BAE requires deep sedation, usually with propofol, but in some Canadian centres with general anesthesia.

ENDOSCOPIC OUTCOMES

Nearly all of the data that exist for small bowel enteroscopy come from DBE studies, with only early outcomes reported for BAE and spiral enteroscopy. DBE yields a positive diagnosis when investigating small bowel diseases approximately 70% of the time, resulting in immediate endoscopic therapy or a subsequent change in management in two-thirds of positive cases (2,7,9,31-37). The most commonly identified pathology among patients investigated for bleeding indications are vascular lesions such as angiodysplasia, inflammatory lesions such as ulcers, and tumours or polyps. Much less data exist for SBE, but early studies suggest a diagnostic yield of 41% to 65%, with 50% to 60% of cases being able to provide therapeutic interventions, rates comparable with what has been achieved using DBE (3,38-40). Much is often made about depths of insertion when comparing methods of small bowel endoscopy, yet despite a standardized method for estimating the extent of insertion (41), this remains a highly subjective measure. A more objective metric is the rate of complete enteroscopy when the entire small intestine is visualized by combining oral and anal approaches. This itself is highly variable for DBE, ranging from as low as 5% in the early US experience (7), to 23% in Germany (42) and to as high as 86% in the study by Yamamoto et al (2), the first pioneer of DBE, in Japan. In contrast, rates of complete enteroscopy using SBE, to date, have been limited to 0% to 25% (3,38-40). A recent study sought to compare the single- and double-balloon techniques by randomly assigning patients to undergo DBE or a ‘single-balloon’ method using the Fujinon DBE and overtube but without a balloon attached to the endoscope to simulate SBE (43). The rate of complete enteroscopy in the DBE group was 66% compared with 22% in the ‘single-balloon’ group (P<0.001). However, this study has been criticized for using endoscopists with extensive experience in DBE but much less with SBE and for simulating the single-balloon technique instead of actually using the Olympus SBE system, and likely does not represent a true comparison of these competing technologies. These limitations were overcome by a clinical trial from Japan that randomly assigned 38 patients to SBE or DBE, and found a complete enteroscopy rate of 0% and 57%, respectively (P=0.002) (8). In fact, this trial was stopped early due to the obvious advantage for the DBE group. Conversely, a multicentre European noninferiority trial that randomly assigned patients to SBE versus DBE found no difference in proximal or distal insertion depths with either method, with rates of complete enteroscopy of 18% for SBE and 18% for DBE (44). Nevertheless, based on our own experience, it is not surprising to observe that SBE seems to have inferior insertion depths when compared with DBE, likely because the SBE hooking manoeuvre with the endoscope tip is less effective at grasping the bowel wall than inflation of the balloon at the tip of the endoscope in DBE, causing the SBE to slip during reduction cycles. However, achieving complete enteroscopy is often not clinically important or necessary, particularly when the majority of lesions, at least in patients in the western world, seem to be found in the proximal small intestine (37). Indeed, the rates of positive diagnoses between the DBE and the SBE groups in the previously mentioned studies were not significantly different despite the impressive difference in rates of complete enteroscopy in the first two of these trials (diagnostic yields of 52% for DBE and 42% for SBE [P=0.42] in the Wiesbaden study [43]; 50% for DBE and 61% for SBE [P=0.49] in the Japanese study [8]). However, achieving complete enteroscopy may provide greater reassurance against the possibility of rebleeding in subsequent follow-up compared with when parts of the small bowel remain unexamined (45).

Endoscopic outcomes are only beginning to be defined for spiral enteroscopy, the latest method of small bowel enteroscopy. Preliminary reports described low diagnostic yields despite significant small bowel insertion depths and rapid average procedural times (5). However, recent studies have demonstrated improved outcomes similar to those obtained with DBE and SBE (46). Furthermore, studies directly comparing spiral enteroscopy via the oral route with SBE (47) and with DBE (48,49) have now been published with somewhat conflicting results, although diagnostic yields did not significantly differ among methods. The only prospective randomized study found significantly shorter procedure times with spiral enteroscopy, but significantly greater insertion depths with DBE (49). Even less is known about the efficacy of spiral enteroscopy performed via the anal route. Although this has been shown to be a feasible technique (50), we expect deep insertion using this method to be limited because the spiral overtube itself is unable to pass through the ileocecal valve in a retrograde fashion. Thus, while spiral enteroscopy has potentially great appeal due to its shorter insertion times, its comparative efficacy still needs to be clarified before adoption in clinical settings.

CLINICAL OUTCOMES

A more important consideration regarding small bowel enteroscopy is the question of how clinically useful these investigations are to
patients in the long term. In fact, very little data regarding long-term follow-up of patients after DBE exist, with most studies having focused on immediate endoscopic results. In a telephone survey of 274 patients who had undergone DBE for OGIB in which 31% agreed to participate in an interview at 30 months’ follow-up, 59% experienced no further bleeding or anemia, 28% had an ongoing need for blood transfusions or iron therapy, and 24% experienced new or recurrent overt bleeding (51). Among patients found to have arteriovenous malformations, 57% experienced rebleeding, or required transfusions and/or iron therapy at 12 months’ follow-up. More rigorous data come from a recent retrospective analysis of 151 patients who underwent DBE for OGIB in Japan. At a mean long-term follow-up of 29.7 months, 63% of patients with a negative DBE had ‘control’ of bleeding, defined as the absence of overt bleeding, a drop in hemoglobin >10 g/L, and blood transfusions or iron therapy (52). In contrast, patients found to have vascular lesions on DBE were most likely to experience rebleeding and had significantly shorter rebleeding-free intervals, with 40% experiencing a recurrent overt bleed within one year of their DBE and only 40% with ‘control’ of OGIB at long-term follow-up. The significant predictors of rebleeding among these patients with vascular lesions were a large transfusion requirement before the initial DBE (mean of 9.7 units in patients with overt rebleeding versus 3.3 units in patients without overt rebleeding [P=0.012]), the finding of multiple vascular lesions compared with a solitary vascular lesion (P=0.01) and the identification of ‘suspicious’ as opposed to ‘definite’ causative lesions (P=0.038), perhaps because these inconclusive lesions were not endoscopically treated. Meanwhile, patients with other findings on DBE seem to experience better long-term outcomes, with 65% control in those with ulcers/erosions and 84% control in those with tumours or polyps (52). It appears that patients with OGIB due to vascular lesions are the most difficult to treat, and the most likely to experience recurrent or ongoing bleeding, suggesting that ongoing clinical follow-up is likely required for this group. Nevertheless, the superior outcomes in patients with other diagnoses and the need to exclude more sinister causes of bleeding such as small bowel tumours, which may be present in as many as 5% to 10% of OGIB patients (53,54), illustrates the importance of performing some form of small bowel endoscopy, be it DBE, SBE or CE.

SAFETY AND COMPLICATIONS

Given the deeply invasive nature of BAE, it is perhaps not surprising to observe complication rates that exceed those encountered with colonoscopy. A large, multicentre survey of 10 institutions in Europe and Asia involving 2362 DBE procedures (55) identified bleeding (0.8%), perforation (0.3%) and pancreatitis (0.3%) as the most common and significant adverse events associated with DBE. Overall, complications were more frequently encountered with therapeutic (4.3%) rather than diagnostic (0.8%) procedures, with 12 of 19 bleeding episodes occurring after polypectomy and five of six perforations occurring after an intervention (two postdilation, three post-argon plasma coagulation). Rates of pancreatitis did not differ between diagnostic and therapeutic procedures but were confined to patients who had undergone antegrade DBE. A similar pattern was observed in 2478 DBE procedures performed at nine centres in the US, where the most notable adverse events remained: perforation (0.4%), bleeding (0.2%) and pancreatitis (0.2%) (56). However, a striking finding of this study was the preponderance of perforations occurring in retrograde DBE procedures performed in patients with surgically altered anatomy, most in purely diagnostic examinations. The perforation rate was much higher in retrograde (1.1%) compared with antegrade (0.2%) cases, with one-half of such perforations in the retrograde procedure occurring in patients with previous ileocolonic or ileoileocolonic anastomoses. In fact, among this subgroup with a surgically altered anatomy, perforations occurred in six of 60 (10%) retrograde but only one of 159 (0.6%) antegrade DBE cases. This finding should raise alarm and signal endoscopists to heed caution when performing retrograde DBE in this patient population. In the early years of BAE, much of the attention regarding complications focused on the occurrence of post-DBE pancreatitis. In response to these concerns, the DBE insertion technique was modified to delay balloon inflation until the tips of both the endoscope and overtube are beyond the ligament of Treitz, which appears to have decreased the incidence of pancreatitis, but asymptomatic hyperamylasemia remains common (57). Indeed, in the first studies of adverse events with SBE and spiral enteroscopy, no episodes of pancreatitis were encountered (58,59). Thus, while pancreatitis continues to be a present, yet possibly diminishing, concern, bleeding and, in particular, perforation, remain major adverse events that must be considered before performing BAE and spiral enteroscopy.

EMERGING APPLICATIONS

Biliary and pancreatic access in surgically altered anatomy

Endoscopic retrograde cholangiopancreatography (ERCP) in patients after partial gastrectomy with Billroth II gastrojejunostomy or after Roux-en-Y anatomyosis (for a variety of surgical indications including Whipple resection, liver transplant and gastric bypass) has long been challenging, particularly in achieving access to the native papilla or pancreatic and/or biliary surgical anastomosis. Over the past few years, the feasibility, safety and efficacy of the new BAE methods to facilitate ERCP have been demonstrated, predominantly in the form of small case series with DBE. Several studies have reported success rates of 80% to 90% (60-63), whereas other series have had much lower success rates in the range of 60% to 63% (64-66). Similar cannulation success rates of between 62% and 75% have also been reported from early case series of SBE-assisted ERCP (67-71). A multicentre, retrospective study compared the use of DBE, SBE and spiral enteroscopy to facilitate 156 ERCP procedures conducted in 129 long-limb surgical bypass patients (72), and no difference was observed among the methods, with overall success rates of 71% for enteroscopy (in terms of reaching the native papilla or pancreatic and/or biliary anastomosis) and 63% for ERCP cannulation. Indeed, achieving successful cannulation is one of the unique challenges posed by BAE-assisted ERCP, particularly because of the need to use a forward-viewing rather than a side-viewing endoscope and because of the lack of an elevator (73). An additional challenge has been the need for dedicated ERCP accessories long enough to be used with the 200 cm DBE or SBE endoscopes. To overcome this limitation, a ‘short’ 152 cm DBE endoscope with a 2.8 mm working channel (EC-450BI5 [Fujinon Inc, Japan]) that is compatible with conventional ERCP accessories has been developed. Early data from one expert Japanese centre demonstrated exceptional outcomes, with ERCP access achieved in 97% and successful cannulation in 95% of 103 short-DBE ERCP cases (74). In summary, while the new methods of BAE and spiral enteroscopy can be effectively used to facilitate ERCP in patients with surgically altered anatomy, the procedure remains challenging.

Incomplete colonoscopy

Another useful, emerging application of BAE is the completion of colonoscopy in patients with previously failed or difficult colonoscopy. Several case series have demonstrated the efficacy and safety of using DBE or SBE endoscopes to perform colonoscopy in patients in whom often multiple previous attempts with conventional colonoscopy failed to reach the cecum (75-79). Among these cohorts, successful cecal intubation was achieved in more than 95% of cases, with no reported complications. While there has yet not been a head-to-head comparison of DBE- and SBE-assisted colonoscopy, a small, single-centre, randomized controlled trial comparing SBE with repeat standard colonoscopy (SC) in 30 patients with previously failed colonoscopy was recently published (80). The cecal intubation rate was 93% and 50% for SBE and SC, respectively, with success rates for reaching the cecum by crossing over to the alternative technique of 100% for SBE and 0% for SC. However, a retrospective review of 90 patients with previously incomplete colonoscopy referred to St Paul's Hospital (Vancouver, British Columbia) between 2005 and 2010, showed that repeat attempts at colonoscopy were successful in 97% of cases (81). Thus, it
is important to emphasize that while balloon-assisted methods are useful options when complete colon examination cannot be achieved, the vast majority of incomplete colonoscopies can be overcome with the use of increased sedation, more time and patience, variable-stiffness or pediatric colonoscopes, or referral to a more experienced endoscopist.

**SUMMARY**

Over the past decade, the advent of DBE, SBE and spiral enteroscopy has revolutionized the accessibility and approach to small bowel diseases, extending beyond the diagnostic capabilities of radiology or CE to enable real-time access, tissue sampling and therapeutic interventions deep within the small intestine. While small bowel enteroscopy was an experimental field only a few years ago, it has now become firmly established as a key component in the evaluation of the gastrointestinal tract (Table 3). What remains unclear is how the various methods truly compare, and the clinical – not just endoscopic – outcomes that are achieved by performing these invasive and time-consuming procedures. Well-designed, prospective, randomized controlled trials with long-term follow-up are needed to provide this clarity. In the meantime, DBE remains the standard for which most data exist, and SBE and spiral enteroscopy will likely continue to be regarded as experimental methods that still need to be shown to be as good as DBE before being adopted outside of a research setting.

**REFERENCES**


**TABLE 3**

**Summary of key messages**

| BAE is safe and effective, enabling real-time diagnosis, tissue sampling and therapeutics throughout the small bowel |
| Assessment for small bowel sources of bleeding should begin with CE, followed by BAE when CE yields positive findings or when clinical suspicion remains high |
| Most data exist for DBE, but evidence continues to emerge for SBE and spiral enteroscopy |
| Randomized controlled trials comparing DBE and SBE show superior rates of ‘complete enteroscopy’ for DBE but equivalent diagnostic yields |
| There is a paucity of data regarding long-term clinical outcomes and benefit from BAE for small bowel bleeding |
| The major complications from BAE are perforation (0.3%-0.4%), pancreatitis (0.2%-0.3%) and bleeding (0.2%-0.8%) |

**BAE Balloon-assisted enteroscopy; CE Capsule endoscopy; DBE Double-balloon enteroscopy; SBE Single-balloon enteroscopy**

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