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Diagnostic yield of deep enteroscopy techniques for small-bowel bleeding and tumors

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ABSTRACT

Endoscopic evaluation and management with deep enteroscopy techniques have largely replaced the role of intraoperative enteroscopy in the management of small-bowel (SB) disorders. While capsule endoscopy (CE) enables visualization of the entire SB, therapeutic deep enteroscopy techniques (balloon-assisted enteroscopy and spiral enteroscopy) facilitate diagnostic and therapeutic management deep within the SB. CE is currently recommended as the third test of choice in the evaluation of obscure gastrointestinal bleeding after a negative bidirectional endoscopy. The test also has a role in the diagnosis of SB tumors and surveillance of familial polyposis syndromes. Therapeutic deep enteroscopy techniques are mainly used for evaluation and management of CE findings, but they may also have a role in patients with a negative CE but high clinical suspicion for an SB disorder. Because preliminary data suggest a comparable diagnostic and therapeutic yield with double-balloon, single-balloon, and spiral enteroscopy, selection of the enteroscope should be based on availability and the endoscopist's experience with the technique.

Introduction

The introduction of a large armamentarium of deep enteroscopy techniques during the past decade has led to a shift toward an endoscopic approach for the management of small-bowel (SB) disorders. While capsule endoscopy (CE) has enabled diagnostic evaluation of the entire SB, balloon-assisted enteroscopy (BAE) (double- and single-balloon [DBE and SBE]) and spiral enteroscopy (SE) have facilitated both diagnostic and therapeutic management deep within the SB, thereby avoiding surgery in many patients. This article is a review of the diagnostic yield of the deep enteroscopy techniques and a comparison of the different modalities for obscure gastrointestinal bleeding (OGIB) and tumors. A description of these technologies and their therapeutic utility is discussed in a separate article.

1. Obscure gastrointestinal bleeding

Most patients with OGIB have SB or "midgut" bleeding, which is defined as bleeding from sources located between the ampulla of Vater and ileocecal valve. The use of push enteroscopy (PE) and intraoperative enteroscopy (IOE) for evaluation of SB bleeding has now been largely replaced by deep enteroscopy techniques.

1.1. Capsule endoscopy

CE is currently recommended as the third test of choice in the evaluation of patients with OGIB, after a negative bidirectional endoscopy [1,2]. This recommendation is based on the results of 2 meta-analyses that unequivocally showed that CE is superior to other diagnostic modalities in OGIB. A meta-analysis of 14 studies found that CE had an incremental yield of 30% (yield, 56% vs 26%) over PE and 36% over SB radiography for clinically significant findings within the SB. In a subanalysis, CE had a higher yield than PE for the detection of vascular and inflammatory lesions [3]. Another meta-analysis that included 9 studies also showed that CE is superior to alternative SB modalities (PE and SB radiography), with a rate difference of 41% for all SB disorders and 37% in OGIB [4].

Compared with IOE as a gold standard test, CE was found to have a diagnostic yield of 74% in a prospective study of 47 patients with OGIB [5]. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of CE in this study were 95%, 75%, 95%, and 86%, respectively. The yield of CE in OGIB ranges from 35% to 76% [6–10], and a pooled analysis of 24 CE trials with 691 patients reported an overall diagnostic yield of 87% with CE [11]. A recent study from Europe surveyed 23 centers for their CE practice during a 7-year period. Forty-three percent of the 2921 CEs had been performed for OGIB, and the diagnostic yield of CE was 66% in these patients [12].

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Several factors, including clinical presentation, patient selection, and timing of the procedure can influence the diagnostic yield of CE. In a single-center study of 250 patients, CE had a significantly higher yield of 60% in patients with overt bleeding as compared with 46% in those with occult bleeding. Moreover, in patients with overt bleeding, the yield was higher in those who had ongoing bleeding (87%) as compared with previous bleeding (56%) [13]. Bresci et al. [14] reported a diagnostic yield of 91% as compared with 34% when CE was performed within and after 2 weeks of the bleeding episode. CE also has a higher likelihood of detecting a bleeding source in patients with >1 episode of bleeding, persistent bleeding for >6 months, or low hemoglobin (<10 g/dL) [15].

Studies have reported favorable outcomes in patients who have undergone CE for evaluation of OGIB. Pennazio et al. [16] reported a sensitivity, specificity, PPV, and NPV of 89%, 95%, 97%, and 83%, respectively, with CE in 100 consecutive patients. Sixty-five percent of the patients had no recurrent bleeding during a mean follow-up period of 18 months after CE-guided interventions. Similarly, Delvaux et al. [17] reported a PPV of 94.4% and NPV of 100% with CE. Follow-up of patients for >12 months revealed no recurrence of bleeding in 83% of patients who had a positive CE and interventions. All the patients with a negative CE finding were subsequently diagnosed with a bleeding source outside the SB. Two other studies have demonstrated favorable outcomes after a negative CE. The cumulative rebleeding rates in these studies were 5.6% and 11% in patients with a negative CE finding as compared with 48% and 42%, respectively in those with a positive examination result [18,19]. Therefore, the International Consensus Committee on CE has recommended that additional invasive testing can be deferred in patients after a negative CE finding, unless there is rebleeding [20].

There is a role for repeat CE in patients who present with recurrent bleeding, after a negative or nondiagnostic examination. A study of 76 patients who underwent repeat CE for recurrent bleeding or experienced a decrease in hemoglobin of >2 g/dL found that the repeat examination was diagnostic in patients whose presentation changed from occult to overt bleeding, and in those with a decrease in hemoglobin of >4 g/dL [21]. Two smaller studies reported a diagnostic yield of 35% and 75% on repeat CE and a change in management in up to 63% of these patients after the second examination [22,23].

1.2. Double-balloon enteroscopy

The depth of SB intubation with DBE ranges from 240 to 360 cm with the antegrade approach and 102 to 140 cm with the retrograde approach, and it is significantly higher compared with PE (90-150 cm) and ileoscopy (50-80 cm) [24–27]. Total enteroscopy with DBE is defined as intubation of the entire SB, using either a single or combined antegrade and retrograde approach. The decision to perform total enteroscopy is based on the degree of clinical suspicion for an SB lesion and/or inability to detect a lesion observed on prior CE or SB imaging at initial DBE. The rate of total enteroscopy with DBE ranges from 0% to 86% and is higher in studies from the East [25,26,28,29].

May et al. [30] compared DBE to PE in 52 patients with OGIB and found that DBE allowed a greater depth of intubation (230 vs 80 cm) and also had a higher diagnostic yield (73% vs 44%) than PE. Furthermore, DBE detected additional lesions in the distal SB in patients who had proximal SB lesions on PE. The diagnostic yield of DBE in patients with OGIB ranges from 50% to 80%, and the test enables successful endoscopic therapeutics in up to 75% of patients [24,25,27,30–33]. A systematic review of 13 studies that included 906 patients with OGIB reported a diagnostic yield of 66% with DBE, predominantly angioectasias [34]. Although vascular lesions are the most prevalent findings on DBE reported from Western studies, inflammatory lesions and tumors have been more commonly described in the East [27,30,35].

A study of 100 consecutive patients with OGIB reported a high sensitivity of 92.7%, specificity of 96.4%, PPV of 98.1%, and NPV of 87.1% with the test. The diagnostic yield of DBE was significantly higher in patients with overt ongoing bleeding (100%) as compared with those with previous overt bleeding (48.4%) or occult bleeding (42.1%) [35]. Similar to CE, the yield of DBE is also higher in patients with a longer duration and multiple episodes of bleeding [36].

The need for DBE and its route are often determined based on findings of previous CE. Gay et al. found a PPV of 94.7% and NPV of 98.3% with CE for reliably predicting a necessity for DBE. Using a time index for SB lesions (ratio of transit time of lesion to the time between ingestion and entrance of capsule into the cecum), the study also showed that an index of >0.75 accurately predicted finding the lesion via a retrograde DBE approach [37]. This performance of a "targeted DBE" has been shown to increase the diagnostic (73%-93%) and therapeutic yield (57%-73%) of the test. Because of deeper intubation of the SB, the antegrade approach is the preferred route for lesions suspected to lie within the proximal 75% of the SB, whereas the retrograde route is used for more distal lesions [38,39].

A small study evaluated the role of emergent DBE without a previous CE in 10 patients with overt ongoing bleeding. The route of DBE in the study was based on presentation of the patient with melena (antegrade approach) or hematochezia (retrograde approach). If initial DBE was negative, the test was performed by the alternate route. The diagnostic and therapeutic yield with DBE was 90% and 50%, respectively, with this approach. This study showed that an emergent DBE is technically feasible and facilitates the diagnosis and management of acute OGIB [40].

DBE has multiple roles in the evaluation and management of OGIB. The test is useful after a positive CE for biopsies or hemostasis, after a negative CE in patients with recurrent bleeding or high clinical suspicion for SB lesion, in patients in whom CE is contraindicated, and in those with active bleeding.

There are only limited data on the outcomes of patients after DBE. Gerson et al. conducted telephone interviews of 85 patients at 30 months follow-up after DBE. There was no recurrent bleeding or iron/transfusion requirements in 59% of patients, whereas 24% reported recurrent bleeding and 18% had ongoing need for iron/transfusions [41]. Another outcomes study of DBE in patients with vascular SB lesions found no recurrent bleeding after a mean follow-up period of 55 months in 58% of patients. There was a decrease in transfusion requirements from 60% to 16% of patients before and after DBE [42].

1.3. Single-balloon enteroscopy

SBE was introduced after DBE and has since been evaluated in a small number of studies. A preliminary study reported a total enteroscopy rate of 15% and a diagnostic yield of 54% with SBE in patients with suspected SB disorders [43]. Frantz et al. [44] evaluated 38 patients who underwent antegrade SBE for suspected SB disorders, 97% with OGIB. The diagnostic yield with SBE was 47%, and the estimated depth of insertion was proximal jejunum (34%), mid jejunum (45%), and distal jejunum (21%). The procedure was successfully performed with conscious sedation in most patients. Similar results were reported in a study from India, with a diagnostic yield of 60% in OGIB, total enteroscopy rate of 25%, and mean depth of intubation of 256 cm with the antegrade approach and 163 cm with the retrograde approach [45]. The largest single-center study from the United States evaluated SBE in 161 patients with suspected SB disorders, of whom 59% had OGIB. The mean depth of intubation in this study was only 133 cm with the antegrade approach and 73 cm with the retrograde approach. However, the yield of SBE was 58%, similar to previous reports on DBE, and included predominantly angioectasias. The concordance between CE and SBE findings was 40%, and SBE detected new findings in 17% of patients [46].