Bleeding from Small Intestine: No Man's Land

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Clin Colon Rectal Surg 2020;33:16–21.

Abstract

Keywords

- ▶ video capsule endoscopy (VCE)
- ▶ deep enteroscopy
- ▶ intraoperative enteroscopy

Bleedings from small intestine account for 5% of all gastrointestinal bleeding. With advanced endoscopic tools, such as video capsule endoscopy and deep enteroscopy, accurate diagnosis and treatment is possible in majority of cases with low mortality and morbidity. Nonoperative management includes endoscopic hemostasis and angiographic embolization. Recurrence after initial treatment is relatively common. Surgery is reserved for the cases that are refractory to endoscopic or angiographic treatment, bleeding from tumor or mass lesions, or hemodynamic instability. At the time of surgical exploration, unless the lesion has been marked by endoscopic tattoo or clip, intraoperative enteroscopy is often necessary to localize the lesion.

Gastrointestinal bleeding (GIB) from small intestines poses significant challenges in localization and treatment. Unlike upper GIB or colonic bleeding, endoscopic access and endoscopic hemostasis are generally not possible with conventional tools. Unlike colonic bleeding, where a partial colectomy or in limited cases, subtotal colectomy is an option, surgeon needs a precise localization for limited resection in small intestine. Fortunately, for physicians and surgeons, bleeding from small intestine is rare. It accounts for about 5% of all GIB,¹ and many can be managed conservatively. Furthermore, in recent years, advent of new diagnostic tools, such as video capsule endoscopy (VCE), and newer endoscopy, such as balloon enteroscopy, has made localization and endoscopic treatment feasible. In fact, majority of what was called “obscure GIB (OGIB)” is small intestinal bleeding. In this article, we will review etiology, diagnostic tools, and management of small intestine bleeding with technical details on deep enteroscopy.

Etiology of Small Intestinal Bleeding

Two most common etiologies that are found in small intestinal bleedings are vascular lesion and ulcerated lesion. Ulcerated lesion is defined by large area of erosion with central exudative area. Vascular lesion is defined by red or raised structure that is different from normal mucosa.²

1. *Vascular lesion*: this is the most common identifiable cause of small intestinal bleeding in Western countries. They include angioectasia, Dieulafoy's lesion, and arteriovenous malformation (AVM). They are amenable to endoscopic treatment, such as argon plasma coagulation (APC) or clipping. The rebleeding (defined by rebleeding within 30 days) risk is relatively high. Several studies have corroborated that rebleeding after therapeutic double balloon enteroscopy (DBE) is a relatively common phenomenon, occurring in 35 to 46% of patients.^{3,4} Factors significantly associated with rebleeding included valvular or arrhythmic heart disease, thrombocytopenia, varices, total number of vascular lesions, and presence of overt bleeding.
2. *Mucosal ulcerative lesion*: this is the most common cause of small intestine bleeding in Eastern Asian countries and, in most cases, related to chronic NSAIDs (Non-Steroidal Anti-Inflammatory Drugs) use.⁵
3. *Benign or malignant lesion*: this includes hemangioma, gastrointestinal stromal tumor (GIST), adenocarcinoma, and lymphoma. In young patients with intestinal polyposis syndrome, such as Peutz-Jegher syndrome, small intestine polyps could bleed profusely.
4. *Congenital lesion*: Meckel's diverticulum is present in 2% of population and most of them are asymptomatic. When it becomes symptomatic, the most common symptoms

are bleeding. Small Meckel's diverticulum that is not apparent on computed tomography (CT) or small bowel series but is bleeding persistently can be challenging. Since technetium-99m scan only provides the presence of ectopic gastric mucosa without precise localization, deep enteroscopy is needed to localize the ulcerated lesion.

Video Capsule Endoscopy

Introduction

Since its development in 1998, VCE has taken on a vital role in the evaluation and management of small bowel bleeding. VCE allows for minimally invasive high resolution imaging of the entire small intestine without the need for sedation or radiation. The capsules measure 26 × 11 mm in dimension and have a battery life lasting 8 to 11 hours. The field of view ranges from 145 to 156 degrees and the capsule can store images at a rate of 2 frames/second.⁶ The images are transmitted directly to a recording device worn on the patient during the exam and are later uploaded to a computer with dedicated image viewing software. VCE has the ability to visualize the entire small bowel in 70 to 90% of patients, making it a first line diagnostic modality for small bowel bleeding after upper and lower GI sources have been ruled out.⁷

There is no standard preparation for VCE. Several methods of preparation exist, including fasting the day before the procedure, clear liquid diet the day before the procedure, or purgative preparation, generally with 2 to 4 L of polyethylene glycol. A meta-analysis of 12 studies showed that purgative preparation prior to VCE compared to clear liquid diet provided a significantly higher diagnostic yield and small bowel visualization quality.⁸ Simethicone is also frequently used as an antifoaming agent to improve visualization in addition to mechanical preparation.

Diagnostic Efficacy

The overall diagnostic yield of VCE for obscure GIB has been reported in several studies and varies from 40 to 77%.^{9,10} VCE has also been shown to have a high positive predictive value and negative predictive value (94.4 and 100%) for obscure GIB, determined by deep enteroscopy and clinical follow-up for 12 months in 44 patients.¹¹ A meta-analysis of three studies comparing VCE to small bowel radiography (88 patients) found that VCE had a significantly higher yield for clinically significant lesions (42 vs. 6%).¹² A study of 28 patients with OGIB demonstrated that a source of bleeding was detected in a higher proportion of patients with VCE compared to CT angiography (72 vs. 24%), but there was no significant difference between VCE and standard angiography.¹³ Several studies have compared the yield of VCE to DBE for OGIB and found them to have similar yields. This has been corroborated by three meta-analyses.¹⁴⁻¹⁶ However, the yield of DBE after a positive VCE (75%) was found to be significantly higher than DBE performed after a negative VCE (27.5%).¹⁶ This underscores the importance of diagnostic VCE in assessing the need for therapeutic deep enteroscopy.

Push Enteroscopy

Push enteroscopy (PE) is an upper endoscopy examination continued into the proximal jejunum. PE is generally performed with a pediatric colonoscope or a dedicated enteroscope measuring 250 cm in length and can reach a depth of 45 to 90 cm beyond the ligament of Treitz. PE is often limited by looping of the endoscope in the small bowel and patient discomfort, especially when being performed with intravenous (IV) conscious sedation. Overtubes have been used in conjunction with PE to increase the depth of insertion; however, their use is limited by patient discomfort and studies have shown no increase in significant findings compared to PE without an overtube. Due to the lack of deep access to the small bowel, PE is often used in conjunction with capsule endoscopy for lesions that are limited to the duodenum or proximal jejunum. PE may also be used as an adjunct to second look endoscopy for obscure GI bleeding.

The diagnostic yield of PE is reported to be 28 to 56%, with AVMs being the most common lesions found.¹⁷ AVMs are often distributed proximally in the small bowel. One study retrospectively examined 428 capsule endoscopies and identified 69 patients with AVMs. Of these lesions, 67% were in the duodenum and 78% were within the first 25% of small bowel transit, suggesting that the majority of these lesions are within the reach of PE.¹⁸ Thus, PE may be useful when VCE localizes lesions to the proximal small bowel.

Deep Enteroscopy

Deep enteroscopy is a generic term that generally implies the use of a specialized device to achieve deep access into the small intestine, and occasionally visualization of the entire small bowel. Deep enteroscopy is usually performed with DBE (Fujinon, Japan), single balloon enteroscopy (SBE; Olympus America Inc., Center Valley, PA), or spiral enteroscopy (SE; Spirus Medical Inc., Stoughton, MA). Each of these techniques will be reviewed separately below.

Double Balloon Enteroscopy

Introduction

The DBE was created in order to address the shortcomings of PE and allow deep access in to the small bowel. Use of a double balloon enteroscope for deep examination of the small bowel was first described by Yamamoto et al¹⁹ in 2001 and has been available in the United States of America since 2004. The DBE procedure involves use of an enteroscope, usually 230 cm in length, with a dedicated overtube measuring 145 cm in length. A shorter version with a 182 cm enteroscope and a 105 cm overtube is also available. The system includes two latex balloons, one at the tip of the enteroscope and another at the end of the overtube. A handheld balloon-pump controller (PB-20; Fujinon; Japan) is used to inflate and deflate the balloons. The balloons are inflated to a predetermined pressure of 5.6 kpa. The controller sounds an alarm if the balloon reaches a higher pressure. The procedure can be performed in both antegrade and retrograde fashion (► Fig. 1).

Fig. 1 Double balloon enteroscope with both overtube balloon and enteroscope balloon inflated.

Technique

The DBE procedure requires two people, the endoscopist and an assistant to operate the overtube. Once the enteroscope and overtube are passed into the duodenum beyond the major papilla, the overtube balloon is inflated to anchor it in place and the endoscope is advanced as far as possible into the jejunum. The endoscope balloon is then inflated to fix it to the intestine and the overtube balloon is deflated and advanced to meet the tip of the endoscope. The overtube balloon is then inflated so as to anchor both balloons in the intestine to obtain a stable position, and the entire system is

gently withdrawn to pleat the bowel over the overtube. This process is repeated serially to minimize looping of the endoscope and thereby maximize insertion depth. A tattoo is often injected at the point of maximal insertion as a reference point for future retrograde examination to allow for complete small bowel visualization. Retrograde examination is performed in a similar fashion to antegrade examination. Total enteroscopy may be performed with a direct antegrade approach or a combined antegrade–retrograde approach; however, successful total enteroscopy is much more likely with a combined approach. DBE may be performed with or without fluoroscopic guidance.²⁰

Withdrawal of the enteroscope is performed with the overtube balloon inflated for stabilization, and the endoscope balloon deflated to allow for slow and controlled inspection of the mucosa. When the endoscope tip reaches the overtube, the endoscope balloon is inflated and the overtube is deflated. The overtube is withdrawn until it meets the hub of the endoscope and the overtube balloon is then inflated and the endoscope balloon deflated. The endoscope is withdrawn and the process is repeated until the examination is completed.

Efficacy and Outcomes for Small Bowel Bleeding

The DBE allows for intubation of the small bowel 240 to 360 cm beyond the pylorus and 100 to 140 cm beyond the ileocecal valve with a retrograde approach. The diagnostic yield for OGIB ranges from 58 to 78% in large studies with a total enteroscopy rate of 57 to 76% and an therapeutic treatment rate of 16 to 49%.^{21,22} A systematic review of 12,823 DBE procedures demonstrated a pooled diagnostic yield for suspected small bowel bleeding of 68% with a total enteroscopy rate (antegrade or combined) of 44%. Total enteroscopy with antegrade approach is uncommon and has been reported in 2% (► Fig. 2).²³

Major complications during DBE are relatively uncommon, reported at 0.7%. The most common major complications are perforation, pancreatitis, bleeding, and aspiration pneumonia. Various studies have described the rate of perforation from 0.3 to 3.4%, with increased risk associated with inflammatory bowel disease, malignancy, and surgically altered anatomy. DBE should be used with caution in patients with such conditions. The rate of pancreatitis has been reported to be 0.3% in a large multicenter prospective study of 2,245 DBE examinations in 1,765 patients. Minor complications resulting from DBE are relatively more common, occurring in 9.1% cases.²⁴

Single Balloon Enteroscopy

Introduction and Technique

The SBE is similar to DBE in most regards, except that only balloon is located on the overtube, as opposed to DBE that has a second balloon on the endoscope tip. SBE was first introduced in the U.S. in 2007 and uses a disposable overtube with a silicone balloon at the end. The overtube length (132 cm) is slightly shorter than the DBE overtube (145 cm), but the overtube diameter (13.2 mm) and the balloon diameter

Fig. 2 Patient with recurrent occult small bowel bleeding from vascular lesion that was successfully treated with double balloon enteroscopy and clip placement.

(4 cm) are the same. A handheld controller device regulates the overtube balloon inflation, which is set to 5.4 kPa. The SBE also has an advantage of quicker setup compared to DBE, as there is no need to apply a balloon to the endoscope. The endoscopic technique of SBE is similar to that of DBE, except that the tip of the endoscope is hooked against the small bowel mucosa to anchor the endoscope in place, rather than using a dedicated endoscope balloon. The enteroscope is advanced deep into the jejunum and the overtube is then advanced with the balloon down while flexing the tip of the endoscope, preferably around a turn. The balloon is then inflated and the entire apparatus is then reduced to pleat the small bowel and the process is repeated until the maximal point of insertion is reached.

Efficacy and Outcomes for SBW

The majority of research in deep enteroscopy has been performed in DBE, with relatively little data available for SBE. However, some important data have been established. The diagnostic yield for SBE has been reported at 41 to 61%²⁵ with a therapeutic yield of 5 to 42%.²⁶ Depth of insertion for SBE has been reported from 204 to 258 cm (antegrade). Several studies have compared SBE to DBE and found SBE to have a lower rate of total enteroscopy.²⁷ However, diagnostic yield has generally been found to be similar between the two techniques. Adverse events with SBE are rare and are similar in nature to complications of DBE.

Spiral Enteroscopy

Introduction and Technique

The SE became available in 2007 as a means of achieving deep enteroscopy in a more efficient fashion. SE utilizes an overtube with raised spiral ridges that are designed to rotate and pleat the small bowel. The Endo-Ease Discovery overtube (Spirus Medical Inc; Stoughton, MA) comes in both standard and low profile height of the spiral ridge (4.5 vs. 5.5 mm), as well as a retrograde version. The antegrade overtube is

compatible with enteroscopes that are 200 cm long and 9.1 to 9.4 mm in diameter. The overtube has a device that couples it to the enteroscope allowing an assistant to rotate the spiral overtube clockwise to pleat the small bowel over the endoscope and advance forward. Conversely, counterclockwise rotation allows for withdrawal. The overtube can then be uncoupled to advance the endoscope freely.

Efficacy and Outcomes for SBW

The majority of studies on SE have established a diagnostic yield of 33 to 75%.^{28,29} A multicenter prospective study evaluated the diagnostic yield of SE in patients that had a positive CE study and found a diagnostic yield of 57%, with arteriovenous malformations being the most common finding.³⁰ SE has been shown to reach depths of 217 to 262 cm with a mean procedure time of 34 to 55 minutes.

Several studies have compared deep enteroscopy using the spiral overtube with balloon enteroscopy. A large prospective multicenter study compared 191 DBEs with 50 SEs and found no statistically significant difference in the diagnostic yield (DBE: 70%; SE: 75%), therapeutic yield (DBE: 66%; SE: 70%), procedure time (DBE: 60 minutes; SE: 55 minutes), or depth of insertion (DBE: 200 cm; SE: 220 cm).²⁸ Other smaller comparative studies have found longer exam times and greater depth of insertion with DBE compared to SE.^{31,32} One study reported a significantly higher rate of complete enteroscopy with DBE (92%) compared to SE (8%); however, the clinical significance of achieving complete enteroscopy remains unclear, as this study showed no difference in diagnostic or therapeutic yield between the two modalities.³¹ SE has also been compared to SBE in a retrospective study by Khashab et al. The study compared 52 SBE procedures with 53 SE procedures and found no difference in diagnostic yield (59.6 vs. 43.4%, respectively) or procedure time (53 vs. 47 minutes, respectively). However, insertion depth for SE was significantly higher than SBE (301 vs. 222 cm).³³

Long-term outcomes of SE were examined by Williamson et al. Follow-up data were gathered for 78 patients who

underwent SE for small bowel GIB over a mean period of 25 months and found that overt bleeding dropped from 62% before the SE procedure to 26% after the procedure. Mean hemoglobin level increased from 10.6 to 12.6g/dL, with associated decrease in need for transfusion, iron supplementation, and additional endoscopic procedures.³⁴ Serious complications are rare with SE, but mucosal tears and sore throat are relatively common minor adverse events.

Management of Obscure Gastrointestinal Bleeding

Once the upper and lower GIB is ruled out, stable patients undergo VCE and/or CT angiography. VCE has been shown to have higher sensitivity in detecting bleeding lesion than CT angiography and, therefore, should be considered as first diagnostic modality in stable patients, when there is no intestinal obstruction.⁷ Since VCE has high-negative predictive value, if VCE is negative and bleeding recurs, repeat EGD (esophagogastroduodenal scope) and colonoscopy is considered to find lesions that may have been missed at initial study. For hemodynamically unstable patients, mesenteric angiography and embolization is the procedure of choice. Injection of methylene blue through supraselective catheter enables selective resection of small bowel that contains bleeding lesion, if embolization is unsuccessful or severe bleeding recurs.³⁵ Once VCE identifies a bleeding lesion, the patient undergoes either push enteroscopy, if it is proximal lesion, or deep enteroscopy. Once endoscopic treatment is successful, the patient is monitored for signs of rebleeding. If the rebleeding occurs, repeat enteroscopy is advisable. At the time of enteroscopy, endoscopic tattooing is helpful for potential surgical resection. Endoscopic tattooing is also helpful for small resectable lesions, such as benign or malignant tumors. When surgical resection is indicated and accurate preoperative localization is not possible, intraoperative enteroscopy should be considered in coordination with experienced gastroenterologist. Enteroscopy can be advanced antegrade from mouth, retrograde from anus, or via enterotomy.³⁶ As endoscopist advances the scope, surgeon pleats small intestine. Distended small intestine makes pleating extremely difficult. For this reason, retrograde access from anus is less successful, because by the time the scope reaches terminal ileum, entire small intestine is distended. It is important to occlude small intestine with finger to minimize distension and examine mucosa as the scope advances, not as it is withdrawn. When the lesion is identified, suture is placed to mark the site before resection.

Conflict of Interest

None declared.

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