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Capsule Endoscopy and Endoscopic Modalities for Deep Enteroscopy

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Long considered the final frontier of endoscopy, over the past decade the small intestine has witnessed the introduction of more technologies than any other portion of the gastrointestinal (GI) tract. Due to extensive loop formation, the length of the small bowel is not compatible with deep penetration by conventional flexible endoscopes. Indeed, until the turn of the 20th century, sonde endoscopy and intraoperative enteroscopy were the only means by which direct mucosal examination of the entire small intestine was possible. Fortunately for both patients and endoscopists, this is no longer the case.

Obscure GI bleeding is the most common indication for small bowel enteroscopy. Defined as GI blood loss or persistent iron deficiency anemia with a negative upper endoscopy and colonoscopy, obscure bleeding accounts for approximately 10% of all cases of GI blood loss. The source in most cases between the ligament of Treitz and the ileocecal valve. Until the introduction of capsule endoscopy in 2000, patients underwent an average of 7 negative diagnostic studies in the course of the work-up of obscure GI bleeding.

Prior to the year 2000, available modalities for detecting sources of obscure GI bleeding included small bowel series, contrast-enhanced computed tomography (CT) scanning, angiography, tagged red blood cell scanning as well as both push and intraoperative enteroscopy. Contrast-enhanced radiography, angiography, and nuclear medicine testing have a diagnostic yield between 0 and 5% for obscure GI bleeding whereas push enteroscopy has

a diagnostic yield of 30%; the latter is the small-bowel equivalent of performing a flexible sigmoidoscopy to search for a colonic bleeding source. The current gold standard for the diagnosis of obscure GI bleeding is intraoperative enteroscopy, which yields a diagnosis in up to 90% of the cases. Unfortunately, it is also the most invasive with a significant rate of post-operative ileus and need for prolonged hospitalization.

■ Capsule Endoscopy

Introduced into clinical practice in 2000,[1] capsule endoscopy (CE) for the first time allowed for non-surgically assisted direct mucosal examination of the entire small intestine. Unlike other forms of endoscopy, CE is a minimally invasive procedure which is performed on an outpatient basis and requires no sedation. Images obtained by the capsule endoscope are transmitted to electrodes worn by the patient and captured on a data recorder. Captured images are then reconstructed into a digital video, which can be viewed by the endoscopist using proprietary software. CE is a safe procedure with the only risk is the capsule being retained. Capsule retention does not occur in normal small intestine; thus, its occurrence denotes some small bowel pathology. The risk of capsule retention is 0.7%;[2] patients with a strong history of non-steroidal anti-inflammatory drug use, prior small bowel surgery, and an established diagnosis of small bowel Crohn's disease are at highest risk.

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Although acute small bowel obstruction and perforation have been reported in the setting of capsule retention, there is no reliable testing to predict in which patient such will occur.[3]

Pennazio and colleagues[4] reported the results of a prospective study involving 100 patients with obscure GI bleeding who underwent capsule endoscopy. Not surprisingly, this cohort had undergone 620 negative diagnostic tests prior to CE. The overall diagnostic yield for capsule endoscopy in this setting was 50%. When viewed in comparison to the 0-5% yield for contrast radiography in the same setting, these data appear even more significant. The diagnostic yield was then stratified by the type of obscure GI bleeding: ongoing overt, previous overt, and occult. Interestingly, there was a positive finding in 92.3% of the patients with ongoing overt obscure GI blood loss, diagnostic yield was 12.9% in patients with previous overt bleeding, and it reached 44.2% in those with occult obscure bleeding. In the case of prior overt obscure bleeding, the diagnostic yield decreased the further out from the index bleeding episode. Therefore, these data highlight the point that timing, more than anything, is the critical factor in maximizing the chances of a positive capsule study in the setting of overt obscure GI bleeding: the closer to the index bleed, the higher the likelihood of a positive study.

The advantages of CE over other technologies are obvious: it is a user-friendly device which is minimally invasive and has a low complication rate and a relatively high diagnostic yield. A meta-analysis performed by Lewis and colleagues,[5] which included 14 studies using CE for obscure GI bleeding found that CE identified new findings in 68.4% of the patients with a miss rate of 12.5%. There was concordance between CE and other diagnostic modalities in 12.5% of patients. A mean of 7.4 negative studies had been performed per patient prior to CE. However, the technology is not without limitations. First, the exam is diagnostic only; the current version of the capsule endoscope has no therapeutic capabilities. The device lacks air insufflation and findings may be obscured by blood, debris or missed altogether by rapid small bowel transit. Indeed, the miss rate for CE in the diagnosis of small bowel mass lesions is 20%.[5,6] Reading time for CE is significant, which may lead to reader fatigue. Finally, interobserver variability is high and, despite software changes and modifications, localization of identified lesions may be difficult.

■ Deep Small Bowel Enteroscopy

Whereas CE has dramatically altered the endoscopic approach to small bowel disorders by providing endoscopists the opportunity to examine the entire small intestine with relative ease, the technology is restricted by the lack of therapeutic or biopsy capabilities. In 2003, Yamamoto described the use of double balloon enteroscopy (DBE).[7-9] The double balloon system is comprised of a 2 m enteroscope with an affixed 140 cm overtube. A latex balloon is attached to the tip of both the enteroscope and the overtube. With serial overtube advancement and balloons inflation and deflation performed in concert with reduction maneuvers, the small bowel is pleated onto the overtube which allows for straightening of the small intestine and, ultimately, deep advancement of the enteroscope into the small intestine. The technique, known as push and pull enteroscopy, can be performed per os or via a retrograde, transcolonic approach. Complete enteroscopy via a single antegrade approach has been reported; more commonly, it it done through a combination of antegrade and retrograde approaches.

Several series from multiple centers have documented the clinical efficacy of DBE in the evaluation and management of obscure GI bleeding.[10-12] Whereas the diagnostic yield ranges between 50 and 70% in most series, a full range of therapeutic capabilities are afforded by the instrument. Aside from bleeding therapy using a heater probe, bipolar electrocautery or argon plasma coagulation, polypectomy, jejunostomy, enteral stent placement, foreign body removal, stricture dilation as well as ERCP in surgically altered anatomy have all been reported. In addition, biopsies can be obtained when required.

Although useful in terms of its diagnostic and therapeutic capabilities, DBE is not without drawbacks. Unlike CE, DBE is invasive, requires sedation and, in some cases, monitored anesthesia care or a general anesthetic; in addition, it is time consuming and demands significant resources. Complications such as perforation and pancreatitis, although rare, have been reported.[12-16] Lack of a reimbursement code in the United States has, unfortunately, limited widespread use of this technology.

Since the introduction of DBE into clinical practice, additional technologies for deep small bowel enteroscopy have emerged. The single balloon

enteroscopy (SBE) system includes a 2 m endoscope with attached 140 cm overtube. As opposed to DBE, the single balloon enteroscope has a balloon affixed to the tip of the overtube only. As such, advancement deep into the small bowel requires the use of the "hook and pull" method. Several reports have documented the clinical utility of SBE in the evaluation and management of small bowel disorders.[17-19]

The spiral enteroscopy (SE) system differs from DBE and SBE in that it does not utilize balloons for deep enteral access. Rather, SE uses an overtube with struts at the distal aspect. The endoscope is advanced deep into the small bowel by a rotational motion of the overtube when closely mated and "locked" to the shaft of the 2 m enteroscope. Like a curtain rod, the small bowel is "pulled" onto the overtube when rotational force is applied. The safety of the spiral enteroscopy system has now been documented in several reports and the clinical utility of this technology is beginning to emerge in large case series.[20-22]

With so many devices now available for deep small bowel endoscopy, the question which often arises regards superiority. To date, the literature has not supported a true clinical advantage of one device over another. Whereas SE and SBE may be performed more quickly than DBE, it is not clear that this translates into improved clinical outcomes. Conversely, DBE likely allows for the deepest advancement into the small bowel and the highest rate of complete enteroscopy. Whether or not this actually makes a difference in clinical practice remains to be established. One major problem in comparing the available technologies is the lack of true outcome studies. Most commonly, available literature on any of these technologies consists mainly of large case series measuring the "diagnostic yield" of a given technology. It must be recalled that all of these devices allow for therapeutic intervention in the small bowel. While it is clear that each of these technologies is able to detect small bowel pathology, what remains to be seen is how this changes clinical outcomes.

Whereas before year 2000, small bowel endoscopy was extremely limited, the dawn of the new millennium has brought a significant number of new technologies designed to allow direct mucosal imaging, and in some cases, therapeutic maneuvers deep within the small bowel with no need for surgical assistance. Given the relative advantages and disadvantages of CE versus DBE, SBE and SE, the typical approach is to first use CE to detect small bowel pathology followed by application of DBE, SBE or SE for therapy. It remains to be seen whether or not this approach will change clinical outcomes, especially in case of obscure GI bleeding. However, compared to surgical enteroscopy, available technologies for deep enteroscopy in 2010 represent a significant improvement in user-friendliness and associated morbidity.

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