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REVIEW

Small Bowel Capsule Endoscopy: Indications, Limitations and Diagnostic Yield

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ABSTRACT

Small bowel capsule endoscopy (CE) is a simple, safe, non-invasive, reliable technique, well accepted and tolerated by the patients, which allows complete exploration of the small intestine. The advent of CE in 2000 has dramatically changed the diagnosis and management of many diseases of the small intestine, such as obscure gastrointestinal bleeding, Crohn's disease, small bowel tumors, polyposis syndromes, *etc*. Capsule endoscopy has become the gold standard for the diagnosis of most diseases of the small bowel. Lately this technique has also been used for esophageal and colonic diseases. The present review focuses on the indications, limitations and diagnostic yield of capsule endoscopy in the investigation of small bowel diseases.

INTRODUCTION

Until a few years ago, the small bowel was an organ which was very difficult to explore with the available endoscopic, radiological and nuclear medicine techniques. In routine practice, only the last few centimeters of the ileum were accessible to retrograde visualization by ileocolonoscopy. Exploration from the proximal side by push, sonde or intraoperative enteroscopy were invasive procedures that did not always allow us to visualize the lesions in the small bowel.[1] Sonde enteroscopy had been abandoned in the 90's because it was a tedious technique (long duration of the procedure) and it had several technical limitations. Push enteroscopy is limited by the depth of insertion of the scope and is poorly tolerated. Intraoperative enteroscopy is the most effective of these techniques, but it is the most invasive with a significant percentage of adverse side effects.[2] Single and double balloon enteroscopy, as well as spiral enteroscopy have also been introduced in recent years; however, they are time consuming and technically demanding and have not been incorporated in every day clinical practice as yet.[2]

With wireless capsule endoscopy (CE) we can provide a simple, safe, non-invasive, reliable procedure, well accepted and tolerated by the patient, which has revolutionized the study of the small bowel. This technique evaluates endoscopically, with high resolution images, the whole small bowel, avoiding any sedation, surgery or radiation exposure.[2]

Abbreviations
CE = capsule endoscopy
CT = computed tomography
HIV = human immunodeficiency virus
NSAID = non-steroidal anti-inflammatory drugs

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TECHNICAL PROPERTIES

The capsule endoscope is a disposable, small, swallowable, wireless, miniature camera which allows us to get a direct visualization of the gastrointestinal mucosa.[3] The initial endoscopy capsule was developed by Given Imaging (Yoqneam, Israel) and approved in Europe by the European Medicines Agency and in the United States by the Food and Drug Administration in 2001.[3] To date this technique is available in over 4500 gastrointestinal centers throughout the world.

The capsule measures only 11 mm × 26 mm and weighs 3.7 g, holds a metal oxide semiconductor imaging-chip video camera, 6 white light-emitting diode illumination sources, 2 silver-oxide batteries and a radio telemetry transmitter. The image filed is 140 degrees, magnification is × 8 and the depth of view is 1 to 30 mm.[4,5]

Before the capsule is swallowed, 8 skin antennas are taped to the patient's anterior abdominal wall and connected to the hard drive. After an overnight fast and a bowel preparation with 2 liters of polythylene electrolyte solution, the patient swallows the capsule with a few sips of water, then the capsule is passively moved along by peristalsis.[6] Two hours after ingestion, the patient is allowed to drink, while eating is allowed after 4 hours. During the procedure the patient may carry on with his/her daily activities.

The camera is activated by removal of the capsule from its magnetic holder and takes 2 images per second and transmits these by means of radio frequency to a sensor array placed on the patient's abdomen and from there to a recording device in a belt that the patient wears for the duration of the battery life (8 hours). The use of the real time viewer may shorten the procedure, as the patient can be disconnected once the cecum is visualized.[5]

After 8 hours, the sensor array and recorded data are removed and the recorded images are downloaded to the computer. The capsule is excreted with the feces, usually within 24 to 48 hours.[7] It takes on average 40-60 min for a trained gastroenterologist to read the images downloaded and one of the limitations of the test is the fact that it is time-consuming.[8,9] Since its development, additional support systems have been added to the software to assist the reader, such as localization capability, suspected blood indicator, a multiviewing feature and quick view modality.[3]

LIMITATIONS OF SMALL BOWEL CAPSULE ENDOSCOPY (TABLE 1)

The retention of the endoscopy capsule is the main complication of the procedure and is defined when the device remains in the digestive tract for a minimum of 2 weeks.[10] The frequency of this problem varies, depending mostly on the clinical indication for CE and ranges from 0% in healthy subjects, to 1.5% in patients with obscure gastrointestinal bleeding, to 5% in patients with suspected Crohn's disease and to 21% in patients with intestinal obstruction.[3] Patency capsule or small bowel follow through should be performed before small bowel capsule endoscopy in patients in whom intestinal obstruction is suspected. This should be particularly sought in patients with Crohn's disease.[6] In patients in whom patency capsule precedes the Pillcam examination, the cost is increased by approximately 30%. At present CE has some technical limitations; it cannot be used to obtain biopsy specimens or for endoscopic treatment and it cannot be controlled remotely.[8] Capsule endoscopy has also some clinical limitations which are problems in sizing and locating small bowel lesions,[2] a possible false-negative CE result, due to the fact that the global miss rate is about 11%, ranging from 0.5% for ulcerative lesions to 18.9% for neoplastic disease and the fact that sometimes we can get findings of uncertain relevance in healthy subjects.[8]

TABLE 1. Current Indications and Limitations for Small Bowel Capsule Endoscopy

Indications
• Obscure gastrointestinal bleeding
• Crohn's disease
• Intestinal tumors
• Celiac disease and other malabsorptive syndromes
• Drug enteropathies (e.g. NSAID)
• Small bowel polyposis syndromes
• HIV patients with gastrointestinal symptoms
• Henoch-Schonlein purpura
• Patients with small bowel transplants and with intestinal graft *versus* host disease (monitoring the response to immunosuppressive therapy)
Limitations
• Retention of endoscopy capsule
• May miss lesions
• Technical limitations
- unable to obtain biopsy specimens
- cannot deliver endoscopic treatment (e.g. drugs or hemostasis)
- cannot be controlled or maneuvered remotely
- limited battery life
• Cost

HIV = human immunodeficiency virus; NSAID = non-steroidal anti-inflammatory drugs

Another drawback is that in almost 20% of procedures the capsule does not reach the cecum while it is active, due to the 8 hour life span of its battery.[9]

INDICATIONS OF SMALL BOWEL CAPSULE ENDOSCOPY (TABLE 1)

Currently, CE is recommended as a third stage examination, after negative gastroscopy and colonoscopy in patients with *obscure gastrointestinal bleeding*.[11-14] Also many studies have established, with a growing body of evidence, that this technique is cost-effective in other clinical situations, such as detection of small bowel lesions in *Crohn's disease* in patients in which other methods have failed to provide a diagnosis, non steroidal anti-inflammatory drug *enteropathies*, *celiac disease*, small bowel *polyposis* syndromes and small bowel *tumors*.[11-14] Other possible indications are HIV patients with gastrointestinal symptoms, malabsorptive syndromes other than celiac disease, Henoch-Schonlein purpura, patients with small bowel transplants and with intestinal graft *versus* host disease, particularly in monitoring the response to immunosuppressive therapy.[11-14]

DIAGNOSTIC YIELD

With regards to the main indication of small bowel capsule endoscopy, i.e. bleeding of obscure origin, this is defined as bleeding of unknown origin that persists or recurs (i.e. recurrent or persistent iron deficiency anemia, fecal occult blood test positivity or visible bleeding) after a negative initial workout including gastroscopy, colonoscopy, small bowel barium follow through or enteroclysis and push enteroscopy.[15] Bleeding of obscure origin is further subdivided in two clinical entities: i) Obscure – occult, as manifested by recurrent iron-deficiency anemia and/or recurrent positive fecal occult blood test results, ii) Obscure – overt, with recurrent passage of visible blood (hematochezia / melena).[15] Management of patients with gastrointestinal bleeding of obscure origin remains a challenging problem in clinical practice. When a bleeding source is not identified in upper or lower gastrointestinal endoscopy, the small bowel is interrogated and wireless capsule endoscopy has become the method of choice for this purpose. Indeed, the diagnostic yield of CE has been demonstrated in a number of comparative studies, which show that capsule endoscopy is superior to push enteroscopy (50% vs 24%)[16] barium follow through (31% vs 5%), computed tomography enteroclysis (59% vs 36%),[17] intraoperative enteroscopy (74.4% vs 68%),[18] double balloon enteroscopy (59% vs 42%)[19] and angiography (72% vs 56%).[20] However, it should be noted that not only in the above mentioned studies, but in many other publications, the diagnostic yield of CE in patients with obscure bleeding varies considerably. These immense variations among reports clearly reflect differences in image interpretation, since a consensus on what represents a positive finding has not been reached as yet. According to a classification proposed by our group,[21] findings are considered positive if they are the actual source of bleeding, while lesions suspected to be the source are classified as findings of uncertain significance. Using the strict criteria adopted in our classification, we reported a diagnostic yield of 41.6% for positive findings in patients subjected to capsule endoscopy for the investigation of obscure gastrointestinal bleeding.[21]

Regarding the other major indication for capsule endoscopy, i.e. patients with suspected or diagnosed Crohn's disease and given the numerous small studies involving CE and the difficulty in quantifying the diagnostic yield of CE from these studies, a meta-analysis was undertaken by Triester et al.[22] A literature search analyzed prospective trials comparing CE to alternative diagnostic modalities to detect lesions beyond the reach of standard upper endoscopy and colonoscopy (not including ileoscopy). A total of 11 trials involving 309 patients were included in the meta-analysis. All trials excluded patients with known strictures. All patients served as their own controls between imaging studies. In the comparison of CE with small bowel barium radiography, the "diagnostic yield" of CE for findings in all patients consistent with a diagnosis of Crohn's disease was 64% versus 24% for barium radiography for an "incremental yield" of 40%. The incremental yield was greater (46%) in patients being evaluated for suspected recurrent Crohn's disease. In the comparison of CE with colonoscopy and ileoscopy, CE had a 61% yield for Crohn's disease in all patients compared to a 46% yield for ileoscopy (incremental yield = 15%). Similarly, the incremental yield (26%) was greater in the established Crohn's disease subset. In the comparison of CE with computed tomography (CT) enterography/enteroclysis, CE had a 69% yield versus 30% for CT with an incremental yield of 39%. The conclusion of the study was that CE did not reveal a statistically significant greater yield of findings (compared to any other modality) in patients with suspected Crohn's disease, but it did identify a greater number of lesions than all alternative modalities in patients with established Crohn's disease.

Small bowel capsule endoscopy is also helpful in celiac disease patients in select situations. It can be performed in patients who are unable or unwilling to undergo conventional endoscopy, those with positive celiac serology with normal duodenal biopsies and those who do not respond to gluten-free diet or develop alarm symptoms.[23]

CONCLUSION AND FUTURE DIRECTIONS

Today, small bowel capsule endoscopy is a valuable tool in

the diagnostic management of patients with obscure gastrointestinal bleeding, as well as those with suspected or diagnosed Crohn's disease. In the future CE may be used to determine medical response to therapy, while new capsules might be able to provide tissue for histological examination in addition to improved views and extended battery life for visualization of the entire small intestine.[24]

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