Capsule Endoscopy - Diagnostic Role in Obscure Gastrointestinal Bleeding

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ABSTRACT Obscure gastrointestinal bleeding accounts for over 5% of the total gastrointestinal bleedings. Due to the nature of the lesions and to the fact that about 5% are located in the small bowel, it is one of the most important indications of capsule endoscopy. Capsule endoscopy is a safe, non invasive diagnostic tool, mainly used to investigate small bowel lesions. It has a very high diagnostic yield especially if the bleeding is ongoing. Several studies prove this technique to be superior to other methods for the detection of suspected lesions and the source of bleeding. Capsule endoscopy has been shown to change the outcome in patients with obscure gastrointestinal bleedings, especially if used in conjunction with double balloon enteroscopy.

KEY WORDS Capsule Endoscopy, Obscure Gastrointestinal Bleeding, Small Bowel

Introduction

Occult Gastrointestinal Bleeding – general facts.

Obscure gastrointestinal bleeding (OGIB) is defined as bleeding from the gastrointestinal (GI) tract that persists or recurs with no obvious etiology after being investigated by esophagogastroduodenoscopy (EGD), colonoscopy and small bowel follow-through or enteroclysis.

It has been divided into two subcategories: obscure occult and obscure overt, based on the absence or presence of clinically evident bleeding. [1,2]

Obscure occult GI bleedings can be suspected by fecal occult blood testing or by the presence of an iron deficiency anemia. Obscure overt GI bleedings present with visible blood loss, either by hematochezia or melena.

OGIBs could be due to lesions that are overlooked (when located in the esophagus, stomach or colon) or lesions in the small intestine, which are difficult to visualize by standard endoscopy. Diagnosis can be missed if the lesion has stopped bleeding during endoscopic investigation, or is obscured by blood clots that are unable to be mobilized during endoscopy, also it is known that significant anemia and hypovolemia cause lesions to look less obvious. [2]

It is estimated that OGIBs accounts for between one and five percent of the total GI bleedings. Out of these, approximately 5% are caused by lesions in the small intestine. [1,2]

A list of possible causes for OGIB can be found in table 1.

Table 1. List of common causes for obscure Gastrointestinal Bleedings (OGIBs).

<table>
<thead>
<tr>
<th>Ulcers</th>
<th>Vascular</th>
<th>Tumors</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peptic</td>
<td>Angiodysplasia*</td>
<td>Polyps</td>
<td>Diverticulosis</td>
</tr>
<tr>
<td>Anastomotic</td>
<td>Dieulafoy lesion</td>
<td>Carcinoid</td>
<td>Meckel’s diverticulum</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory</td>
<td>Varices</td>
<td>Lymphoma</td>
<td>Hemobilia</td>
</tr>
<tr>
<td>NSAID medication</td>
<td>Lymphangiomas</td>
<td>Gastrointestinal stromal</td>
<td>Hemosuccus pancreaticus</td>
</tr>
<tr>
<td>Gastro Esophageal Reflux Disease (GERD)</td>
<td>Other infections</td>
<td>tumor (GIST)</td>
<td>Aortoenteric fistula</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td></td>
<td>Carcinoma</td>
<td></td>
</tr>
<tr>
<td>Cytomegalovirus /viral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other infections</td>
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* - most common cause of small bowel OGIBs.
Until recently the small bowel represented a part of the GI tract difficult to explore. The need to explore the relatively inaccessible small bowel led to the development of the capsule endoscopy (CE).

**Technical characteristics of the video capsule system**

The video capsule endoscope (VCE) is a wireless 11/26mm disposable device which weights only 3.7g. The image has a field of view of 140 degrees, 1:8 magnification, 1 to 30 mm depth of field and a minimum size for detection of about 0.1 mm. [3] (see figure 2)

**Figure 2.**

There are currently in use three VCE systems, Pillcam SB (Given Imaging Ltd, Yoqneam, Israel), Olympus Endocapsule (Olympus, Japan) and OMOM (Jinshan Science and Technology Group, Chongqing, China).

VCE consists of an optic dome, lens, LEDs (light emitting diodes), a CMOS camera sensor (complementary metal oxide silicone), ASIC (application specific integrated circuit) and an antenna. Images captured by the capsule are transmitted to electrodes attached to the patient’s body allowing storage on a small portable recorder. The capsule transmits at a rate of 2 images per second, 50000 images being obtained within 8 hours of recording time. [4] Analyzing the images require between 40-60 minutes and 2-3 hours depending on the experience of the physician.

**Advantages.**

The main advantages of CE include patient comfort, the ability to review the images, procedure safety, the ability to conduct the procedure in a variety of settings, image quality comparable to other forms of endoscopy, and the possibility to explore the entire length of the small bowel.

There are some limitations of the VCE that include the impossibility of air insufflation, the relatively high cost, the unavailability of taking biopsies or treating lesions. [5]

**Safety measures.**

Patency capsule

A patency capsule, with a biodegradable body, spontaneously dissolving after a given time, similar in size to normal wireless capsules, has been recently developed to assess bowel patency and degree of stenosis. If its passage is blocked, the capsule dissolves in 40 to 100 h. It replaced the early lactose-body model, which had questionable safety and efficiency [6] The new patency capsule should be used prior to conventional CE in order to minimize the risk of retention or impaction. [7]

Currently, a few conclusions regarding the CE investigatory technique were drawn:

- On some occasions, the capsule had to be retrieved from the cricopharyngeus [8] and an appendiceal stump. [9]
- Capsules had to be surgically retrieved in unsuspected tight strictures, caused by non steroidal anti-inflammatory drugs (NSAIDs) and Crohn’s disease. [10]
- A gastrointestinal radiograph should be performed prior to the investigation, in order to exclude adhesive or inflammatory obstruction.
- Colon diverticulitis poses no threat to the safety of capsule endoscopy.
- Batteries have been reported to be non-toxic, leakage or exposure posing no threat.
- Absolute contraindications:
  - gastrointestinal obstruction
  - pseudo-obstruction.
- Relative contraindications:
  - gastrointestinal motility disorders (for instance severe gastroparesis);
  - pregnancy;
  - known or suspected fistulae or strictures;
  - presence of a cardiac pacemaker or other implanted electromedical device;
  - large or numerous small intestinal diverticuli;
  - Zenker’s diverticulum;
  - extensive Crohn’s enteritis;
  - prior pelvic or abdominal surgery.
Diagnostic yield of CE. Impact on clinical outcome.

Both the efficacy and accuracy of this procedure needs to be assessed. CE has an extremely variable [11-17] diagnostic yield, from over 70% when the studied lot contains 20 or less patients, down to under 60% in larger studies, with 50 or more subjects. Subgroup analysis shows that the diagnostic yield reaches 92.3% in patients with ongoing overt GI bleedings, compared to 44.2% in obscure occult bleeding. [18] Timing of the procedure is very important while optimizing the yield of CE in OGIB. [19] In this direction, the International Consensus on Capsule Endoscopy (2005) recommended CE as an early investigation, preferably within 2 weeks while investigating the patients [20] (see figure 3)

Figure 3.

Positive results should be emphasized when considering clinical outcome. A positive outcome in the case of OGIB is represented by the stoppage of bleeding. A large majority of studies involving CE in OGIB management refer to changes in management, rather than a change in outcome. Only a few studies assessed the clinical outcome and changes in management.

In a recent study, Compean et al [21] presented the impact of therapeutic interventions based on CE findings on long term outcome. They refer to 40 patients with chronic OGIB who underwent CE investigation in the 2003-2005 timeframe. He concluded that CE results had a favorable influence in patient outcome, specific treatment making recurrent bleeding less likely.

Pennazio et al [11] determined the outcome in 56 patients, with a mean follow up of 18 months. 85.9% of the patients with ongoing overt GIB suffered complete resolution of bleeding, compared with 69.2% in occult OGIB and 41.4% in past OGIB. Alberts et al [22] assessed in his multicentric study the impact of CE on clinical outcome. In more than 66% of the 247 patients included in this study had a change of management or were recommended for a specific intervention, after receiving a definite diagnosis by CE. Similarly, another recent study reported definitive treatment changes in 70% of the patients positively diagnosed by CE. Delvaux et al [23] reported 1-year follow-up experience in 44 patients. CE had a positive predictive value of 94.4%, and the negative predictive value was 100% in patients with normal findings on capsule examination. On the contrary, positive clinical outcome was reported in only 16% patients according to Rastogi et al. [17]

Variations in outcome may be explained by differences in the studied population, lack of standardized management, different policies applied by each medical center. There is however no doubt that CE plays a definite role in management planning of patients with OGIB.

Comparison of CE with other investigations.

A number of other investigations are available for assessing OGIB: barium follow through, push enteroscopy (PE), enteroclysis, angiography, nuclear scanning and more recently single or double-balloon enteroscopy.

A number of studies compared CE to barium follow through and PE. In all cases, CE had the highest detection frequency of clinically relevant intestinal abnormalities. Costamagna [24] and Eliakim [25] conducted studies on a small number of patients (20 in each case), reporting more than double diagnostic rates when using CE in comparison with barium follow through. A meta analysis [26] comprising three studies with a total of 88 subjects found a 59% incremental diagnostic yield for CE (67% for CE compared to only 8% for barium follow through).

When comparing CE to PE the diagnostic yield is double for CE. [27-36] Diagnostic yield increases when there are more patients with occult bleedings than with overt. [11,27,32,36] Most of the above studies also report fewer complications and less discomfort associated with CE. Together, these reports show a 63% (250/297) yield for CE and a 23% (93/397) yield for PE. A different meta analysis [26] referring to 14 different studies, with 396 patients, found an incremental yield of 35% (63% for CE versus 28% for PE). A number of issues were quoted when summarizing these trials,
such as small populations, different eligibility criteria, and potential selection biases.

The same meta-analysis also compared the diagnosis yield of CE with CT enteroclysis, mesenteric angiography and small bowel MRI, showing the superiority of CE.

Recently, some studies have compared CE with Double Balloon Enteroscopy (DBE). CE had a significantly higher detection rate for potential bleeding when compared with DBE. [37] Hadithi et al [38] have concluded after performing a retrospective study on 35 patients, that CE is more likely to detect the presence of a possible bleeding (80% versus 60%) when compared with DBE. However he concluded two procedures should be considered complimentary and not competitive, as an early CE diagnose can be followed by an interventional or therapeutic DBE.

Cost effectiveness of CE

Several studies have assessed the cost effectiveness of CE when used to diagnose OGIBs. Oradei et al [39] made cost calculations on a population of 76 individuals with OGIB admitted in a major Italian hospital, by performing different diagnostic tests and studying synthetic indicators. Their conclusions was that the use of CE is appropriate when diagnosing disease of the small bowel, especially if he or she presents active bleeding, and that it allows significant cost reduction in different patients subgroups. In an assessment of CE as the evaluation technique for OGIB conducted in Australia by Dyer et al [40] The diagnostic yield for CE was in line with literature (58%), and was significantly higher when compared with small bowel series radiography (only 4%). This findings, combined with the fact that the patient needed no further diagnostic tests if CE was positive and a significant reduction in managements costs determined the Australian Government to provide public funding for CE in OGIB patients. Kamal et al [41] evaluated initial DBE in comparison with CE followed by DBE (if CE detected the presence of a lesion) and other diagnostic methods, such as PE, angiography and intraoperative-enteroscopy for the diagnosis and management of OGIB. Simple DBE proved to be more cost effective, however CE followed by DBE was found to be more cost effective if DBE found a probability of less than 59% for angiectasia.

Conclusions

CE is an important tool in the management of OGIB. Improved software has greatly reduced reading time for CE recordings. The technology improves each day, and with the prospect of more advanced capsules, with sensor capabilities for biological constants or even capsules with curative principles on board, it is certainly one of the leading technologies in GI endoscopy.

References

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