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REVIEW

Capsule endoscopy in clinical practice: concise up-to-date overview

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Abstract: Until recently, the small bowel was considered a 'no man's land' as the imaging modalities available for its investigation were laborious, invasive, costly, or involve significant radiation exposure. Wireless capsule endoscopy (WCE) has changed the field dramatically, over the last eight years. The established indications for small bowel WCE are obscure gastrointestinal bleed/anemia, Crohn's disease, hereditary polyposis syndromes, and to a lesser extent, evaluation of side effects of nonsteroidal anti-inflammatory medications and coeliac disease. We herein present an overview of the capsule examination, which seems to be a quickly improving area.
Keywords: capsule, imaging, small bowel, Crohn's, celiac, GI bleed

Introduction

Since its introduction into clinical practice during the last decade, wireless capsule endoscopy (WCE) is now widely accepted as a first-line examination technique for the small bowel. Published medical literature now includes several high impact papers, as well as a large number of reviews on the various capsule endoscopy modalities employed today. A total of more than 700,000 wireless video capsules (WVC) have been swallowed since 2001; this number rises exponentially since an introduction of this service to several major district hospitals and tertiary centers around the world. The aim of this paper is to review available equipment and devices, their indications for clinical use (along with potential complications) and potential future applications.

History and progress

Until recently, the small bowel was considered the 'no man's land' of the gastrointestinal tract (GI) tract as the imaging modalities available for investigation of this area (ie, small bowel follow through, CT enteroclysis, and push enteroscopy) are laborious, invasive, costly, and involve significant radiation exposure. These issues do not apply to WCE and, whilst more traditional methods of small bowel imaging are still utilized, diagnostic yield of these techniques falls short when compared with WCE.[1,2]

The examination of the small bowel is currently possible using WCE systems available from a handful of manufacturers ie, PillCam® SB2 (Given Imaging, Yoqneam, Israel), the Olympus EndoCapsule® (Olympus, Tokyo, Japan), and the OMOM® capsule (ChongQing JinShan Science & Technology Co., Ltd, ChongQing, China). The WVC is an ingestible camera of cylindrical shape, which is not bigger than a vitamin pill (11 × 26 mm, weight 3.7 gr) and an image capture rate of two frames per second. The camera is powered by a battery with an approximate life of eight hours.

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This equates to more than 50,000 images per test (average duration 7–8 hours). Newer generation WVCs (from 2008 onwards) offer an advanced automatic light control system and a wider angle of view (156° vs 140°). They provide 1:8 magnifications, and an estimated 1–30 mm depth of view.

The images are transmitted, via digital radio frequency communication, to external electrode sensors. These are placed in the lower chest and abdomen in a predetermined pattern and the transmitted digital images are stored in a lightweight data recorder, which patients can wear on their waist or carry like a handbag for the duration of the test. The recorder has a rechargeable battery, and the acquired images are downloaded onto the reading platform for review. The Korean company, Intromedic, has also recently released its MiroCam® capsule for use in small bowel investigations. The MiroCam® technical specifications include longer battery lifetime (11 hours), high-resolution image capture, a sampling rate of three frames per second, and an alternative, conductive method of data transmission. However, no data are currently available regarding its clinical use.[3]

Given Imaging (Yoqneam, Israel) also market an esophageal (the PillCam®Eso2) and a colon (the PillCam®Colon) capsule. The esophageal capsule has been available for clinical use since 2004. It is similar in size to the enteric capsule, but is equipped with two optical domes instead of one, allowing an image capture rate of 14 images per second (seven images per optical dome). It is due to this high capture rate and accelerated battery depletion that the operating time of the esophageal capsule is limited to 20 min.[3] The colonic capsule was released in 2006. It is larger than the company's enteric capsule (11 × 31 mm vs 11 × 26 mm). It has two optical domes capturing two frames per second each, and a wide angle of view similar to that of the updated enteric capsule. Despite the fact that both the esophagus and colon are easily accessible to conventional endoscopes, potential complications arising from diagnostic endoscopic investigations have a reasonable mortality rate[4] and WCE may be a useful alternative in those patients in whom invasive techniques are contraindicated (eg, multiple co-morbidities). WCE may also be used in patients intolerant of conventional endoscopy or as a supplemental technique in GI-screening programs.

Additional technologies and advancements

Reader station software of the GIVEN system has been significantly updated and now offers higher quality images, faster image download time, and aids to image review. A handheld device (connected via USB port with the data recorder) is now frequently used which gives the investigator the ability to follow the capsule in a real-time mode and confirm the capsule entry into small bowel and colon. Using this device, failed studies due to gastric retention are minimized as prokinetics may be administered to aid transit of the capsule through the pylorus. Retention further down the GI tract is also immediately apparent avoiding delays in taking remedial action. This equipment is not widely available yet, but it is hailed as the next step in improvement of the diagnostic algorithm for obscure/occult GI bleed and stricturing Crohn's disease.

The potential problems of capsule retention can be minimized using radiology and/or the patency (Agile®) capsule. The capsule currently in use (second generation – Agile® from Given Imaging) has a centrally placed radiofrequency identifiable tag (13 × 3 mm,with a tiny antenna and magnet, but no battery) which can receive electromagnetic waves at a frequency of 128 KHz, it then emits similar waves at 64 KHz. The device is contained in a lactose shell, which dissolves quickly and completely once inside the GI tract. It also contains a small amount of barium to enable fluoroscopic visualization (if needed). The lactose shell itself is contained within an outer plastic coat that prevents entrance of digestive fluids into the capsule. The capsule is complete with two timer plugs on both sides, which are designed to resolve over a period of 12 hours. Excretion of the patency capsule can be confirmed by X-ray or through the handheld scanner that will detect the emitted electromagnetic signal. If the patency capsule is excreted within 30 hours of ingestion, or if it is excreted intact, the patient can then safely undergo WCE.

As with most tests, WCE requires prior patient consent, despite being one of the safest procedures in gastroenterology. The informing health care provider will have to fully explain the procedure to the patient as well as mention the potential complications of the procedure. These are retention of the capsule, inconclusive findings, contraindication of magnetic resonance imaging (MRI) until capsule passage is confirmed, and finally capsule aspiration.[5–7] Initially the presence of indwelling cardiac pacemaker/implantable defibrillator or other electromedical devices was considered a contraindication to WCE; however, recent data suggest that the radiofrequency signal of the capsule endoscope does not interfere significantly with cardiac pacemakers.[3,9] In patients with swallowing difficulties, in children, and in cases where the device has previously failed to enter the small bowel, even after the use of prokinetics, the capsule can be introduced into the duodenum with the use of an endoscope and either

a Roth® net or the specially designed AdvanCE® delivery device.

All patients should attend the day of their test after a 12-hour fast and medications such as iron tablets, opiates, and antimony drugs should be avoided for a few days prior to the test. Some centers advise the use of polyethylene glycol (PEG) electrolyte purgative solution in order to improve bowel cleanliness, however there is accumulating evidence that bowel preparation has questionable benefits in WCE. Most units in UK do not use bowel preparation.[10–12]

The major task after obtaining the video sequence is analysis of the data. There are still many areas of concern as to accreditation of gastroenterology trainees for interpretation of WCE data, ideal reading conditions (ie, distance from the screen, amount of light in the room, reading speed, and time required for careful and complete reading) and the involvement of nonspecialized medical health care professionals in data interpretation.[13]

Indications

The established indications for small bowel WCE are obscure GI bleed, investigation of Crohn's disease, hereditary polyposis syndromes, and to a lesser extent, evaluation of side effects of nonsteroidal anti-inflammatory medications (NSAIDs) and coeliac disease.[14]

Obscure GI bleeding (OGIB)

Obscure bleeding, defined as recurrent episodes of GI bleeding (ie, melaena, hematemesis or hematochezia), a positive fecal occult blood (FOB) test, or chronic iron deficiency anemia, is by far the most frequent indication for WCE. A recent meta-analysis confirmed the superiority of WCE against all other modalities (including push enteroscopy, but not double balloon enteroscopy [DBE] or mesenteric angiography) in patients with obscure GI bleeding.[2] In a meta-analysis in which cumulative data of all the double balloon enteroscopy studies against the use of WCE, the diagnostic yield of the two procedures was found to be fairly similar.[15] A very recent multicenter study of the concordance of capsule endoscopy and DBE showed good agreement for vascular and inflammatory lesions, but not for polyps or neoplasia. DBE seems to provide valuable adjunctive information, particularly in patients with neoplasia or polyp at capsule endoscopy. DBE clarified the origin of bleeding in two-thirds of patients with capsule endoscopy showing only blood in the lumen.[16]

Pennazio and colleagues have shown that WCE has a higher diagnostic yield in patients with ongoing intestinal bleeding at the time of the procedure, or when the procedure was done soon after the bleeding episode.[17] On the other hand, the positive predictive value of WCE is inversely correlated with the overall diagnostic yield; therefore every lesion found by WCE should not be regarded as a relevant source of bleeding.[3]

A recent study from Scotland showed that a negative WCE study in patients with OGIB is associated with a low rate of recurrent bleeding in the long term (11%). The investigators suggested an expectant approach with these patients, thus avoiding the need for unnecessary additional investigations.[18]

Investigators from Greece demonstrated that in patients with obscure GI bleeding, a diagnostic WCE is more likely to lead to therapeutic interventions and a favorable outcome. Patients, who had a previously noninformative test, would definitely benefit from a second-look WCE, if the bleeding presentation changes from occult to overt, or if the hemoglobin value drops ≥4 g/dL.[19]

Crohn's disease

Historically, the diagnosis of Crohn's disease has been based on clinical, hematological, biochemical, radiological, and endoscopic data, with no gold standard in place. In addition to contributing to the initial diagnosis of Crohn's disease, proper small bowel evaluation allows accurate determination of both the location and the extent of small bowel disease.[20] The average time between onset of symptoms and Crohn's diagnosis can be more than couple of years, whilst earlier treatment of the disease can lead to better clinical outcome and improved life quality. It was only natural for WCE to find one more 'solid' indication.

In another recent meta-analysis, the results of various modalities in the diagnosis of Crohn's were summarized, and it was shown that WCE is superior to any one other test in detecting the intestinal lesions of Crohn's disease.[1] WCE allows the detection of intestinal lesions in a large subset of patients with known Crohn's disease, but also frequently the detection of intestinal lesions in patients with a clinical and/or biological suspicion of Crohn's disease with a diagnostic yield of 43%–71%. Admittedly, patients with raised inflammatory indexes (C-reactive protein, erythrocite sedimentation rate) or high fecal calprotectin present better yield in comparison to those referred for WCE on the basis of diarrhea or abdominal pain.

In 2006, Golder and colleagues compared the diagnostic yield of capsule endoscopy and magnetic resonance enteroclysis (MRE) in the detection of small bowel

pathologies. They studied a total of 36 patients out of which 18 had proven or suspected small bowel Crohn's disease. They found that in patients with Crohn's disease, WCE detected significantly more inflammatory lesions in the first two segments of the small bowel compared with MRE (12 patients vs one patient; $p = 0.016$). One patient had scattered inflammation of the mucosa. MRE did not reveal any intestinal abnormalities in this patient group.[21]

Marmo and colleagues compared WCE and enteroclysis while Voderholzer and colleagues studied WCE versus CT enteroclysis in evaluating the extent of small bowel involvement in Crohn's disease. Both groups found that WCE is superior to enteroclysis/CT enteroclysis in estimating the presence and extent of small bowel Crohn's disease.[22,23]

A simple Capsule Endoscopy Crohn's Disease Activity Index (CECDAI) has been recently devised, in order to allow for grading of the severity of small bowel capsule endoscopy findings in such cases.[24] The investigators divided the small bowel into proximal and distal segments (according to transit times), and then rated each segment on the basis of three parameters: inflammation (A), extent of disease (B), and presence of strictures (C). To determine each segmental (proximal and distal) score the three subscores were used ($A \times B + C$). The CECDAI index is calculated by adding both segmental scores.[24]

A different approach was proposed by Solem and colleagues after a blind, prospective study which aimed to assess the sensitivity and specificity of WCE, CTE, ileocolonoscopy, and small bowel follow-through (SBFT) in the diagnosis of small bowel Crohn's disease. The patients included underwent all four tests over a four-day period. The investigators concluded that the sensitivity of WCE for active small bowel Crohn's disease was not significantly different from CTE, ileocolonoscopy, or SBFT. However, the utility of CTE as a first-line test for Crohn's disease may be limited by low specificity, and by the need for prior small bowel radiography (due to the high frequency of asymptomatic partial small bowel obstruction).[25]

CTE and MRE can be used for evaluation of bowel wall thickness and enhancement, supporting the diagnosis of Crohn's disease. These techniques have the added benefit of not only investigating the intestinal wall, but also detecting the presence of extra-intestinal abnormalities such as abscess formation. Unfortunately, MRE is costly and availability is a problem in many regions. It may be effective to use CTE as a first-line diagnostic tool and reserving WCE for patients suspicious for Crohn's despite a negative evaluation with ileocolonoscopy and CTE.[26] Certainly, the recent World Organization of Digestive Endoscopy – European Colitis and Crohn's Organization (OMED–ECCO) consensus guideline set the scene for the standard use of capsule endoscopy in the investigation algorithm of small bowel Crohn's disease.[27]

Polyps/small bowel malignancies

Tumors in the small intestine present with abdominal pain or intestinal obstruction, weight loss, abdominal mass, and anorexia or jaundice rather than GI bleed, therefore only one third of these are investigated for OGIB. Small bowel neoplasms are uncommon (accounting for approximately 1%–3% of GI tumors) and abdominal pain is a late sign of small bowel cancer. In a recent study, small bowel tumors were found to account for 5%–7% of patients presenting with obscure bleeding. It is the most common cause in patients under 50 years of age presenting with obscure GI bleeding.[28] Angioectasias, although a common capsule finding in all age groups, tend to present more frequent in the elderly. Approximately 60% of tumors are malignant. The most common location for both epithelial and nonepithelial small bowel tumors is the jejunum, while carcinoids are more common in the ileum.[25] GI stromal tumors are the most common bleeding tumors.

Coeliac disease

The diagnosis of coeliac disease is made by demonstrating the characteristic histopathological changes of subtotal partial atrophy and increased intraepithelial lymphocytes on intestinal biopsy obtained by upper GI endoscopy. Serological tests include antiendomysial and antitissue transglutaminase antibodies. However, there is a definite place for WCE in the diagnosis of this disease, as it provides eight-fold magnification, and allows the acquisition of views similar to those obtained during dissecting microscopy.[29]

It can be used not only as an attractive first diagnostic step, but also as a monitoring tool in patients with known celiac disease to check for healing of the small bowel. Some of the limitations of the 'gold standard' ie, the difficulty to obtain proper oriented tissue samples, the tendency to present as patchy mucosal lesions that can too easily be missed on biopsy, and the limited portion of the duodenum examined by an upper GI endoscopy, along with the risk of failing to diagnose coeliac complications are considered the major strengths of WCE.[29]

On the other hand, lesser degrees of villous atrophy can be easily missed by WCE, and also the lesions identified by capsule endoscopy (especially in cases of complicated coeliac disease) will eventually need a biopsy. Overall, capsule

endoscopy seems to be able to recognize the endoscopic markers of coeliac disease described in the literature.[30]

Esophageal WCE

The esophagus is easily accessed by upper GI endoscopies, but some patients are concerned about the invasiveness of the test, the effects of sedation, and pharyngeal discomfort. On top of that, in the Western world there are recently issues regarding endoscopy equipment decontamination in relation with variant Creutzfeldt-Jakob disease (vCJD). Various studies have proved the validity of esophageal capsule for Barrett's esophagus and esophagitis, while its use for the detection of varices is undergoing evaluation after few studies showed encouraging results.[31]

Colon WCE

The use of colon capsule is on the take-off; however, there are still numerous factors that need addressing prior to a wider application of the technique. First of all, the purgative regimen used to maintain the cleanliness of the colon throughout the transit of the capsule is cumbersome and real time viewer is ideal in order to avoid unsuccessful investigations. Colon WCE should act as complementary to conventional colonoscopy and could be an appropriate solution for those patients who are either unwilling or have failed colonoscopy, as well as in cases where conventional colonoscopy is contraindicated.[32] The main long-term primary objective of the colon WCE is the average risk population undergoing colorectal cancer screening. A recent study of a total of 328 patients (mean age, 58.6 years) showed that the sensitivity and specificity of capsule endoscopy for detecting polyps that were 6 mm in size or bigger were 64% and 84%, respectively and for detecting advanced adenoma, the sensitivity and specificity were 73% and 79%, respectively. Of the 19 cancers detected by colonoscopy, only 14 were detected by capsule endoscopy (sensitivity, 74%; 95% confidence interval [CI]: 52 to 88). For all lesions, the sensitivity of capsule endoscopy was higher in patients with good or excellent colon cleanliness than in those with fair or poor colon cleanliness. Mild-to-moderate adverse events were reported in 26 patients (7.9%) and were mostly related to the colon preparation.[33] As colon WCE has still some limitations (inability to insufflate air, clean or take biopsies), future capsule prototypes seem to be necessary.[32]

Conclusion

A new era has begun with the use of wireless capsule in the investigation of the GI tract. The once inapproachable small bowel has become a familiar territory and pathologies and variations of normality are now images portfolios and atlases. It is only certain that the new technology will find more applications in the form of controllable capsule endoscopy and why not, therapeutic as well.

Disclosures

The authors report no conflicts of interest in this work.

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