Small Bowel Capsule Endoscopy: Have We Conquered the Last Frontier?

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Abstract

Capsule endoscopy was launched at the beginning of this millennium and has since become a well-established tool for evaluating the entire small bowel for manifold pathologies. CE far exceeded our early expectations by providing us with a tool to establish the correct diagnosis for such elusive gastrointestinal conditions as obscure gastrointestinal bleeding, Crohn's disease, polyposis syndrome and others. Recent evidence has shown CE to be superior to other imaging modalities – such as small bowel follow-through X-ray, colonoscopy with ileoscopy, computerized tomographic enterography, magnetic resonance enteroclysis and push enteroscopy – for diagnosing small bowel pathologies. Since the emergence of CE, more than 650,000 capsules have been swallowed worldwide, and more than 700 peer-reviewed publications have appeared in the literature. This review summarizes the essential data that emerged from these studies.

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The small bowel is the most difficult part of the gastrointestinal anatomy to examine. Endoscopic examination of the small bowel is limited by its considerable length and its distance from the mouth and the anus. Barium X-rays and enteroscopy had traditionally been the primary methods for screening the small bowel, but the diagnostic value of these tests is low for a wide variety of specific lesions. A barium small bowel series, the most commonly used investigation, cannot demonstrate flat lesions, such as angiodysplasias, one of the most common pathological lesions found in the GI tract [1]. A barium X-ray of the small bowel is currently the primary radiographic means of diagnosing a small bowel neoplasm and the best way to locate small bowel lesions, but its sensitivity is only 30–44% [2]. Magnetic resonance enteroclysis has been adapted for clinical application in imaging the small bowel. This modality has excellent soft tissue contrast and three-dimensional capabilities that may be of importance when studying the small intestine [3].

Enteroscopy provides direct visual inspection of the small bowel mucosa beyond the reach of standard upper endoscopes. Push-enteroscopy takes between 15 and 45 minutes to perform, it is uncomfortable, often painful, usually requires sedation and analgesia, bears the danger of perforation and requires a skilled endoscopist [2]. In addition, the instrument can only examine 80–120 cm beyond the ligament of Trietz [2]. Occasional complications may occur, usually related to the use of an overtube for facilitating deep intubation of the small bowel. Double-balloon enteroscopy [4], a new method, is an invasive time-consuming procedure and is associated with a recognized risk of complications and higher costs as well as the need for a high level of technical skill. Another approach for examining the entire small bowel is intraoperative enteroscopy [5], which is used to identify lesions responsible for obscure GI bleeding or other pathologies. Intraoperative enteroscopy involves anesthesia and laparotomy, but it does have a high degree of accuracy and the ability to provide visualization of the entire small bowel in selected patients together with the possibility of carrying out biopsies and therapeutic procedures.

It is generally accepted that the imaging methods currently available to the gastroenterologist for diagnosing small bowel diseases and disorders are unsatisfactory [1,2].

Capsule endoscopy

The desire to explore the relatively inaccessible small bowel led to the development of an ingestible miniature camera. Capsule endoscopy provides visualization of the entire small bowel by transmitting wireless images from a disposable capsule to a data recorder worn by the patient. Iddan et al. [6] were the first to describe this new type of endoscope, which consists of a wireless swallowable capsule capable of transmitting moving color television images of the GI tract. Later, in a randomized trial, our group compared CE with push-enteroscopy for the detection of small bowel lesions in canines [7]. After CE had been proven to be a safe and painless procedure in healthy volunteers, it was used for the first time in patients with suspected small bowel pathology in a prospective clinical study in two medical centers in Israel [8].

The capsule

The Given® capsule was approved by the American Food and Drug Administration in August 2000 and, to date, more than

CE = capsule endoscopy
GI = gastrointestinal

650,000 capsules have been ingested (Given Imaging Ltd. Database, personal communication). The first publication on the diagnosis of pathological conditions in the human small bowel that was made using this new painless and harmless endoscopic system appeared in 2002 [8,9]. At the time of this writing, the Given Imaging Ltd (Yokneam, Israel) PillCam™ SB system is the only one that has received FDA clearance. Another similar capsular system from Olympus Medical System Corp (Tokyo, Japan) held two clinical trials [10,11] but the results were not published in a peer-reviewed format. The Given® system consists of three components: the capsule, a data recorder, and software. The capsule measures 11 x 26 mm, weighs 3.7 g and contains four light-emitting diodes, a lens, a color camera chip, two batteries, a radiofrequency transmitter, and an antenna. The camera uses a complementary metal oxide semiconductor chip, which requires less power than the charged coupled device chips currently found in video endoscopes. It transmits continuous images at two frames per second, permitting the acquisition of more than 50,000 images during the 6 to 8 hour procedure as it passes through the GI tract. Video images are transmitted from the capsule via ultra-high frequency band radio telemetry to sensor arrays taped to the patient's abdomen and stored on a portable solid-state recorder worn around the patient's waist. The recording allows physicians to locate lesions in the small intestine as well as calculate gastric emptying time and small bowel transit time.

Capsule endoscopy's highest diagnostic yield is in patients with obscure gastrointestinal bleeding

The CE procedure

CE is a painless non-invasive diagnostic procedure that is performed on an outpatient basis. The patient fasts overnight and, on the morning of the procedure, swallows the capsule with a small amount of water. A trained nurse can instruct the patient in carrying out the simple steps involved. Some physicians administer an oral purging solution and/or prokinetic drug prior to the swallowing of the capsule. The duration of the procedure is approximately 8 hours during which the patient is free to continue his/her daily activities.

Indications

The CE was approved for visualization of the small bowel in adults and in children over the age of 10. There has been clinical experience in children as young as 3 years old after endoscopic placement [12]. The most common indications are obscure GI bleeding. When the results of upper and lower GI endoscopy are normal, the small bowel becomes the most likely source of OGIB [13]. Many clinical studies examined the ability of CE to detect bleeding sources in OGIB patients [8,9,14,15], confirming the superiority of CE in evaluating OGIB over all the conventional imaging modalities. The most favorable candidates for CE study are those with obscure *overt* GI bleeding (with a diagnostic yield of 92–100%) compared to patients with obscure *occult* GI bleeding (with a diagnostic yield of 50–53%) [15]. A meta-analysis of a total of 14 studies (396 patients altogether) compared the yield of CE with that of push-enteroscopy and that of small bowel barium radiography for detecting OGIB, and found that CE was superior to the other two methods for diagnosing clinically significant small bowel pathology in patients with OGIB [16]

The initial study by Fireman et al. [17] on the use of CE in the diagnosis of Crohn's disease reported a 71% yield in diagnosing small bowel Crohn's disease: 12 of 17 patients with a normal small bowel series and colonoscopy but with a high clinical suspicion of having the disease were found by CE to have lesions consistent with Crohn's. In their study of 20 patients with suspected Crohn's disease, Eliakim and co-authors [18] found that in 14 of these patients CE confirmed lesions that were considered to be medically significant or that explained the patient's reason for referral (ulcers and erosions, erythema, aphthae, absent or blunted villi). Triester et al. [19] recently reported a meta-analysis that was conducted on the yield of CE compared to other diagnostic modalities in patients with non-stricturing small bowel Crohn's disease. Their results showed that CE had a higher diagnostic yield for Crohn's than small bowel barium studies, computed tomography enterography, push-enteroscopy, and colonoscopy with ileoscopy. Hara and team [20] compared four diagnostic modalities (CT enterography, colonoscopy with ileoscopy, small bowel follow-through X-ray, and CE) in small groups of patients known to have or suspected of having non-obstructive Crohn's disease. They concluded that CE is better for assessing proximal or early mucosal disease, whereas CT enterography is better for detecting transmural and extraluminal abnormalities. Most important, CE and CT enterography may depict non-obstructive Crohn's of the small bowel when conventional techniques, such as ileoscopy or SBFT, produce negative or inconclusive findings. In comparing the diagnostic yield of CE to that of magnetic resonance imaging enteroscopy in small bowel Crohn's disease, CE revealed significantly more inflammatory lesions in the proximal and middle part of the small bowel than MRI enteroclysis. In contrast, MRI was more helpful in identifying transmural Crohn's and extraluminal lesions, and could exclude strictures. Albert et al. [21] concluded that CE and MRI are complementary methods for diagnosing small bowel Crohn's disease.

For tumors of the small bowel, several studies found CE beneficial in patients with known or suspected polyposis syndromes [22,23], indicating that CE could detect significantly more small bowel tumors that are often missed by other methods of inves-

FDA = Food and Drug Administration

OGIB = obscure GI bleeding
SBFT = small bowel follow-through

tigation. CE is able to detect more polypoid lesions than barium examinations, such as SBFT and MRI: while CE did not differ from SBFT and MRI in identifying polyps that were larger than 15 mm, it detected small polyps more often than the others could [24].

CE had a low yield in the evaluation of chronic abdominal pain according to the results of several studies and can not be recommended as a first-line test without further study [25,26]. On the basis of the published data, CE can not be recommended for patients whose only symptom is chronic abdominal pain.

CE also serves as a modality for identifying small bowel atrophy and other endoscopic findings suggestive of celiac disease. Celiac disease is based on histological findings and response to a gluten-free diet. CE may be an option to recognize villous atrophy in patients with a positive serology test who are unwilling or unable to undergo gastroscopy [27]. The ability of CE to view the entire small bowel is especially advantageous for patients with refractory celiac disease that might be complicated by a variety of conditions, i.e., ulcerative jejunitis [28], small intestinal adenocarcinoma, or small intestinal lymphoma [29]. In this subgroup, CE studies have correctly documented pathological lesions in up to 45% of the cases [30].

The evaluation of postoperative monitoring of patients with small bowel transplantation for the early detection of post-transplant complications and for the assessment of the graft's integrity (published in a case report [31]), as well as the use of CE for the diagnosis of acute intestinal graft-versus-host disease [32] has shown its utility in possibly avoiding repeated endoscopic procedures with biopsies. Larger studies are needed to confirm these observations.

Numerous studies have demonstrated that the disposable capsule is well tolerated and highly effective in adult patients. The procedure has also been performed safely in a small series of pediatric patients after ingestion or endoscopic placement of the capsule. The high yield of abnormal findings was comparable to those in adults [8,9,12,15].

The procedure's limitations

Despite the expected life span of ~8 hours, the capsule battery may run out before the entire small bowel is visualized, particularly in cases of delayed small bowel transit time [10,14,15]. A critical region of interest may remain unevaluated, as in the terminal ileum in Crohn's disease. Some lesions may be missed since the capsule direction and passage velocity are not controllable. Image quality is sometimes inferior to that of flexible video endoscopy, since the lesions cannot be washed or re-examined. The camera may be obscured by residual debris, such as bile, food, contrast barium or feces. The capsule's inability to perform biopsies limits histopathological correlation and diagnostic accuracy.

Complications and safety

The capsule may be retained in the GI tract and may require endoscopic or surgical removal. Pathologies that may cause retention include benign strictures or adhesions, Crohn disease strictures, and lesions (e.g., carcinoid tumor or adenomas) [33]. Retention rarely occurs at Zenker's or Meckel's diverticula [34,35]. The overall incidence of capsule retention is low (0.1–5%), and most of the cases are due to Crohn-related strictures [36,37]: capsule retention occurs in < 1% of patients without evident disease [37], but retention rates of 4–6% are reported in patients with established Crohn's. Cheifetz et al. [37] retrospectively reviewed the records of 983 CE procedures performed at three private gastroenterology practices. Capsule retention occurred in 13% of patients with known Crohn's, but in only 1.6% of patients with suspected disease. A retained capsule may indicate unsuspected strictures in Crohn's disease that may require an unexpected, but therapeutic surgical intervention. Patients and physicians should be aware of these potential risks when considering CE in Crohn patients.

Capsule endoscopy has been proven to be an effective tool in the diagnosis and follow-up of patients with small bowel Crohn's disease

The Agile™ patency System (Given Imaging Ltd) is a dissolvable capsule propelled through the GI tract by natural peristalsis. It is 26 mm long and 11 mm in diameter (the same dimensions as the PillCam™ SB) and it was designed in an effort to avoid retention of a capsule when there is some suspicion of a stricture in patients who were candidates to undergo CE. The Agile™ is capable of evaluating the presence of obstructional strictures in the GI tract and stays intact in the GI system for approximately 30 hours post-ingestion after which it begins to disintegrate. It contains a small radiofrequency tag that can be detected by a scanner. One recent study [38] confirmed it to be a useful tool for identifying those individuals who may safely undergo CE without capsule retention.

Contraindications

CE is contraindicated in pregnancy, in patients with known or suspected small bowel stricture, previous major abdominal surgery, dysphagia, or with implanted cardiac pacemakers, although Payeras and collaborators [39] recently reported that 20 patients with implanted pacemakers underwent CE studies without any electrical interferences. Endoscopic delivery of the capsule in patients with dysphagia, anatomic abnormality, or gastroparesis has been reported as safe and effective in pediatric patients as well [12].

Conclusions

It can be said that the invention of CE marked the start of a new age of diagnostic imaging and opened up the final frontier of endoscopy. CE's highest diagnostic yield is in patients with obscure GI bleeding and it therefore should be performed early on in the workup of patients who have negative upper and lower

endoscopic results. CE has been proven to be an effective tool in the diagnosis and follow-up of patients with Crohn's disease. Refinement of the technology by prospective comparative studies with adequate control groups and predefined clinical endpoints can be expected to establish CE as a valuable tool in the diagnosis and treatment of Crohn's. The ultimate CE needs a kind of reservoir for collecting body fluids for diagnosis and analysis, and the ideal capsule will also be able to take biopsies.

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