

Capsule Endoscopy in the Evaluation of Patients with Suspected Crohn's Disease: Expanding Experience into the Pediatric Age Group

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Crohn's disease is an idiopathic chronic inflammatory disease that can involve any portion of the gastrointestinal tract in both children and adults. Crohn's disease is a transmural disease that may present as discontinuous areas of inflammation, scarring and fistulization. Ileocolonic disease is found in 37.5% of cases, ileal disease in 26.9% of cases, colonic disease in 19%, and jejunal and upper gastrointestinal disease in 16.6% of cases [1].

Historically, the diagnosis of Crohn's disease has been based on clinical, hematological, biochemical, radiological and endoscopic examinations. A relatively new technology, wireless video capsule endoscopy, was approved by the U.S. Food and Drug Administration in 2001 for use in the diagnosis of small bowel diseases. Since then, CE has established itself as an important tool in the evaluation of the small bowel.

Capsule endoscopy may be performed in an outpatient setting. Preparation prior to the examination includes a 12 hour fast or clear liquid diet. Some centers employ a bowel preparation the night before in order to improve visualization and to improve the chances of the capsule reaching the colon prior to the end of the exam [3,4]. Two hours into the test a clear liquid diet is allowed and a regular diet may be given after 4 hours. In children who are unable to swallow the capsule, the examination may be done by introducing the capsule directly into the duodenum endoscopically [5].

The most frequent indication for CE has been obscure gastrointestinal bleeding. This method was shown to be superior to other diagnostic tools, including barium radiography and push enteroscopy, in the evaluation of obscure gastrointestinal bleeding [6-9]. It was also found useful for detecting small bowel polyps in patients with familial polyposis syndromes [10]. Several studies have demonstrated the possible usefulness of CE in the diagnosis of celiac disease [11,12].

Capsule endoscopy has proven itself as a sensitive tool for the diagnosis of small bowel Crohn's disease

The PillCam SB, produced by Given Imaging Limited (Yoqneam, Israel), was the first wireless CE system approved by the FDA. The system comprises a wireless capsule endoscope and a recording system. The CE measures 11 mm in diameter, 26 mm in length and weighs 3.7 g. Image features include a 140° field of view and 1.8 magnification. The capsule captures two frames per second, resulting in 55,000 images in a routine 8 hour study. Peristalsis advances the capsule through the bowel as it transmits images to the recording system. Battery life and thus the duration of capsule studies are typically about 8 hours. The average reading time, often determined by reader experience and bowel transit time, ranges from about 30 to 120 minutes [2]. Recently, the Olympus Medical Systems Corporation (Tokyo) introduced a new CE for evaluating the small bowel. There has been less experience with this system.

Capsule endoscopy in Crohn's disease

Since Crohn's disease frequently involves the small intestine, much of which is not accessible to standard upper endoscopy and colonoscopy, tests that provide more information than standard small bowel series may be extremely useful in the evaluation of these patients. In addition to contributing to the initial diagnosis of Crohn's disease, proper small bowel evaluation allows accurate determination of the location and extent of small bowel disease [Figure 1]. This is important when choosing medications and when considering surgery. CE enables visualization of the entire small bowel and is therefore of great interest with regard to Crohn's disease.

To define the role of CE, it was necessary to compare its efficacy with that of other more traditional diagnostic modalities. Fireman et al. [13] diagnosed small bowel Crohn's disease by CE in 12 of 17 patients who had a normal small bowel series, esophagogastroduodenoscopy and colonoscopy but with a strong clinical suspicion of Crohn's disease due to abdominal pain, fever, weight loss, anemia and elevated erythrocyte sedimentation rate. Capsule findings included mucosal erosions, ulcers and strictures. All 12 patients were treated with mesalamine or steroids and had a good clinical response. Eliakim and co-authors [14] examined 20 patients with suspected Crohn's disease on

CE = capsule endoscopy
FDA = Food and Drug Administration



Figure 1. Capsule endoscopic image showing multiple ulcerations of the small bowel compatible with Crohn's disease.

the basis of abdominal pain, diarrhea and weight loss. They showed that CE established new diagnoses, confirmed existing diagnoses, enlarged the extent of the disease, and ruled out the suspicion of Crohn's disease in 70% of the patients. In addition, this evaluation detected all the lesions diagnosed by the small bowel series and computed tomographic enterography as well as finding additional lesions that were not detected by other modalities in 47% of the cases, and ruled out lesions that were detected by other modalities in 16% ($P < 0.05$). In an extension of this study, a total of 35 patients with suspected Crohn's disease were evaluated. A diagnosis was made by CE in 77% of patients, compared with a small bowel series diagnostic yield of 23% and CT enterography where the yield was 20% [15]. Herreras et al. [16] studied 21 patients who underwent CE as part of the evaluation for Crohn's disease because of abdominal pain, diarrhea, weight loss, fever, anemia and elevated C-reactive protein. Colonoscopy and small bowel series were negative in all patients. In nine patients the CE findings were compatible with Crohn's disease. These findings included aphthae, linear or irregular ulcers and mucosal fissures. Patients were subsequently found to be in remission after starting treatment [16]. Voderholzer et al. [17] prospectively compared CE and CT enteroclysis in 41 patients with known and suspected Crohn's disease. Twenty-five of these patients were found to have jejunal or ileal lesions by CE compared to 12 by CT enteroclysis. The new information was mainly due to the detection of small mucosal lesions such as multiple aphthae and erosions. Treatment was changed as a result of the capsule findings in 10 patients. In a study by Dubcenco and team [18], CE demonstrated a sensitivity of 89.6%, specificity of 100%, positive predictive value of 100% and negative

predictive value of 76.9% versus small bowel series with respective values of 27.6%, 100%, 100% and 32.3%.

A meta-analysis of nine prospective comparative studies reported that the yield of CE for diagnosing Crohn's disease was 63% versus 23% for small bowel barium radiography. Four prospective comparative studies demonstrated an overall yield for CE of 61% vs. 46% for ileoscopy in finding small bowel disease consistent with Crohn's disease. In three studies the CE yield was 69% compared to 30% with CT enterography/CT enteroclysis [19].

Postoperative recurrence of Crohn's disease is a common challenge for the gastroenterologist. CE was performed in eight patients with a history of small bowel resection for Crohn's disease who were suspected of relapse and had a negative conventional workup including an upper endoscopy, colonoscopy, ultrasound, barium contrast study, CT and push enteroscopy. In six of the eight patients, CE showed recurrence of small bowel disease, which led to a change in therapy and subsequent clinical remission.

There are fewer studies evaluating the role of capsule endoscopy in children with suspected Crohn's disease. Seidman et al. [21] studied 20 children with suspected Crohn's disease who had negative small bowel series and colonoscopy. In 10 of them CE demonstrated multiple erosions and ulcers thought to be consistent with Crohn's disease. Arguelles-Arias and collaborators [22] used CE in 12 patients aged 12–16 with a weight range of 43–87 kg. The indication was a clinical suspicion of Crohn's disease with a normal gastroscopy, colonoscopy, and small bowel follow-through series. Ileoscopy was performed in 50% of the patients and showed normal ileal mucosa and biopsies. CE identified lesions suggestive of Crohn's disease in 7 of the 12 patients (58.3%), with the majority of the lesions located in the ileum.

We recently reviewed our experience with the first 45 children undergoing CE in our practice. The indications for this modality included unresponsive Crohn's disease; possible intestinal polyps; unexplained iron deficiency anemia; growth failure associated with symptoms suggestive of an underlying intestinal disorder, and others [Table 1]. A total of 28 CE tests were abnormal. These included nine patients who were newly diagnosed with Crohn's disease and nine known Crohn patients who were newly diagnosed with small bowel involvement. Of the 9 who were newly diagnosed with Crohn's disease, 8 (89%) began treatment based on the findings of the CE test while one patient remains

Table 1. Indications for capsule endoscopy

Indication for CE	No. of patients (%)
Unresponsive Crohn's disease	16 (36%)
Possible intestinal polyps	11 (24%)
Unexplained iron deficiency anemia	7 (16%)
Growth failure	5 (11%)
Unresponsive ulcerative colitis	3 (7%)
Persistent abdominal pain	1 (2%)
Protein losing enteropathy	1 (2%)
Allergic enteropathy with GI bleeding	1 (2%)

asymptomatic and is not taking any medication. Among the 9 patients with Crohn's disease who were newly diagnosed with small bowel involvement based on the CE, 7 (78%) had their treatment changed after the procedure [23].

We subsequently reviewed our experience with children who underwent CE for the evaluation of unexplained growth failure. Indications for the procedure included growth failure associated with abdominal pain in three patients, diarrhea and aphthous ulcers in one patient, mild anemia in one, delayed puberty in one and a family history of Crohn's disease in one. Small bowel series, esophagogastroduodenoscopy and colonoscopy were normal in all patients. CE demonstrated multiple aphthae and ulcers consistent with Crohn's disease in the small bowel in five of seven patients. All five patients began treatment and subsequently demonstrated improved growth [24].

CE allows the gastroenterologist to view the mucosa of the entire small bowel. The lesions seen – such as mucosal breaks, erythema, aphthae, erosions and ulcers – are often considered to be consistent with Crohn's disease. However, with CE there is no histological correlation. Therefore, there is a need to establish a system to objectively determine what findings on CE are diagnostic of Crohn's disease. Goldstein and associates [25] found a 13.8% incidence of small bowel lesions with CE in apparently healthy asymptomatic volunteers who were not taking non-steroidal anti-inflammatory medications and with no history of gastrointestinal disease. In addition, CE detected small bowel mucosal breaks in 55% of patients using naproxen, 16% of patients on celecoxib and in 7% of placebo patients. This study demonstrates that NSAIDs are associated with a high prevalence of injury to the bowel [25]. Kornbluth et al. [26] have devised a scoring system for description of small bowel lesions detected by CE in adults being evaluated for Crohn's disease.

The most significant complication associated with capsule endoscopy is capsule retention due to a stricture

In the evaluation of children, only one preliminary study has looked at the specificity of CE findings for Crohn's disease. We recently studied 17 consecutive children diagnosed by CE as having small bowel Crohn's disease. The children were divided into three groups based on their CE findings and were followed for 6 months. We demonstrated that those with the more significant CE findings were most likely to respond to Crohn's disease treatment, while those with the milder lesions were less likely to have clinical improvement [Figure 2]. We suggested that less severe CE findings are not sufficient to diagnose Crohn's disease and therefore should not be used to guide medical therapy [27]. It is therefore important to recognize that not all mucosal changes

NSAID = non-steroidal anti-inflammatory drug

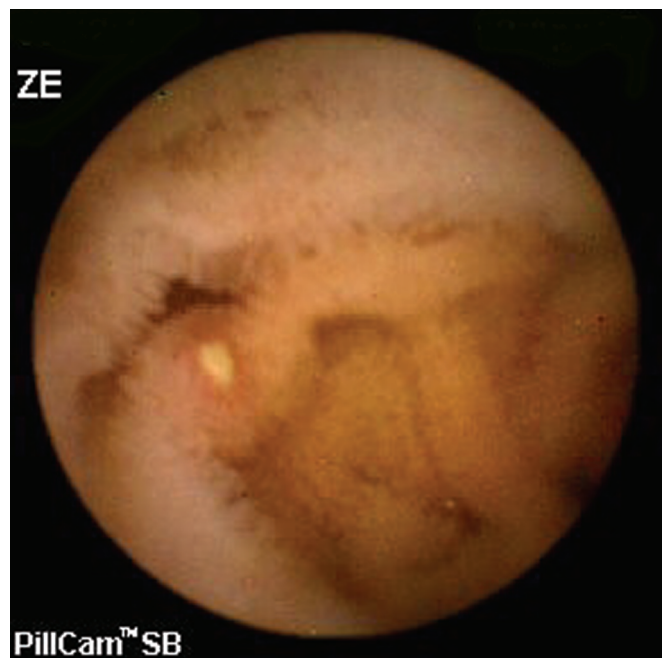


Figure 2. Isolated aphthous ulcer in the small bowel. The significance of such isolated findings needs to be determined.

are a result of Crohn's disease, and that before labeling a patient with a life-long diagnosis or making changes in treatment one must take into account the clinical picture and other diagnostic tests.

Complications

Complications of CE are thought to be infrequent, the most significant being capsule retention due to a stricture. Capsule retention in the intestine may necessitate removing it either by endoscopy or surgery. In cases of narrowing secondary to inflammation, high dose steroids has occasionally allowed for passage of a retained capsule. One study noted retention of the capsule in 2 of 30 adult patients with Crohn's disease, all of whom had normal small bowel series [28]. In the largest series reported to date, capsule retention occurred in 0.7% of 900 adult patients evaluated primarily for obscure bleeding; most of them were patients with normal small bowel series preceding capsule ingestion [29]. Cave et al. [30] reported 5 retained capsules in their series of 137 adults evaluated primarily for obscure bleeding. In a series assessing adult patients with known Crohn's disease, capsule retention occurred in 4 of 55 patients. None of these patients had strictures, which were suspected based on the clinical presentation or small bowel follow-through [26]. In pediatrics, Seidman [21] reported capsule retention in 1 of 30 patients evaluated for small bowel Crohn's disease, polyps or obscure gastrointestinal bleeding. In our recent review of patients who underwent CE we noted that 9 of the 45 subjects had adverse events. Five patients had delayed passage from the stomach, with two requiring endoscopic retrieval of the CE. Four had delayed passage from the small intestine (> 5 days) with

two requiring surgical removal. One responded to steroids and one required an ileocolic resection 2 months after the CE for an undiagnosed ileal stricture. All the children with capsule retention had normal small bowel series prior to CE and all the children with small intestine capsule retention were found to have Crohn's disease [23].

To reduce the chances of a retained capsule, Given imaging developed a patency capsule that is ingestible and dissolvable and is the same size as the Given capsule. It consists of a biodegradable and mixed material body (including barium) surrounding a small radiofrequency ID tag. If the capsule is passed intact then patency is confirmed. The patency scanner is used to detect a signal from the radiofrequency ID tag. If the scanner detects the capsule then the patency of the gastrointestinal tract is not confirmed. If the patency capsule remains in the body for more than 2 days it starts to disintegrate, thus diminishing the chances of stricture complications. However, with the initial model of the patency capsule there have been reports of capsule retention requiring emergency surgery [31]. Recent modifications of the patency capsule may decrease the likelihood of patency capsule retention. Studies of this new patency capsule should be available shortly.

Conclusions

Capsule endoscopy is a sensitive method for evaluating the small bowel. It is helpful in diagnosing small bowel Crohn's disease and for determining the extent of small bowel disease. It has strengthened our diagnostic armamentarium but there remains much to be clarified. Studies are needed to establish what findings on CE are diagnostic of Crohn's disease. In addition, further evaluation is needed to clarify the place of CE in the diagnostic tree of Crohn's disease.

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