

Clinical utility of capsule endoscopy in small intestinal diseases, experience of single referral center with 125 cases

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Abstract

Aim: To evaluate the clinical utility of capsule endoscopy in diagnosing small bowel disease.

Material and methods: A retrospective review of 125 capsule endoscopy (CE) examinations from September 2003 to March 2009 was performed.

Results: The average patient age was 47.7 ± 18.2 (min: 13, max: 97), 49 were female (39.2%). Indications for CE were obscure gastrointestinal bleeding (OGIB) (56.0% of cases), diarrhea (14.0%), abdominal pain (7.2%), other indications such as known Crohn's disease, and surveillance for polyposis syndromes. The CE completely evaluated the entire small bowel in 92 patients (73.6%). Capsule endoscopy study was normal without any finding in 22.4% of patients. The overall diagnostic yield of capsule endoscopy was 74.4% (93/125). The diagnostic yield of obscure gastrointestinal bleeding by capsule endoscopy was 77.1%. No complication related to the capsule was observed.

Conclusions: Capsule endoscopy is safe and well tolerated diagnostic tool in the evaluation of small bowel diseases.

Introduction

Diseases of the small bowel are rare and diagnosis of them is a challenge. Because symptoms of diseases are nonspecific and endoscopic access to the small bowel is very laborious due to its length, location and relative tortuosity. Various techniques have been used for exploring the small bowel such as; radiologic (small bowel follow through, enteroclysis, abdominal computed tomography and abdominal magnetic resonance imaging), angiographic, nuclear medicine and endoscopic techniques (push enteroscopy and intraoperative enteroscopy). All these imaging techniques are far from ideal and have their limitations including inconvenience, invasiveness, risk, the possibility of incomplete visualization and insensitivity. For example, radiological techniques permit examination of the whole small bowel but have disadvantages of low diagnostic yield and radiation exposure, push enteroscopy has been used in few reference centers, and intraoperative enteroscopy requires general anesthesia and laparotomy [1-3].

Capsule endoscopy (CE), which was introduced in 2000, is an ideal method for examination of the small bowel. The capsule is a device in the shape

and size of a pill (26 mm long, 11 mm wide and 3.7 g in weight) that contains a light source, video camera, battery and antenna for image transmission. Once swallowed, the capsule moves through the intestine via peristalsis and excreted in the stool. Capsule endoscopy is minimally invasive and can evaluate the entire small bowel. Obscure gastrointestinal bleeding (OGIB) is the main clinical indication for CE. Additionally, CE has been used to investigate polyposis syndromes, Crohn's disease, celiac disease, chronic abdominal pain and diarrhea. Although, the a low frame rate may result in miss of some mucosal lesions [4-6], CE revealed that the small bowel can be silently involved in several inflammatory or vascular diseases.

Aim

The aim of the present paper is to briefly review our institutional results with CE for the study of the small bowel diseases in a single referral center in Turkey.

Material and methods

Gastroenterology Department of Hacettepe University is the first center in Turkey that implemented

the CE for the diagnosis of the SB diseases at 2002 and is a major referral center for CE nationwide. Patient names, age, gender, indications for CE, results of prior diagnostic tests were recorded into database. Capsule endoscopy findings were recorded and backed up for future evaluations. Since parts of our cohort were published previously [7-9], the present database is the basis for retrospective evaluation of the characteristics and findings of 125 consecutive of patients who underwent CE examination between September 2003 and April 2009. All of the patients had upper and lower GI endoscopies before CE study. There was no clinical sign of intestinal obstruction, additionally; patients with suspected Crohn's disease (CD) had radiologic examinations to exclude obstruction.

Given M2A (Given Imaging, Yoqneam, Israel) video capsule was used for all the procedures. All patients gave their informed consent before undergoing the CE study. Bowel cleansing was performed with 3 l of polyethylene-glycol solution and fasting for at least 12 h before taking the capsule. No premedication was given. After ingestion of the capsule, patients were allowed to drink clear liquids after 2 h, eat a light meal after 4 h and were observed for 8 h at the study site. Once the study was completed, the recording device and sensor arrays were removed and the images were downloaded to the computer with Reporting and Processing of Images and Data (RAPID, Given imaging) software that displays the video images on a computer monitor. The capsule endoscopic images were reviewed at a rate of 15 images per second by experienced and competent capsule readers.

If a found lesion clearly satisfied the study indication, than it was denoted as diagnosis made. These lesions included active bleeding, existence of polyps and tumors, suggestive findings of Crohn's

disease such as mucosal atrophy, nodularity and ulcers. For the patients with anemia and GI bleeding, non-active lesions of angiodysplasia and multiple ulcers that could potentially cause the patient's problem were labeled as diagnosis suspected.

The location of the lesion detected by CE was estimated as duodenal, jejunal or ileal based on total small bowel transit time of capsule from entrance into the duodenum to ileocecal valve and the endoscopic appearance of the mucosa. The anatomic landmarks were used such as the duodenum was defined as entrance of capsule through the pylorus; the jejunum was characterized by prominent folds with high and narrow villi, whereas ileum has fewer folds with shorter villi.

Descriptive statistics were used for demographic features, clinical characteristics and capsule endoscopic findings. Categorical variables are presented as percentages and numerical variables as means and ranges. All the statistical analyses were performed with the statistical software SPSS version 10.5.

Results

Out of 120 patients, 76 (60.8%) were male and 49 (39.2) were female; mean age of the patients was 47.9 \pm 18.0 (range 13-97) years (Table I). The main indication was OGIB (56%). Other indications included evaluation of abnormal radiographic findings, celiac disease, common variable immunodeficiency and polyp surveillance in Peutz Jeghers disease.

Capsule endoscopy successfully evaluated the entire small bowel in 74.2% of patients (Table II). The most common cause for incomplete examination was premature battery failure (16.6% of cases). Technical problems with capsule or transmission were the cause of incomplete examination in 7 cases. Three patients had insufficient bowel cleaning and obscured

Table I. Demographic characteristics of the patients ($n = 125$)

Age [year] (mean \pm SD)	47.9 \pm 18.0	
Male : female	76 : 49	
Indication ($n, \%$)		
OGIB	70	56.0
Anemia	10	8.0
Diarrhea	18	14.4
Abdominal pain	9	7.2
Crohn's disease	8	6.4
Other	10	8.0

OGIB – obscure gastrointestinal bleeding

Table II. Outcomes of capsule endoscopy examinations ($n = 125$)

Outcomes	n (%)
Examination	
Complete	92 (73.6)
Incomplete	33 (26.4)
Findings	
Normal study	28 (22.4)
AVMs	16 (12.8)
Ulcers/erosions	44 (35.2)
Neoplasm/polyp	8 (6.4)
Other	29 (23.2)

AVM – arterio-venous malformations

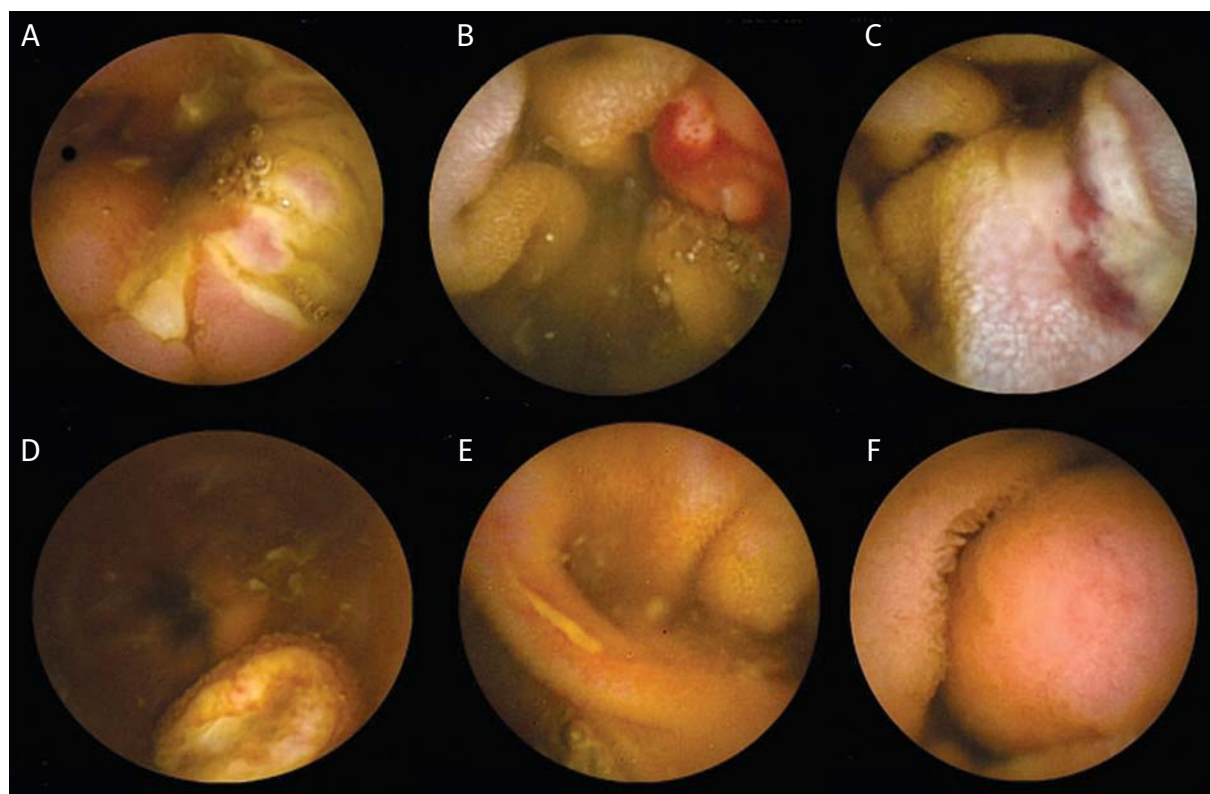


Fig. 1. Causes of small intestinal bleeding: (A) non-steroid anti inflammatory drug induced ulcer in the ileum, (B) actively bleeding mass, (C) cancer in the jejunum, (D) renal cell cancer metastasis to small intestine seen as an ulcerated polyp, (E) diffuse intestinal ulcers found in a patient with multiple myeloma, (F) a large polyp in the jejunum

view of the capsule in spite of bowel cleansing. Regional transit abnormality, which was defined as failure to passage longer than an hour, occurred in 1 patient having strictures of Crohn's disease and in another patient whose capsule stayed in the ileum for 3 h before the battery died. This second patient was later found to have ileal adenocarcinoma, which caused intestinal perforation 2 days after CE study. However, no capsule retention was seen in preoperative abdominal radiograms. No complication related directly to the CE study was observed in our series. Second CE study was performed in 5 patients because of technical failure. Second look CE revealed an ulcerated lipoma of the ileum, which was not detected during the first study. CE could not detect any lesion and reported to be as normal in 28 patients (22.4%) (Table II). Aphthous ulcer, mucosal erosion, ulcerated stenosis and nodular pattern were detected in 47 patients (Figure 1A). The lesions were mainly distributed in proximal small bowel jejunum 21 (44.7%), ileum 16 (34.0%) and diffuse in 10 patients (21.3%). Out of 8 patients with diagnosis of malignancy, the diagnosis was confirmed by surgery in 5 patients (4%). Histologic findings of tumors were

1 adenocarcinoma (Figure 1B, 1C), 1 lipoma, 1 gastrointestinal stromal tumor (GIST) and 2 metastatic tumors which were extensive polypoid small bowel metastasis of renal cell carcinoma (Figure 1D). One patient with OGIB was found to have multiple myeloma which was presented as ulcer, nodularity and irregularity of the mucosa (Figure 1E). Although we did not have any histologic confirmation of intestinal involvement, patient is in remission after chemotherapy and no intestinal complaints including bleeding was observed 2 years after the diagnosis.

A bleeding source was identified in 54 out of 70 patients. The most frequent reason for bleeding was ulcers or erosions in 28 patients and secondly angiodysplasia in 12 patients. Active bleeding without any identified source of bleeding was observed in 10 patients (8%). Bleeding angiodysplasia were the most common reason in these patients. However, CE missed a mass lesion, which was diagnosed as GIST after single balloon enteroscopy, located in the distal duodenum. Diagnostic yield for OGIB was 77.1%. In this analysis we excluded the patients with anemia, combining results of these patients

Table III. Diagnostic yield of CE according to indication

Indication for CE	N	Definitive diagnosis n (%)	Suspected diagnosis n (%)	Total yield [%]
OGIB	70	37 (52.8)	17 (24.3)	77.1
Chronic diarrhea	18	2 (11.1)	7 (38.9)	50.0
CD	8	6 (75.0)	6 (75.0)	75.0
Abdominal pain	9	2 (22.2)	3 (33.3)	55.5
Other	20	8 (40.0)	6 (30.0)	70.0

OGIB – obscure gastrointestinal bleeding, CD – Crohn's disease

Table IV. Capsule endoscopy findings by study indication

	OGIB (n = 70)	Diarrhea (n = 18)	CD (n = 8)	Pain (n = 9)	Other (n = 20)
Ulcers	28 (40)	3 (16)	6 (75)	3 (33)	4 (20)
AVM	12 (17)	1 (5)	0 (0)	1 (11)	2 (10)
Mass/polyp	7 (10)	1 (5)	0 (0)	0 (0)	0 (0)
Other	8 (11)	4 (22)	0 (0)	1 (11)	8 (40)

Data are presented as n (%) according to indications, OGIB – obscure gastrointestinal bleeding, CD – Crohn's disease

lowers the diagnostic yield to 69.6%. Figure 1F shows a large polyp detected in a patient with Peutz Jeghers disease.

Patients with abdominal pain and diarrhea had the lowest diagnostic yield (Table III). On the other hand patients with Crohn's disease (CD) had the highest yield by CE study. Most of the patients with CD had typical small bowel ulcers. Ulcers were the most common finding, presented in 40% of patients with OGIB. AVMs were mostly encountered in patient with OGIB (Table IV).

Discussion

No doubt for that Capsule endoscopy has changed our way of management of small intestinal diseases. Capsule endoscopy has become preferred method for visualization of small bowel.

As expected, OGIB was the most common indication for the CE examination. Cause of bleeding was found in 74% of patients. Data from the current studies have reported a diagnostic yield around 70%, though lower figures were also reported, which may be directly related to the patient selection criteria. The time interval and type of bleeding might influence diagnostic yield. The diagnostic yield of CE in OGIB depends on the type of bleeding; the highest yield of CE was in patients with active bleeding (92.3%) compared to those with obscure occult bleeding (44.2%) [10].

Researchers observed a reverse relationship between findings and time after last bleeding episode. The longer the time from last bleed, the lower the diagnostic yield. Although we did not include this data, 5 patients had active bleeding that was demonstrated during the CE, which necessitated surgical operations and done in 4 patients. One patient with bleeding angiodysplasia did not accept operation and he is still alive without any bleeding episode. Capsule endoscopy discovers more lesions but do they have any bleeding potential or clinical importance in terms of management change? Saurin *et al.* [11] showed that CE detects more lesions, but only half of them have true bleeding potential.

Crohn's disease (CD) is an important indication for capsule endoscopy, and via using this method SB involvement can be discovered in a significant portion of patients with suspected CD. Eight patients referred for search for SB involvement had known CD, with either ileocaecal or colonic involvement. An interesting finding is 12 patients with OGIB had previously not been diagnosed with this disease, and capsule endoscopy revealed findings highly suggestive of CD and changed the management strategy. Mucosal ulcerations were the most common finding in our patient series, determined in almost one out of four patients. Crohn's disease was the third most common indication for CE study (6.4% of patients). Patients

with CD had severe ulcerations and two patients had strictures that resulted in regional transit abnormality. However, no capsule retention occurred in this group. Moreover, CE changed the management strategy in 10% of patients with a new diagnosis of CD. Another finding was that 37.5% of the patients diagnosed as suspected CD did not have complete examination. Nonspecific jejunoileitis and NSAID-induced erosions were observed in 6.4% of patients.

Results from the CE procedure must be reviewed very carefully and sometimes patients past history of diseases may give a clue for the diagnosis. In our patient cohort we have seen patients with Behçet's disease, vasculitis and tuberculosis. Lesions found in the small intestine were not different from others in terms of shape, location or distribution. However these patients' survival was very short. A patient with vasculitis and intestinal involvement was deceased within 6 months after the CE. Another one with diffuse jejunal ulcers was misleded by the patient's history of non-steroid anti inflammatory drug use, whom diagnosed as non specific jejunoileitis. This patient had miliary tuberculosis and deceased because of sepsis and meningeal involvement. That's why we think this patient as intestinal tuberculosis. These cases showed us if there is an intestinal involvement in systemic disorder, course of the disease could be detrimental. Moreover, according to Neves intestinal lesions in Behçet disease could be more frequent than previously thought, regardless of disease activity. They reported to found lesions in 80% of patients regardless of activity [12].

Small intestinal lesions can be found in healthy adults, which may make it difficult to interpret such findings in some patients [13, 14].

Capsule endoscopy's ability to detect mucosal atrophy has been reported in several studies. Unsuspected celiac disease can be diagnosed in variety of complaints such as abdominal pain, diarrhea and anemia. Unfortunately, we had only one patient with celiac disease and mucosal atrophy, which was diagnosed after the CE study. Several studies report that evidence of celiac disease was found in the distal duodenum or proximal jejunum, beyond the reach of an endoscope. Capsule endoscopy could be a valuable tool in patients with milder forms of celiac disease that had not classical picture of malabsorption or diarrhea and may also play a role in patients with CD who are unresponsive to gluten-free diet or with symptoms such as weight loss, persistent or recurrent abdominal pain, and occult gastrointestinal bleeding to exclude complications of celiac disease [15, 16].

Chronic diarrhea was the second most common indication for CE study in our series. Half of these

patients did not have any condition that may cause diarrhea and diagnostic yield of CE was very low. Use of CE for the evaluation of abdominal pain is debated. Although some serious causes are identified in such patients, CE is mostly unyielding. In our series only 2 cases (22.2%) were diagnosed by CE over other diagnostic modalities. If patients with other signs and symptoms of inflammation were selected, than the diagnostic yield may be considerably higher [1, 10].

No serious complications related to procedure were noted. All of the patients had previous diagnostic work up, some including small bowel radiology, thus no case of retention was noted. However, almost one out of four procedures was unsuccessful. Incomplete study rate is 25.8%, which was reported to be approximately 20 to 30% in most studies [16-19]. Risk factors for incomplete study include delayed gastric emptying (longer than 45 min), previous small intestinal surgery, hospitalization, poor bowel cleansing and diabetes mellitus. Prokinetics and different bowel cleansing regimes do not offer any benefit. Although, incomplete examination rate is high, we believe incomplete does not mean inadequate except the technical failure of the capsule itself. Incomplete CE examination may necessitate repeat of the procedure.

Although some studies have demonstrated that bowel preparation can lead to high quality pictures and have benefits for completion of the procedure, it is still debated [20]. We had only three patients with poor bowel cleansing. Therefore we recommend the routine use of bowel preparation for CE procedure. Even ingesting a small amount of polyethylene glycol may significantly improve CE quality [21].

Further diagnostic work-up after a positive CE study may be needed; for instance, fresh blood in the absence of a definitive lesion, or visualized polyp or mass that result in further imaging tests to confirm the diagnosis. Balloon assisted enteroscopes, which includes single and double balloon enteroscope, are widely available and safe techniques that gained acceptance in recent years. Combined use of CE and balloon assisted devices may give higher diagnostic yield and therapy of the suspected lesions.

In conclusion, capsule endoscopy is a major advance in the diagnosis of small bowel diseases but it is not the gold standard. We should recognize the down sides and reassess the clinical utility of the CE in various indications. OGIB and Crohn's disease are seemed to be the major indications with high diagnostic yield and clinical impact on the course and treatment of disease.

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