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ORIGINAL ARTICLE

URGENT CAPSULE ENDOSCOPY IS USEFUL IN SEVERE OBSCURE-OVERT GASTROINTESTINAL BLEEDING

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Aim: With capsule endoscopy (CE) it is possible to examine the entire small bowel. The present study assessed the diagnostic yield of CE in severe obscure-overt gastrointestinal bleeding (OOGIB).

Methods: During a 3-year period, 15 capsule examinations (4.5% of all CE in a single institution) were carried out in 15 patients (11 men; mean age 69.9 ± 20.1 years) with severe ongoing bleeding, defined as persistent melena and/or hematochezia, with hemodynamic instability and the need for significant red blood cell transfusion. CE was carried out after non-diagnostic standard upper and lower endoscopy. The mean time from admission until CE was 4.1 ± 4.4 days (0–15 days).

Results: CE revealed active bleeding in seven patients and signs of recent bleeding in four. Etiology of bleeding was correctly diagnosed in 11 patients (73.3%) (portal hypertension enteropathy, three patients; subepithelial ulcerated lesion, two patients; angiodysplasia, two patients; jejunal ulcer with visible vessel, one patient; multiple small bowel ulcers, one patient; jejunal tumor, one patient; jejunal mucosa irregularity with adherent clot, one patient). One patient (6.7%) had active bleeding but no visible lesion. As a consequence of the capsule findings, specific therapeutic measures were undertaken in 11 patients (73.3%) with five managed conservatively, four endoscopically and two surgically. Two patients experienced bleeding recurrence. One of them, with a probable small bowel tumor, refused any other interventions.

Conclusions: CE is useful in patients with severe OOGIB by providing positive findings in the majority of patients, with subsequent impact on therapeutic procedures.

Key words: capsule endoscopy, mid-gastrointestinal bleeding, severe overt-obscure gastrointestinal bleeding.

INTRODUCTION

Obscure gastrointestinal bleeding (OGIB) is blood loss from an unknown source that persists or recurs after a negative initial endoscopic (colonoscopy, upper endoscopy) and radiological evaluation.[1] Obscure bleeding may be obscure-occult (i.e. not visible) or obscure-overt (OOGIB) (i.e. continued passage of visible blood).[1] These patients represent 2–10% of all patients with digestive bleeding, and they frequently undergo multiple diagnostic procedures and blood transfusions with increased consumption of health-care resources.[2,3]

OGIB is considered severe when any of the following criteria are present: overt presentation, recurrent episodes of acute bleeding, transfusion dependence and the need for hospitalization.[4] Severe OGIB represents 1% of all overt digestive bleedings.[4]

Intraoperative enteroscopy with a diagnostic yield of 70–100% in OGIB and considered for many years the gold standard for endoscopic small bowel imaging must be compared with new methods.[5] In fact, capsule endoscopy (CE) allows the examination of the entire small bowel with similar diagnostic yield and double balloon enteroscopy (DBE) permits real-time exploration of the small bowel with full diagnostic and therapeutic capabilities.[5–7] The advent of these two methods is linked to the emergence of a new definition in gastroenterology: mid-gastrointestinal bleeding.[8]

OGIB is the main indication for CE, considered the most efficient strategy regarding diagnosis, positively predicting the intestinal diagnosis or normal status in 95.5% of cases.[3,9] However, the use of CE after initial negative upper endoscopy and colonoscopy without a second standard endoscopic evaluation is controversial because some studies report that a number of lesions detected by CE are within the reach of standard endoscopy.[10–15]

CE has a high positive (95%) and negative predictive values (83–100%), but the diagnostic yield is influenced by the timing of the examination and the nature of the bleeding.[5,9,16] In fact, patients with ongoing OOGIB are the ones that benefit the most from CE when compared with patients with obscure-occult bleeding.[5,16–18] Even if no lesion is found, CE has the potential to, at least, determine the location of the bleeding.[18]

In the present study, we aimed to determine the diagnostic yield, therapeutic changes and final outcome of CE performed shortly after standard endoscopic evaluation in patients with severe OOGIB.

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METHODS

A total of 330 examinations with CE performed with PillCam SB (Given Imaging, Yoqneam, Israel) between January 2005 and December 2007 at a single institution were retrospectively evaluated. We considered eligible for study all patients with severe ongoing bleeding, defined as persistent melena and/or hematochezia, with periods of hemodynamic instability and the need for red blood cell (RBC) transfusion, submitted for CE after non-diagnostic standard upper and lower endoscopy. Only urgent CE, defined as non-scheduled examinations carried out in patients with clinical and analytical signs of ongoing bleeding, immediately after negative standard upper and lower endoscopies were included.

All but one patient were submitted for colonoscopy in the previous 24 h, and were fasting for more than 12 h. The patient that did not undergo colonoscopy had multiple previous episodes of OGIB with extensive previous work-up, including colonoscopy and elective CE. As no diagnosis was previously established, we decided to carry out a CE soon after the start of a new bleeding episode.

Metoclopramide (10 mg, i.v.) was given to all patients. After 8 h, the sensor array and the recording device were removed and the digital video image streams of the examinations were downloaded to the RAPID system (Given Imaging). The CE digital image stream was assessed and interpreted by four gastroenterologists with experience in CE.

Age, sex, time of hospitalization, previous episodes of GI bleeding and recent medications, results of previous diagnostic work-up tests, including upper endoscopy, colonoscopy, previous CE, contrast radiography, tagged red blood cell scintigraphy and angiography, were registered. Complications of the procedure, limitations, rate of total enteroscopy and specific therapeutic interventions resulting from the CE findings were also registered. Rebleeding rate was assessed by analyzing medical records or contacting the referring physicians.

The findings were classified according to a system already adopted in other studies:[9,19] P0 lesions, such as visible submucosal veins, diverticula without the presence of blood and nodules without mucosal break, considered to have no bleeding potential; P1 lesions, such as mucosal red spots or small/isolated erosions, having uncertain or intermediate hemorrhagic potential; and P2 lesions, such as typical angiomas or angiodysplasias, varices, tumors, large ulcerations and multiple erosions, considered to have large bleeding potential. Active bleeding, even without identification of the hemorrhagic source, was also considered a positive important finding. Portal hypertension enteropathy, described as areas of mucosa with a reticulate pattern, was considered a P1 lesion, as its clinical significance regarding digestive bleeding, is uncertain.[20]

Descriptive statistics were used to describe the patient's demographic features, clinical characteristics, endoscopic findings and therapeutic procedures. Categorical variables were presented as percentages and numerical variables as means and ranges.

All ethical and legal considerations were strictly respected.

RESULTS

Fifteen cases of patients with severe ongoing OOGIB submitted for CE were identified (4.5% of the examinations carried out during the considered period) (11 men; mean age 69.9 ± 20.1 years, range 29–94 years). All patients presented with melena and/or hematochezia. In eight patients it was the first episode of severe bleeding. The remaining seven had suffered previous episodes, but the etiology of the bleeding was unknown. Mean hemoglobin (Hb) level at the time of the exam was 8.4 ± 1.2 g/dL (range 5.9–10 g/dL) with a mean transfusion requirement of 6.3 ± 4.1 RBC units (range 2–16 units).

Table 1. Demographic data and clinical history of patients with severe OOGIB after standard endoscopic evaluation

	N	Range
No. patients	15	
Gender (M/F)	11/4	
Mean age (years)	69.9 ± 20.1	29–94
Males	65.6 ± 21.5	29–94
Females	81.8 ± 8.5	75–94
Mean Hb level at time of CE (g/dL)	8.4 ± 1.2	5.9–10
Mean blood transfusions (units)	6.3 ± 4.1	2–16

CE, capsule endoscopy; Hb, hemoglobin; OOGIB, obscure-overt gastrointestinal bleeding.

The mean time from admission until endoscopic examination by capsule was 4.1 ± 4.4 days (range 0–15 days), but, in four patients, CE was carried out in the first 12 h after hospitalization. The demographic and clinical data of the patients are presented in Table 1.

The capsule was easily swallowed by all patients, no technical problems or complications occurred during the examinations and the capsule was naturally excreted in all patients. Total enteroscopy was achieved in 11 patients (73.3%), with four cases of partial enteroscopy resulting from slow small bowel transit.

The patients were divided into four groups in accordance with the findings (Table 2). Group A included seven patients with active bleeding in the small bowel (Figs 1–3); group B included four patients with signs of recent bleeding in the small bowel and lesions with hemorrhagic potential (Fig. 4); group C included two patients with cecal blood residues but no potential bleeding lesions in the small bowel (Fig. 5) and group D included two patients without blood or clots in the GI tract but jejunal lesions.

Positive relevant findings concerning bleeding were detected in 80% of patients. The etiology of the bleeding was diagnosed in 11 patients (73.3%). In one additional patient, active bleeding in the small bowel was seen, but no causative lesion was identified.

We found P2 lesions in eight patients (53.3%), active bleeding with P1 lesion in one (6.7%), active bleeding but no lesion in another one (6.7%) and P1 lesions without active bleeding in three (20%). Specific therapeutic measures were proposed in 12 patients (80%) but carried out in 11 (73.3%) because one refused surgery. Of the 11 patients, two were managed surgically with resection of a small bowel tumor (gastrointestinal stromal tumor [GIST]). Four were managed endoscopically with DBE and fulguration of angiodysplasias in two, DBE followed by intraoperative enteroscopy in one and endoscopic resection of a large subepithelial ulcerated lesion (lipoma) in the final patient. Five patients were

Table 2. CE findings, therapeutic procedures and final outcome of patients with severe OOGIB after standard endoscopic evaluation

Group/Patients	Findings	Therapy	Rebleeding
Group A	Active small bowel bleeding		
Male, 74 years	Subepithelial ulcerated lesion	Surgery: GIST	No
Male, 68 years	Irregular area of mucosa	Surgery: GIST	No
Female, 81 years	Active bleeding; angiodysplasia	Enteroscopy: argon-plasma	No
Male, 92 years	Active bleeding; angiodysplasia	Enteroscopy: argon-plasma	No
Male, 72 years	Subepithelial ulcerated lesion	Endoscopic excision: large ileocecal lipoma	No
Female, 94 years	Jejunal tumor	Refused surgery: probable carcinoma	Yes
Female, 77 years	Active bleeding; no lesion identified	No	No
Group B	Signs of recent bleeding		
Male, 64 years	Portal hypertension enteropathy	Beta-blockers	No
Male, 58 years	Portal hypertension enteropathy	Beta-blockers	No
Male, 41 years	Portal hypertension enteropathy	Beta-blockers	No
Male, 87 years	Multiple small bowel ulcers	Suspended NSAIDs	No
Group C	Clots in cecum; no small bowel lesion		
Male, 94 years	No relevant lesion	No	No
Female, 75 years	No relevant lesion	No	No
Group D	No blood in GI tract		
Male, 29 years	Jejunal ulcer	DBE and intraoperative enteroscopy	Yes
Male, 42 years	Jejunal ulcer with visible vessel	Chemotherapy: disseminated B-cell lymphoma	No

CE, capsule endoscopy; DBE, double balloon enteroscopy; GIST, gastrointestinal stromal tumor; NSAIDs, non-steroidal anti-inflammatory drugs; OOGIB, obscure-overt gastrointestinal bleeding.

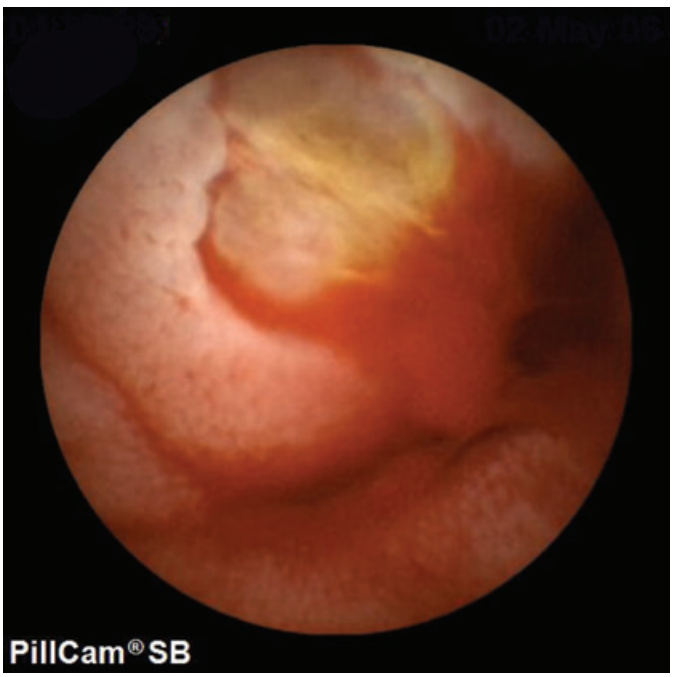

Fig. 1. Subepithelial ulcerated lesion with active bleeding.

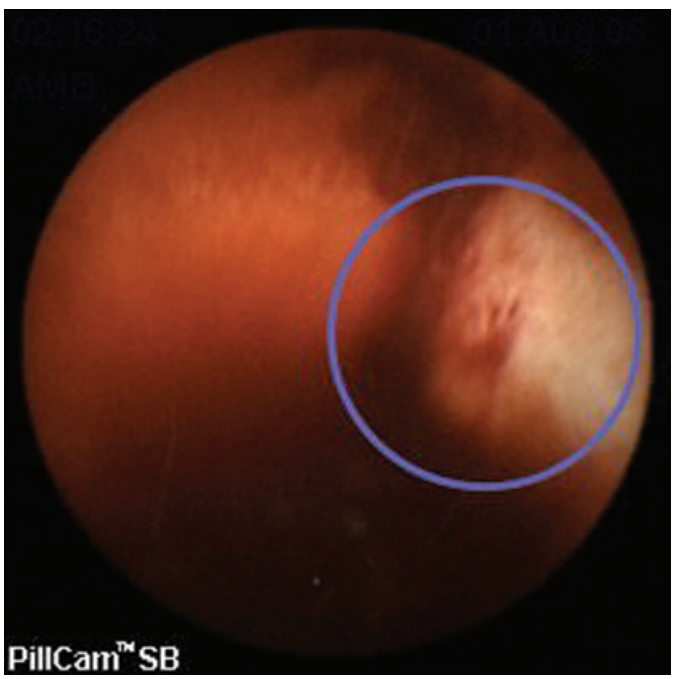

Fig. 2. Irregular area of mucosa with blood and an adherent clot.

managed conservatively with the introduction of beta-blockers in patients with portal hypertension enteropathy, chemotherapy in a patient with disseminated B-cell lymphoma and suspension of NSAIDs in one patient with iatrogenic small bowel lesions.

Rebleeding occurred in two patients, with one requiring specific measures after CE. This patient, in group D, found to have a jejunal ulcer not considered to be the cause of the hemorrhage, was given a DBE. This procedure was inconclusive and was followed by an intraoperative enteroscopy that revealed the presence of duodenal varices (fourth portion). This patient was the only one who had red blood cell scintigraphy and angiography, with both methods being unsuccessful in showing the cause of the bleeding.

Both patients in group C were given a second colonoscopy that did not fid any relevant lesion.

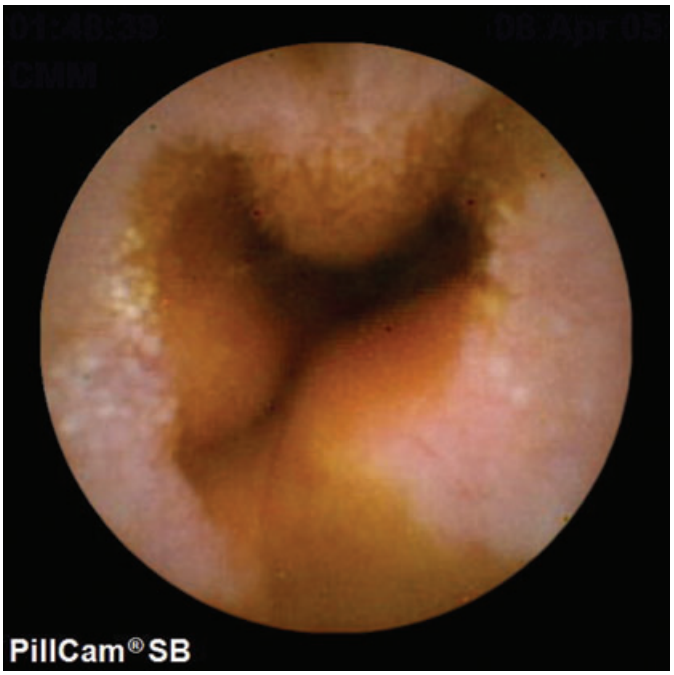

Fig. 3. Irregular, congestive, friable lesion suggestive of small bowel carcinoma.

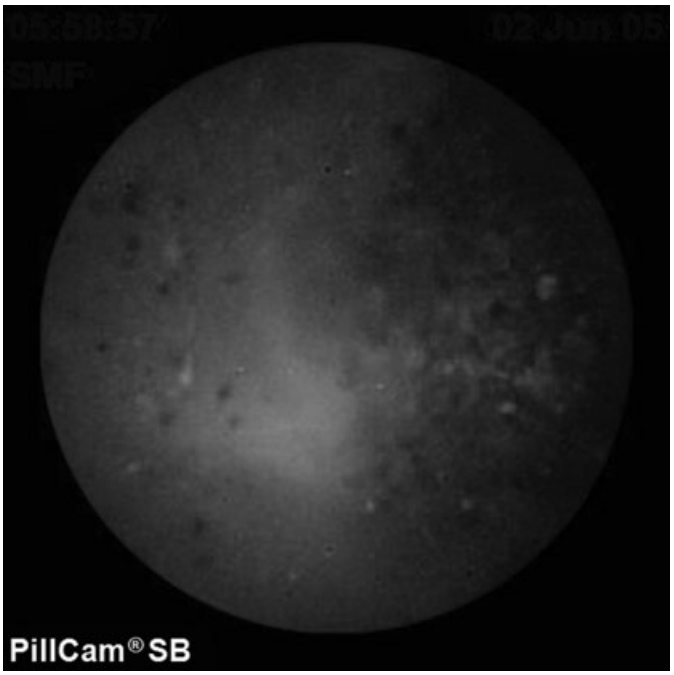

Fig. 5. Blood residues in the cecum.

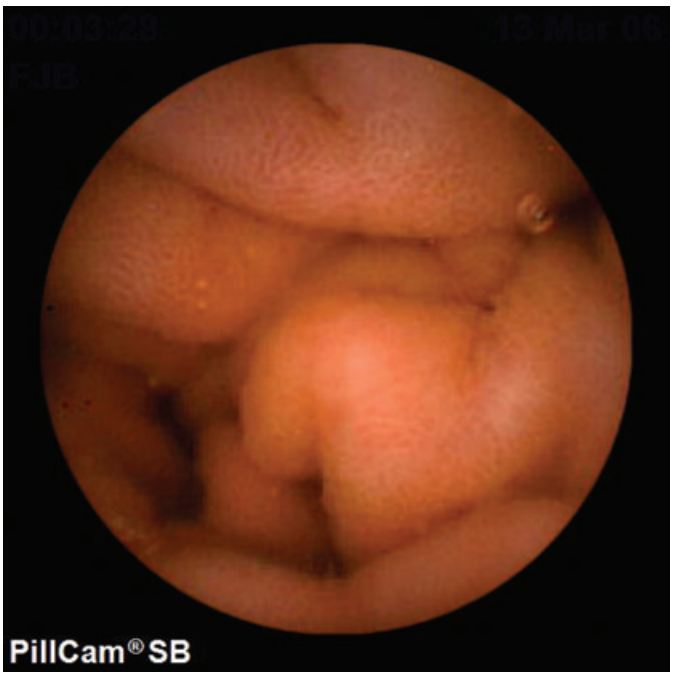

Fig. 4. Portal hypertension enteropathy.

DISCUSSION

Using CE early in the course of OOGIB is attractive because it has no major complications, it is easy to perform with no discomfort to the patient, its diagnostic yield is larger in these cases and will, at least, reveal the location of the bleeding.[1,5,16–18] In fact, in the present study, only two patients had no blood residues in the digestive tract and seven patients presented active bleeding at the time of the exam, clearly revealing the source/location of the hemorrhage, with no need for further diagnostic work-up. In the absence of blood or lesions, there is no need to proceed with further investigations unless rebleeding occurs, avoiding unnecessary human and financial costs.[4]

In a prospective study, Apostolopoulos *et al.*, had already stated that CE appeared to have a high diagnostic yield in patients with acute, mild-to-moderate, active bleeding but patients with severe hemorrhage were excluded.[18] Our report, albeit retrospective and with a limited number of patients, seems to demonstrate that CE can also be helpful in patients with severe, ongoing OGIB. In fact, CE was helpful in all cases but one, establishing the location or the etiology of the lesions, most of them P2 type, with a positive impact on the subsequent investigation or chosen therapy.

Angiography, a procedure that has an overall positivity rate in acute lower GI bleeding of 27%–77% (mean 47%), is another option in these patients.[21] Therapeutic procedures are possible with angiography, but the number of patients successfully treated with this technique is small and the complications are frequent and sometimes severe.[22] In fact, CE has a higher diagnostic yield than angiography in acute OOGIB.[23] In our series, angiography was used in the only case in which CE failed to find the etiology of a recurrent gastrointestinal hemorrhage. However, angiography also failed in identifying the source of bleeding.

DBE is also an option in these patients. The diagnostic and therapeutic capabilities of this technique allow it to be a reasonable alternative to CE in patients with severe ongoing OOGIB. In fact, the use of push enteroscopy, followed, in the case of failure, by CE, was proposed by Dulai and Jensen,[4] although the opposite sequence has also been suggested by Fleischer.[24] The recommended approach in suspected small-bowel bleeding is that DBE should be used after initial diagnosis with CE.[25] The same applies, in our

opinion, to patients with severe ongoing OOGIB. In fact, in these patients, after the initial standard endoscopic evaluation, CE should be the procedure of choice, followed by DBE in accordance with the findings. This approach would avoid a long endoscopic procedure with DBE, probably not diagnostic in many cases given the known difficulty in performing total enteroscopy with this technique.[26] Choosing CE as the first diagnostic procedure is advantageous also because it is helpful in determining the route of insertion of the enteroscope.[27]

The drawbacks associated with the use of CE in patients with OOGIB must also be considered. The first is the absence of control of the image acquisition process that, in the presence of debris, may jeopardize the observation. However, a bowel-cleaning preparation probably allows a better examination, but may interfere with interpretation, as blood residues are eliminated in the process. In our series, some CE examinations were carried out immediately after colonoscopy and, apparently, the previous bowel preparation did not interfere with the interpretation of the images. Another difficulty with CE is the assessment of the exact location of findings. It can grossly be estimated by considering the time that elapsed after the first duodenal image, total time of transit in the small bowel and macroscopic characteristics of the surrounding mucosa.[28] Another drawback associated with the use of CE in these patients is that the result of the enteroscopy is obtained hours after swallowing the capsule. Rapid alternating between two different recorders, allowing an almost real-time reading, can solve this problem.[29] The 'Rapid Access' system may also allow a similar approach.[28] The possibility of an incomplete examination of the small bowel, missing lesions in the distal segments, must also be considered. The reported frequency of this occurrence is variable, but may reach up to one-third of the exams.[4] In our series, this occurred in four patients (26.7%). A second CE or retrograde DBE may be helpful if the bleeding persists or recurs.[30] Fortunately, in our four patients, there was no need for further studies because the lesions were well documented in the obtained video. Finally, the absence of therapeutic capabilities is also a major limitation of this technique.

There are other risks and difficulties associated with CE that may be increased in patients actively bleeding, including incapability to swallow the capsule, risk of vomiting/aspiration, delayed gastric emptying time and masking the sources of bleeding by blood and clots. Our patients had no difficulties in swallowing the device. We used a prokinetic as it can increase the likelihood of complete small bowel examination with CE.[31] In our series, in only one case of active bleeding was no lesion identified. On the contrary, our major diagnostic failure occurred in the setting of the absence of blood. In fact, CE failed to identify duodenal varices in one patient. Even DBE, with cautious observation of the duodenum, was insufficient to establish diagnosis, achieved only by transillumination during intraoperative enteroscopy.

In conclusion, our results show that CE might be useful in patients with severe OOGIB because, without discomfort to the patient or major complications, this methodology provides positive findings in the majority of patients, avoiding further diagnostic procedures and allowing specific therapeutic measures.

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