The Role of Capsule Endoscopy in Obscure GI Bleeding: Experience of a Tertiary Center in Romania

Lucian Negreanu1, Ana Filimon1, Ana Stemate1, Theodor Voiosu2, Bogdan Mateescu2

Abstract

Obscure gastrointestinal bleeding OGIB represents about 5% of the digestive hemorrhages. The introduction of the endoscopic videocapsule in the current clinical practice caused a major change in the diagnostic and treatment paradigm of these patients. **Aim:** In Romania capsule endoscopy is not reimbursed and although available in many centers is not an investigation readily accessible in all patients. Also, device assisted enteroscopy is performed in few centers only. We present a series of forty patients with obscure GI bleeding and the role of capsule endoscopy in their diagnosis, treatment decision and follow up. **Methods:** This is a retrospective, single center study. Examinations were performed using second and third generation small bowel capsules SB2/SB3 and the second generation of colon capsule PillCam Colon 2. The choice of capsule was arbitrary decided by their availability in the unit at the moment of the examination. **Results:** The source of bleeding was identified in 33 patients (83% of the cases). The most frequent lesions were angiomas in 14 patients, small bowel Crohn’s disease in 9 cases and NSAID’s enteropathy in 4 cases. Endoscopic therapeutic procedures were used in five patients, three undergone surgery, medical treatment was initiated in 11 patients, gluten free diet in one, and discontinuation of NSAID’s in three. **Conclusion:** Capsule endoscopy was useful in the diagnostic and the therapeutic decision in the majority of cases. Angiomas, ileal Crohn’s disease and NSAID enteropathy were the main causes for obscure bleeding. Due to capsule endoscopy examination costs, a careful and complete exploration of the patients with routine ileoscopy before capsule is advisable.

**Keywords:** obscure bleeding, Crohn’s disease, angioma, capsule endoscopy

Rezumat

Videocapsula endoscopică are un rol primordial în diagnosticul hemoragiilor digestive de cauză obscură. Investigația se face în tandem cu o enteroscopie (simplu sau dublu balon sau spirală) care permite biopsii sau gesturi terapeutice. Accesul la investigarea cu videocapsulă sau la enteroscopie este limitat în România în câteva centre și terapia pacienților presupune un efort multidisciplinar și uneori multicentric. Este prezentată experiența din două centre terțiere, retrospectiv, cu un număr important de pacienți care au avut leziuni de boală Crohn. Această particularitate este posibil explicată de specializarea în boli inflamatorii a celor două centre.

**Cuvinte cheie:** hemoragie obscură, videocapsulă, enteroscopie, boala Crohn

---

1 Second Department of Internal Medicine and Gastroenterology, Emergency University Hospital, Bucharest, Romania
2 Department of Gastroenterology, Colentina Hospital, “Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

**Corresponding author:**
Lucian Negreanu
Second Department of Internal Medicine, Emergency University Hospital, 169 Splaiul Independentei, 5th District, Bucharest, Romania
INTRODUCTION

Obscure gastrointestinal bleeding OGIB represents about 5% of those patients with gastrointestinal bleeding of any type. It is defined as persistent or recurrent bleeding of unknown origin (i.e., recurrent or persistent iron-deficiency anemia, positive fecal occult blood test, or visible bleeding) with a negative upper and/or lower gastrointestinal endoscopy.

In the majority of cases, OGIB originates in the small bowel and can result from a series of conditions, including vascular lesions, tumors, drug induced and immune mediated lesions. It is classified as “overt” when there are manifestations of bleeding such as hematochezia or melena, and as “occult” when fecal occult blood tests are positive or iron deficiency anemia is presumed to be caused by gastrointestinal blood loss.

Over the last decade with the introduction in clinical practice of new diagnostic and therapeutic procedures (i.e. Capsule Endoscopy, Computed Tomographic Enterography, Magnetic Resonance Enterography, and Device Assisted Enteroscopy) the diagnostic and treatment paradigm of patients with obscure gastrointestinal bleed has completely changed.

Capsule endoscopy and device assisted enteroscopy are regarded as complementary methods in the management of OGIB. Their availability is increasing and they now became an integral part of the diagnostic and therapeutic recommendations for OGIB in most parts of the world.

AIM

To present a series of forty patients with obscure GI bleeding and the role of capsule endoscopy in their diagnosis treatment and follow up.

Because in Romania capsule endoscopy is not reimbursed, although available in many centers is not an investigation readily accessible in all patients. Device assisted enteroscopy is performed in only few centers.

PATIENTS AND METHODS

This is a retrospective, single center study.

Starting February 2011 a total of 150 capsule examinations were performed in our unit. Forty patients, 20 women and 20 men, with a mean age of 51.3 years (range 22 – 89) were investigated for obscure gastrointestinal bleeding (Table 1).

The patients were initially investigated in our center or referred from other gastroenterology centers, were they all had upper endoscopies and colonoscopies for the exclusion of other causes of bleeding. After capsule endoscopy we referred the patients needing enteroscopy in another unit, since we lack the equipment.

ETHICAL CONSIDERATIONS

Capsule endoscopy examination protocol, informed consent and examination agreement were approved by the ethics committee of the University Hospital of
Bucharest in 2011 and renewed in 2013. All patients signed an informed consent for the investigation.

**PROCEDURE**

All types of capsules from Given Imaging (Yokneam Israel) were used in this study: second and third generation small bowel capsule and the second generation of colon capsule PillCam Colon 2. The choice of capsule was arbitrary dictated by their availability in the unit at the moment of the examination. We used the DR3 recorder.

Initially the Rapid reader 7 software was used in this study. Starting 2012 we used a Rapid 8 prototype and from December 2013 the commercial version of Rapid 8.

The preparation consisted in a low-residue diet starting 48 hours before investigation. One liter of polyethylene glycol (PEG) Fortrans® (Macrogol 4000, Ibsen, France) was administered in the evening before capsule ingestion. Capsule ingestion was performed between 9-10 a.m.

---

*Figure 1.* Polip ulcerat - sd Peutz Jeghers.

*Figure 2.* Ulcer ileal cu sangerare activa.

*Figure 3.* Angiodisplazie.

*Figure 4.* Angiodisplazie.

*Figure 5.* Sangerare activa exulceratie Dieulafoy.

*Figure 6.* Sangerarea active din malformatie arteriovenoasa.
In two patients with multiple angiomas a single balloon enteroscopy with APC and a double balloon enteroscopy with APC were performed in two different centers. In a patient the single balloon enteroscopy which also failed to reach his vascular lesions and then a surgical ileal resection. He has currently a good clinical status without recurrent anemia.

Another two patients were treated surgically: the jejunal GIST patient undergone resection with excellent results and a right hemicolectomy was performed for the colon cancer patient.

A gluten free diet was prescribed for the celiac disease patient after bioptic and serologic confirmation. The patient with a gastric ulcer underwent a second endoscopy that confirmed the lesion. One morbid obesity patient had an active severe bleeding of a jejunal ulcer and he died before surgery due to cardiovascular complications. Both patients received proton pump inhibitors.

Discontinuation of NSAID's was possible in three out of four patients.

All the nine patients with Crohn’s disease are currently treated and in clinical remission.

Technical failures
We had two technical difficulties: one due to a recorder dysfunction which required replacement with another recorder and one SB3 capsule malfunction which was replaced with a PC2 capsule.

Complications
We had an asymptomatic capsule retention due to a Crohn’s disease stenosis. She was completely asymptomatic without any occlusive symptoms or abdominal pain and was addressed for iron deficiency anemia and she had normal upper endoscopy and colonoscopy. After failure to excrete the capsule, the retention was
confirmed by plane radiography two weeks after the examination. The patient refused surgery and started medical treatment with budesonide with capsule elimination after three months.

DISCUSSION

In our study we find lesions that could explain the OGIB in 33 patients (82.5% of cases). In a meta-analysis including 227 studies and including 22840 CE procedures, the diagnostic yield for OGIB was 61%. In another study published subsequently including 911 patients with OGIB, 56% patients had positive finding at CE. Our increased success rate can be explained by the highly selected population (based on global limited access to capsule due to economic reasons) and the small number of patients presented.

As a result of the findings, a specific intervention was made in 66% of patients who had a positive capsule finding. Endoscopic therapeutic procedures were used in five patients, three undergone surgery, medical treatment was initiated in 11 patients, gluten free diet in one, and discontinuation of NSAID’s in three patients. This is comparable with other studies.

Negative CE in the setting of OGIB, has been shown to predict the outcome. In fact, the risk of re-bleeding rate after negative CE is very low, and these patients could be managed by a conservative approach. In our group of seven patients with negative capsule findings only three patients (two women, one man) still have mild recurrent iron deficiency anemia.

The particularity of our series is the important number of patients (9/40) who had lesions that were suggestive for Crohn's disease. Currently capsule endoscopy is considered a valuable tool to diagnose or exclude CD. A high index of clinical suspicion (digestive symptoms plus either extraintestinal manifestations, inflammatory markers or abnormal imaging studies) together with suggestive capsule findings is necessary to increase the diagnostic yield.

After careful examination associated symptoms such as diarrhea and weight loss were found in all patients. Also inflammation markers and fecal calprotectin were elevated in all nine patients.

The classical indications of VCE in Crohn's disease are indeterminate colitis, Crohn's disease of the small bowel excluding last ileal loop, clinical/endoscopical discrepancy, post surgery and mucosal healing monitoring. Failure/refuse of colonoscopy is an indication for colon capsule in selected patients.

Ileal involvement was the rule in our patients but unfortunately although a complete colonoscopy was performed in all cases, in none of them the last ileal loop was visualised. After capsule examination results, Crohn's disease was confirmed by colonoscopy with catheterization of the terminal ileum and biopsies in five cases; for the other four patients the therapeutic decision was based on clinical setting, capsule findings and inflammatory markers. We excluded lesions due to the use of non-steroidal anti-inflammatory drugs (NSAIDs), vasculitis, lymphoma, ischemic or infectious lesions. At the moment all the nine patients are treated and in clinical and biological remission. A careful examination of the data showed that in five out of nine patients the capsule examination could have been avoided if a visualization of the last ileal loop would have been realized during colonoscopy.

The mean age of the nine patients diagnosed with Crohn's disease was 37 years. Similar results were reported in a study of 385 patients with obscure gastrointestinal bleeding, where the young adults (17-40 years) were most likely to have Crohn's disease, small intestine tumors or non-specific enteritis.

One of the most feared problems in capsule endoscopy is capsule retention. Crohn's disease is an independent risk factor for capsule retention confirmed in many studies. The rate of capsule retention was 1.6% in cases of suspected CD and peaked as high as 13% in patients with known CD. Sometimes obtaining a careful history might be the best single method to detect the possibility of retention according to some experts but this is highly debated since retentions were encountered in asymptomatic patients. In our study the retention occurred in an asymptomatic patient that remained asymptomatic for the three months until capsule excretion.

In three patients (7.5%) the lesions discovered by capsule endoscopy were accessible by upper endoscopy (gastric ulcer, celiac disease) and colonoscopy (colon cancer). This is not unusual since lesions in upper or lower GI tract can be missed in as much as about 28% of patients submitted to CE for obscure bleeding.

CE may play an important role in identifying the lesions missed at conventional endoscopy and careful evaluation of the images should be realized.

We currently changed our approach to the patients with OGIB. Before recommending an expensive and not reimbursed examination by capsule we make sure that a complete colonoscopy with visualization of the terminal ileum was performed.

CONCLUSIONS

The rate of patients without an explaining lesion was small (13%). Capsule endoscopy was paramount in the therapeutic decision in the majority of cases.
An important number of patients investigated for obscure GI bleeding turned out to have small bowel Crohn’s disease in our group. Due to capsule endoscopy examination costs, a careful and complete exploration of the patients with routine ileoscopy before capsule is advisable.

The access to therapeutic enteroscopy is still limited and close networking between centers is necessary to provide the necessary care for the patients.

Conflicts of interests: none declared.

Author contributions: All authors equally contributed to the article.

References