

Capsule endoscopy examination of patients with obscure gastrointestinal bleeding : evaluation of clinical impact

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Abstract

Background : Wireless video capsule endoscopy (WVCE) has been reported to contribute to the diagnostic management of patients with obscure gastrointestinal bleeding (OGB). Nevertheless, clinical impact data is lacking. The aim of our study was to determine the clinical outcome of patients undergoing WVCE for OGB.

Patients and Methods : 38 patients who were referred for OGB and who underwent WVCE examination were included in this study. A questionnaire was sent to the referring doctors after the capsule investigation. The following items were investigated : the final diagnosis of OGB, treatment applied and clinical outcome.

Results : Data was recorded for 26 patients out of 38 (17F, 9M). The mean age was 63 years (range, 21-84). A positive finding was noted in 11 patients. Findings included small bowel lesions in 7 cases and gastroduodenal lesions in 4 cases. As a result of the capsule investigation, specific therapy was administered in 9 patients. Six of the 9 patients treated had no further anemia. Final diagnosis of OGB was in agreement with positive findings of WVCE in all these 11 patients.

Among the 15 patients with a negative WVCE, 9 had a digestive lesion (3 small bowel lesions) as a final diagnosis.

Conclusion : Patients with a positive result at WVCE had further intervention in 82% and were successfully treated in 67% of cases. We had no false positive results in this study, which suggest a high positive predictive value of WVCE. Moreover, negative WVCE had also an indirect clinical impact. (*Acta gastroenterol. belg.*, 2005, 68, 10-14).

Introduction

Endoscopic techniques for examining the small bowel are limited, by the length of the small intestine (3,35-7,85 m) (1) and by a complex looped configuration resulting from its free intraperitoneal location constrained by mesenteric attachments. Push enteroscopy techniques allow the visualisation of the superior jejunum but endoscopic exploration for the remaining small bowel is still a medical challenge.

The wireless video-capsule endoscopy (WVCE) (Given Imaging, Yoqneam, Israel) is a new promising technique for small bowel exploration. It was described for the first time in 2000 (2) and then was commercialized by the Israelian society Given Imaging. This technique was approved by the FDA in august 2001.

Its efficacy and safety were first tested in an animal model (3). Up to now, more than 60000 WVCE exams have been performed in the world. Based on this enlarging experience, we can conclude that WVCE allows a satisfactory visualization of the entire small bowel in the majority of cases, is well tolerated and is not associated with major adverse effects (4).

Obscure gastrointestinal bleeding (OGB) is defined as recurrent bleeding for which no definite source has been identified by routine endoscopic and barium contrast studies (5), and is the main indication for WVCE in order to identify the responsible lesion.

Several groups have compared WVCE with push enteroscopy and with small bowel radiographs in OGB. The overall diagnostic yield of WVCE varies from 42 to 88% and is superior to push enteroscopy and small bowel radiography in several trials (6,7,8).

WVCE could also contribute in establishing the diagnosis of Crohn's disease but, for the time being, sufficient data is lacking (9). Furthermore, its role is currently assessed in other domains of gastrointestinal diseases as unexplained abdominal pain (10) and familial polyposis (11).

Although sufficient data is available regarding the diagnostic yield of WVCE for OGB, limited information is currently disposed concerning the clinical impact of this diagnostic method on the therapeutic strategy and the patient's outcome. These findings will be very helpful in defining the place of WVCE in the diagnostic approach of OGB.

The aim of our study is to evaluate the impact of WVCE on subsequent therapeutic strategy and clinical outcome of the patient presenting with OGB.

Patients and methods

Patients

Forty patients who underwent WVCE were reevaluated by the practitioner who had referred the patient to our institution. Thirty-eight out of the forty patients underwent this examination for OGB.

OGB was defined either as recurrent overt bleeding (rectal discharge of blood) or chronic iron-deficient anemia (the serum hemoglobin level at least below 10 g/dl) with positive blood research on stools, for which no source had been identified after a work-up including at least esogastroduodenoscopy and total colonoscopy.

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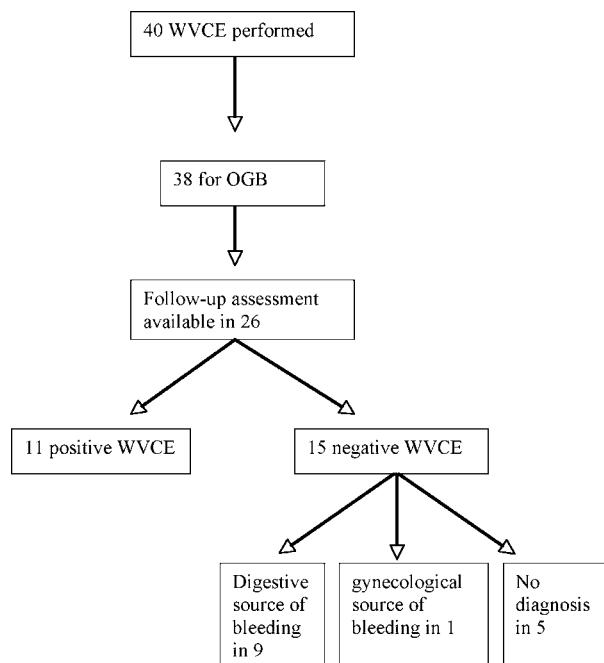


Fig. 1. — Study population

WVCE : wireless video capsule endoscopy ; OGB : obscure gastrointestinal bleeding.

Exclusion criteria included pregnancy, known or suspected stricture of the small bowel ; previous abdominal surgery ; swallowing disorder ; ongoing unstable or uncontrolled medical conditions ; presence of a cardiac pacemaker or other implanted electromedical devices and the need to undergo magnetic resonance imaging (MRI) before the elimination of the enteroscopic wireless-capsule.

All the patients have been explored by an esogastro-duodenoscopy and total colonoscopy before WVCE. WVCE had been performed in these patients between March 2001 and February 2003.

Evaluation

Data concerning follow-up were collected with the help of a standard questionnaire, which was sent by post to the referring physician. The questionnaire involves three sections : one concerning the diagnosis (final diagnosis and diagnostic procedure which lead to diagnosis), a second one concerning the type of therapy applied and its clinical effect (persistent anemia ? hospitalisations ?) and a third one concerning the clinical evolution of the patient following therapy. Completed questionnaires are then sent to our service and are analysed by two gastroenterologists.

WVCE was considered positive when it detected a potential hemorrhagic lesion which can explain anemia.

The global diagnostic yield included all lesions detected in the upper gastrointestinal tract and the visualized small bowel, and the specific diagnostic yield included only lesions located beyond the reach of routine esogastroduodenoscopy.

WVCE was considered to have a positive therapeutic impact when it had directly influenced the therapeutic strategy, independantly of the treatment applied (medical, endoscopic, surgical).

The wireless videocapsule

WVCE was performed with the M2A videocapsule system designed by Given Imaging Ltd (Yoqneam, Israel). Briefly, the capsule includes a complementary metal oxide silicon imaging chip, a miniature processor, a white-light emitting diode, a lens with a short focal length, a miniature transmitter and an antenna powered by silver oxide batteries. The video images are transmitted by a radiofrequency signal (about 410 MHz), at a rate of two frames per second, to an array of eight aerials attached to the abdominal wall that allow image capture. The images are stored on a portable recorder carried on a belt, and can subsequently be downloaded in a specifically designed workstation.

The capsule was ingested in the morning (between 8 and 9.30 am) at least twelve hours after the last meal, without any special preparation. Patients were allowed to drink and eat one hour and three hours after capsule ingestion, respectively.

Statistical analysis

Continuous variables are expressed by mean and range. Differences between categorical values were analysed with the chi-square test.

We analysed sensitivity, specificity, positive predictive value and negative predictive value of WVCE in detecting small bowel lesions, considering as gold standard for the diagnosis surgery, push enteroscopy or small bowel radiography. Analysis was based on the following definitions : *true positive* : confirmation of WVCE positive diagnosis by surgical exploration, push enteroscopy or small bowel radiography ; *true negative* : negative WVCE study and OGB resolved with no further treatment or lesions responsible for OGB detected elsewhere than the small bowel ; *false positive* : positive WVCE study not confirmed by following exams ; *false negative* : negative WVCE study but small bowel lesions explaining OGB identified by surgical exploration, push enteroscopy or small bowel series.

Results

Only the 38 patients who had WVCE for OGB were included. Out of the thirty-eight questionnaires sent out concerning patients who underwent WVCE for OGB, twenty-six (68,4%) were completed and sent back, allowing data collection.

Among these twenty-six patients, there are 17 females and 9 males. Mean age was 63,1 years (range : 21-84). They presented with occult bleeding in sixteen cases (61,5%) and with overt bleeding in ten cases (38,5%). Follow-up ranged from four to twenty-six months.

Positive findings and therapeutic impact

WVCE exam was positive in eleven patients out of the twenty-six evaluated for OGB (42,3%). Among these eleven positive patients, six had occult bleeding and five overt bleeding.

The following lesions were visualized : small bowel adenocarcinoma (n = 1), small bowel ischemia (n = 1), ileal ulcer (n = 1), hypertensive enteropathy (n = 2), Rendu-Osler disease with small bowel angioectasia (n = 1), Crohn's disease (n = 1), erosive gastritis (n = 2), gastric ulceration (n = 1) and erosive duodenitis (n = 1). Global diagnostic yield including all lesions detected in the upper gastrointestinal tract and the visualized small bowel was 42,3% (11/26). Specific diagnostic yield including only lesions located beyond the reach of routine esogastroduodenoscopy was 26,9% (7/26). Among the eleven positive exams, the visualized lesion could explain anemia in all cases.

If we only consider small bowel lesions, the specificity of WVCE was 100% and its positive predictive value was also 100%.

Subsequent treatment was surgery in two cases, endoscopic treatment in two cases, medical treatment in five cases and no treatment in two cases (table 1). Surgery was indicated in one patient who did not receive therapy ; however surgery was postponed because of rapidly progressive heart failure. The second patient who did not receive therapy died from terminal cirrhosis with hepatic failure.

After treatment, anemia persisted in five cases and was resolved in six cases.

Two patients died during follow-up. Cause of death was terminal cirrhosis state in one case and terminal renal failure in the other case. OGB was due to GI bleeding due to portal hypertensive enteropathy and to erosive duodenitis, respectively ; however, in these two cases death was not directly linked to the GI bleeding.

Totally nine out of the eleven "positive" patients received a treatment based on the results of the WVCE. Therefore, therapeutic impact is 34,6% (9/26).

Negative findings

WVCE exam was negative in fifteen patients out of the twenty-six investigated for OGB (57,7%). Among these fifteen positive patients, ten had occult bleeding and five overt bleeding.

Concerning final etiology of OGB, a digestive source was identified in nine cases and a gynecological source in one case. No diagnosis was obtained in five patients. In the group of anemia from digestive origin, an endo-

scopic exam or surgery finally certified the diagnosis after WVCE. In this group, the following lesions were identified : Cameron ulcerations (n = 2), hiatal hernia (n = 1), gastric Dieulafoy ulceration (n = 1), right colon neoplasia (n = 1) initially misdiagnosed because of initial incomplete colonoscopy and finally diagnosed by a second colonoscopy performed after WVCE, colonic diverticulosis (n = 1), small bowel angioectasia (n = 1) diagnosed and treated by push enteroscopy, terminal ileal varices (n = 1) diagnosed and treated by surgery (small bowel resection) and jejunal diverticula (n = 1) identified by small bowel radiograph and push enteroscopy.

In all, there were three small bowel lesions who were not identified by WVCE. Negative predictive value of WVCE for small bowel exploration is 80% (12/15). Sensitivity of WVCE for small bowel lesions is 78,6%.

Among these nine patients, subsequent treatment involved surgical resection in three cases, endoscopic treatment in one case, medical treatment in four cases and no treatment in one case (table 2).

In this same group of patients, after treatment, anemia persisted in two cases, was resolved in six cases and specific data was missing in one case.

In the group of anemia without diagnosis, anemia persisted in two cases of five and was resolved in the three remaining cases.

Finally, anemia was resolved after hysterectomy in the patient who had OGB from gynaecologic origin.

Discussion

Since the beginning of its application, WVCE has attracted significant interest ; in fact, it's a revolutionary investigation method of the small bowel allowing for the first time to visualize the entire small bowel, which is very difficult to study with conventional radiologic and endoscopic methods. Its role in small bowel exploration allows us to assume that it will soon become a key element in the diagnostic strategy of OGB, which is often difficult and costly.

However, diagnostic yield of WVCE for this indication varies, depending on patient characteristics but also on the extent of the previous work-up and there is only few data regarding clinical impact of this new technique on the ulterior therapeutic strategy and patient outcome.

In this series where data was recorded for twenty-six patients, WVCE was considered positive in 42,3% and negative in 57,7% of cases. These results show a lower rate of positive results compared to other series, but more recent studies also show a lower diagnostic yield compared to previous publications (12). These discordant results can be explained by the fact that positivity criteria vary between investigators (4,6,7,12,13). Moreover imaging interpretation can enhance this heterogeneity. Interpretation of the results remains subjective and there is no standardization for a "positive image".

Table 1. — Patients with positive findings at WVCE

Details concerning gender, age, lesion seen at WVCE, therapy performed and the treatment's effect on anemia in patients with positive WVCE

N°	gender ; age	Lesion at WVCE	Treatment performed	Effect on anemia
1	Male ; 82	Adenocarcinoma	Surgery	Yes
2	Female ; 75	Mesenteric ischemia	Surgery	No
3	Female ; 84	Ileal ulcer	No treatment (surgery indicated)	No
4	Female ; 58	Hypertensive enteropathy	Endoscopic	Yes
5	Male ; 79	Rendu-Osler (multiple angioectasia)	Endoscopic	No
6	Male ; 81	Hypertensive enteropathy	No treatment (patient deceased)	No
7	Female ; 34	Crohn's disease	Medical (5-ASA, budesonide)	No
8	Male ; 76	Erosive gastritis	Medical (PPI, IV iron supplementation)	Yes
9	Female ; 46	Erosive gastritis	Medical (oral iron supplementation)	Yes
10	Male ; 36	Gastric ulcer	Medical (PPI)	Yes
11	Male ; 83	Erosive duodenitis	Medical (PPI, oral iron supplementation) (patient deceased)	Yes

PPI : proton pump inhibitor ; WVCE : wireless video capsule endoscopy ; IV : intravenous.

Table 2. — Patients with negative findings at WVCE (digestive origin of anemia)

Details concerning gender, age, lesion seen at WVCE, therapy performed and the treatment's effect on anemia in patients with negative WVCE (digestive origin of anemia)

N°	gender ; age	Diagnosis	Treatment performed	Effect on anemia
1	Female ; 54	Cameron ulceration	Medical (PPI, oral iron supplementation)	Yes
2	Male ; 68	Cameron ulceration	Medical (PPI, oral iron supplementation)	No
3	Female ; 78	Hiatal hernia	Medical (PPI, oral iron supplementation)	No
4	Female ; 77	Jejunal diverticula	Medical (IV iron supplementation, stop antiaggregant)	Yes
5	Female ; 53	Right colon neoplasia	Surgery	Yes
6	Male ; 52	Dieulafoy ulceration	Surgery	Yes
7	Female ; 48	Ileal varices	Surgery	Yes
8	Female ; 82	Small bowel Angioectasia	Endoscopy	?
9	Female ; 80	Colon diverticula	No	Yes

PPI : proton pump inhibitor ; WVCE : wireless video capsule endoscopy ; IV : intravenous.

Some investigators have tried to avoid this problem by classifying detected lesions in high, intermediate and low pertinence (13). In our study, WVCE was considered positive when a potential hemorrhagic lesion which can explain anemia was seen ; this definition has the disadvantage of being very subjective ; however, it is strict and excludes lesions of intermediate and low pertinence. It is also noteworthy that in healthy subjects examined by WVCE, small bowel lesions were identified in 22,6% of cases (14).

Interestingly, if we regard only small bowel lesions (specific diagnostic yield), the percentage of positive cases is only 26,9% (7/26). This confirms that in OGB, upper gastrointestinal tract lesions are frequently identified, even following a negative esogastro-duodenoscopy (15).

It is interesting to note that diagnostic yield tends to vary according to the characteristics of bleeding : it is of 50 percent in the group with overt bleeding (5/10) and 37,5 percent in the group with occult bleeding (6/16) but this difference does not reach significance.

We wanted to assess the sensitivity and specificity of WVCE for the detection of small bowel lesions ; this is hampered by the lack of a gold standard to verify the accuracy of the diagnosis. Nevertheless, we considered

as gold standard surgical small bowel exploration when possible and small bowel radiographs or push enteroscopy in the remaining patients who had not undergone surgery. Based on these criteria sensitivity and specificity concerning the diagnosis of small bowel lesions with WVCE are 78,6% and 100% respectively. The negative predictive value is 80% and the positive predictive value is 100%. Thus, because all lesions identified by WVCE were confirmed by other techniques considered as a gold standard, the specificity of this examination is excellent. Among the lesions missed by WVCE, there was one case of small bowel angioectasia diagnosed and treated by push enteroscopy, one case of small bowel varices identified by surgical exploration and one case of jejunal diverticula revealed by small bowel X-ray and push enteroscopy.

In assessing the value of a diagnostic tool, an important point is the evaluation of the impact of such tool on subsequent patient management. Among the 11 patients with positive WVCE, we have distinguished small bowel lesions from upper gastrointestinal tract lesions. Seven patients had small bowel lesions and five of them have been treated, two by surgery, two by endoscopy and one medically. Among these five patients, anemia was resolved in three. Concerning the remaining two

patients, one has a Rendu-Osler disease with multiple small bowel angioectasia and was treated by endoscopy but with ulterior bleeding relapse, and the other has Crohn's disease (ileal location) responsible for relapsing obscure bleeding. Among the two patients who were not treated, one had severe cardiovascular morbidity contraindicating surgery and the other died because of hepatic failure. Four patients had upper gastrointestinal tract lesions initially missed by a first esogastroduodenoscopy; all were medically treated with success. Globally, among the 11 patients with positive WVCE, nine were treated, six of them successfully. Thus, the therapeutic impact of WVCE is 34,6 percent (9/26). One limitation in the interpretation of these results is that many patients were referred to us for WVCE by other hospitals, and there was no standardized therapeutic approach after WVCE. In general, clinical impact depends on the rates of positive lesions, the potential therapeutic but also the global characteristic of the patient.

In the nine cases of negative WVCE in which final diagnosis was bleeding from digestive origin, a small bowel lesion was reasonably excluded and a lesion from another part of the digestive tract was retained as the final cause of anemia in four cases; these lesions (hiatal hernia with or without Cameron ulcerations in three cases and colic diverticulosis in one case) had been visualized before WVCE and had been retained as responsible from anemia after excluding a small bowel lesion. Even, after negative WVCE, repeated endoscopic examination permitted to diagnose a Dieulafoy gastric ulceration and right colon neoplasia initially missed by an incomplete colonoscopy. Thus, negative WVCE has also an indirect clinical impact in reasonably excluding a small bowel lesion as responsible for anemia.

In this present study, although a lower diagnostic yield compared to previous publications, we show that WVCE has an excellent specificity, an excellent positive predictive value and a lower sensitivity and negative predictive value. The impact on the ulterior therapeutic strategy is also good, confirming that this technique has its place in the diagnostic strategy of OGB. Finally, the

important percentage of lesions identified in the upper digestive tract must incite to repeat careful endoscopic examination when source of bleeding is not identified in the small bowel.

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