Diagnostic yield and therapeutic implications of capsule endoscopy in obscure gastrointestinal bleeding

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SUMMARY

Aim — The main aim of this study was to evaluate efficacy and therapeutic impact of capsule endoscopy (CE) in obscure gastrointestinal bleeding (OGIB). In addition, we evaluated the software for automatic detection of red zones (SBI, Given Imaging).

Patients and methods — From June 2002 to June 2003, thirty-five patients with OGIB underwent capsule endoscopy after negative upper and lower digestive endoscopy. Capsule endoscopy was performed following a 12-hour fasting period and some received 2 L of PEG the night before for bowel preparation.

Results — CE was performed for occult (N = 18) or overt (N = 17) OGIB. Potentially bleeding lesions were found in 16/35 patients (45.7%). Lesions were angiodysplasias (N = 8), ulcerations (N = 4), tumors (N = 2) and active bleeding without visible lesion (N = 2). Lesions were located in gastric antrum (N = 1), duodenum (N = 2) and jejunum ileum (N = 13). Endoscopic (N = 10), surgical (N = 2) or medical (N = 1) treatments were performed in 13/35 (37%). SBI was retrospectively evaluated in 24 patients with sensitivity, specificity, positive and negative predictive value of respectively 45%, 73%, 50% and 69%. CE retention during 10 days occurred in a patient with a small bowel NSAID-induced stricture.

Conclusion — CE is a safe and effective procedure in the management of OGIB and had a therapeutic impact in more than one third of patients.

Introduction

Approximately 5% of gastrointestinal bleeding arise from the small bowel [1, 2]. Bleeding is called obscure when upper and lower endoscopy is unable to reveal a potential explanation [2]. Clinically, obscure gastrointestinal bleeding (OGIB) raises a double diagnostic and therapeutic challenge [3, 4]. Upper and lower gastrointestinal endoscopy are unable to localize and treat small bowel lesions. If standard endoscopic procedures are negative, non-invasive (barium study, scintigraphy with labelled red cells, angiogram, enteroscan) or invasive (arteriography, enteroscopy) investigations may be performed if available. The diagnostic yield is at best moderate for technetium-99m-labelled red cell scintigraphy [5-8] and near 5% for barium study [9-11]. Selective arteriography is not indicated except for severe acute gastrointestinal bleeding and the enteroscan is a new imaging technique which has not been evaluated in this indication. Capsule endoscopy (CE) (Given Imaging, Yoqneam, Israel) is a recent innovating technique proposed for small bowel exploration [12-14] as an alternative to push enteroscopy [15-19] for the diagnosis of OGIB arising from the small bowel. Five controlled trials [20-24] have compared CE with push enteroscopy in patients with OGIB. All have demonstrated the superior diagnostic yield of CE for this indication, particularly for lesions of the mid portion of the small bowel inaccessible to enteroscopy. The

RÉSUMÉ

Résultats et implications thérapeutiques de l’exploration par vidéo-capsule des saignements digestifs obscurs

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Malades et méthodes — De juin 2002 à juin 2003, trente-cinq malades ayant un SDO extériorisé ou occulte ont été explorés par vidéo-capsule après un bilan endoscopique digestif haut et bas normal. Les malades étaient laissés à jeun depuis la veille au soir et recevaient ou non une préparation par 2 litres de PEG la veille de l’examen.

Résultats — Une vidéo-capsule a été réalisée pour une anémie par carence mariale sans hémorragie extériorisée (N = 18) ou une hémorragie basse extériorisée d’origine indéterminée (N = 17). Des lésions digestives potentiellement hémorragiques ont été retrouvées chez 16/35 patients (45,7 %). Il s’agissait d’angiodysplasies (N = 8), d’ulcérations (N = 4), de tumeurs (N = 2) et d’hémorragies actives sans lésion visible (N = 2). Ces lésions siègentaient dans l’antre (N = 1), le duodénum (N = 2) et l’intestin grêle (N = 13). L’impact thérapeutique était de 13/35 (37 %) et comprenait un traitement endoscopique (N = 10), chirurgical (N = 2) ou médical (N = 1). Le système de détection des zones rouges a été évalué rétrospectivement chez 24 malades et avait une sensibilité, une spécificité, une valeur prédictive positive et négative de respectivement 45 %, 73 %, 50 % et 69 % pour le diagnostic de maladies porteurs d’une lésion d’imputabilité certaine. La seule complication a été une rétention prolongée de la capsule pendant 10 jours.

Conclusion — La vidéo-capsule est une méthode diagnostique d’utilisation simple et sûre qui permet une prise en charge diagnostique efficace des SDO extériorisés ou occultes. La vidéo-capsule a permis ultérieurement une prise en charge thérapeutique dans plus d’un tiers des cas.
only reports on the therapeutic contribution of CE in patients with OGIB have been published in abstract form [25-28]. The main objectives of this study were to evaluate the contribution of CE to the diagnosis of obscure gastrointestinal bleeding and to determine its therapeutic impact. The secondary aim was to evaluate the technique of automated detection of red zones (SBI, Suspected Blood Indicator™; Given Imaging).

Patients and methods

This study was conducted from June 2002 to June 2003 in patients with OGIB. Patients were included if they presented with occult (anemia and microcytisemia and low serum ferritin for more than six months) or overt OGIB (melena or hematochezia). In both situations, gastroscopy (with duodenal and gastric biopsies in anemic patients) and total colonoscopy performed under general anesthesia with a video-endoscope were negative. A gynecological cause had to be ruled out in women with occult OGIB. If the patient was free of recent abdominal pain, was not taking NSAID regularly, and did not have known Crohn's disease, no further radiological examination was recommended to rule out small bowel stenosis before performing CE. Nevertheless, for patients with occult anemia, a barium study or an enteroscan was performed before CE in eight and six patients, respectively.

Exclusion criteria were massive cataclysmic bleeding which could not be controlled by medical treatment, hematemesis, pregnancy, cancer, pacemaker, swallowing disorders and known gastrointestinal stenosis. Before inclusion, patients underwent a physical examination. Oral iron supplementation was interrupted ten days before capsule procedure and patients fasted since 10 p.m. the night before. Bowel preparation was not performed in the first fourteen patients. Following modifications in expert recommendations, all patients except two were given 2 L PEG twelve hours before the procedure. All procedures were conducted at 9 a.m. in the gastrointestinal endoscopy unit. After ingestion of CE with a glass of water, recordings were made for 8 hours. The procedure was performed in the first fourteen patients. Following modifications in expert recommendations, all patients except two were given 2 L PEG twelve hours before the procedure. All procedures were conducted at 9 a.m. in the gastrointestinal endoscopy unit. After ingestion of CE with a glass of water, recordings were made for 8 hours. The procedure was performed in outpatients, day-hospital setting or during hospitalization in case of overt OGIB (melena or hematochezia). In both situations, gastroscopy (N = 3), upper enteroscopy (N = 6), or lower enteroscopy (N = 2). The therapeutic decision was not affected by the clinical presentation (table I). Eight patients with angiodysplasias were treated with argon plasma coagulation delivered during gastroscopy (N = 3), upper enteroscopy (N = 4), or lower enteroscopy (N = 1). Endoscopic polypectomy was performed in one patient with a 25-mm pedunculated polyp in the first jejunal loop which was identified as an endocrine tumor at the pathology examination (figures 2, 3, 4). Two patients had a Dieulafoy ulcer which appeared as active bleeding with no visible lesion on capsule recording and which was treated during upper enteroscopy by epinephrine injection and hemoclip. One of these two patients also required local resection of the proximal jejunum after failure of endoscopic treatment. A second segmentary resection of the small bowel was performed during per-operative enteroscopy in one patient with multiple angiodysplasias in the proximal ileum which had been underestimated by capsule endoscopy. This patient had severe Willebrand disease and experienced multiple episodes of lower gastrointestinal bleeding. A patient was treated by corticosteroids because the clinical context and the aspect of the lesions was highly suggestive of Crohn's disease. A subsequent therapeutic intervention was not performed in only three patients with P2 lesions. Surgical exploration of a moderate-sized polyp in the mid portion of the small bowel was not attempted in the first patient due to his poor general status (cerebrovascular accident). In the two other patients, ulcersations of the small bowel which appeared to be related to NSAID were not treated after spontaneous interruption of the bleeding. Among patients with negative capsule endoscopy, the cause of bleeding could not be established for 14. Another site was identified for five patients whose bleeding arose from stomach (N = 1), colon (N = 2), or a gynecological disorder (N = 1). An hematological disorder explained anemia in one patient.

The value of red zones identified by the Suspected Blood Indicator™ was evaluated retrospectively in 24 patients with P1 or P2 lesions. The sensitivity, specificity, positive predictive value and negative predictive value of the SBI were 43%, 73%, 50% and 69%, respectively, comparatively to capsule reading, considered as “gold standard”. All lesions identified by the SBI were known before the procedure. In three patients, recognized lesions were not identified by SBI.

Discussion

Management of patients presenting OGIB is a difficult and costly challenge. Capsule endoscopy, a major technological progress, allows complete non-invasive exploration of the small bowel with a single-use device. Moreover, this exploration is often performed in outpatients (40% of our patients) [14, 29]. Early experimental animal studies demonstrated safety of CE and its diagnostic efficacy for exploration of lesions of the small bowel [30]. Several clinical trials have demonstrated the diagnostic yield of CE and its superiority over push enteroscopy in
Fig. 1 – Small bowel lesions visible with the wireless capsule Endoscopy. a) whitish superficial ulcer; b) prolonged obstruction due to a stenosing circumferential ulcer (patient taking non-steroidal anti-inflammatory drugs); c) overt bleeding with visible lesion; d) solitary zone of angiodysplasia in the mid portion of the small bowel; e) polypoid mass in the proximal jejunum.

Différents aspects lésionnels de l’intestin grêle visibles après une exploration par vidéo-capsule. a) ulcération superficielle blanchâtre de l’intestin grêle ; b) obstruction prolongée de la capsule sur une ulcération circonférentielle et sténosante liée à une prise chronique d’AINS ; c) saignement actif sans lésion visible ; d) angiodysplasie unique localisée au niveau de la partie moyenne de l’intestin grêle ; e) masse polypoïde localisé dans le jéjunum proximal.
patients with OGIB [20-24]. Our results confirmed the diagnostic contribution of this technique for obscure gastrointestinal bleeding, since one or several lesions likely to be the cause of bleeding were found in 45% of our patients. We found angiodysplasias (56%), ulcers (31%) and tumors (13%). Only P2 lesions were chosen for analysis. Using this approach, the diagnostic yield and therapeutic impact of capsule endoscopy were similar, whether OGIB was occult or overt.

Thirty-seven percent of patients who underwent capsule endoscopy were treated by endoscopy, surgical or medical treatment. These treatments were not attempted in three patients who had P2 lesions detected by capsule endoscopy and anemia persisted in two patients whose capsule endoscopy was negative. There are few data in the literature about the therapeutic impact of capsule endoscopy in patients with obscure gastrointestinal bleeding. In four recent studies [25-28] including 22, 44, 45, and 137 patients respectively, subsequent management was modified because of CE findings in 32 to 45%. In our series, treatment was proposed in one-third of the patients after capsule endoscopy, a rate similar to the earlier French study reported by Delvaux et al. [26]. Considering small bowel lesions alone in their series of 44 patients explored for obscure gastrointestinal bleeding and followed-up for one year, the procedure had a therapeutic impact in 33%; considering all (including upper and lower) capsule-detected lesions the rate was 45%. Enns et al. [31] also reported in abstract form a multivariate analysis which showed that the only predictive factor of positive CE was negativity of at least two prior upper GI endoscopies. In our series, 24 patients (69%) had undergone at least two upper endoscopic procedures before capsule endoscopy. Two of the three patients whose capsule exploration revealed gastroduodenal lesions had had two prior gastroscopic procedures. In these two patients, capsule endoscopy revealed active bleeding in the genu superius (N = 1) and in the second portion of the duodenum (N = 1) without a focal lesion. These two patients had angiodysplasia (N = 1) and a Dieulafoy ulcer (N = 1). In the third patient, antral angiodysplasia had been missed at gastroscopy.

The capsule was retained for a long period in only one woman who was taking NSAID chronically. In this patient, capsule endoscopy was an emergency procedure following acute massive hematochezia. At the present time, it appears advisable to perform an enteroscan before CE in patients taking NSAID chronically. Earlier CE reports have found that more than 30% of patients with chronic NSAID intake have severe small bowel lesions (32%).

Since CE became available for clinical use, three new functions have been added to the RAPID™ software. The first is Multi-view™, a reading system which enables simultaneous visualization of two successive images. The second is a system for localization of CE. The third is the Suspected Blood Indicator™ which detects red zones on the recording. We evaluated the Suspected Blood Indicator™ retrospectively in our last 24 patients. The sensitivity of this system was 45% and its specificity 73%. It is a rapid screening method which does not at the present time appear to be particularly useful. In any case, careful reading of the recordings remains necessary. The main present problem is localization of CE. The new localization system should, in theory, provide improvement. This function has not been evaluated in this study. The Multi-view™ system appears to improve the diagnostic yield (at equal speed) and to shorten reading time [33].

In conclusion, capsule endoscopy is a major diagnostic tool in patients with small bowel bleeding. This safe, easy-to-use method has demonstrated diagnostic efficacy, leading to effective treatment of diagnosed lesions in one third of the patients.
REFERENCES


Fig. 4 – Pathology section (stains: hematein eosin safran). a) normal intestinal mucosa lining the polyp (magnification × 2.5); b) diagnosis: well-differentiated endocrine tumor (magnification × 40).

Coupe anatomopathologique du polype (coloration: hématéine éosine safran). a) le polype est entièrement bordé par une muqueuse intestinale normale (grossissement × 2.5) ; b) affirme le diagnostic de tumeur endocrine bien différenciée (grossissement × 40).


