Diagnostic yield of repeat capsule endoscopy and the effect on subsequent patient management

Sigrid Svarta MD, Brandon Segal BHK, Joanna Law MD, Ajit Sandhar MD, Ricky Kwok BSc
Andrew Jacques MD, Pardis Lakzadeh BSc, Robert Enns MD

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BACKGROUND: Capsule endoscopy (CE) has been shown to produce a high diagnostic yield in patients with obscure gastrointestinal bleeding (OGIB); however, in those with negative studies, management is controversial. Very few studies have reported on repeat CE in the same patient; data regarding this diagnostic strategy are limited.

OBJECTIVE: To determine the diagnostic yield of repeated CE studies and how this yield affects subsequent patient management.

METHODS: A retrospective chart review of all patients who underwent CE at St Paul's Hospital (Vancouver, British Columbia) between December 2001 and June 2009 was conducted. Patients who underwent subsequent repeat CE were identified and divided into one of four subgroups. Findings were classified as positive or negative.

RESULTS: Eighty-two of 676 patients underwent more than one CE study. Group 1 (incomplete study) included 22 patients (27%) and yielded 10 positive findings (45%). Group 2 (screening) comprised four patients (5%) and yielded two positive findings (50%). Group 3 (ongoing symptoms despite previous negative study) totalled 26 patients (32%) and yielded 10 positive findings (38%). Group 4 (previous positive study with treatment/investigation) included 30 patients (37%) and yielded 23 positive findings (77%). Overall, the present study found positive findings in 55% (45 of 82) of repeated CE cases, which resulted in a change in management in 39% (n=32) of the patients.

CONCLUSION: Due to the high diagnostic yield and noninvasive nature of CE, repeat CE appears to be of benefit and should be considered for specific patients before other types of small bowel studies.

Key Words: Patient management; Repeat capsule endoscopy; Yield

Since the development of the first video capsule endoscope in 2000 (1), it has proven to be the most effective non-invasive means of imaging the mucosa of the small intestine. Capsule endoscopy (CE) has proven to be superior to other diagnostic modalities such as small bowel (SB) barium radiography (ie, SB follow-through and enteroclysis), computed tomography enteroclysis, mesenteric angiogram and SB magnetic resonance imaging in patients with obscure gastrointestinal bleeding (OGIB) (2). Furthermore, a meta-analysis of CE (3) demonstrated diagnostic yield results comparable with those of double-balloon enteroscopy (DBE) in patients with SB disease, including OGIB (3).

The inception of technology that enabled the direct visualization of the mucosa of the small intestine led to the reclassification of OGIB into three separate categories: upper, mid and

Rendement diagnostique de l'endoscopie capsulaire répétée et effet sur la prise en charge des patients

HISTORIQUE : Il a été démontré que l'endoscopie capsulaire (EC) donne un bon rendement diagnostique chez les patients souffrant d'hémorragie digestive occulte (HDO). Toutefois, le traitement ne ferait pas l'unanimité lorsque les examens sont négatifs. Très peu d'études ont fait état d'EC répétées chez un même patient. Les données sur cette stratégie diagnostique sont limitées.

OBJECTIFS : Déterminer le rendement diagnostique des EC répétées et la façon dont ce rendement influe sur la prise en charge des patients.

MÉTHODES : Examen rétrospectif des dossiers de tous les patients ayant subi une EC à l'hôpital St. Paul's (Vancouver, Colombie-Britannique) entre décembre 2001 et juin 2009. Les patients ayant subi des EC répétées ont été recensés et répartis en quatre sous-groupes. Les résultats ont été classés selon qu'ils étaient positifs ou négatifs.

RÉSULTATS : Quatre-vingt-deux patients sur 676 ont subi plus d'une EC. Le groupe 1 (examen incomplet) comprenait 22 patients (27 %) et a donné dix résultats positifs (45 %). Le groupe 2 (dépistage) regroupait quatre patients (5 %) et a donné deux résultats positifs (50 %). Le groupe 3 (symptômes persistants malgré résultats négatifs à l'examen) regroupait 26 patients (32 %) et a révélé dix résultats positifs (38 %). Le groupe 4 (résultats positifs à un examen précédent avec traitement/investigation) regroupait 30 patients (37 %) et a donné 23 résultats positifs (77 %). Dans l'ensemble, cette étude a dégagé des résultats positifs dans 55 % (45/82) des cas d'EC répétées, ce qui a donné lieu à une modification de la prise en charge chez 39 % (n = 32) des patients.

CONCLUSIONS : Compte tenu du rendement diagnostique élevé et de la nature non effractive de l'EC, la répétition de l'intervention semble avantageuse et devrait être envisagée chez certains patients avant le recours à d'autres types d'examens du grêle.

lower gastrointestinal bleeding (4). Previous diagnostic techniques to directly visualize the location of bleeding within the small intestine in patients with OGIB have been insufficient. It has been reported that through the use of CE, OGIB sites can be identified in up to two-thirds of cases (5).

However, there appears to be very little data supporting the reproducibility of CE when repeated procedures are performed. Therefore, the present study assessed the indications and the diagnostic yield of repeat CE as well as the subsequent effects on patient management.

METHODS

In an effort to determine the diagnostic yield of repeat CE, approximately seven years of patient information regarding CE cases from a tertiary care, hospital-based endoscopy unit were

Department of Medicine, Division of Gastroenterology, St Paul's Hospital, Vancouver, British Columbia

Correspondence: Dr Robert Enns, Division of Gastroenterology, St Paul's Hospital, University of British Columbia, 770-1190 Hornby Street,

Vancouver, British Columbia V6Z 2K5. Telephone 604-688-6332, fax 604-689-2004, e-mail renns@interchange.ubc.ca

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TABLE 1
Summary of findings

Group	Patients, n (positive findings on repeat CE, n)	Diagnostic yield, %	Change in management, %
1	22 (10)	45	27
2	4 (2)	50	25
3	26 (10)	38	27
4	30 (23)	77	60

CE Capsule endoscopy

reviewed. As the sole provider of this service to residents of British Columbia, the gastroenterology clinic at St Paul's Hospital (Vancouver, British Columbia) serves a population base of 4.4 million (6).

A retrospective chart review of patients who underwent CE between December 2001 and June 2009 was conducted. Patients who underwent repeat CE were identified and divided into one of four subgroups as follows: group 1 (incomplete study) was defined as gastric/esophageal retention, poor/incomplete preparation (greater than 25% of mucosa not visible) and/or capsule transmission failure (less than 1 h of SB imaging); group 2 (screening for polyposis syndrome) included patients with previously diagnosed Peutz-Jeghers (PJ) syndrome, familial adenomatous polyposis (FAP) and Muir-Torre syndrome; group 3 included patients with ongoing symptoms despite previous negative CE studies; and group 4 was comprised of patients who complained of ongoing symptoms despite previous positive findings and subsequent ineffective treatment.

Findings were classified as either positive or negative. Positive findings were defined as the identification of ulcers, tumours, strictures, polyps, blood, and actively bleeding angiodysplasia occurring between and including the stomach and the cecum.

RESULTS

A total of 676 patients (54% women, mean [$\pm$ SD] age 57.6 ± 18.56 years, range 12 to 92 years). Eighty-two of these 676 patients (50% women, mean age 58.6 ± 17.93 years, range 16 to 88 years) had undergone multiple CE procedures, totaling 184 CE procedures (69 patients underwent two CE procedures, nine patients underwent three CE procedures, one patient underwent four CE procedures and three patients underwent five CE procedures). The indications for repeat CE were recurrent gastrointestinal bleeding, anemia, screening for polyposis syndromes, abdominal pain and failure of the first CE procedure (Table 1).

Findings in the initial incomplete studies of group 1 patients were secondary to either retention of the capsule in the stomach, capsule transmission failure or excessive debris within the small intestine that limited visibility. Group 1 (incomplete studies) consisted of 22 of the 82 patients (27%) who had undergone repeated studies, 10 of whom (45%) had positive findings on repeat CE. Of these 10 patients, one (4.5%) revealed a positive finding only after a third CE procedure. Six repeat CE procedures (27%) resulted in no findings due to another incomplete procedure, and six patients (27%) had normal negative results on the second CE procedure. Findings in the 10 positive studies included the following: bright red blood in the SB (n=3), ulcerations and erosions (n=4), multiple blue blebs throughout the SB (n=1) and coarsened/flat-tened folds in the SB (n=1). In addition, one patient with

known hepatic cirrhosis had very prominent veins throughout the SB that were suspected to be varices.

Six of the 22 (27%) patients who had positive findings on repeat CE underwent a change in management. The changes in management included the following: SB resection because lesions could not be reached with esophagogastroduodenoscopy (EGD) or colonoscopy (n=2); intensified treatment for Crohn's disease (n=2); beta-blockade (n=1); and colonoscopy with argon plasma coagulation (APC) of vascular lesions in the colon seen on CE (n=1). Supportive therapy with iron supplementation (n=3) was not considered to be a change in management. The patient with multiple blue blebs received no further treatment.

Screening for polyposis syndrome (group 2) comprised four patients (5%; two men). Two patients underwent three CE procedures and two patients underwent two procedures. Fifty per cent of the patients in group 2 had positive findings on their repeat CE, with findings of polyps (n=2). In one of these patients, the polyps were seen on all CE procedures for which the patient subsequently underwent endoscopic polyp removal. In the other patient, the first CE showed no polyp. The patients are currently being followed every two to three years with surveillance CE.

Participants with ongoing symptoms despite previous negative CE studies (group 3) comprised 26 of the 82 patients (32%). On repeat CE, 10 studies (38%) resulted in positive findings. This included one patient who underwent four CE procedures in which only the final procedure reported positive findings. Sixteen studies (62%) yielded negative (ie, normal) results, including three patients who underwent three CE procedures. The 10 positive studies demonstrated bright red blood in the small intestine in eight cases, and significant SB ulcerations in two cases.

Patient management in this group changed in seven patients (27%) who had positive findings on repeat CE. The changes in management included colonoscopy with APC of angiodysplastic lesions seen on CE (n=2), and colonoscopy because of lesions in the cecum seen on CE (n=1, this patient finally underwent subtotal colectomy to remove the bleeding lesions initially seen on CE), SB resection due to tumours seen in the duodenum suspected to be malignant (n=1), SB resection because of several ulcers seen in the SB (n=1) and treatment for Crohn's disease (n=2). Similar to group 1, this group also comprised two patients who received supportive therapy, typically long-term iron supplementation with routine laboratory monitoring. The last patient died of cardiac arrhythmia (unrelated to his CE study) before a planned EGD.

Thirty of 82 (37%) patients underwent repeat CE despite a previous positive study. The positive findings from the initial studies resulted in further treatment and/or investigation, but did not result in the cessation of symptoms. Twenty-three of 30 procedures (77%) resulted in a positive finding on repeat CE. Three patients underwent three CE procedures, while three patients underwent five CE procedures. The positive findings included actively bleeding angiodysplastic lesions (n=5), blood within the small intestine (n=6), ulcerations (n=7), polyps (n=1), stricture (n=1), multiple vascular lesions (n=1), inflammation (n=1) and a mass (n=1).

Of the 23 patients who had positive findings on repeat CE, 60% (18 of 30) underwent a change in management.

The changes in management included EGD with APC (n=4), and EGD with endoclip (n=1). These procedures were all performed because lesions were seen on CE in either the stomach or the proximal SB. Other changes in management included DBE with APC (n=1), enteroscopy with oversewing of lesions (n=1), enteroscopy with APC (n=2), intraoperative enteroscopy with removal of polyp (n=1), treatment for Crohn's disease (n=4), SB resection (n=2) because of bleeding in the SB, and estrogen therapy because of angiodysplastic lesions (n=1). A computed tomography scan, performed after a suspected mass was seen on CE, was unremarkable. The patient underwent a bone marrow biopsy to determine the hematological source of bleeding and revealed multiple myeloma with pancytopenia (n=1). This group also contained five patients who underwent supportive therapy with iron supplementation, similar to the other groups.

DISCUSSION

The present study is one of the few that report on the diagnostic yield of repeated CE. Our study found an overall yield (positive findings) of 55% and an overall change in the management of 39% of the patients who underwent repeat CE. This supports current trends with regard to the effectiveness of CE. The present study also validates the repeated use of CE and its utility in the subsequent management of patients with specific gastrointestinal ailments.

With increasing evidence supporting CE as an effective modality, general standards regarding patient care have been developed. Current standards discussed at the Sixth International Conference on Capsule Endoscopy held in Madrid, Spain, in 2007, maintain that a secondary CE investigation should be completed for patients with recurring OGIB and/or unexplained gastrointestinal pain, who have undergone an initial, previously negative, CE procedure.

The main indications for repeat CE in our study were recurrent gastrointestinal bleeding, iron deficiency anemia and a previous incomplete study. Similar indications for secondary CE were also reported by Jones et al (7) in 2005. In this smaller study, 75% (18 of 24) of the patients who underwent a repeated study had additional positive findings that led to a change in management in 62% of them. A more recent study by Viazis et al (8) reported on 76 patients with new evidence of overt bleeding or a decrease in hemoglobin who underwent a second-look CE procedure. There were positive findings in 37 patients (49%) on second CE, findings of uncertain significance in 22 patients (29%) and 17 patients had no findings. The study concluded that certain patients would benefit from a second-look CE procedure.

As previously noted, subjects in our study were classified into four separate subgroups (Table 1). In group 1 (incomplete studies) changes in management occurred in 27% of the patients studied, implicitly supporting a strong benefit for repeat CE studies in this group. On repeat CE, there were six patients who, again, had incomplete studies, three of whom experienced gastric retention of the capsule on both the first and second procedure. These patients were considered for endoscopic placement of the capsule within the duodenum.

All patients in our study were instructed to ingest a bowel preparation in the form of polyethylene glycol (PEG,

GoLYTLEY, Braintree Laboratories, USA); however, there were still three patients who presented with poor preparation following both CE studies. Because CE is still a fairly new technique, there is currently no strong consensus regarding the effectiveness of the use of bowel preparation and/or prokinetics before CE procedures, and the views regarding this subject remain divided. Two previous studies found PEG to decrease gastric and SB transit time (9,10), and reported no improvement in the quality of the images produced (10). Conversely, other studies (11,12) have found the opposite, stating that PEG does improve quality as well as diagnostic yield (13). Because we only included patients who ingested bowel preparations, we cannot conclude that it improved image quality; larger prospective, randomized studies are needed. However, our most recent practice is that patients with an initial incomplete study or a study with excessive debris should undergo 'full preparation' before repeat CE.

Group 2 consisted of patients who suffered from hereditary polyposis syndromes. These syndromes include FAP, PJ syndrome, juvenile polyposis and their subtypes. Additionally, this group also included a patient with Muir-Torre syndrome, which is a subgroup of hereditary nonpolyposis colorectal cancer (14,15). It is well known that the lifetime risk of developing SB malignancy in patients with these syndromes is increased (16-18) and, therefore, is an important issue for these patients. Giardiello et al (16) found that patients with PJ syndrome had a statistically significant increase in the RR of cancers in the small intestine. Giardiello and Offerhaus (17) reported that upper gastrointestinal tract cancers, including adenocarcinoma of the duodenum and the ampullary region, were second to the colorectum as a site of malignancy in FAP patients. Vasen et al (18) tried to assess age-specific cancer risk in patients with hereditary nonpolyposis colorectal cancer. They reported an RR of more than 100 for SB cancer in their study. More recently, Schulmann et al (19) suggested CE to be of value in patients with polyposis syndrome because it is safe, noninvasive and has a high yield. Iaquinio et al (20) found CE to be safe for surveillance of jejunal-ileal polyps in selected patients with FAP; however, they also concluded that CE was not useful for surveillance of the duodenum. Currently, these patients represent the smallest group; however, we believe that this will become a much larger group in the future. It is important to recognize that the capsule has limited visibility within the duodenum and, therefore, in addition to CE, our practice is always to perform enteroscopy (to view the distal duodenum) and side viewing assessment of the papilla in those at significant risk for duodenal polyps.

In patients with a previous negative study, repeat CE had a diagnostic yield of 38%, with a change in management in 27% of the patients in this group. Again, we found a clear benefit for a repeat CE study and, therefore, conclude that repeat CE should be performed in this group to guide other invasive procedures and/or further medical treatment.

Many patients with positive CE results are managed conservatively for a period of time. For the group of patients who underwent repeated studies despite previous positive studies, CE had a diagnostic yield of 77%, which resulted in a change in management in 60% following a secondary CE procedure. The ongoing symptoms imply that the lesion was not cured by the initial management strategy.

The role of DBE after an initial negative CE has been demonstrated in some studies to find lesions that were missed on the initial CE study (21,22). Ross et al (21) compared DBE and CE in patients who had SB mass lesions. In their study, 15 of the patients who had SB mass lesions on DBE previously underwent a CE procedure. In the study, CE revealed a mass lesion in five patients, fresh luminal blood in seven patients, and erythema and erosions in three patients. They concluded that patients with OGIB with nonspecific or negative findings on CE should undergo DBE or intraoperative enteroscopy. Chong et al (22) believed that the two procedures – DBE and CE – are complementary, and concluded that DBE should be performed if the CE was negative and if a high suspicion of SB pathology remained. Early in our study, DBE was not available. In general, even at this stage, because of the invasive nature of

DBE, we tend to repeat a CE procedure rather than use DBE if an initial study was negative. If the repeat CE is negative, we usually treat the patient supportively. Only positive CE studies are followed up with DBE.

Using repeated CE, the diagnostic yield of positive findings totalled 45 of 82 (55%) cases. This figure is artificially elevated by the high yield of patients who have had positive findings and ongoing symptoms despite treatment (ie, failed/inadequate treatment [77% yield]). Regardless, it appears that the use of repeat CE is beneficial for patients with recurrent gastrointestinal bleeding, anemia and for screening purposes. Due to the high diagnostic yield and noninvasive nature of this modality, as well as the changes in management that follow, we conclude that a repeat CE appears to be of benefit and should be considered for specific patients before subsequent SB studies.

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