Wireless capsule endoscopy for obscure gastrointestinal bleeding: A single-centre, one-year experience

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BACKGROUND: Wireless capsule endoscopy (CE) is increasingly being used in the investigation of obscure gastrointestinal (GI) bleeding, but some studies have found that many of the bleeding lesions recognized by this technique are within the reach of conventional endoscopy.

METHODS: The results of CE performed in the authors' centre in a 12 month period for obscure GI bleeding were retrospectively reviewed.

RESULTS: Of the 46 patients with obscure GI bleeding, CE found a definite or probable cause in 19 (41%) and a possible cause in another 10 (22%), with an overall diagnostic yield of 63%. One of these lesions was found to be within reach of conventional gastroscopy, two were within reach of push enteroscopy, four were within reach of colonoscopy and one was within reach of retrograde enteroscopy through a stoma. The percentage of patients with a bleeding source within reach of routine endoscopy but missed during pre-CE endoscopy was significantly higher for those patients having endoscopy only in the community (30% [eight of 27]) versus in the authors' centre (0% [zero of 19]).

CONCLUSIONS: CE was valuable for diagnosing bleeding lesions not only within the small bowel, but also in the stomach and colon. However, 'second-look' endoscopy may be considered before ordering CE for obscure GI bleeding when local expertise is available.

Key Words: Capsule regional transit abnormality; Endoscopy; Gastrointestinal bleeding; Wireless capsule endoscopy

La capsule endoscopique sans fil pour un saignement gastro-intestinal obscur : Une étude unicentrique d’un an

HISTORIQUE : La capsule endoscopique (CE) sans fil est de plus en plus utilisée pour explorer des saignements gastro-intestinaux (GI) obscurs, mais selon certaines études, bon nombre des lésions hémorragiques décelées par cette technique seraient accessibles par endoscopie classique.

MÉTHODOLOGIE : Les résultats des CE utilisées pour déceler des saignements GI obscurs dans le centre de l’auteur au cours d’une période de 12 mois ont fait l’objet d’un examen rétrospectif.

RÉSULTATS : Parmi les 46 patients présentant un saignement GI obscur, la CE a permis de découvrir une cause définitive ou probable dans 19 cas (41 %) et une cause possible dans 10 autres cas (22 %), pour un rendement diagnostique global de 63 %. L’une de ces lésions aurait été visible par gastroscopie classique, deux par entéroscopie pousseuse, quatre par coloscopie, et une par entéroscopie rétrograde dans une stomie. Le pourcentage de patients manifestant une source hémorragique qui aurait pu être visible par endoscopie systématique mais non perçue à l’endoscopie avant le recours à la CE était beaucoup plus élevé chez les patients ayant subi l’endoscopie dans la collectivité (30 %, ou huit sur 27) plutôt que dans le centre de l’auteur (0 %, ou zéro sur 19).

CONCLUSIONS : La CE est précieuse pour diagnostiquer des lésions hémorragiques, non seulement dans l’intestin grêle, mais également dans l’estomac et le côlon. Cependant, une deuxième endoscopie pourrait être envisagée avant d’opter pour la CE afin de découvrir un saignement GI obscur en présence de compétences techniques locales.
open-access procedure (24). On the other hand, there is a growing recognition that many lesions detected by CE are within the reach of standard endoscopy (21-23,25). Lo et al (21) studied 95 patients with obscure GI bleeding, finding 23 patients (24%) with lesions that could be reached by either upper endoscopy or colonoscopy. These 23 patients represented 37% of their positive CE studies. Costamagna et al (22) reported on six patients with lesions within the reach of a gastroscope in a study of 20 patients with suspected small bowel pathologies. Janowski et al (23) reported that, of 37 patients who underwent CE, five had gastric lesions diagnosed by CE. Van Gossum et al (25) compared push endoscopy with CE in 21 patients with obscure GI bleeding. They found 12 patients (57%) with lesions such as esophageal varices, upper GI ulcers and cecal angioectasia within the reach of routine endoscopy. In addition, there has been a reported case of colonic cancer missed by colonoscopy but detected with CE (26).

To further evaluate this controversy, we reviewed all cases of CE performed at our centre over a 12 month period. Data collected on all patients with obscure GI bleeding undergoing CE at our centre were analyzed. All patients referred for CE by our university-based endoscopists had negative prior endoscopy, including enteroscopy. We reviewed and compared CE findings in patients who had enteroscopy performed by university-based endoscopists from our centre with those having undergone endoscopy in the community.

**PATIENTS AND METHODS**

A retrospective evaluation was undertaken of all cases of obscure GI bleeding with anemia investigated with CE at The Center for Therapeutic Endoscopy and Endoscopic Oncology, St Michael's Hospital, Toronto, Ontario between July 2002 and June 2003. Obscure GI bleeding was defined as persistent or recurrent GI bleeding with no bleeding source found at initial upper and lower endoscopy (ie, recurrent or persistent iron-deficiency anemia, fecal occult blood test positivity or visible bleeding). In patients with iron-deficiency anemia but without gross GI bleeding, small bowel biopsy was performed to rule out celiac disease. Before CE, patient history and data, including radiological and endoscopic investigation for GI bleeding, were collected. Endoscopic investigation included esophagogastroduodenoscopy (EGD), push enteroscopy and colonoscopy. The study hospital is a tertiary medical institution with a referral centre for advanced and therapeutic endoscopy. Patients were referred from practising gastroenterologists (NM, PK, GH, GK). The video taken within the esophagus, stomach and small bowel was viewed and assessed at a frame rate of 15 frames/second. Colonic videos were read at a faster rate (25 frames/second). The entire video recording was completely assessed in each patient.

**CE image interpretation and classification**

Currently, there is no standard system of classification for CE video image interpretation. The wide range of diagnostic yields reported in different studies partially reflects differences in image interpretation. We used the following criteria for assessing and classifying CE findings (26):

- **Angioectasia**: A flat, red mucosal lesion with visible ‘legs’ or borders.
- **Ulcer**: An interruption of the mucosa with visible ‘legs’ or borders.
- **Fresh blood localization without definite lesion identified**: Blood seen but no underlying lesion visualized.

Once a specific lesion is identified at CE or with other investigations, the fresh blood or ‘localization without definite lesion identified’ is considered to be a ‘definite finding’ on CE. If further investigation, including intraoperative enteroscopy, fails to detect the specific lesion accounting for the fresh blood seen on CE, ‘fresh blood localization without definite lesion identified’ is classified as a separate category. In the authors’ experience, bleeding angioectasia and small ulcers account for most cases of ‘fresh blood localization without definite lesion identified’. An indeterminate red spot was defined as a pinpoint, faintly red spot and was considered to be a subtle finding bearing no clinical significance. Other subtle findings such as focal erythema, prominent submucosal veins or venous blebs were deemed to be clinically irrelevant. In certain cases, capsule transit was significantly delayed within a segment of small bowel with or without visible pathology. Such delay was often accompanied by capsule pressing on the mucosa (26). This finding frequently exceeded 15 min. This finding was termed ‘regional transit abnormality (RTA)’ and was considered to be a ‘red flag’ sign alerting the capsule endoscopist to
the possibility of underlying pathology. Table 1 shows the classification of diagnostic findings on CE.

Statistical analysis

Patient attributes are expressed as counts or percentages. Means and standard deviations are provided for clinical parameters. Percentages and counts for different groups were compared using the Fisher’s exact test or its generalization to three groups, due to low cell counts. Pre-CE hemoglobin, number of EGDs and number of colonoscopies were compared among groups using one-way ANOVA, after square roots were taken of the latter two variables to reduce their inherent skewness as counts. Statistical significance was asserted for P<0.05. It is recognized that there was multiple testing of outcome data. The P values are presented without correction and it is noted that no findings of statistical significance would have been removed by application of Bonferroni’s method of correction, where the results for three groups would not be counted among the main statistical tests being exploratory tests of secondary results.

RESULTS

During the 12 month period, 50 patients underwent CE at the authors’ centre. In 47 patients, the indication was obscure GI bleeding. The remaining three patients underwent CE to investigate small bowel lesions noted on computed tomography or small bowel barium follow-through (SBFT). Of the 47 patients with obscure GI bleeding, 28 were men and 19 were women, with a mean age of 62 years (range 33 to 86 years). Fourteen patients were taking nonsteroidal anti-inflammatory drugs; eight of these patients had stopped this medication after the development of GI bleeding. Four of the 47 patients were on anticoagulation therapy for atrial fibrillation or cardiac valvular replacement. These patients were instructed to continue anticoagulation therapy before and during CE. In terms of comorbid conditions, one patient had hepatic cirrhosis and another had portal and mesenteric thrombosis (27). Small bowel varices were seen on CE in these two patients. One patient had severe heart disease (congestive heart failure).

Before the CE, a total of 283 GI investigations had been performed on these 47 patients: 109 EGD, 24 push enteroscopies, 33 SBFTs and 117 colonoscopies. Twenty-six patients (55%) had a history of blood transfusion for anemia due to obscure GI bleeding. Twenty-five patients (53%) had obscure-overt bleeding and 22 (47%) had obscure-occult bleeding.

Before the CE, thirteen of the 47 patients (28%) had push enteroscopy performed by an endoscopist at the authors’ centre. Four of these 13 patients (31%) had positive findings at enteroscopy: small bowel angioectasia (three patients) and small bowel ulcer (one patient). All four patients underwent CE with the suspicion of similar, more distal lesions beyond the reach of the enteroscope. In each case, CE confirmed this clinical suspicion. During analysis, these four patients were considered to have diagnostic findings at both push enteroscopy and CE. Four patients underwent repeat colonoscopy at the authors’ centre. No new lesions were identified.

In one patient, the capsule failed to enter the small bowel and this patient was excluded from data analysis. For the remaining 46 patients with GI bleeding, 45 patients tolerated the CE well. No symptoms were reported during the 7 h study period. One patient with a Billroth II gastrectomy had the capsule placed endoscopically, using a Roth basket, into the efferent limb of the small bowel. Although a cardiac pacemaker is considered to be a contraindication to CE, there are reported cases of CE safely performed in patients with cardiac pacemaker (28). After consultation with a cardiac electrophysiologist and with the informed consent of the patient, CE was successfully and uneventfully performed in one patient with a cardiac pacemaker. A post-CE pacemaker check showed no interference with the pacemaker during the CE. One patient experienced capsule impaction at the site of a carcinoid tumour, requiring removal at the time of surgical resection. Complete small bowel examination was achieved in all but 12 patients (26%). Of these, eight (67%) patients had underlying small bowel pathology that impeded capsule transit.

Of the 46 patients who successfully completed CE, a definite or probable bleeding source was found in 19 patients (41%) and a suspected bleeding source was found in another 10 patients (22%). The overall diagnostic yield for definite, probable or suspected bleeding source was 63% (29 of 46 patients). Table 2 shows the diagnostic findings of CE in the present study. Of 29 patients with positive CE findings classified as either definite or suspected source of bleeding, definitive treatment targeted at these findings was carried out in 10 patients. These definitive treatments included endoscopic and surgical interventions.

Excluding the four patients with positive findings on push enteroscopy before CE, eight of 42 patients (19%) had probable or suspected lesions within the reach of EGD (n=1), push enteroscopy (n=2), retrograde enteroscopy through the stoma (n=1) or colonoscopy (n=4): one patient had a bleeding Cameron ulcer, one had an oozing angioectasia in the proximal jejunum, one had a large tumour at the fourth portion of the duodenum, one patient had a surgical staple-related small bowel ulcer close to the ileostomy stoma and four patients were found to have cecal or colonic angioectases (Table 3). Active bleeding was documented on CE in three of four cases of colonic angioectases (Figures 1-3).
represent one patient with a large oozing cecal angioectasia). No patients with bleeding lesions or fresh blood seen were anticoagulated at the time of CE. Of the eight patients with a definite, probable or suspected lesion within the reach of standard endoscopy, no patient had undergone pre-CE endoscopy by an endoscopist from the authors’ centre. Five of these eight patients had successful endoscopic treatment of the bleeding source. The percentage of patients with a bleeding source within reach of routine endoscopy but missed during pre-CE endoscopy was significantly higher for those patients having endoscopy only in the community than at the authors’ centre: 30% (eight of 27) versus 0% (zero of 19), P=0.014.

Comparing the obscure-overt bleeding group with the obscure-occult group, there was no significant difference in diagnostic yield from CE (Table 4). In the present study, 12 patients (26%) had a definite, probable or suspected lesion within the reach of EGD (n=1), push enteroscopy (n=6), retrograde enteroscopy through the stoma (n=1) or colonoscopy (n=4).

In 38 patients (83%), there were lesions not reachable by enteroscopy. The diagnostic yield of CE in these 38 patients was: 34% (13 of 38) for definite or probable source of bleeding; 24% (nine of 38) for suspected source of bleeding; and the overall diagnostic yield was 58% (22 of 38). Even after the four patients who had diagnostic findings on pre-CE push

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**TABLE 3**

Eight cases of obscure gastrointestinal bleeding with the bleeding source within reach of the standard endoscope in patients who had endoscopy performed before capsule endoscopy (CE) by one or more community-based endoscopist(s)

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/sex</th>
<th>EGD</th>
<th>Colonoscopy</th>
<th>SBFT</th>
<th>Push enteroscopy</th>
<th>Definite CE finding</th>
<th>Suspected findings</th>
<th>Final diagnosis</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>43/F</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>RTA*</td>
<td>Ulcerated GIST</td>
<td>Surgery</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>46/F</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Fresh blood in the stomach</td>
<td>Bleeding Cameron ulcer</td>
<td>Hernia repair</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>82/F</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>Fresh blood in the jejunum</td>
<td>Angioectasia found in the proximal jejunum</td>
<td>Treated endoscopically</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>61/M</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>Distal SB ulcer</td>
<td>Two surgical staples with large SB ulcer close to the stoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>74/F</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>Oozing cecal angioectasia</td>
<td>Cecal angioectasia</td>
<td>Treated endoscopically</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>78/M</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>Oozing cecal angioectasia</td>
<td>Cecal angioectasia</td>
<td>Treated endoscopically</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>78/M</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>Large cecal angioectasia</td>
<td>Cecal angioectasia</td>
<td>Treated endoscopically</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>85/M</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>Fresh blood in the colon</td>
<td>Oozing angiectasia in the ascending colon</td>
<td>Treated endoscopically</td>
<td></td>
</tr>
</tbody>
</table>

*Capsule regional transit abnormality (RTA): normal small bowel (SB) mucosa pressed against the camera window and stopped for 40 min in the proximal SB. When the capsule popped through, it failed to demonstrate the tumour or any mucosal abnormalities. EGD Esophagogastroduodenoscopy; F Female; GIST Gastrointestinal stromal tumour; M Male; SBFT Small bowel barium follow-through
enteroscopy by the tertiary centre endoscopists were excluded (all of whom had further distal lesions on CE), the diagnostic yield of CE in the remaining 34 patients was still high: 32% (11 of 34) for definite or probable source of bleeding and 21% (seven of 34) for suspected source of bleeding, for an overall diagnostic yield of 53% (18 of 34). Of the 38 patients, 20 patients (53%) had obscure-overt bleeding and 18 patients (47%) had obscure-occult bleeding. There was no significant difference in diagnostic yield between the obscure-overt and obscure-occult groups (P=0.917).

‘Fresh blood localization without definite lesion identified’ was present in three patients. A specific lesion was found in each case after further investigation: a bleeding Cameron’s ulcer (n=1) or an angioectasia (n=2) (Table 2). Therefore, ‘fresh blood localization without definite lesion identified’ was considered to be a ‘definite’ or ‘probable’ finding on CE among all three cases. Among the eight patients with capsule RTA, six had underlying small bowel pathologies. In one patient, acute duodenal ulcer was blamed for RTA after a normal push enteroscopy. The eighth patient with RTA will undergo further investigation such as standard or computed tomography enteroclysis if her anemia persists. There were a total of three patients in the study who had a history of bowel surgery with the possibility of adhesions. RTA was present in one of these patients due to underlying small bowel anastomotic varices and presumed anastomotic strictures.

DISCUSSION
In agreement with most other studies, we found that CE had a high diagnostic yield in obscure bleeding, namely, 63% (41% for definite or probable and 22% for suspected causes). However, in contrast to many other studies, we noted that in 28% (12 of 42) of cases the lesion was within the reach of conventional endoscopy. A recent study from another Canadian expert centre (28) also found that 28% (23 of 83) of lesions found on CE were within the reach of conventional endoscopy and were missed by primary endoscopy. This figure provides a guideline for each clinician to determine whether repeat conventional repeat endoscopy is preferable to CE in obscure GI bleeding. That only a minority of these within-the-reach-of-conventional-endoscopy lesions were, in fact, found at conventional endoscopy emphasizes the importance of ‘repeat endoscopy’ being done by an endoscopist with an interest in this area. This is underscored by our finding that there was a statistically significant higher chance of endoscopy done at our university centre finding a bleeding source than if the endoscopy was done in the community. Our findings differ from other studies, probably because of differences in patient selection, quality of pre-CE endoscopic investigation and non-standardized interpretation on CE imaging.

The major limitations of the present study are its retrospective nature and lack of long-term follow-up data. Besides the agreement of some patients to undertake a second-opinion endoscopy at our centre, there was no predefined standard in selecting patients for repeat endoscopy. We did not evaluate the quality of endoscopic evaluations made in the community. In the present study, CE and push enteroscopy proceduralists

| TABLE 4 | Diagnostic yields of capsule endoscopy among obscure-overt and obscure-occult bleeding groups |
|---------|--------------------------------------------------|----------|--------|
|          | Definite/probable source (n=9) | Suspected source (n=10) | Overall |
| Obscure-overt | 11 (44%) | 5 (20%) | 16 (64%) |
| Obscure-occult | 8 (38%) | 5 (24%) | 13 (62%) |
| Overt versus occult | | | P=0.93 |

Figure 2) Oozing of the same cecal angioectasia

Figure 3) Colonoscopic view of the same cecal angioectasia. It was treated using argon plasma coagulation

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were not blinded to one another, potentially influencing interpretation of the second test. There was also potential referral bias in our study. Because the procedure and cost of the wireless capsule were not covered by the Canadian health care system, unlike in some other countries, there was potential bias for both patients and physicians to choose second-look endoscopy over CE. Due to the retrospective nature of this study and relatively small numbers, we were unable to generate predictors for lesions best identified by each procedure. Future prospective randomized trials should address these limitations. 

In the present study, we found several small bowel tumours that were missed by SBFT. This reiterates the poor sensitivity of SBFT in the investigation of obscure GI bleeding (2). A recent study (22) specifically demonstrated the superior diagnostic yield of CE to that of SBFT in small bowel disease, and some authors have recommended that CE replace SBFT in the investigation of obscure GI bleeding (22,29). Furthermore, in a recent study (30), CE detected small bowel ulcers in three patients with normal results from state-of-the-art birefringent enteroclysis using barium and methylcellulose.

During the past year, we have serviced many CE studies by finding a significant lesion on second-look endoscopy and enabling endoscopic intervention. Given the current cost of CE and its inability to intervene therapeutically, sample tissue, or examine the stomach and colon in their entirety, CE should not, at least at the current time, replace push enteroscopy in the algorithm of investigation for obscure GI bleeding (31,32,33). This is supported by our observation and the results of other studies (32) that the vast majority of bleeding lesions are located within reach of an enteroscope or colonoscope with the potential for therapeutic intervention (32). In a canine study (34), push enteroscopy demonstrated a higher diagnostic yield within the reach of the endoscope than that from CE (94% versus 53%, respectively). We illustrated several scenarios where CE could miss important diagnostic findings (35). 

CONCLUSIONS

The current study demonstrates a high diagnostic yield of CE for both definite and suspected bleeding sources in patients with obscure GI bleeding. CE was also valuable in diagnosing and localizing the source of non-small bowel GI bleeding. However, our study revealed a high percentage of cases with a source of bleeding within reach of a push enteroscope or colonoscope. Furthermore, all such cases referred for CE came from the community as opposed to patients who had undergone enteroscopy and/or repeat colonoscopy by a tertiary centre endoscopist from our centre. Possible explanations to account for a higher yield by this group include: benefits of a ‘second look’; the endoscopist’s interest, training and skills; or the progression of underlying disease between the two endoscopies. This study suggests that in a tertiary endoscopy centre, a second-look endoscopy, including a push enteroscopy and in selected cases, repeat colonoscopy, be performed in patients with obscure GI bleeding before proceeding with CE. Under circumstances where push enteroscopy or experienced endoscopists are not available, CE maybe used to investigate obscure GI bleeding after unexplainatory initial endoscopy because of its seemingly high diagnostic yield.

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7. Landi B, Tkoub M, Gaudric M, et al. Diagnostic yield of SBFT in the investigation of obscure GI bleeding (2). A recent study (22) specifically demonstrated the superior diagnostic yield of CE to that of SBFT in small bowel disease, and some authors have recommended that CE replace SBFT in the investigation of obscure GI bleeding (22,29). Furthermore, in a recent study (30), CE detected small bowel ulcers in three patients with normal results from state-of-the-art birefringent enteroclysis using barium and methylcellulose.


