Diagnostic Yield of Capsule Endoscopy in a Tertiary Hospital in Patients with Obscure Gastrointestinal Bleeding

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Abstract

Background & Aims. Capsule endoscopy is applicable to several clinical conditions, but obscure gastrointestinal bleeding remains the main indication. This study aims at determining the diagnostic yield of capsule endoscopy for obscure gastrointestinal bleeding using a structured terminology in a large cohort in an academic hospital.

Methods. In this retrospective study, 592 capsule endoscopy procedures performed in a tertiary hospital were analysed using the Capsule Endoscopy Structural Terminology. Main indications were gastrointestinal bleeding (n=142) and iron deficiency anaemia (n=240).

Results. Capsule endoscopy identified abnormalities in 44% of patients with iron deficiency anaemia and in 58% of patients with gastrointestinal bleeding, resulting in a diagnostic yield of 49% for obscure gastrointestinal bleeding. In 32 patients the cause was found in the stomach and in 8 in the colon.

Conclusion. Capsule endoscopy evidenced a diagnostic yield of 49% for obscure gastrointestinal bleeding. Repeating endoscopy before capsule endoscopy should be considered since a reasonable proportion of lesions were found outside the small intestine.

Key words


Introduction

Capsule endoscopy (CE) is a relatively new procedure used for the investigation of the mucosa of the small intestine. It is also known as M2A (mouth to anus), VCE (video capsule endoscopy) and WCE (wireless capsule endoscopy). Although this procedure has been found to be applicable for the evaluation of several clinical conditions, including Crohn’s disease, celiac disease and small bowel tumours [1, 2], it is primarily used for the evaluation of patients with obscure gastrointestinal bleeding (OGIB). Obscure gastrointestinal bleeding is defined by the American Gastroenterological Association as persistent or recurrent gastrointestinal (GI) bleeding, undetected by gastroduodenoscopy (GDS) and colonoscopy. This is further divided in either obscure-occult bleeding presenting as persistent iron deficiency anaemia (IDA) or a positive faecal occult blood test, or obscure-overt bleeding when visible blood is found (melena, hematemeses, hematochezia) [3]. In the future, small-bowel bleeding with a cause located between the papilla and the ileocecal valve might be classified as mid-gastrointestinal bleeding (MGIB) [4].

Capsule endoscopy has advantages and disadvantages compared to other diagnostic modalities which evaluate the small intestine. The main advantage of CE is that it is a non-invasive technique with little or no side effects or complications. Capsule endoscopy is now an important diagnostic modality for the analysis of OGIB, as it has a higher diagnostic yield compared to other imaging techniques of the small bowel, including push enteroscopy (PE) and small bowel barium radiography [5], and a comparable diagnostic yield as double balloon endoscopy (DBE) [6]. The main disadvantage of CE is the lack of therapeutic opportunities and tissue sampling, and the risk of stagnation of the capsule in a patient with small bowel obstruction. However, stagnation of the capsule does not seem to occur frequently and DBE might be a relatively easy method for capsule retrieval [7].

Determining the value of CE for diagnosing causes of OGIB remains difficult. Initially, many different descriptions were used for the indications and findings of CE. In order to structure and standardise the nomenclature used in CE, Delvaux et al [8] introduced the Capsule Endoscopy Structural Terminology (CEST). The diagnostic yield of CE in the detection of OGIB has been analyzed before,
predominantly in small groups of patients. Up till now, there have been few studies with at least 200 patients and structured scoring systems.

In the present study we therefore analyzed the diagnostic yield of CE in a large group of patients with OGIB in daily practice in an academic referral hospital using a structured terminology.

Material and methods

Cases

In this retrospective study, data of the first 592 CEs performed from February 2003 until June 2007 at the VU University Medical Centre Amsterdam were analyzed. The mean age of the patients was 57 years (range 14-99), of whom 287 (49%) were male and 305 (51%) were female.

In this study population, OGIB accounted for 65% of the indications for CE. Among those, 240 patients (41%) had IDA and their indication for CE was classified as obscure-occult GI bleeding, whereas 142 patients (24%) had overt GI bleeding and were classified as obscure-overt GI bleeding. Another 34 subjects had anaemia, of which the exact classification was unclear and these patients were excluded for analysis. Individuals who suffered from both IDA and overt GI bleeding were classified as GI bleeding because anaemia was considered the consequence from GI bleeding. The other indications included diagnosis or evaluation of Crohn’s disease (n = 47; 8%); celiac disease (n = 50; 8%) and Peutz-Jeghers or other polyposis syndromes (n = 31; 5%). A total of 27 patients were evaluated in the workup of chronic abdominal pain.

Methods

All patients with GI bleeding and/or anaemia underwent GDS and colonoscopy before referral for CE. A subgroup of patients was subjected to other investigations, including MR-enteroclysis, small bowel follow-through, CT abdomen, or Meckels’ scan; all with negative results. Every patient was asked to stop iron supplementation a week before the procedure of CE. Medication which delays small bowel peristalsis (e.g. codeine) was stopped as well. Standard preparation of the small bowel was by ingestion of 2 litres of sodium sulphate/sodium bicarbonate solution (Klean-Prep®, Norgine B.V., Amsterdam, The Netherlands) 10 hours before swallowing CE and overnight fasting. Since both exercise and bed rest may influence CE transit time, patients were advised to adhere to daily routine during the investigation without excessive exercise. Patients were told not to smoke before and in the first 2.5 hours after ingestion of the capsule. To prevent interfering with data processing from the video capsule to hard disk, patients were told to stay away from shoplifting detection fences, as well as wireless internet systems (WIFI), MRI and other electromagnetic fields.

Contraindications for CE examination were known or suspected intestinal obstruction or strictures. Relative contraindications were a cardiac pacemaker, pregnancy and diabetic gastroparesis. All patients were told to check their stools carefully for retrieval of the video capsule and were asked to return the capsule.

Diagnostic imaging system of CE

The M2A capsules by Given (Given Imaging Ltd., Yoqneam, Israel) were used in all patients. This 11 x 27 mm capsule weighs 3.7g and takes two photos every second in a 140° field of view and 8:1 magnification. The technical description has been described before [9]. This capsule proceeds by intestinal peristalsis only. The data are transmitted to a hard disk worn on a belt by the patient. Total recording time for this device is 8 hours. Pictures were pre-screened by a trained specialised nurse and subsequently by a physician. The review time by the investigators was in general one hour. In case of discrepancy between the two reviewers, data were discussed in an expert panel.

In 14 patients, a capsule endoscope delivery device (AdvanceCE™, USendoscopy, USA) was used. This system uses a 2.5 mm single sheathed device for transcatheter delivery of the Given Video Capsule to the stomach or duodenum. The reasons for using this device included stomach retention during previous CE (n=7), and miscellaneous indications, including inability to swallow the capsule, pyloric stenosis or a Billroth-II stomach.

Outcome variables

Retrospectively, diagnostic reports were scored for angiectasia, erythematous mucosa, erosions, ulcers, aphthae, blood or clots, polyps, diverticula, abnormal villi, tumours and stenosis, according to the CEST nomenclature [8]. As no gold standard exists for small bowel evaluation, sensitivity and specificity could not be determined. Therefore, investigators scored findings as a ‘definite’ explanation, a ‘probable’ explanation, an ‘improbable’ explanation, or as a ‘definite negative’ explanation for the indication. A definite explanation for the indication OGIB was given when the diagnostic report showed a concrete answer for blood loss or anaemia (e.g., angiectasia, ulcer, blood, or based on the interpretation of the investigator). Erosions, submucosal bleedings and mass lesions were considered as a probable explanation. The presence of moderate erythematous mucosa, small red spots, small polyps and superficial aphthae were considered as improbable explanations. If the results were normal or clinically irrelevant, it was scored as definite not an explanation for OGIB. Diagnostic yield of CE was defined positive when a definite or probable cause of OGIB was found determined by the above named criteria. This scoring method is very similar to a previously used classification [10].

When CE did not show clear pictures of the intestine because of contamination and did not reveal abnormalities, the procedure was scored as failed. Most of these patients were given a second video capsule. However, when the recorded images were not optimal for inspection but did show abnormalities which may explain the indication, this procedure was scored as succeeded and scored as a definite or probable explanation.

Macroscopic signs of significant gastritis (including erosions and/or hematina) were considered a probable explanation for OGIB if no other abnormalities were found.
As atrophic gastritis, celiac disease and Helicobacter pylori infection possibly have a negative influence on iron and/or vitamin B12 absorption [3, 11], the first named finding on CE was also considered a probable cause of IDA if no other abnormalities were found in or outside the small intestine.

Statistical analysis

The statistical programme SPSS 14.0 (SPSS Inc., Chicago, IL) was used for all frequency analysis and descriptive statistics.

Results

Procedural aspects and safety

From February 2003 until June 2007 CE was performed 592 times, in 571 patients. The maximum recording time of 480 minutes was reached in the majority of patients. Mean transit time after ingestion of the capsule to reach the duodenum was 41 minutes (SD 60; range 0-480 min). Small bowel transit time was highly variable, ranging from as short as 7 minutes to longer than 8 hours, the maximum recording time of the capsule used in this study. The colon was reached in 77% of cases before batteries expired. Among the 592 CE procedures, failure occurred in 47 patients (7.9%). In this case, patients were re-examined and in most CE was repeated or other diagnostics methods were used for further evaluation. The reasons for failure are shown in Table I.

In 6 patients, the capsule was not spontaneously released with the stools. The indications to perform CE in these cases were IDA (n = 2), celiac disease (n = 2), macroscopic blood loss (n = 1) and Crohn’s disease (n = 1). In all cases, the entrapped CE was successfully retrieved with DBE [7]. In 5 of 6 patients an obstructing malignancy or polyps were the underlying cause of the retention; the patient with Crohn’s disease had benign fibrostenotic disease.

Diagnostic yield

A total of 240 patients were subjected to CE because of IDA. In 44% of these patients (n=106), a plausible explanation for the anaemia was found by CE. A plausible explanation is hereby defined as findings that were interpreted by the physician who reviewed the video as a ‘definite’ or ‘probable’ explanation for the anaemia (Table II). The abnormalities which were interpreted as a definite or probable explanation included the presence of blood or clots, angiectasia, erosions, or ulcers. In 120 (50%) patients, no explanation was found for the anaemia.

Subsequently, we analyzed the 142 patients who underwent CE because of overt GI bleeding (i.e. haematemesis, rectal blood loss or melena, or (sub)acute fall in Hb requiring transfusion). In this group of patients, the diagnostic yield of CE was somewhat higher (58%; n=82) as shown in Table 2. No explanation for the GI bleeding was found in 35%. In a subgroup of 20 patients who had substantial blood loss requiring blood transfusion, the diagnostic yield was 70% (14/20). According to the AGA guidelines, both GI bleeding and IDA are considered a cause of OGIB [3]. Therefore, in this study, when figures are combined, the detection ratio for OGIB by using CE is 49%.

Discussion

In the current study we retrospectively analyzed the first 592 CE procedures in a tertiary referral hospital over a period of almost 4 years, to study the diagnostic yield of this small bowel diagnostic modality for detecting the cause of OGIB.

In 382 CE procedures performed for OGIB in our study, a diagnostic yield of 49% was accomplished. This is in concordance with a recent publication in this journal [12] and a review by Concha et al [11], showing that the
diagnostic yield of CE varies from 32 to 76%. It is well established that patient selection and timing of the CE procedure largely influence outcome percentages [13-15]. Bresci et al [13] showed a detection rate of 92% when CE was performed within 15 days after diagnosing OGIB, compared to only 34% when CE was conducted more than 15 days after diagnosis. In the present study, referral time is variable. Negative performance of other small bowel diagnostic methods before CE may decrease the likelihood of positive findings on CE. As such other diagnostic methods may be performed more often in patients referred to tertiary hospitals, the detection level of CE may be underestimated. When these factors are taken into consideration, it is to be expected that the diagnostic yield of CE found in the present study may further increase when it is performed earlier in the diagnostic process of a patient with OGIB.

In the present study, a further subdivision of OGIB was made in obscure overt GI bleeding on one hand and obscure occult GI bleeding (IDA) on the other hand. In patients known to have IDA, the diagnostic yield was 44%, whereas detection ratios in patients with overt GI bleeding were somewhat higher (58%). This is in agreement with a study by Carey et al describing a smaller study population [16]. Angiectasia were the major cause of OGIB, both in IDA and GI bleeding subgroups.

This study has some limitations, one of them being its retrospective design. Diagnostic yield of CE might be influenced by many factors including severity of anaemia and the timeframe in which it develops. However, too little data in our patients with anaemia were available to report, mainly because of the retrospective design of our study and the fact that our hospital is a tertiary hospital for many surrounding clinics. Blood transfusion requirement may be another factor of influence on diagnostic yield. Indeed, the diagnostic yield in a subgroup of 20 individuals who required blood transfusion in this study was substantially higher than in the remaining patients with overt OGIB. Previous studies have also shown an association of detection levels with age [15] and anticoagulants [12]. The latter also seems to apply to the patients from our hospital (van Weyenberg et al, submitted).

An important observation in our study relates to the fact that with the use of CE not only abnormalities were identified in the small intestine, but also in the stomach and colon despite the fact that CE is not primarily intended to detect abnormalities in these organs. Thus, in 27% of patients with IDA and in 13% of patients with GI bleeding, the cause was found in either the stomach or colon. Recommendations to carefully review the entire recording time of CE or repeat GDS and colonoscopy before CE have been made before [17, 18], as this may result in finding lesions in 35-75% [11]. The results from our large cohort confirm these findings and support a repeat GDS before small bowel evaluation. Based on our data, adherence to these recommendations would result in anticipated detection rates for the small bowel of 32% for IDA and 50% for GI bleeding.

Of the 592 CEs performed in this study, 47 (7.9%) failed. Major causes are slow passage and/or retention of the capsule

### Table III. Abnormalities found in positive CEs in the small intestine in patients with obscure-occult and obscure-overt gastrointestinal bleeding.

<table>
<thead>
<tr>
<th>Abnormalities found in the small intestine</th>
<th>Number of abnormalities in obscure-occult GI bleeding (n = 77)*</th>
<th>Percentage of positive CEs with this abnormality</th>
<th>Number of abnormalities in obscure-overt GI bleeding (n = 71)*</th>
<th>% with this abnormality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiectasia</td>
<td>56</td>
<td>52.8%</td>
<td>42</td>
<td>51.2%</td>
</tr>
<tr>
<td>Erosion(s)</td>
<td>9</td>
<td>8.5%</td>
<td>16</td>
<td>19.5%</td>
</tr>
<tr>
<td>Ulcer(s)</td>
<td>9</td>
<td>8.5%</td>
<td>6</td>
<td>7.3%</td>
</tr>
<tr>
<td>Blood or clots</td>
<td>19</td>
<td>17.9%</td>
<td>34</td>
<td>41.5%</td>
</tr>
</tbody>
</table>

*more abnormalities in one patient possible.

### Table IV. Abnormalities found in positive CEs outside the small intestine in patients with iron deficiency anaemia (IDA) and gastrointestinal (GI) bleeding.

<table>
<thead>
<tr>
<th>Abnormalities found considered as the relevant explanation*</th>
<th>Number of abnormalities in IDA in the stomach (n = 24) or in the colon (n = 5)</th>
<th>Number of abnormalities in GI bleeding in the stomach (n = 8) or in the colon (n = 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormalities in the stomach</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Macroscopic signs of gastritis/erosions</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>Ulcer</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Hematin</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Blood</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Abnormalities in the colon</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angiectasia</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Erosions</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Blood</td>
<td>1</td>
<td>-</td>
</tr>
</tbody>
</table>

*in some patients more than one abnormality was found
in oesophagus or stomach (n = 16) and technical problems (n = 13). This indicates that performance can be improved significantly. A real-time viewer is now used for the early detection of stagnation in the stomach. If the capsule retains in the stomach, capsule progression can be stimulated by erythromycin [19] or endoscopic assistance [20]. The percentage of stomach retention in this study (1.0%) is in accordance with findings from the literature (1.7% up to 4.2%) [21, 22].

The non-excretion rates in the present study (1.0%) are in agreement with results from studies with strict exclusion criteria (0.8% to 1.9%) [23]. In 5 of 6 patients a (partially) obstructing tumour or polyp was found that could not be anticipated based upon history or prior investigation and therefore no patency capsule procedure was performed prior to CE. According to the literature, entrapped capsules are principally removed surgically. In our experience, all entrapped capsules could be successfully retrieved by DBE [7].

In conclusion, this study supports the importance of CE for the detection of causes of OGIB. With a diagnostic yield of 49% in a large tertiary study population using a structured scoring system, CE is suggested to be a valuable diagnostic modality after GDS and colonoscopy. Careful patient selection might be helpful in increasing diagnostic rates and repeating GDS and colonoscopy before CE might be preferred.

Conflicts of interest

There are no conflicts of interest regarding this study.

Contribution

Sietze van Turenhout had full access to all the data in the study and participated in the design, data acquisition, data analysis, data interpretation of the study as well as in writing of the manuscript and has the final responsibility for the decision to publish the study. Stijn van Weyenberg, Maarten Jacobs, Chris Mulder and Gerd Bouma participated in the design, data analysis and interpretation, supervision of the study and writing of the manuscript. Erik Herdes, Fred Stam and Gerd Bouma participated in the data acquisition. All authors have seen and approved the final version.

References