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ENDOSCOPY

Safety, Reliability, and Limitations of the Given Patency Capsule in Patients at Risk of Capsule Retention: A 3-Year Technical Review

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Abstract *Introduction* The patency capsule may prevent capsule retention in high-risk patients. However data on its use in routine clinical practice is limited. *Methods* Patients referred to our institution between Feb-04 and Jan-07 were reviewed. The following data was collected: presenting symptoms; medical/surgical history; medication; radiology; patency/video capsule result; subsequent investigations; clinical outcomes. *Results* 373 patients were referred. In 315 (84%) 'low-risk' patients (no patency capsule): delayed transit occurred in three, with no cases of capsule retention. In 58 (16%) 'high risk' patients (patency capsule): asymptomatic retention occurred in eight, all with pathology despite normal prior barium studies in six; in four cases patency location was incorrectly assessed radiologically, leading to video capsule retention and surgery in one. *Discussion* Most patients can safely undergo capsule endoscopy without a patency capsule. The patency capsule appears safe and is indicative of pathology when retained. Assessment of patency capsule location post ingestion can be difficult, and if barium radiology is equivocal a limited abdominal computed tomography (CT) scan is suggested.

Keywords Wireless capsule endoscopy · Patency capsule · Capsule retention · Barium follow-through X-ray · Limitations

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Introduction

Capsule endoscopy is emerging as the investigation of choice for obscure gastrointestinal bleeding [1–3] with promising data supporting its role for investigating suspected small-bowel Crohn's disease [4], assessment of refractory coeliac disease [5], small-bowel tumour detection [6] and polyposis syndrome surveillance [7]. Capsule endoscopy has proved to be safe and well tolerated by patients but capsule retention remains the most significant complication, occurring in approximately 0.75% of studies overall [8]. Retention is defined as the presence of a capsule within the gastrointestinal tract for more than 2 weeks and usually leads to some form of medical, endoscopic or surgical intervention [9]. Certain groups are considered to be at higher risk: patients with obstructive symptoms, known Crohn's disease, previous small-bowel surgery or chronic NSAID users [8, 9]. Retention typically indicates underlying pathology and is generally asymptomatic, although acute abdominal pain or obstruction due to capsule impaction has been reported [10, 11].

Barium radiography has been used to help assess small-bowel patency prior to capsule endoscopy for patients who are considered at risk of retention, but strictures may be missed [1, 9, 12, 13]. As an alternative screening test, Given Imaging Ltd. (Yoqneam, Israel) developed the patency capsule—a dummy pill swallowed by high-risk patients prior to capsule endoscopy. Successful excretion of the patency capsule indicates that capsule endoscopy can be performed safely, while retention of the patency capsule implies potential small-bowel stricturing disease is present and capsule endoscopy should not be performed. Published data on the safety, reliability and limitations of the patency capsule is limited and its role in clinical practice is unclear with wide variations in its use between capsule endoscopists [14–18].

The aim of this technical review was to clarify the role and optimal use of the patency capsule in routine clinical practice. Specifically, we examined:

(i) indications for patency capsule use;
(ii) safety of the patency capsule when retained and reliability for predicting underlying pathology;
(iii) accuracy of the patency capsule versus with barium enterography;
(iv) technical limitations of the patency capsule.

Methods

The records of all patients referred for capsule endoscopy to our centre between February 2004 and January 2007 were reviewed. The decision to use a patency capsule was based on the clinical referral letter and patient telephone interview with regard to presenting symptoms, medical and surgical history, medication use and previous radiological tests.

Our practice is to use a patency capsule in the following patients:

(i) documented Crohn's disease, including colonic and peri-anal disease, even if recent small-bowel radiology is unremarkable;
(ii) history of small-bowel resection;
(iii) typical obstructive abdominal symptoms (i.e. post-prandial colicky abdominal pain/bloating/vomiting);
(iv) chronic (>6 months) regular (non-aspirin) NSAID use;
(v) suspected strictures or adhesions on recent radiology (within 12 months).

A patency capsule was not used in a small minority of patients in whom there was a low clinical index of suspicion for obstructive disease and recent (within 12 months) small-bowel radiology was unremarkable. The second-generation Agile patency capsule was used in place of the first-generation M2A patency capsule from September 2006.

For the purposes of this review complete passage of the patency capsule was defined as the absence of the patency capsule on abdominal radiography performed at 30–36 h post patency capsule ingestion. Capsule retention was defined as retention of the video capsule within the gastro-intestinal tract for more than 2 weeks, requiring subsequent medical, endoscopic or surgical intervention. Delayed transit was defined as retention of the video capsule within the gastro-intestinal tract from between 72 h and 14 days post ingestion, with subsequent spontaneous passage. To identify these cases, abdominal radiography was performed in all patients who had not noticed the video capsule pass by 72 h post ingestion and in whom the colon had not been reached on review of the capsule video.

The Patency Capsule

The Agile patency capsule (Given Imaging Ltd., Yoqneam, Israel) is a dummy capsule identical in size to the PillCam SB small-bowel capsule (26 mm × 11 mm) with a radio-opaque lactose and barium body that contains a radiofrequency identification tag. In the event of retention the patency capsule is visible on an abdominal radiograph or is detectable using a handheld radio scanner which is passed over the abdomen. The patency capsule's resistant parylene coating is absent at both ends of the body, allowing luminal fluid access to two paraffin timer plugs that dissolve over 30 h, following which rapid disintegration of the rest of the patency capsule occurs. The M2A patency capsule had a single timer plug at one end only and disintegrated after 36 h (Fig. 1).

Ingestion Protocol for Patency Capsule

Patients considered at high risk of retention received a patency capsule by mail with instructions to swallow the Agile or M2A patency capsule either 30 or 36 h, respectively, before capsule endoscopy. An abdominal radiograph was performed at the end of this period, usually on the morning of capsule endoscopy. If the patency capsule was not visible on abdominal radiograph, capsule endoscopy was performed. If the patient experienced significant abdominal discomfort following ingestion of the patency capsule, or the patency capsule was still visible on abdominal radiograph, capsule endoscopy was not performed. Review of the abdominal radiograph was then undertaken by one of the

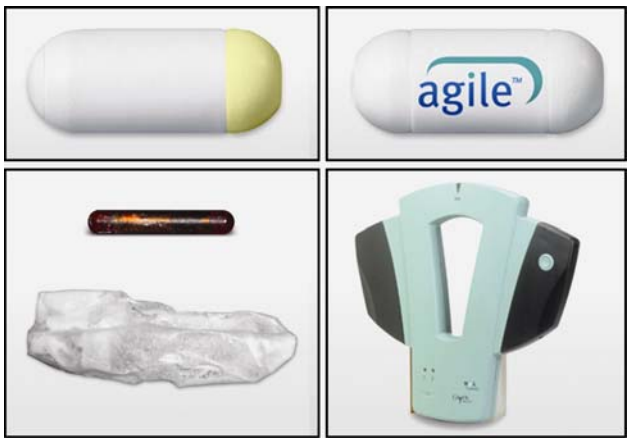

Fig. 1 M2A (top left) and Agile patency capsules (top right), disintegrated patency capsule with radiofrequency tag (bottom left) and patency capsule scanner (bottom right)

three experienced gastro-intestinal (GI) radiologists at our centre. If localisation of the patency capsule on abdominal radiographic appearance alone remained difficult, patients underwent same-day limited fluoroscopy following air or Gastrografin (Schering, UK) enema with insufflation of the rectum and sigmoid colon via a thin rectal catheter (16F Foley catheter) to localise the patency capsule to the small or large bowel. Capsule endoscopy was not performed if retention was suspected and alternative imaging tests (barium, CT or MRI enterography) were then organised.

Results

Three hundred and seventy-three patients were referred for capsule endoscopy [167 male (45%), 206 female (55%)] during the review period. Investigation of iron deficiency anaemia and/or obscure gastro-intestinal bleeding was the commonest indication in 174/373 (47%) patients followed by known or suspected Crohn's disease in 147/373 (39%) patients.

'Low Risk' for Capsule Retention

Of the patients, 315/373 (84%) were considered 'low risk' for video capsule retention and underwent capsule endoscopy without a prior patency capsule. The indications for capsule endoscopy in this group are shown (Fig. 2).

Significant findings were identified in 100/315 patients (32%). There were no significant complications or cases of video capsule retention requiring intervention in the 'low-risk' group. However there were three cases of delayed transit:

Case 1

A 51-year-old male with abdominal pain, bloating and positive faecal occult blood testing, and normal upper and lower endoscopies and barium enterography. The capsule was retained without symptoms within an inflamed and narrowed segment of ileum. Capsule images suggested active small-bowel Crohn's disease. Sequential abdominal radiographs documented passage of the capsule by day 17 without specific therapy.

Case 2

A 66-year-old female with recurrent iron-deficiency anaemia and chronic NSAID use. Normal upper and lower endoscopies and barium enterography. The capsule was retained without symptoms by several NSAID-related ileal diaphragms before spontaneous passage by day 7.

Case 3

A 73-year-old female with recurrent iron deficiency anaemia, systemic lupus and chronic NSAID use. Previous barium enterography suggested mucosal oedema in the ileum but no strictures. The retained capsule caused some mild abdominal discomfort for several days before entering the colon following oral administration of 200 ml Gastrografin used to localise the site of delay. Capsule images showed an NSAID-related ileal stricture.

'High Risk' for Capsule Retention

58/373 patients (16%) were considered to be at high risk of capsule retention and were given a patency capsule. The first 45 patients received an M2A patency capsule, while the remaining 13 patients received the Agile patency capsule. The indications for capsule endoscopy in these patients are shown (Fig. 3). Complete passage of the patency capsule (as demonstrated by absence of the capsule on abdominal radiograph) was achieved in 25/58 (43%) of patients. The patency capsule was still present on abdominal radiograph in the remaining 33/58 (57%) patients. Of these, true small-bowel retention of the patency capsule had occurred in eight patients (i.e. 14% of those given a PC or 24% of those in whom the PC was visible on abdominal

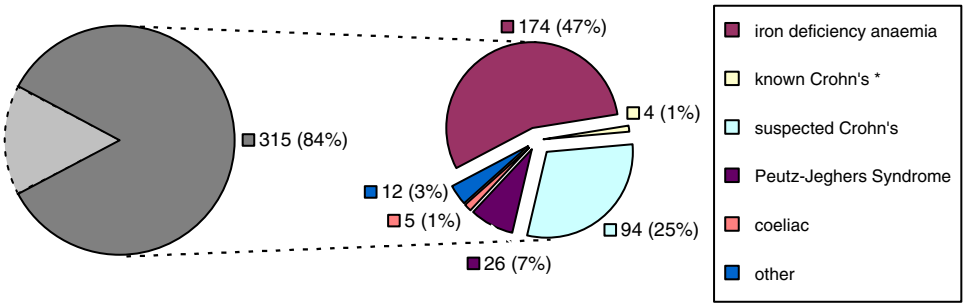

Fig. 2 Indication for capsule endoscopy ('low-risk' group)

* inadvertent inclusion in 'low-risk' group

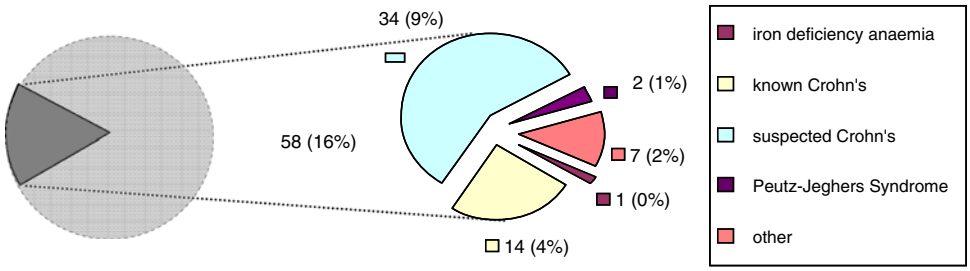

Fig. 3 Indication for capsule endoscopy ('high-risk' group)

radiograph). Of the 50/58 high-risk patients who did not retain the patency capsule, one patient declined subsequent capsule endoscopy and significant findings were identified in 16 of the remaining 49 cases (33%).

Safety and Reliability of Patency Capsule

No adverse symptoms or complications were associated with the patency capsule whether or not retention occurred. Subsequent investigation (barium x-ray, CT enterography or double-balloon enteroscopy) confirmed significant small-bowel pathology in seven of the eight patients who had retained the patency capsule (Table 1, Fig. 4), with the remaining patient declining further investigation. The patency capsule passed successfully in 50/58 (86%) patients, all but one of whom proceeded to uncomplicated capsule endoscopy (one patient declined subsequent capsule endoscopy).

Reliability of Barium Enterography for Assessment of Small-Bowel Patency

Six of the eight patients with patency capsule retention had undergone recent barium enterography before receiving a patency capsule. These had been reported either as normal (2/6 patients) or else showing only minor abnormalities (4/6 patients). In one patient a second barium enterography performed after their first patency capsule was retained was again reported as normal but subsequent CT enterography demonstrated stricturing ileal Crohn's disease. Of the 50 high-risk patients that passed the patency capsule, strictures were previously demonstrated by barium enterography in three patients: in two patients, capsule endoscopy was uneventful and in one patient transient hold up occurred before successful transit of the capsule.

Of the 315 low-risk patients in whom no patency capsules were used, there were three cases of delayed transit during capsule endoscopy as a result of small-bowel disease (cases 1, 2, and 3), despite no significant abnormalities being identified by previous barium enterography.

Limitations of the Patency Capsule

The patency capsule remained visible on abdominal radiography 30–36 h post ingestion in 33/58 (57%) patients, but only in 8/33 cases was the PC retained within the small bowel with the remainder (25/33) in the colon. Retention rates for the M2A and Agile patency capsules were similar. Localisation of the patency capsule either to the small or large bowel was made by the GI radiologist based on abdominal radiographic appearances alone in 17/33 (52%) patients. Additional imaging in the form of fluoroscopy with air or Gastrografin enema was required for the remaining 16/33 (48%) patients. Small-bowel retention of the patency capsule was initially reported by the radiologists in ten patients. However, final analysis revealed that, of these ten patients, three patency capsules were incorrectly localised to the small bowel when in fact they were in the colon (i.e. three false positives for retention), while one patency capsule was localised to the colon when in fact it was retained in the small bowel (i.e. one false negative). In the latter case this resulted in asymptomatic video capsule retention following capsule endoscopy in a 36-year-old male with Crohn's disease and long-standing obstructive symptoms. Treatment with a course of oral corticosteroids was ineffective and the patient subsequently underwent elective surgery (Fig. 5).

Discussion

Capsule retention is the main complication associated with capsule endoscopy, occurring in approximately 0.75% of all cases, but rates are higher for patients with a history of Crohn's disease, chronic NSAID use or small-bowel resection [8, 9, 19, 20]. Prior to the introduction of the patency capsule it was difficult to identify with confidence the patients for whom capsule endoscopy was contraindicated. Clinical symptoms suggestive of obstruction as described by patients are heterogeneous and not always reliable. Small-bowel radiology, in particular barium enterography may miss strictures [1, 9, 12, 13]. The development of the M2A patency capsule, superseded by the

Table 1 Details of the eight patients who retained the patency capsule (PC) in small bowel

Patient	Clinical history and presenting complaint	Prior radiology	Investigations after retained PC
1	59M previous lymphoma and small-bowel resection with recurrent obstructive symptoms	None	BFT: adhesion related jejunal hold-up with proximal dilatation
2	41F obscure GI bleeding and obstructive symptoms	BFT: possible thickening at ileo-caecal valve	Symptoms resolved and declined further investigation
3	33F eosinophilic enteritis and small-bowel resection with recurrent obstructive symptoms	BFT: thickened small-bowel mucosa	Double-balloon enteroscopy: two tight ileal strictures
4	34M Crohn's disease and small-bowel resections with chronic abdominal pain	BFT: 'featureless loop' of proximal ileum	Repeat BFT: active ileal Crohn's disease with stricturing
5	30F diarrhoea and anaemia. Minor ileal ulceration at colonoscopy of indeterminate histology	None	BFT: 30 cm of ileal Crohn's disease with luminal narrowing
6	43F Crohn's disease and small-bowel resection with recurrent obstructive symptoms	BFT: normal	Subsequent BFT normal. Repeat PC retained. CT enterography: stricturing ileal Crohn's
7	46F diarrhoea. Minor ileal ulceration at colonoscopy of indeterminate histology	BFT: terminal ileal inflammation	BFT: Spigelian hernia
8	36M Crohn's disease with recurrent obstructive symptoms	BFT: normal	CE retained in Crohn's stricture, confirmed on subsequent BFT

BFT—barium follow through X-ray; PC—patency capsule; CE—capsule endoscopy

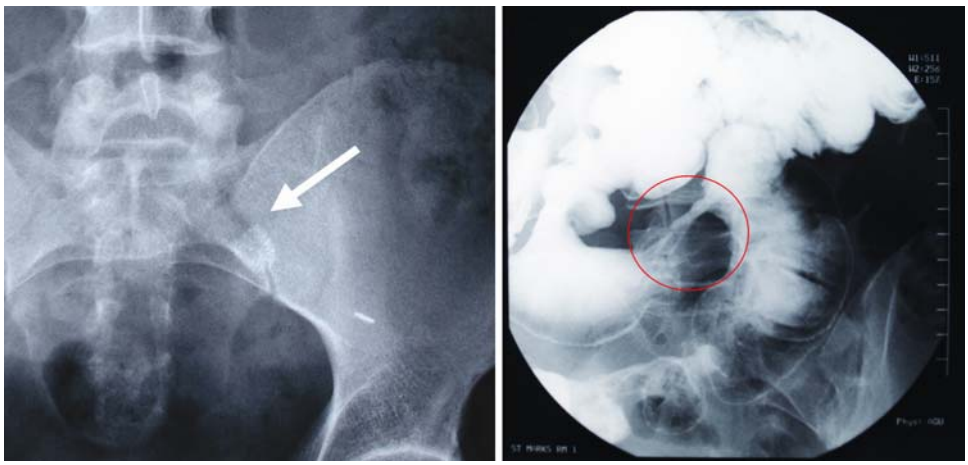

Fig. 4 34-year-old male with Crohn's disease. Retained patency capsule (left) and subsequent barium enterography (right)

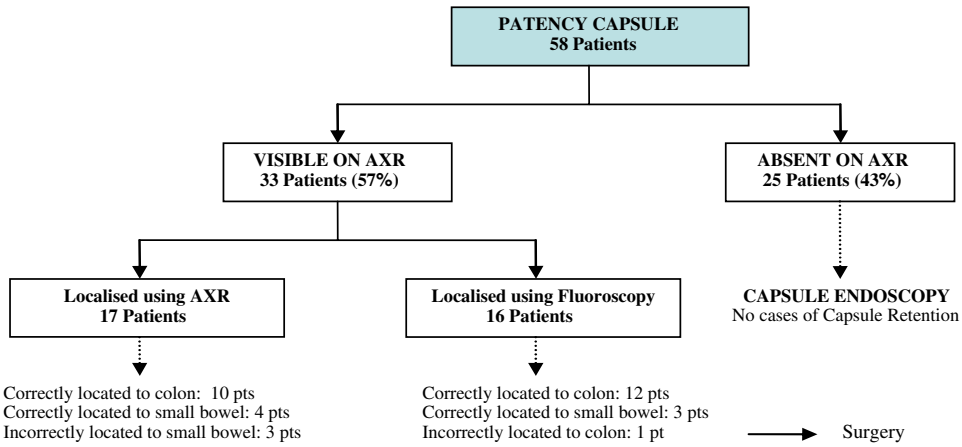

Fig. 5 Use of radiology for patency capsule localisation

Agile patency capsule, provides an alternative screening test for clinicians wishing to perform capsule endoscopy in patients considered to be at risk of retention.

Our review confirms that clinical criteria can be applied to determine the likelihood of capsule retention in patients referred for capsule endoscopy and that the majority of patients do not need a patency capsule. True patency capsule retention occurred in 14% (8/58) or one in seven of the high-risk group, and was most commonly due to Crohn's disease related small-bowel strictures. There were no adverse events resulting from the patency capsule whether retention occurred or not. In addition all patients in whom patency capsule transit was complete underwent subsequent capsule endoscopy successfully, and a high diagnostic yield was achieved in this group (33%).

Our data supports the widely reported observation that barium enterography can miss significant strictures and also that radiologically identified strictures may still be functionally patent. The two cases of delayed video capsule transit in chronic NSAID users with unremarkable preceding barium radiology suggests that a low threshold for patency capsule use should be considered in this patient group. A recent multicentre study of the Agile patency capsule in patients with known small-bowel strictures has examined the role of the patency capsule for identification of functionally patent, radiologically proven strictures to determine whether patients may still undergo capsule endoscopy [21, 22].

Currently there is little consensus regarding the approach to patients in whom the patency capsule is retained at 30–36 h post ingestion (on abdominal radiograph or by patency scanner). In the majority of such cases (60% in our review) it will be located in the colon. However if it is decided that capsule endoscopy is contraindicated at this point, it is likely that clinically relevant diagnoses will be missed or delayed in patients in whom capsule endoscopy would have been safe. Some authors have recommended retrieval of the excreted patency capsule over the following 48–72 h following careful stool examinations, with painless passage of an intact capsule suggesting functional patency of the small bowel [16, 18]. However, our preferred option is for immediate further radiological assessment to localise the capsule position to the small or large bowel. This has the significant advantage of allowing subsequent capsule endoscopy to be performed on the same day, which is both more convenient for the patient and allows for efficient running of a busy capsule endoscopy service. In contrast, self-examination of the stool in routine clinical practice is unlikely to be either popular or reliable, and would significantly reduce the appeal of an otherwise patient-friendly procedure. Furthermore capsules excreted after the 30 h time window may have already started to disintegrate, and as a result small-bowel luminal patency can no longer be confirmed with confidence [15, 16].

However, radiological assessment of patency capsule location is not without problems, with the main limitations being the high rate of incomplete transit, and the subsequent difficulty in accurate radiological localisation of the patency capsule to the small or large bowel (along with the associated risks of radiation exposure and the financial cost). We found that 57% of patency capsules were still present within the abdomen when assessed by abdominal radiography despite ingestion 30–36 h earlier. Subsequent accurate localisation of patency capsules to the small or large bowel in this situation is difficult when using two-dimensional plain abdominal radiographs alone and on occasion even with the assistance of additional fluoroscopy (with air or Gastrografin enemas). As a result if patency capsule location is not clearly demonstrated we currently perform an unprepared low-dose limited abdominal CT scan as an alternative to an air or Gastrografin enema following abdominal radiography.

There are also cost and safety implications with a patency capsule protocol that involves the use of radiology. The radiation exposure from an abdominal radiograph is relatively small at around 1 mSv (equivalent to 3 months of natural background radiation). However, those requiring further imaging, e.g. fluoroscopy with air or Gastrografin enema or limited abdominal CT, are exposed to an additional 2–4 mSv (8–16 months background radiation) [23]. In our opinion, the additional screening is worthwhile as the majority of patency capsules are in the colon by this point and these patients remain suitable for capsule endoscopy. In our review the use of a patency scanner would have avoided the initial abdominal radiograph in 25/58 (43%) patients in whom patency capsule transit was complete, and for this reason we recommend the use of this simple noninvasive technique for the initial assessment. However, subsequent radiological assessment would still have been required in 33/58 (57%) patients in whom the patency capsule was still present.

The Agile patency capsule's 30 h disintegration time is a compromise between achieving successful excretion while reducing the risk of symptomatic impaction, although this is a rare occurrence and did not occur in our at risk group. Complete excretion of the patency capsule occurred in only 43% of patients. In order to maximise excretion rates within this 30 h time window (and therefore minimise the need for further radiological assessment) we are currently investigating the use of bowel preparation for patients that require a patency capsule.

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