Small bowel enteroclysis with magnetic resonance imaging and computed tomography in patients with obscure delivery of patency capsule

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Abstract

Background. Video capsule enteroscopy (VCE) has revolutionised gastrointestinal endoscopy as it offers a detailed examination of the mucousa of the entire small bowel. Indirect small bowel examination with magnetic resonance imaging (MRI) and computed tomography (CT) enteroclysis have replaced conventional barium-based enteroclysis. A new indication for MRI and CT enteroclysis is the clinical suspicion of small bowel obstruction as indicated by delayed or non-delivery of a test capsule given before a VCE examination to exclude possible stenosing lesions. The aim of this study was to define the clinical value of subsequent MRI and CT examinations in patients in whom a test capsule did not present itself in due time.

Methods. Seventy patients were identified with a delayed or un-noticed delivery of the test capsule. These patients were subsequently examined with either MRI (44) or CT (26). All medical records and imaging studies were reviewed for the presence of symptoms, laboratory analyses and findings on the examinations.

Results. No abnormality was disclosed at follow-up enteroclysis in 60 and only minor organic abnormalities in 10. This observation would therefore allow a VCE to be carried out with no risk of the capsule becoming stuck. However, only 20 VCEs were finally performed and mainly in younger patients. In the rest of the patients, the referred physician got sufficient clinical information from the MRI and CT studies. In total, 8 cases of suspected Crohn´s disease were found. There was no correlation between symptoms and finding on imaging studies. Patients without alarm symptoms and pathological laboratory analyses did never show any erosions in the small bowel mucosa.

Conclusion. Our prime explanation for the intended VCE to be cancelled is that the MRI and CT enteroclysis reports are sufficiently informative for the clinician to base their clinical management, and thus omit VCE or at least postpone it for later usage.
Key words:
Small bowel, enteroclysis, magnetic resonance imaging, computed tomography, patency capsule, video capsule enteroscopy
Background

The least invasive imaging tool that demonstrates the mucous membrane of the whole small bowel in detail is the swallowable video capsule for enteroscopy (VCE). The capsule is an environmentally friendly, high-tech miniature endoscope, designed for spontaneous passage through the small bowel. Logically, VCE soon established itself as a first-line diagnostic procedure of small bowel diseases [1, 2] although it carries a minute risk of getting stuck. In order to avoid this calamity, a self disintegrating sham capsule, also known as the Patency Capsule (PC), equal in size and shape to the video capsule, was soon introduced to prove a non-obstructive small bowel passage. The capsule is naturally excreted within 18 hours. If not noted, a dedicated screening tool for external abdominal application is used to trace it. If screen outcome is positive or doubtful, a follow-up radiological examination of the small bowel is performed to rule out any stenotic lesion before a diagnostic VCE is contemplated. A retained PC will spontaneously disintegrate after 36 hours to prevent bowel obstruction.

Radiology of the small bowel is performed as an enteroclysis, either by means of magnetic resonance imaging (MRI) or computed tomography (CT). Both techniques are well established in routine medicine [3] and are highly sensitive for the detection of organic masses as well as extra-intestinal complications such as abscesses, fistulas and involvement of other organs [4-8]. MRI has the advantage of combining high diagnostic performance and lack of ionizing radiation and this is reflected in an increasing clinical demand. This series on MRI and CT examinations is part of our continuous audit of imaging techniques and diagnostic quality [9]. Our hypothesis was that after an unnoticed PC-delivery, or a true impaction of the PC, the diagnostic value of follow-up examination with MRI or CT is sufficiently comprehensive for the
clinician to waive or postpone the intended VCE for later use. To the best of our knowledge no such information is available in the literature.

Thus, our primary aim of this study was to define the clinical value of subsequent MRI and CT examinations in patients in whom a test capsule did not present itself in due time.
Methods

All medical data were dealt with in agreement with the ethical principles for medical research established in the Helsinki Declaration of 1975 and as per standard practice at our department. The study was approved by the Ethics committee and patients gave their informed consent to let us dispose their clinical files and small bowel images for this partly retrospective review.

Study design

Consecutive out-patients from the Department of Gastroenterology at our University Hospital with clinically suspected or known disease of the small bowel, mostly Crohn’s disease, were retrospectively included in this study. All had an initial PC-test that resulted in a late or unconfirmed excretion of the capsule. These patients were subsequently examined with either MRI or CT. Patient recruitment extended over a three year period from January 1, 2005, until January 31, 2008, with a further follow-up period stretching until mid 2010. Seventy-five consecutive patients were informed by letter. Seventy agreed to participate.

All appropriate medical records and imaging studies were reviewed and following data per patient were noted: gender, age at the clinical consultation, duration and type of symptoms (abdominal pains, diarrhoea, weight loss, nausea and anaemia), laboratory analyses (hemoglobin, C-reactive protein (CRP), leukocytes, orosomucoid and albumin in serum, and calprotectin in feces), indication for the intended VCE, passage delay of PC, type, quality and diagnoses of imaging studies. Duration of patients’ symptoms until time for to the PC-test, often only given as an estimate in the medical files, were classified as symptoms for less than 12 months, up to 29 months, and longer. Following symptoms and signs were classified as alarm symptoms: weight loss,
haematochezia, anemia, nocturnal diarrhoea, ileus, fistulas and abscesses. In case a final VCE had been performed, its indication was registered and diagnosis considered to be the true one. Time between various examinations was calculated.

The diagnostic accuracy of MRI and CT enteroclyses were bio-statistically calculated, defining true diagnoses to be primarily based on endoscopic follow-up procedures, otherwise on clinical observations during up to 24 months after the latest imaging procedure.

**MRI- and CT-Enteroclysis**

The following technical considerations were valid for both methods: patients were allowed free fluid but otherwise nil by mouth after midnight. After lubrication of the nasal mucosa with lidocaine hydrochloride 2% gel (Xyloxeine®, AstraZeneca, Gothenburg, Sweden) a 13-F naso-jejunal catheter was advanced under fluoroscopic guidance beyond the duodeno-jejunal junction. No conscious sedation was used. Adequate small bowel luminal distension was achieved by infusing an iso-osmotic polyethylene glycol solution. It is neutral on CT images (HU = 0), black on T1-weighted MR-images and white on T2. The infusion rate was adjusted to 100 ml/min to a total of 1500 +/- 250 ml, and administered via an electric roller pump (Watson Marlow 323®, Wilmington, MA, USA). Lesion detection was improved by the administration of an intravenous contrast agent. Scanning commenced when caecal filling was established and peristalsis eliminated (20 mg Buscopan® (Boeringer Ingelheim, Stockholm, Sweden) or 0.3 mg Glucagon® (Novo Nordic, Malmö, Sweden) intravenously).
Magnetic resonance imaging (MRI)

MRI was performed on a 1.5 Tesla MR-system (Magnetom Symphony, Siemens Medical Solutions, Erlangen, Germany), with a phased array coil with four elements being placed on the abdomen. The transit of the polyethylene solution was monitored with a turbo spin-echo T2 weighted half Fourier acquired single-shot turbo spin echo (HASTE) sequence, and motility was studied with a coronal dynamic true fast imaging with steady-state precision (true FISP) sequence [10]. Small bowel morphology was examined with a true FISP sequence (TR/TE 6ms/3ms, slice thickness 3mm) and HASTE images (TR/TE = infinite/90 ms, slice thickness 5mm) applied in axial and coronal planes; image matrix 256 x 256. Following intravenous application of 0.2mmol/kg bodyweight Gd-DOTA meglumine (Dotarem®, Guerbet, Aulnaysous-Bois, France) a coronal 2D gradient-echo (FLASH) sequence with fat saturation (TR/TE = 103/7.2 ms, thickness 4mm, image matrix 256 x 512) during breath holding was applied [6].

Computed tomography (CT)

All patients received an intravenous injection of 120 mls of iohexol (Omnipaque®, GE Healthcare, Oslo, Norway) with an iodine concentration of 300 mgJ/ml. The rate of injection was set at 4 ml/s with an automatic power injector followed by a saline flush of 50 ml. The volumetric acquisition was performed in the late arterial dominant phase, 35s after start of injection. CT-scanning was performed on a multi channel detector CT (Somatom Sensation 16, Siemens Medical Systems, Erlangen, Germany) in prone position, from dome of diaphragm to pubic symphysis. Scan parameters were 16 x 0.75mm collimation with a reconstruction interval of 1.0mm, rotation time 0.5s, tube
voltage 100 kV and 240mAs. Reformats at 3mm in transverse, coronal and sagittal planes were sent to the picture archiving system [11-14].

**Evaluation of enteroclysis**

All MRI- and CT-enteroclysis examinations were re-evaluated by two radiologists, one of whom board-certified and specialised in gastrointestinal radiology and endoscopy. The overall image quality and small bowel distension was defined as good, sufficient or insufficient separately for the duodenum and jejunum, the proximal and mid-ileum, and the distal and terminal ileum.

The enteroclyses were all reclassified and following features were looked for: masses, stenotic lesions, pre-stenotic dilatation, regional contrast enhancement of the mucous membrane and gut wall as compared to unaffected parts and nearby vessels, mucosal surface irregularities, mural and transmural involvement, fissures, engorged vessels and fibrofatty proliferation of the mesentery and abnormalities of the peritoneum. Radiologic signs were summarised into three groups, those compatible with Crohn’s disease, an alleged bleeding source, and miscellaneous findings such as adhesions, benign adenopathy, impaired peristalis in an otherwise normal small bowel, and other non-specific observations.

**Video capsule endoscopy (VCE)**

The Given Diagnostic Imaging System® (Yoqneam, Israel) consists of the PillCam SB capsule, which includes a miniature video camera, an external antenna with attached portable computer, and a workstation with appropriate software for review, interpretation, and reporting of images. The capsule provides 2 frames per second over about 8 hours, at 1:8 magnifications, with a
140° field- and 1 to 30 mm depth of view. The capsule is passively progressed through the gastrointestinal tract and excreted the natural way. The patients fasted overnight before swallowing the capsule. They were advised to drink liquids after 2 h and have a light meal after 4 h. The patients wore a belt with a power supply and a small hard drive for receiving images. Before ingesting the capsule, a sensor array was fixed to the patient’s abdominal wall and connected to the hard drive. The patients were encouraged to live as normally as possible during the 8 h video recording. The equipment was returned to the Endoscopy Unit the following day, and the data downloaded to a computer for evaluation. The video recordings, featuring more than 50 000 images, were down-loaded from the portable recorder to the workstation. After an evaluation about one hour requiring the physician was able to save images and create reports to be viewed and printed. The RAPID™ application software also provided a localization diagram of the capsule’s progress through the small bowel [15]. A PC was used to establish free passage through the small bowel tract before the proper VCE.

VCE offers a magnified view of the small bowel mucosal lining, i.e. tiny capillaries and small clusters of villi are disclosed in coloured detail. Superficial lesions and any bleeding source are readily detected. A normal lumen width is in most instances easy to evaluate, whereas the reason for a narrowed lumen is more difficult to rule out, be it thickened mucosa, fistulous opening or an extra-intestinal manifestation, as VCE cannot reveal any pathologic processes beyond the mucosa itself [16].
Statistical analyses

Fisher’s exact test was used to calculate associations between the presence of alarm symptoms, laboratory analyses and findings on examinations. P<0.05 was considered statistical significance.

Results

Patient characteristics

Seventy patients, 50 women and 20 men, mean age 45 years, range 10-83 years (Table 1), were finally included in this series, all with a non-documented passage of the PC. Five patients had difficulties in swallowing the PC; one patient with neurogenic swallowing dysfunction had the PC deposited in the duodenum through gastroscopic deliverance. The clinical indications for the intended VCE were Crohn’s disease in 47 patients, small bowel bleeding in 13 patients, and abdominal discomfort, mainly related to bowel dysfunction, in 10 patients.

Patient history was less than 12 months in 22 patients, up to 29 months in 24 others, and more than 30 months in 22. The distribution of patients to small bowel findings at enteroclyses and VCEs is given in Figure 1.

Magnetic resonance imaging (MRI) and computed tomography (CT)

The series includes 44 MRI- and 26 CT-enteroclysis examinations. Fluoroscopy of the abdomen before the MRIs showed no trace of a retained PC. The quality of radiological examinations was rated excellent in 64 cases, sufficient for diagnosis in four (one CT and three MRI examinations) and suboptimal in two female patients, one of whom later had a second PC prior to
a final VCE. The other woman was re-evaluated clinically with no further imaging study requested.

No abnormality was found at MRI- and CT-enteroclyses in 60 out of 70 patients, including all 13 cases of clinical occult bleeding and nine of 10 cases with abdominal discomfort. Signs of Crohn’s disease were revealed in six cases out of 47 with the same clinical diagnosis. Miscellaneous findings were revealed in four other cases on MRI examination where the diagnoses were: adhesions in two patients after bowel resection for Crohn’s disease, increased number of normal mesenteric lymph nodes in one and increased contrast enhancement of normal sized, mesenteric lymph nodes in a fourth patient; both the latter demonstrated normal follow-up VCEs. Pathologic findings to gender are evident from table 2.

**Video capsule enteroscopy (VCE)**

Twenty-three patients were finally referred for a VCE examination (Figure 1). The clinical indications were Crohn’s disease in 15 patients; occult bleeding in five patients, and other indications in three. At study end no VCE had been carried out in three: two patients refused the examination and one was cancelled by the referring clinician. Hence 20 VCEs were left for analysis, accomplished in 15 of 44 patients previously investigated with MRI (34%), and five of 26 patients examined with CT (19%). Half of them were done in young patients up to 30 years of age. Pathologic findings at VCE were documented in five women and three men (Table 2).

In 15 patients with clinically suspected Crohn’s disease, final VCE verified the disease in four. Only one of them had signs of Crohn’s disease on MRI, giving three new cases. Two of these had jejunal erosions on VCE, so far
not further verified. On MRI examination 14 days earlier one of these two had
an increased number of normal mesenteric lymph nodes but no signs of
inflammatory bowel disease at a follow-up ileocolonoscopy examination four
months later. VCE in the third patient showed minimal changes in the
duodenum and numerous erosions in the terminal ileum. A follow-up
ileocolonoscopy performed two months later revealed tiny petechiae and
histology of obtained biopsies from terminal ileum revealed nothing but
lymphatic hyperplasia.

The VCE revealed NSAID type of erosions and mucosal scarring in one
patient; subtle inflammation in the terminal ileum and a tiny ulcerated polypoid
lesion in another, and non-specific mild ileitis with a single small ulcer in a
third patient with normal MRI and ileocolonoscopy studies. The last patient
had previously undergone surgical removal of a duodenal cancer and presented
with gastric retention at VCE. In the five patients with clinically suspected
occult bleeding, no abnormalities were revealed at VCE.

At study end

In 50 of 70 patients, 71%, none of the primarily intended VCE
examinations was ever performed. Of the 10 patients, initially referred for
“abdominal discomfort”, the intended VCE was never performed in eight. The
same was true for seven of nine patients with an abnormal MRI (Figure 1).
Morphologic signs of abnormality based on one of three imaging techniques
were disclosed in 17 patients, 12 under age 50, five men and 12 women.
Pathology was demonstrated by two methods in one male patient. The mean
time between the PC-test and enteroclysis was 3 months, range 0 – 18 months,
and between enteroclysis and final VCE-examination 1.5 months, range 0.5 to
four months in 18 patients. The time lag for the last two patients exceeded 23
months. Seven of ten patients with abnormal findings had examination in close connection with their referral, although no significance could be proven.

No correlation between alarm symptoms and morphologic findings could be established by any of the three imaging modalities (data not shown). In contrast, elevated calprotectin levels in feces were associated with an abnormal VCE (p=0.009) and pathological laboratory analyses were associated with an abnormal MRI (p=0.05). All patients without alarm symptoms and with normal laboratory analyses had also normal examinations (data not shown).

**Complications and limitations**

The only complication was a non-serious esophageal contact bleeding after gastroscopic delivery of a PC to the duodenal cap in one dysphagic patient. One patient refused VCE because of fear of the capsule getting stuck and two enteroclyses were technically suboptimal.
Discussion

This study showed that none of the patients with undelivered PC had any gastrointestinal obstruction. Furthermore, the majority of patients were never referred for the planned VCE after that MRI and CT examinations had been performed.

Continuous quality control of imaging techniques and diagnostic performance is important for patient safety and sound utility of expensive imaging procedures. We have observed an increasing number of patients referred for MRI- and CT-enteroclyses after being tested with a PC as a security measure before an intended VCE. We were asked to rule out any organic or functional small bowel reason for the delays in PC delivery. As evident from our results, 60 of 70 consecutive patients had normal enteroclyses studies. What happened to these patients next? What was the clinician’s understanding of our cross-sectional imaging results, and what impact had these on patient management? As no such information was found in the literature, we undertook this partly retrospective study to get a qualified estimate of the clinical value of our imaging performances.

VCE has proven to be the most effective examination in depicting small bowel mucosal lesions, including subtle signs of chronic inflammatory diseases [17] and obscure bleeding [18]. New capsule endoscopes designed for esophageal and colonic exploration are being introduced on the market [19]. In patients with a risk of capsule retention (4%), total enteroscopy is still possible in more than four out of five patients [20, 21]. Small bowel neoplasia remains rare but half of them might be revealed by VCE, i.e. VCE is diagnostically
more efficient than any other imaging modality [22]. The overall diagnostic success with VCE has allowed gastroenterologists to proclaim VCE to be a first line procedure in ruling out small bowel disease [23]. However, the detailed depiction of the inner gut surface with VCE sometimes gives rise to interpretation difficulties as the specificity for detecting Crohn’s disease is only 53% [24]. Accordingly, erosions of the small bowel do not ultimately lead to a diagnosis of Crohn’s disease [25]. In the present study we encountered three such cases with alleged erosions in the terminal ileum, not confirmed at subsequent ileocolonoscopies.

We were able to make two interesting observations. One was that no organic lesion was diagnosed by us in 60 cases by MRI and CT, i.e. the imaging results did not mirror the clinical suspicion of active small bowel disease. The other was that in most cases the gastroenterologist did not proceed with the primarily intended VCE examination, neither to confirm imaging results nor to verify their preliminary clinical suspicion. It was evident from notes in the patients’ files that the results of MRI and/or CT together with a clinical re-evaluation of the patient’s situation, gave the gastroenterologist sufficient data not to undertake further enteroscopies.

In a patient with biopsy proven diagnosis of inflammatory bowel disease, future examinations of the bowel are probably more focused on complications than on confirmation of diagnosis. In a case like that, case cross sectional imaging with MRI or CT ought to be performed before deciding on a VCE, saving the costs for at least a PC. Furthermore, a strategy that spares a VCE examination, especially when preceded by a PC, would save health care costs and minimize inconveniences, at least for the few and selected patients.
Patients under age of 45 years are, at our department, allocated to MRI, and older ones to CT. As Crohn’s disease mostly starts in a younger patient group, signs of active Crohn’s disease are found more often with MRI than with CT. Crohn’s disease is established when verified endoscopically and proven at microscopy of biopsy specimen [26]. Early diagnosis of Crohn’s disease is important as tailored treatment is of importance both to reverse active disease and prevent complications. Younger patients with symptoms attributed to the small bowel are likely to harbour early and superficial lesions, that might be difficult to reveal on MRI and CT examinations, but visible on VCE. A thorough diagnosis is difficult in early disease, mirrored in our series by the observation that referring doctors seemed to be more prone to send younger patients to a final VCE after MRI-enteroclysis, 15 cases, than after CT, five cases.

All patients were selected and referred by gastroenterologists from one hospital. The fact that the sample population consisted of 2.5 times as many women (50/20) suggests that there might be an imbalance in the inclusion process of patients with a failed PC tests. The skewed selection may partly be explained by the limited size of our sample population. However, reports in the literature indicate that women seek health care services for their symptoms more frequently than men, not least for symptoms related to the intestines [27]. The total amount of pathological diagnoses was 23% in women and 20% in men, which may indicate that men are less prone to seek health services. Furthermore, it has been shown that women have longer bowel transit times than men, which may indicate that the acceptable PC-transit time in women ought to be longer than the 48 hours stated [28].
Given the limited size of our material sample, e.g. only 8 cases of established Crohn’s disease, solid statistical analyses of the temporal aspects of various diagnostic delays were not possible to fulfill. However, patients diagnosed with Crohn’s disease had examinations performed closer in time than the others. Analysis of our data could not disclose any correlation between clinical symptoms and findings at imaging examinations.

**Conclusion**

No small bowel obstruction was revealed in any of our 70 patients with PC retention. It seems justified to conclude that the diagnostic value of MRI and CT is sufficient for clinical management of most patients with alleged small bowel disease. We were able to document that an intended VCE for ruling out small bowel disease was cancelled or postponed in two out of three cases and that almost half of the VCEs performed confirmed the diagnoses from preceding MRI and CT enteroclyses. This might save a considerable amount of health care resources for the better use in other patients. It is unknown to us to what extent any additional diagnostic information from the MRI- and CT-examinations influenced clinical decision making. Patients without alarm symptoms and pathological laboratory analyses should primarily not be referred to further examinations.

**Lists of Abbreviations:**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>CT</td>
<td>Computed tomography</td>
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<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
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<td>PC</td>
<td>Patency capsule</td>
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<td>VCE</td>
<td>Video capsule enteroscopy</td>
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Competing interests

The authors declare that they have no competing interests.

Authors´contributions

FTF: Initiating the study, tutoring NK and SK, finalizing the manuscript

NK: Collecting clinical and imaging data

SK: Second reader of imaging studies

BO: Interpreting medical data, statistical analysis, contributing to the
manuscript

Acknowledgements

This study was supported by grants from the Development Foundations of
Region Skane (BO).
References


Legends to figures

Figure 1. Flow chart of patients and examinations. Figures denote number of patients and gender (male/female). N= normal; abN= abnormal; 0= not examined. A final video capsule enteroscopy (VCE) was not considered necessary after magnetic resonance imaging (MRI)- and computed tomography (CT)-enteroclysis in 71% (50/70 patients)
Tables

Table 1. Number of patients related to age-, gender and method of enteroclysis

<table>
<thead>
<tr>
<th>Age group</th>
<th>N</th>
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<th>CT</th>
<th>Final VCE</th>
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<td>TOTAL</td>
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<td>34</td>
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N=number of patients, MRI=magnetic resonance imaging, CT=computed tomography, VCE=video capsule endoscopy
**Table 2.** Diagnostic results related to gender, age and method of examination

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Sub-total</th>
<th>Gender</th>
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<tr>
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<tr>
<td></td>
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<td>4</td>
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<td>16</td>
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<tr>
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<td>1</td>
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CD = Crohn’s disease; M = miscellaneous findings (adhesion, stricture, diverticulae, etc.)
Figure 1