

## Non-small-bowel abnormalities identified during small bowel capsule endoscopy

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**Author contributions:** Hoedemaker RA and Westerhof J acquired the data, performed statistical analysis and wrote the manuscript; Weersma RK and Koornstra JJ were responsible for the study concept and design, and were involved in editing the manuscript.

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Received: August 30, 2012 Revised: April 20, 2013

Accepted: May 18, 2013

Published online: April 14, 2014

### Abstract

**AIM:** To investigate the incidence of non-small-bowel abnormalities in patients referred for small bowel capsule endoscopy, this single center study was performed.

**METHODS:** Small bowel capsule endoscopy is an accepted technique to investigate obscure gastrointestinal bleeding. This is defined as bleeding from the digestive tract that persists or recurs without an obvious etiology after a normal gastroduodenoscopy and colonoscopy. Nevertheless, capsule endoscopy sometimes reveals findings outside the small bowel, *i.e.*, within reach of conventional endoscopes. In this retrospective single center study, 595 patients undergoing capsule endoscopy between 2003 and 2009 were studied. The incidence of non-small bowel abnormalities was defined as visible abnormalities detected by capsule endoscopy that are located within reach of conventional endoscopes.

**RESULTS:** In 595 patients, referred for obscure gas-

trointestinal bleeding or for suspected Crohn's disease, abnormalities were found in 306 (51.4%). Of these 306 patients, 85 (27.7%) had abnormalities within reach of conventional endoscopes; 63 had abnormalities apparently overlooked at previous conventional endoscopies, 10 patients had not undergone upper and lower endoscopy prior to capsule endoscopy and 12 had abnormalities that were already known prior to capsule endoscopy. The most common type of missed lesions were vascular lesions ( $n = 47$ ). Non-small-bowel abnormalities were located in the stomach ( $n = 15$ ), proximal small bowel ( $n = 22$ ), terminal ileum ( $n = 21$ ), colon ( $n = 19$ ) or at other or multiple locations ( $n = 8$ ). Ten patients with abnormal findings in the terminal ileum had not undergone examination of the ileum during colonoscopy.

**CONCLUSION:** A significant proportion of patients undergoing small bowel capsule endoscopy had lesions within reach of conventional endoscopes, indicating that capsule endoscopy was unnecessarily performed.

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**Key words:** Capsule endoscopy; Small bowel; Findings; Colon; Stomach

**Core tip:** Capsule endoscopy (CE) is a technique to detect small bowel pathology which sometimes reveals non-small bowel abnormalities (NSBAs). There are no data on the incidence of NSBAs in capsule endoscopy. In this study, 595 capsule endoscopy procedures were included. Abnormalities were found in 306 (51.4%) of cases. Of these 306 patients, 85 (27.7%) had abnormalities within reach of conventional endoscopes. The fact that a significant proportion of patients referred for small bowel CE had lesions within the reach of conventional endoscopes indicates that CE was unnecessarily performed and emphasizes the importance of critical selection of patients for capsule endoscopy.

Hoedemaker RA, Westerhof J, Weersma RK, Koornstra JJ. Non-small-bowel abnormalities identified during small bowel capsule endoscopy. *World J Gastroenterol* 2014; 20(14): 4025-4029 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v20/i14/4025.htm> DOI: <http://dx.doi.org/10.3748/wjg.v20.i14.4025>

## INTRODUCTION

Small bowel capsule endoscopy (CE) has become an established method for visualization of the small bowel<sup>[1-4]</sup>. One of the main indications for CE is obscure gastrointestinal bleeding. Obscure gastrointestinal bleeding is defined as bleeding from the digestive tract that persists or recurs without an obvious etiology after a normal esophagogastroduodenoscopy and colonoscopy<sup>[1]</sup>. It can be categorized into overt and occult obscure gastrointestinal bleeding based on the presence or absence of clinically evident bleeding. Approximately 5% of patients presenting with gastrointestinal bleeding have no identified source on upper endoscopy and colonoscopy<sup>[1]</sup>. The cause of obscure gastrointestinal bleeding is usually a lesion located in the small bowel, but also includes lesions that were overlooked during conventional endoscopy, either because of intermittent bleeding or truly missed lesions. Another important indication for small bowel capsule endoscopy is suspected Crohn's disease (CD). Usually, prior to the procedure, colonoscopy is being performed, preferably including endoscopic inspection of the terminal ileum. So, most patients referred for small bowel capsule endoscopy have undergone conventional endoscopies prior to the procedure.

Another method to investigate the small bowel is single- or double balloon enteroscopy<sup>[5,6]</sup>. As in capsule endoscopy, most patients referred for balloon enteroscopy have undergone conventional upper and lower endoscopy before the procedure is conducted<sup>[7]</sup>. It is known that balloon enteroscopy reveals abnormalities within reach of conventional endoscopes in up to 15%-24% of patients<sup>[8,9]</sup>. These findings are generally referred to as non-small-bowel abnormalities (NSBAs)<sup>[8-10]</sup>. There are no firm data on the incidence of NSBAs in capsule endoscopy. The aim of this study was therefore to determine the incidence of findings within reach of conventional endoscopes in patients referred for CE.

## MATERIALS AND METHODS

### Patients and techniques

Data from all consecutive CE studies performed at the University Medical Centre Groningen, the Netherlands, between September 2003 and January 2009 were prospectively collected. Our hospital is a tertiary-care centre with a referral base drawing from the northern part of the Netherlands. Data were collected on patient demographics, indications for the procedure, procedural

data, including gastric and small bowel transit time, and findings of the procedure. CE was considered complete when the cecum was reached within recording time. NSBAs were defined as all abnormal findings found at capsule endoscopy located in the stomach, proximal small bowel, terminal ileum, and colon. Data were retrieved with respect to the extent and number of endoscopies performed prior to CE and whether or not ileoscopy was performed during colonoscopy. In case of missing data from externally referred patients, the referring hospital was contacted or visited.

### CE procedure

All patients received the same bowel preparation during the study period. The patients were given standardized instructions before the procedure, and informed consent was obtained. The patients were asked to stop iron supplements seven days before CE and to use a low-fiber diet 3 d before CE. The patients started a fasting period at midnight before the procedure. Bowel preparation consisted of four liters of polyethylene glycol (PEG), given as 3 L the evening before the procedure and 1 L in the morning. The capsule (Pillcam; Given Imaging Ltd, Yoqneam, Israel) was swallowed in the morning. The patients were allowed to drink fluids after 3 h and to consume a light meal after 5 h. Before capsule ingestion, 100 mL of antifoam and a prokinetic agent was given, 10 mg of domperidone (before July 1<sup>st</sup> 2008,  $n = 641$ ) or 250 mg of erythromycin (after July 1<sup>st</sup> 2008,  $n = 69$ ). All CE procedures were reviewed by two gastroenterologists, experienced with capsule endoscopy (Weersma R and Koornstra JJ). Controversial findings were discussed, and consensus was reached upon the final diagnosis. The most relevant findings obtained from CE were documented and categorized according to standard terminology (10) as angiectasia(s); ulcer(s); active bleeding of unknown origin; erosion(s); polyp(s)/tumor(s); incidental abnormality of esophagus, stomach, or colon; no abnormality; or unable to make a diagnosis.

### Statistical analysis

*P* values below 0.05 were considered significant. SPSS 14.0 for Windows software (SPSS Inc., Chicago, IL, United States) were used for statistical analyses.

## RESULTS

During the study period, 710 capsule endoscopy procedures were performed in 674 patients. 389 patients were female (54.8%) and the average age was 55 years (range 9-93, SD 18). Most of the patients were referred for capsule endoscopy for analysis of obscure-occult gastrointestinal bleeding ( $n = 392$ , 55.2%), obscure-overt gastrointestinal bleeding ( $n = 87$ , 12.3%) or suspected CD ( $n = 116$ , 16.3%). Given the aim of our study, further analysis was limited to these 595 patients. 331 patients (55.6%) were referred by physicians from other hospitals.

**Table 1 Findings of capsule endoscopy procedures (595 procedures) *n* (%)**

Procedures	<i>n</i> = 595
No abnormalities	289 (48.6)
Angiodysplasia(s)	115 (19.3)
Erosion(s)	68 (11.4)
Ulcer(s)	34 (5.7)
Polyp/tumor	31 (5.2)
Active bleeding	28 (4.7)
Other	30 (5.0)

### Previous examinations and capsule endoscopy findings

Patients had undergone a mean number of 1.1 (range 0-5) esophagogastroduodenoscopy procedures and 1.1 (range 0-9) colonoscopy procedures prior to capsule endoscopy. During colonoscopy, the terminal ileum had been intubated in 41.2% of patients. In addition to conventional endoscopy procedures, 20.6% of patients had undergone a small-bowel-follow-through examination and 9.9% of patients had undergone a push-enteroscopy prior to CE. The cecum was reached within recording time in 487 (81.8%) of capsule endoscopy procedures. Findings of capsule endoscopy are summarized in Table 1. In 291 CE procedures, abnormalities were found. The most common abnormal findings were angiodysplasias (*n* = 115, 19.3%) and erosion(s) (*n* = 68, 11.4%).

### Non-small-bowel abnormalities

In 85 patients (14.3%), abnormalities were found within reach of conventional endoscopes, summarized in Table 2. In most patients (*n* = 63, 10.6%), this concerned unknown abnormalities in patients that had undergone both gastroduodenoscopy and colonoscopy prior to CE. In 10 patients (1.7%), NSBAs were found while patients had not undergone esophagogastroduodenoscopy and ileocolonoscopy prior to CE and in 12 patients (2.0%), NSBAs were found that were already known prior to capsule endoscopy. NSBAs were located in: stomach (*n* = 15), duodenum (*n* = 12), proximal jejunum (*n* = 10), terminal ileum (*n* = 21), colon (*n* = 19) or at other or at multiple locations (*n* = 8). The types of lesions encountered are summarized in Table 2: angiodysplasias (*n* = 32, 37.6%), erosion(s) (*n* = 16, 18.8%), active bleeding (*n* = 15, 17.6%) and inflammatory lesions (*n* = 12, 14.1%). 59 of 85 patients (69.4%) with NSBAs concerned patients referred from other hospitals. CD was suspected in 116 of 595 patients (19%). Abnormalities in the terminal ileum were seen in 39 patients (33.6%). In only 12 of these 39 patients (30.8%), the terminal ileum had been inspected during previous colonoscopy.

## DISCUSSION

In this study, we found that in patients referred for capsule endoscopy it is not uncommon to find non-small-bowel abnormalities, so findings within the reach of conventional esophagogastroduodenoscopy or ileocolo-

**Table 2 Non-small-bowel abnormalities in capsule endoscopy *n* (%)**

Procedures	Value
Abnormalities	291 (48.9)
NSBA	85 (14.3)
NSBA known before CE	12 (2.0)
NSBA unknown before CE	63 (10.6)
sNSBA with incomplete previous examinations	10 (1.7)
Location of NSBA	
Stomach	15 (17.6)
Duodenum	12 (14.1)
Proximal jejunum	10 (11.8)
Terminal ileum	21 (24.7)
Colon	19 (22.4)
Other	8 (9.4)
Type of NSBA	
Angiodysplasia(s)	32 (37.6)
Erosion(s)	16 (18.8)
Active bleeding	15 (17.6)
Inflammation	12 (14.1)
Polyp/tumor	6 (7.1)
Other	4 (4.7)

NSBA: Non-small bowel abnormalitie; CE: Capsule endoscopy.

noscopy related to the indication for the procedure. We included only patients who were referred for obscure or occult bleeding and for suspected CD, because patients with other indications for CE, such as suspicion of carcinoma do not generally undergo both esophagogastroduodenoscopy and ileocolonoscopy prior to CE.

Non-small-bowel abnormalities within reach of conventional endoscopes were found in 14.3% of all procedures and could be present in the upper and lower gastrointestinal tract. Vascular lesions were the abnormalities most often found. It must be noted that two-thirds of these patients had undergone conventional upper and lower tract endoscopy with ileoscopy before the capsule endoscopy procedure. One could assume that these lesions were truly overlooked at previous examinations. Alternatively, it may concern intermittently bleeding lesions.

Data on the incidence of non small bowel abnormalities in CE are limited. To the best of our knowledge, only two studies investigated this subject. In a series of 140 capsule endoscopy procedures for obscure gastrointestinal bleeding, NSBA were found in 9 patients (6.4%)<sup>[7]</sup>. In another series of 317 CE procedures, NSBA were found in 11 patients (3.5%), in which the investigators differentiated between referred patients (6.3%) and non-referred patients (1.2%). In this study, the terminal ileum was not defined as a location for NSBA<sup>[11]</sup>. The incidence of NSBA has also been investigated in double balloon endoscopy (DBE) procedures<sup>[8,9]</sup>. In these studies, NSBAs were found in 14.3 % and 24 % of cases respectively. One could assume that the sensitivity of DBE is slightly higher for small bowel abnormalities than that of CE, although most studies indicate a similar diagnostic yield<sup>[5,12-21]</sup>.

In this study we investigated the incidence of NSBAs in relation to prior examinations. A limitation of our

study is that we do not have follow-up data on the patients in whom NSBAs were found. We therefore are not informed of the results of repeat conventional endoscopies after CE. A strong point of our patient cohort is that by selecting only patients who were referred for obscure of occult blood loss and for suspected CD, a group of patients generally fully examined with conventional endoscopies prior to CE.

In conclusion, a significant proportion of patients referred for small bowel CE had lesions within the reach of conventional endoscopes, indicating that CE was unnecessarily performed. Before planning a CE procedure, careful upper and lower endoscopies should be performed including ileoscopy. Repeating these investigations, if not properly performed before CE, should be considered.

## COMMENTS

### Background

Capsule endoscopy (CE) is a very sensitive diagnostic technique to detect small bowel pathology. Another method to investigate the small bowel is single- or double-balloon enteroscopy. As in capsule endoscopy, most patients referred for balloon enteroscopy have undergone conventional upper and lower endoscopy before the procedure is conducted. It is known that balloon enteroscopy reveals abnormalities within reach of conventional endoscopes in up to 15%-24% of patients. These findings are generally referred to as non-small-bowel abnormalities. There are no robust data on the incidence of NSBAs in capsule endoscopy. This was the subject of this study.

### Research frontiers

This the first study that investigated the incidence of non-small-bowel abnormalities in small bowel capsule endoscopy.

### Innovations and breakthroughs

In this study, 595 capsule endoscopy procedures were included. Patients were referred for obscure gastrointestinal bleeding or for suspected Crohn's disease. Abnormalities were found in 306 (51.4%) of cases. Of these 306 patients, 85 (27.7%) had abnormalities within reach of conventional endoscopies; 63 had abnormalities apparently overlooked at previous conventional endoscopies, 10 patients had not undergone upper and lower endoscopy prior to capsule endoscopy and 12 had abnormalities that were already known prior to capsule endoscopy. The most common type of missed lesions were vascular lesions ( $n = 47$ ). Non-small-bowel abnormalities were located in the stomach ( $n = 15$ ), proximal small bowel ( $n = 22$ ), terminal ileum ( $n = 21$ ), colon ( $n = 19$ ) or at other or multiple locations ( $n = 8$ ). Ten patients with abnormal findings in the terminal ileum had not undergone examination of the ileum during colonoscopy.

### Applications

What does this mean for clinical practice? The fact that a significant proportion of patients referred for small bowel CE had lesions within the reach of conventional endoscopes indicates that CE was unnecessarily performed. Before planning a CE procedure, careful upper and lower endoscopies should be performed including ileoscopy. Repeating these investigations, if not properly performed before CE, should be considered.

### Peer review

This work emphasizes the importance of critical selection of patients for capsule endoscopy.

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ISSN 1007-9327



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