Abdominal pain accompanied by weight loss may increase the diagnostic yield of capsule endoscopy: A Korean multicenter study

KI-NAM SHIM1, YONG-SIK KIM2, KYUNG-JO KIM3, YOUNG-HO KIM4, TAE-IL KIM5, JAE-HYUK DO6, JI-KON RYU7, JEONG-SEOP MOON8, SOO-HEON PARK9, CHEOL HEE PARK10, KEE-MYUNG LEE11, IN-SEOK LEE9, HOON-JAI CHUN3, IN-SEOP JUNG12 & MYUNG-GYU CHOI9 FOR THE KOREAN GUT IMAGE STUDY GROUP

1Ewha Womans University College of Medicine, 2Korea University College of Medicine, 3Yang Hospital, 4Sungkyunkwan University School of Medicine, 5Yonsei University College of Medicine, 6Chung Ang University College of Medicine, 7Seoul National University College of Medicine, 8Inje University College of Medicine, 9The Catholic University of Korea, 10Hallym University College of Medicine, 11Ajou University College of Medicine, and 12Soon Chun Hyang University College of Medicine, Seoul, Korea

Abstract

Objective. Capsule endoscopy (CE) is approved for the evaluation of obscure gastrointestinal (GI) bleeding and its use has increased in the assessment of patients with various small-bowel disorders. The yield of CE for indications of disorders other than GI bleeding is not yet well described. The aim of the present study was to determine in which subgroup of patients with unexplained abdominal pain, CE would be a helpful evaluation tool. Material and methods. The results of CE in 110 patients (70 M, 40 F, mean age 50.8±14.1 years) with unexplained abdominal pain from 12 tertiary referral centers between September 2002 and September 2004 were retrospectively analyzed. Results. The visualization of the small bowel to the cecum was successfully carried out in 69.1% of the patients. Nineteen out of the 110 cases revealed positive findings that explained the symptoms of the patient (diagnostic yield 17.3%). Diagnosis included small-bowel stricture (5), Crohn's disease (3), small-bowel tumor (2), radiation-induced enteritis (1), NSAID-induced enteropathy (1), ischemic ileitis (1), diffuse lymphangiectasia (1), and significant erosion or ulceration (5). By univariate logistic regression analysis, the positive findings of CE were significantly associated with weight loss (odds ratio (OR), 11.9; 95% CI [2.0, 70.6]), elevated erythrocyte sedimentation rate (ESR) (≥20 mm/h) (OR, 11.5; 95% CI [1.9, 69.5]), elevated C-reactive protein (CRP) (≥0.4 mg/dL) (OR, 5.0; 95% CI [1.6, 15.9]), and hypoalbuminemia (albumin <3 g/dL) (OR, 23.1; 95% CI [2.4, 223.1]). Using a multivariate analysis, weight loss was found to be a significant risk factor for positive findings of CE (OR, 18.6; 95% CI [1.6, 222.4], p = 0.02). Conclusions. The results of this study suggest that CE can be helpful in patients suffering from abdominal pain that cannot be explained by established examinations, if the pain is accompanied by weight loss.

Key Words: Abdominal pain, capsule endoscopy

Introduction

Abdominal pain is a common problem that is frequently seen in gastroenterology practice. The range of possible causes includes functional, organic, metabolic, toxicologic, and psychiatric disorders [1–4]. Together with headache and lower back pain, abdominal pain is likely to remain medically unexplained in those who frequently attend secondary health care. The diagnostic work-up includes both invasive and non-invasive procedures, including extensive laboratory tests, upper and lower gastrointestinal endoscopy, abdominal ultrasound, computed tomography (CT), and occasionally, push enteroscopy. In many patients, this extensive and expensive work-up yields negative results, while the cause of the abdominal pain often remains obscure. In some of these cases, disorders of
the small bowel may be suspected; in contrast to the imaging examinations of the upper and lower gastrointestinal (GI) tract, the imagery obtained from the small bowel is often unsatisfactory [5–7]. Owing to its length, location, and tortuosity, the small intestine is relatively inaccessible by endoscopic examination. Small-bowel follow-through cannot detect flat lesions such as angiodysplasia, as well as being an insensitive method of detecting fine mucosal disease and raised lesions [8], while push enteroscopy visualizes only the proximal small bowel.

Capsule endoscopy (CE) is approved for the evaluation of obscure GI bleeding [9–12] and is increasingly used in preliminary examinations for the evaluation of other small-bowel disorders. Even though patients with chronic abdominal pain have been included in many studies on CE, few of the studies have focused on this indication. Bardan et al. [13] reported that CE did not appear to have any significant clinical value in the evaluation of patients with obscure chronic abdominal pain in Israel. We attempted to complement their relatively small, single-center study by using CE to evaluate unexplained abdominal pain. The aim of the present study was to determine in which subgroup of patients with unexplained abdominal pain, CE would be a helpful evaluation tool.

Material and methods

This study retrospectively analyzed the medical records and the findings of CE of 110 patients (70 M, 40 F, mean age 50.8 ± 14.1 years) who had undergone examination due to abdominal pain at 12 tertiary referral centers in the Republic of Korea from September 2002 until September 2004. Patients with known intestinal obstruction, a history of major abdominal surgery, and pregnant women were excluded from the study. The study was approved by our Human Research Review Committee, and informed consent was obtained from all the patients.

The characteristics of the abdominal pain were heterogeneous in terms of location and association with other abdominal symptoms. The duration of abdominal pain was 19.5 ± 30.9 months (range 1–180 months). Six of the cases were accompanied by weight loss. Three cases of non-steroidal anti-inflammatory drug (NSAID) ingestion, 1 case of anticoagulant ingestion, and 1 case of steroid ingestion were observed. Laboratory tests, including total blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and a liver function test, were checked (Table I).

CE was performed when there were no specific abnormalities detected in the conventional work-up for the abdominal pain of the patients. The inclusion criteria were only the main complaints of patients, and the clinical characteristics of patients were markedly heterogeneous. Because this study included patients referred from the 1st and 2nd referral centers, routine work-ups such as gastro-duodenoscopy, colonoscopy, abdominal ultrasound, and abdominal CT scan had been performed prior to CE. The CE was carried out to detect or rule out any organic cause of small-bowel disease. The patients swallowed the capsules after an overnight fast only (7), or after the ingestion of PEG 4L (84), sodium phosphate (9), clear water with alaxyl (9), or PEG 2L (1). A standard 8-sensor array attached to a recorder/battery belt-pack device was used. After the ingestion of the capsules, the patients fasted for 2 h, after which they were permitted to ingest only water. Four hours after capsule ingestion, a small snack was permitted. Eight hours later, the sensor array and the recorder/battery belt-pack were disconnected, and the data were then downloaded to a computer equipped with software for image viewing.

In this study, a univariate logistic regression analysis was used to examine the relationships among the significant findings of CE to explain the symptoms of the patients, the clinical characteristics of the patients, and the results of the laboratory tests, while a multivariate logistic regression analysis was used to determine the relationships between significant variables and the results of CE. These statistical analyses made use of SPSS software (v. 11.0; SPSS Inc.). Differences were assumed to be significant at $p$-values of less than 0.05.
Results

None of the patients had any problems with swallowing the capsule, and it stayed in the stomach for an average of 74.6 ± 69.3 min (range 1–281 min). The small-bowel transit time was 279.1 ± 99.8 min (range 24–480 min). In 34 patients, the capsule failed to pass through the ileocecal valve during the study time (range 157–583 min).

Visualization of the small bowel to the cecum was achieved in 69.1% of the patients. Nineteen of the 110 cases revealed positive findings that explained the symptoms of the patient (diagnostic yield = 17.3%). Diagnosis included small-bowel stricture (5), Crohn's disease (3), small-bowel tumor (2), radiation-induced enteritis (1), NSAID-induced enteropathy (1), ischemic ileitis (1), diffuse lymphangiectasia (1), and significant erosion or ulceration (5). The various diagnoses were made by the capsule findings combined with the clinical histories of the patients. In terms of the diagnosis of 5 cases of small-bowel stricture, 4 cases had past histories such as eosinophilic enteritis and minor abdominal surgery for duodenal ulcer perforation, sigmoid fistula due to diverticulum, and intestinal obstruction. In the remaining case of stricture, no specific cause could be found to explain the lesion. In the diagnosis of Crohn's disease, CE showed multiple erosions, ulcerations, or strictures of the small bowel, and the history-taking and clinical course of the patients were considered before a diagnosis of Crohn's disease was reached. In the two cases of small-bowel tumors, lymphoma was confirmed. One of these was confirmed by the operation of the lesion, and the other was confirmed by intra-abdominal lymph node biopsy. In the case of NSAID-induced enteropathy, abdominal pain resolved after discontinuation of the NSAID. In the case of ischemic ileitis, perforation of the small bowel was observed after the capsule endoscopy. An operation was carried out for definite treatment, and the correct diagnosis was made by pathologic confirmation. In cases of erosions or ulcerations, the etiology of the lesions could not be explained by their clinical histories, and the lesions were in the jejunum or ileum, which could not be reached by the upper GI endoscopy. The clinical details of the patients with positive CE are presented in Table II.

A univariate logistic regression analysis was implemented to evaluate the relationships among the clinical characteristics, blood test findings, and CE results that could be used to explain the symptoms, positive findings of CE were significantly associated with weight loss (more than 10% of previous body-weight) (odds ratio (OR), 11.87; 95% CI (1.99, 70.6)), elevated ESR (>20 mm/h) (OR, 11.5; 95% CI (1.9, 69.5)), elevated CRP (≥0.4 mg/dL) (OR, 5.0; 95% CI (1.6, 15.9)), and hypoalbuminemia (albumin <3 g/dL) (OR, 23.1; 95% CI (2.4, 223.1)) (Table III). No significant relationship was found between gender, age, duration of symptoms, passage of CE through the ileocecal valve, anemia, or leukocytosis and a positive finding of CE. Using a multivariate logistic regression analysis, it was found that weight loss was a significant risk factor for positive findings of CE (OR, 18.6; 95% CI (1.6, 222.4), p = 0.02) (Table IV).

Discussion

It is clear that CE is a powerful tool that can be used to assess the small intestine. Its role in occult GI bleeding is becoming clearly defined [9–12], and it is likely that this tool will become more commonly used at earlier stages in the investigation algorithms of these patients [14]. With the current technology, barium radiology will remain the first-line investigation of suspected small intestinal Crohn's disease, but CE should be used in difficult cases and in the characterization of indeterminate colitis [15]. CE also seems to be useful in the screening of polyposis syndromes [6,16,17] and may have a role in the detection of small-intestinal lesions in celiac disease [18], although few studies have been conducted.

Although patients with chronic abdominal pain have been included in many studies on CE, few of those studies have focused on this indication. A retrospective analysis of CE in 493 patients at three centers included 63 patients with unexplained abdominal pain without GI bleeding. The CE findings were able to explain the symptoms in 54% of these patients, but 62% of the cases explained by CE were likely to be within reach of standard endoscopy [19]. In a study of 20 patients with chronic abdominal pain who had negative diagnostic work-ups, including upper and lower GI endoscopy, small-bowel follow-through, abdominal CT scans, and enteroscopy, 14 of these patients had normal findings on CE. The remaining 6 patients had insignificant findings that did not explain the abdominal pain [13]. In a multicenter study with various indications, only 1 out of 24 patients with abdominal pain or irritable bowel syndrome had a positive finding on CE [20]. This was compatible with the results of enteroclysis and push enteroscopy. In contrast to the above results, another retrospective analysis of CE in 21 patients with chronic diarrhea alone or together with abdominal pain suggested that CE might be valuable in patients with chronic diarrhea if accompanied by signs of inflammation and/or malabsorption, and diarrhea...
Table II. Clinical details of the patients with positive results of capsule endoscopy.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age</th>
<th>Gender</th>
<th>Duration of Sx (month)</th>
<th>Weight loss</th>
<th>Hb (g/dL)</th>
<th>WBC (mm³)</th>
<th>ESR (mm/hour)</th>
<th>CRP (mg/dL)</th>
<th>Albumin (g/dL)</th>
<th>Positive findings</th>
<th>Location</th>
<th>Diagnosis</th>
<th>Treatment</th>
<th>Symptom improvement after CE</th>
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<td>Yes</td>
<td>14</td>
<td>4,600</td>
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<td>0.1</td>
<td>4</td>
<td>Lymphangiectasia</td>
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<td>SB stricture (H/O eosinophilic enteritis)</td>
<td>Conservative Tx</td>
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</tr>
<tr>
<td>2</td>
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<td>F</td>
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<td>No</td>
<td>12</td>
<td>4,200</td>
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<td>4</td>
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<td>Jejunum</td>
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<td>ND</td>
<td>ND</td>
<td>3.89</td>
<td>Hyperemic, edematous mucosal nodularities with suspicious strictures</td>
<td>Entire SB</td>
<td>SB stricture</td>
<td>Oral steroid (prednisolone 5 mg)</td>
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</tr>
<tr>
<td>4</td>
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<td>F</td>
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<td>36</td>
<td>36.1</td>
<td>2.7</td>
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<td>Ileum</td>
<td>SB tumor (lymphoma)</td>
<td>Operation and CTx</td>
<td>Death*</td>
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<td>Conservative Tx</td>
<td>Death¹</td>
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<td>ND</td>
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<td>Jejunum</td>
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<td>Jejunum and ileum</td>
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<td>Lost follow-up</td>
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<td>18</td>
<td>4.2</td>
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<td>Ileal stricture</td>
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<td>Jejunal stricture</td>
<td>Conservative Tx</td>
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</table>

Abbreviations: CE = capsule endoscopy; CTx = chemotherapy; Hb = hemoglobin; LGE = lymphangiectasia; ND = not done; SB = small bowel; Sx = Symptom.
*Death due to disease progression; ¹death due to disease-unrelated problem.
In the present study, univariate analysis of the data of the 110 patients who underwent CE for the investigation of abdominal pain showed that weight loss, inflammatory signs such as elevated ESR or CRP, and hypoalbuminemia were factors that were associated with positive findings on CE, and multivariate analysis showed that, of these factors, weight loss was significantly related to positive CE findings that could explain abdominal pain. Our study supports the results of previous studies by Keuchel et al. [21,22]. The yield of positive diagnosis of 17.3% in our study seems high, even in this selected group of patients. One of the possible explanations is the selection bias in favor of organic pathology as a consequence of the heterogeneous inclusion criteria.

The present study has several limitations. The possibility of selection bias is an important limitation of this retrospective study. Furthermore, blood tests could not be performed in all cases, and so it is possible that if they had been performed in all of them, better data could have been obtained for elucidating the relationships between the findings of blood tests and those of CE.

Additionally, in this study, CE did not reach the colon in 31% of the patients, which resulted in incomplete studies of the small intestine. It is still possible, therefore, that these patients had pathology in the terminal ileum. The next generation of capsules, which will have longer recording times, is likely to solve this problem.

In conclusion, the analysis of the present study sheds light on the relationship between a positive finding of CE and abdominal pain accompanied by weight loss. This study suggests that CE may be helpful in assessing patients suffering from abdominal pain that cannot be explained by established examinations if the pain is accompanied by elevated ESR, CRP, or hypoalbuminemia. We believe that, in this selective group of patients, it is important to determine whether CE can alter the investigation algorithms used for examination and reduce further diagnostic studies or provide significant modifications of the therapeutic approaches. It is hoped that this study will lead to prospective studies of larger numbers of patients to elucidate the exact role of CE in the assessment of unexplained abdominal pain.

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References