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Does Back-To-Back Capsule Endoscopy Increase the Diagnostic Yield over a Single Examination in Patients with Obscure Gastrointestinal Bleeding?

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Background/Aims: Video capsule endoscopy (CE) can provide a negative result despite the presence of clinically significant small-bowel lesions. We therefore performed a prospective study to elucidate whether repeated back-to-back CE increases the diagnostic yield over a single CE in patients with obscure gastrointestinal bleeding (OGIB). **Methods:** Sixteen patients with OGIB were prospectively enrolled and underwent back-to-back CE investigation with a 24-hour interval. All CE videos were interpreted by two experienced readers at a maximum 15 frames/second in a random order. **Results:** The diagnostic yield of the single CE was 37.5% for the first CE, 43.8% for the second CE, and 62.5% for the back-to-back CE. The overall mean lesion-detection rates of the first and second CEs were 42.2% and 64.6%, respectively. The bowel preparation status of the second CE was improved in 37.5% and unchanged in 62.5% of cases as compared with that of the first CE. **Conclusions:** These results indicate that back-to-back CE may increase the diagnostic yield and lesion-detection rate over a single CE in patients with OGIB. Therefore, if the first CE is not diagnostic in a patient with OGIB, repeat back-to-back CE may be considered as a candidate for further workup. **(Gut Liver 2010;4:54-59)**

Key Words: Capsule endoscopy; Diagnostic yield; Obscure gastrointestinal bleeding

INTRODUCTION

Currently, video capsule endoscopy (CE) is acknowledged as the most effective noninvasive method of small bowel visualization for the detection of the source of obscure gastrointestinal bleeding (OGIB).[1-4] However, technical and clinical limitations of CE on diagnostic yield are also recognized due to its inherent features: The current capsule for small bowel imaging has a camera at only one end. Attached camera can take only about 2 image frames per second and provide only 140°-156° field of view. In addition, it cannot insufflate the bowel lumen and cannot specifically target suspected lesions for closer examination as it just moves passively through the GI tract by peristalsis and gravity.[5-7]

Recently, several studies addressed limited diagnostic yield of CE. Two studies evaluated the ability of CE to detect the major duodenal papilla as surrogate marker and reported the sensitivity of 10.4% and 43.6%.[7,8] One study validated the effectiveness of CE in patients with OGIB based on the outcome after 12 months of follow-up.[9] The best method to estimate the diagnostic sensitivity and specificity of CE is to compare the result of CE with the reliable gold standard, or intraoperative enteroscopy.[10,11] However, intraoperative enteroscopy is too invasive and it is practically impossible to use this

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method to validate the result of CE in various clinical situations. As mentioned above, CE is currently the most effective noninvasive method of small bowel visualization and it is highly expected that repeated "back-to-back" CE can improve the diagnostic yield. Therefore, "back-to-back" CE may serve as a practical and promising way for improving the lesion detection rate and diagnostic yield of single CE. Until now, there have been two studies on back-to-back CE. However, these studies concentrated on the comparison of two different type of CE (Pillcam SB and Endocapsule), not the evaluation of the lesion detection rate and diagnostic yield of back- to-back CE.[12,13]

The aims of this prospective study were to elucidate whether repeat back-to-back CE increases diagnostic yield over a single CE and to test the potential value of back-to-back CE in the patients with OGIB.

MATERIALS AND METHODS

1. Patients

Patients with suspected small-bowel bleeding and negative findings on recent upper endoscopy and colonoscopy were selected and considered for enrollment in this study. Patients were prospectively recruited in Samsung Medical Center and Catholic Medical Center between May 2007 and April 2008. Patients aged less than 18 years, and those with dysphasia, suspected small-bowel stenosis, history of abdominal surgery or radiation, unstable vital sign or massive bleeding on presentation, and small bowel mass larger than 2 cm on computed tomography (CT) were excluded from the trial. Patients with an implanted cardiac device and pregnant women were also excluded. All enrolled patients were informed about the CE procedures and gave their written consents. Our institutional review board approved the study protocol.

2. Capsule endoscopy

We used the Given M2A wireless video capsule system (Given Diagnostic Imaging System; Given Imaging Ltd., Yoqneam, Israel) for this study. Enrolled patients were prescribed to take 45 mL of sodium phosphate solution and 1 L of water 12 hours before the procedure. After taking this laxative, patients were instructed to fast for 12 hours except taking simethicone solution 20 minutes before swallowing the CE device. CE investigation was performed for 8 hours after ingesting activated capsule and no oral intake was allowed except water during this period. If there was no sign or symptoms of CE retention or no massive bleeding during and after the first CE procedure, the second CE was performed next day with the same protocol as the first day CE. Therefore, the interval between two CEs was 24 hours in all enrolled cases.

Bowel preparation status was classified into 4 categories: excellent, ideal visualization of the small bowel mucosa; good, some fluid or debris present that did not interfere with the quality of the examination; fair, enough fluid or debris present to preclude a completely reliable examination; poor, significant fluid or debris present such that the examination was unreliable.

3. Data analysis

Data were reviewed by two experts (reviewer 1 and reviewer 2) in CE reading, who were blinded to the patient history and the results from previous workup. Two reviewers performed CE reading in opposite order each other (e.g., Reviewer 1: first CE and then second CE, Reviewer 2: Second CE and then first CE) and this order was randomly assigned. One reviewer was also blinded to the reading results from the other reviewer during review process. RAPID application software v 5 (Given Diagnostic Imaging System) was used for image review with the maximum reading rate of 15 frames per second. Significant findings were recorded by thumbnail images and described using standardized terminology.[14,15]

Data analysis was performed in two different ways: diagnostic yield and lesion detection rate. Diagnostic yield was defined as the ratio of the number of cases with suspected or definite small bowel findings responsible for OGIB to the number of all cases examined. Lesion detection rate was defined as the ratio of the number of small bowel lesions found in each single CE to the number of total small bowel lesions found in the first and second CEs by two reviewers.

RESULTS

During study period, total 16 patients with OGIB were enrolled. These 16 enrolled patients comprised of 13 men and 3 women and had a median age of 51.0 years (range, 32-74 years). Cecal arrival rates were 43.8% for the first CE and 50.0% for the second CE, respectively and the cecal arrival rate per patient was 62.5% by back-to-back CE. Median gastric passage times were 13 minutes (range, 1-80 minutes) and 35 minutes (range, 6-248 minutes) for cases with and without cecal arrival, respectively. Median small bowel passage time for cases with cecal arrival was 327 minutes (range, 73-425 minutes). In the present study, duodenal papilla was detected in only 1 CE among total 32 CEs (3.1%). No significant adverse event was observed in any of 32 CEs.

There were total 10 cases with suspected or definite

small bowel findings responsible for OGIB: 1 case with jejunal Dieulafoy's ulcer, 2 cases with angiodysplasias, 6 cases with erosions, and 1 case with multiple polyps. Diagnostic yield of the single CE was 37.5% for the first CE and 43.8% for the second CE, respectively. Diagnostic yield of the back-to-back CE increased up to 62.5% (Table 1).

Table 1 shows mean lesion detection rate of the first and second CE in 10 cases with small bowel lesions and Table 2 demonstrates the lesion detection rate of the first and second CE, bowel preparation status, and indication in each case. The overall mean lesion detection rates of

Table 1. Mean Diagnostic Yield and Lesion Detection Rate of the First and Second CE and Back-to-Back CE according to Reader

	1st CE		2nd CE		Back-to-back CE	
	Diagnostic yield (n=16)	Detection rate (n=10)*	Diagnostic yield (n=16)	Detection rate (n=10)*	Diagnostic yield (n=16)	Detection rate (n=10)*
Reviewer 1 (%)	37.5	41.8	37.5	52.9	56.3	88.2
Reviewer 2 (%)	25	28.4	37.5	37.8	50	59.4
Overall (%)	37.5	42.2	43.8	64.6	62.5	100

CE, capsule endoscopy.
*Only cases with small bowel lesions were used for the calculation of lesion detection rate.

Table 2. Lesion Detection Rate, Bowel Preparation Status and Indication of the First and Second Capsule Endoscopy

		1st CE	2nd CE	Back-to-back CE	Bowel preparation (1st CE/2nd CE)	Indication
Case 1	Detection rate (%)	38.5	61.5	100	Fair/Fair	Occult
	No. of lesion	5	8	13		
Case 2	Detection rate (%)	No lesion	No lesion	No lesion	Good/Good	Overt
	No. of lesion	0	0	0		
Case 3	Detection rate (%)	No lesion	No lesion	No lesion	Poor/Poor	Occult
	No. of lesion	0	0	0		
Case 4	Detection rate (%)	100	0	100	Fair/Good	Overt
	No. of lesion	2	0	2		
Case 5	Detection rate (%)	No lesion	No lesion	No lesion	Fair/Good	Overt
	No. of lesion	0	0	0		
Case 6	Detection rate (%)	68.2	100	100	Fair/Good	Occult
	No. of lesion	15	22	22		
Case 7	Detection rate (%)	No lesion	No lesion	No lesion	Fair/Good	Occult
	No. of lesion	0	0	0		
Case 8	Detection rate (%)	100	0	100	Fair/Fair	Overt
	No. of lesion	1	0	1		
Case 9	Detection rate (%)	100	0	100	Good/Good	Overt
	No. of lesion	2	0	2		
Case 10	Detection rate (%)	No lesion	No lesion	No lesion	Fair/Fair	Occult
	No. of lesion	0	0	0		
Case 11	Detection rate (%)	0	100	100	Fair/Fair	Overt
	No. of lesion	0	2	2		
Case 12	Detection rate (%)	No lesion	No lesion	No lesion	Good/Good	Occult
	No. of lesion	0	0	0		
Case 13	Detection rate (%)	0	100	100	Poor/Fair	Overt
	No. of lesion	0	25	25		
Case 14	Detection rate (%)	0	100	100	Fair/Fair	Overt
	No. of lesion	0	2	2		
Case 15	Detection rate (%)	15.4	84.6	100	Poor/Fair	Overt
	No. of lesion	2	11	13		
Case 16	Detection rate (%)	0	100	100	Good/Good	Overt
	No. of lesion	0	2	2		

CE, capsule endoscopy.

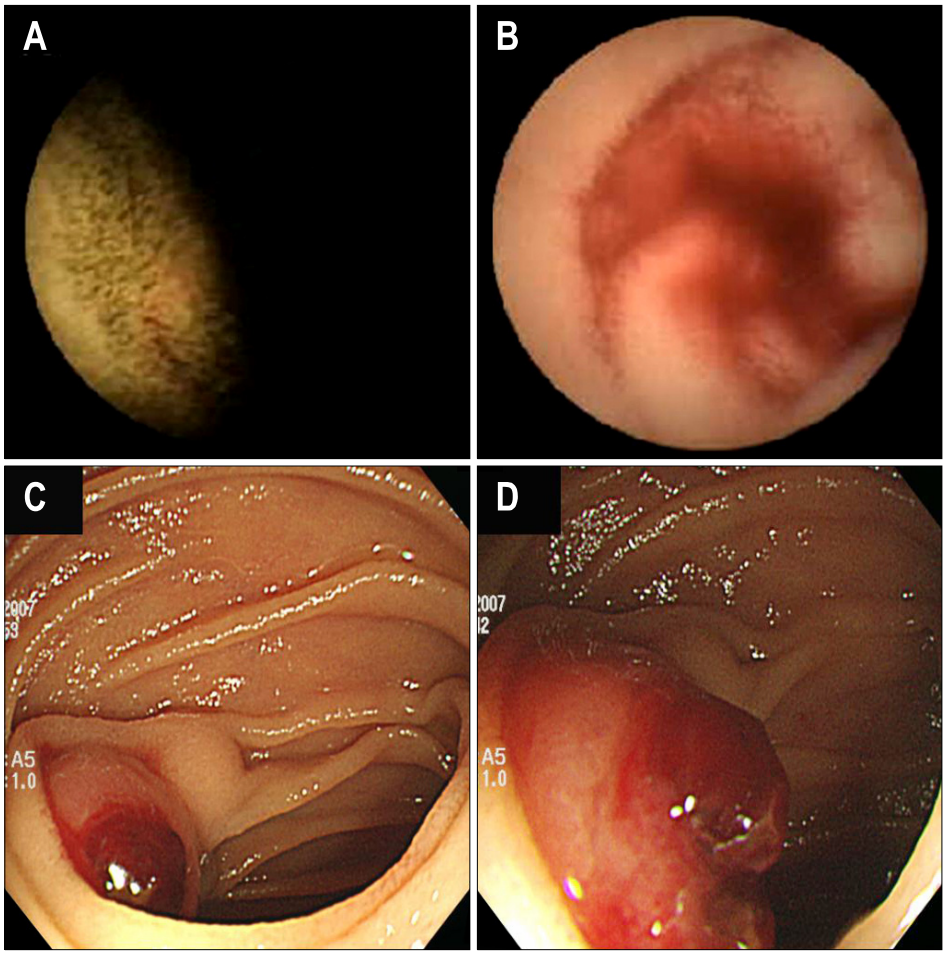

Fig. 1. Case of a jejunal Dieulafoy's ulcer in which back-to-back capsule endoscopy (CE) changed the clinical course. (A) Non-specific findings at an area considered to be the proximal jejunum, observed in the first CE with poor bowel preparation. (B) Fresh floating blood at the area considered to be the proximal jejunum that was detected in the second CE with good bowel preparation. (C) Distant view of a jejunal Dieulafoy's ulcer mimicking a submucosal tumor on the proximal jejunum that was found by push enteroscopy. This lesion was accompanied by active bleeding. (D) Close view of a jejunal Dieulafoy's ulcer that was found by push enteroscopy.

the first and second CE were 42.2% and 64.6%, respectively (Table 1). Bowel preparation status of second CE was improved in 37.5% and unchanged in 62.5% of cases as compared with that of first CE. For the cases with improved bowel preparation status in second CE, the overall lesion detection rates of the first and second CE were 30.6% and 93.5%, respectively. For the cases with unchanged bowel preparation status in second CE, the overall detection rates of the first and second CE were 36.4% and 54.5%, respectively. When analyzing according to the bowel preparation status, the mean lesion detection rates were 50.0%, 62.7%, and 7.7% for good, fair, and poor bowel preparation, respectively. When analyzing according to the indication, the mean lesion detection rates were 67.1% and 50.0% for occult and overt OGIB, respectively. When analyzing according to the cecal arrival, the mean lesion detection rates were 52.0% and 54.5% for cases without and with cecal arrival, respectively.

During study period we experienced one case in which back-to-back CE changed the clinical course (Fig. 1). Patient was 37-year-old male and presented as overt OGIB with hematochezia. Initial CT scan did not provide any information for the source of bleeding and then back-to-back CE was performed. The bowel preparation status of the first CE was poor and no definite or probable source of bleeding except old blood clots was found on the first CE. On the second CE with good bowel preparation, however, fresh floating blood was detected at the area considered as distal duodenum or proximal jejunum. On the basis of this localization suggestive of relatively easy access, push enteroscopy was performed and the about 1.5 cm sized lesion with active bleeding mimicking submucosal tumor was found on the proximal jejunum. This lesion was finally diagnosed as jejunal Dieulafoy's ulcer by wedge resection. In this case patient could avoid risky clinical observation with wait-and-see strategy and undergoing costly double balloon enteroscopy by back-to-back CE investigation.

DISCUSSION

Although the effectiveness of CE is well established in the setting of OGIB,[1-4] its limitation on diagnostic yield

has also been recognized.[7,8] The original Food and Drug Administration trial of the Given M2A wireless video capsule system showed a diagnostic yield of only 55% and following studies demonstrated comparable results.[1,16] Despite this limited diagnostic yield, however, CE is currently the most effective noninvasive method of small bowel visualization. Recently introduced double balloon enteroscopy also showed inferior or comparable diagnostic yield to CE in the patients with OGIB although it has several advantages over CE such as capability of insufflating the bowel lumen and close examination of specific target lesions.[17-20]

Considering the random tumbling movement of CE and the experience from the back-to-back colonoscopy, it is highly expected that repeated back-to-back CE can improve the diagnostic yield.[12] The results of the present study supported this hypothesis. In this study, diagnostic yield of the single CE was 37.5% for the first CE and 43.8% for the second CE, respectively. However, diagnostic yield of the repeated back-to-back CE was increased up to 62.5%. This improvement could be attributable to the additional image frames obtained by back-to-back CE and the improved bowel preparation status in several cases of the second CE. In addition, the absence of adverse events and the excellent tolerance during back-to-back CE proved its value as a practical and safe method.

Currently, no established guideline is available for guiding further workup after negative CE in the patients with OGIB. Therefore the strategy after negative CE is different among institutions. Recent consensus statements on CE suggested the possibility that repeated back-to-back CE might increase the diagnostic yield and guide further treatment in case of nondiagnostic initial CE.[2] At the time of these consensus statements, however, supporting data was lacking. The result of this study revealed that the overall lesion detection rates and diagnostic yield of the second CE and back-to-back CE were markedly better than those of the first CE and supported the suggested possibility in consensus statements. As the order of reading in this study was randomly assigned, this difference between the first and second CE might be mainly due to the improved bowel preparation status in the second CE.

In the last two studies using major duodenal papilla as surrogate marker for the evaluation of CE missing rate, the sensitivity of CE for detection of major papilla were 10.4% and 43.6%, respectively.[7,8] The present study also showed the low detection rate of 3.1%. These results raised the concern that CE and even back-to-back CE may have a drawback in detecting the flat or slightly elevated lesions located in a sharply angulated bowel loop or vertically positioned loop, just like the duodenal papilla. In this study, we experienced the case in which CE did not directly detect the about 1.5 cm sized jejunal Dieulafoy's ulcer mimicking submucosal tumor on the proximal jejunum although the second CE detected fresh floating blood around this area and made an obvious contribution to the diagnosis (Fig. 1).

This study had several limitations. First, the number of patients enrolled in the present study was relatively small. Second, there were difficulties with interpretation of the images with suspected lesions which might cause observer variability, although the two reviewers in this study were experts in capsule endoscopy reading.

In conclusion, the results of this study indicated that back-to-back CE might increase diagnostic yield and lesion detection rate over a single CE in the patients with OGIB. In addition, we experienced the case in which back-to-back CE changed the clinical course. These results supported the suggested possibility that repeat back-to-back CE might increase the diagnostic yield and guide further treatment in case of nondiagnostic initial CE. Additional large prospective studies are needed to prove the role and value of repeat back-to-back CE in patients with OGIB. Given high cost of CE, cost-benefit analysis of back-to-back CE is also required.

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