CLINICAL ENDOSCOPY

Roles of Capsule Endoscopy and Single-Balloon Enteroscopy in Diagnosing Unexplained Gastrointestinal Bleeding

Shohei Ooka, Kiyonori Kobayashi, Kana Kawagishi, Masaru Kodo, Kaoru Yokoyama, Miwa Sada, Satoshi Tanabe and Wasaburo Koizumi

Department of Gastroenterology, Kitasato University School of Medicine, Sagamihara, Japan

Background/Aims: The diagnostic algorithms used for selecting patients with obscure gastrointestinal bleeding (OGIB) for capsule endoscopy (CE) or balloon-assisted enteroscopy (BE) vary among facilities. We aimed to demonstrate the appropriate selection criteria of CE and single balloon-assisted enteroscopy (SBE) for patients with OGIB according to their conditions, by retrospectively comparing the diagnostic performances of CE and BE for detecting the source of the OGIB.
Methods: We investigated 194 patients who underwent CE and/or BE. The rate of positive findings, details of the findings, accidental symptoms, and hemostasis methods were examined and analyzed.
Results: CE and SBE were performed in 103 and 91 patients, respectively, and 26 patients underwent both examinations. The rate of positive findings was significantly higher with SBE (73.6%) than with CE (47.5%, $p<0.01$). The rate of positive findings was higher in overt bleeding cases than in occult bleeding cases for both BE and SBE. Among the overt bleeding cases, the rate was significantly higher in ongoing bleeding cases than in previous bleeding cases.
Conclusions: Both CE and SBE are useful to diagnose OGIB. For overt bleeding cases and ongoing bleeding cases, SBE may be more appropriate than CE because endoscopic diagnosis and treatment can be completed simultaneously. **Clin Endosc 2016;49:56-60**

Key Words: Capsule endoscopy; Enteroscopy; Gastrointestinal bleeding

INTRODUCTION

Gastrointestinal bleeding is commonly encountered in clinical practice. In 10% to 20% of gastrointestinal bleeding cases, the bleeding source may not be evident on initial evaluation. Moreover, repeated bleeding has been reported in approximately half of these patients, resulting in recurrent hospitalizations and massive transfusions.[1]

Gastrointestinal bleeding with an unidentified bleeding source is defined as obscure gastrointestinal bleeding (OGIB).

As endoscopy of the upper and lower gastrointestinal tract cannot identify the bleeding source in many patients with OGIB, the small bowel is generally suspected as the bleeding source in these patients. Although intraoperative enteroscopy and push enteroscopy have been routinely performed to detect the bleeding source since approximately 2000, these approaches are invasive, and it is difficult to evaluate the entire small bowel.[2] Capsule endoscopy (CE), first described in 2000, has become a useful option to diagnose patients suspected of small-bowel bleeding. CE reduces the patient's physical burden and allows the evaluation of the entire small-bowel, irrespective of its condition.[3] On the other hand, single balloon-assisted enteroscopy (SBE), consisting of a balloon and an overtube, enables deep intubation of the small bowel. The combination of oral and rectal approaches enables the examiner to simultaneously evaluate the small bowel, collect biopsy samples, remove polyps, and perform endoscopic hemostasis for the entire small bowel.[4,5]

Currently, diagnostic algorithms, such as those used to

select patients with OGIB for CE or balloon-assisted enteroscopy (BE), vary among facilities. In this study, we aimed to demonstrate the appropriate selection criteria of CE and SBE for patients with OGIB according to their conditions, by retrospectively comparing the diagnostic performances of CE and BE for detecting the source of OGIB.

MATERIALS AND METHODS

Patients

This is a retrospective case series study from a single institution. A total of 194 patients underwent CE and/or BE to detect the source of OGIB at Kitasato University East Hospital and Kitasato University Hospital between January 2005 and December 2014 (Table 1).

The rate of positive findings, details of the findings, accidental symptoms, and hemostasis methods were examined in the patients who underwent CE, SBE, or both. OGIB was classified as overt or occult according to its bleeding behavior.[5,6] In the present study, among the overt bleeding cases, those that underwent the examination within 48 hours after bleeding were defined as "ongoing," whereas those that underwent the examination 48 hours or later after bleeding were defined as "previous." The physician in charge determined whether to perform CE or SBE based on the clinical condition of the patient, contrast-enhanced computed tomography (CT) findings, and/or radiological enteroclysis results.

This study was approved by the Institutional Review Board of Kitasato University. All patients received information about the procedure before the examination, and written informed consent was obtained from the patients.

Capsule endoscopy method

Small-bowel video capsule endoscopy (VCE) is an endolu-minal examination of the small bowel that involves the use of a wireless disposable capsule-shaped device that is swallowed. The device is then propelled by gut motility through the gastrointestinal tract. From the gastrointestinal tract, it transmits images wirelessly to a data recorder worn by the patient.

The VCE systems used in the present study (PillCam, Covidien plc, Dublin, Ireland; Endocapsule, Olympus Optical Co. Ltd., Tokyo, Japan) consist of the following three main components: a capsule endoscope, a sensing system with a data recorder, and a personal computer workstation with proprietary software for image review and interpretation. These systems allow real-time review of images during VCE examinations.

The patients were instructed to fast for 12 hours before the examination and were administered 800 mL of magnesium citrate solution after capsule ingestion. The captured images were later downloaded to the personal computer workstation.[3] An experienced gastroenterologist interpreted all videos.

Single balloon-assisted enteroscopy method

A high-resolution endoscope (Olympus SIF-Q260Y; Olympus; working length 200 cm, external diameter 9.2 mm, forceps diameter 2.8 mm) was used for SBE. A silicone balloon was attached to the tip of a flexible silicon overtube (XST-SB1; Olympus; external diameter 13.2 mm, working length 140 cm) and was dilated/contracted using a pressure-controlled pump system (XMAJ-1725; Olympus; pressure settings –6.0 to +6.0 mm Hg). The overtube has a hydrophilic inner surface moisturized with 10 to 20 mL of physiological saline to reduce friction between the endoscope and overtube.

The patients were administered 1,000 to 2,000 mL of polyethylene glycol before endoscope insertion. The insertion approach (oral/rectal) was selected based on clinical findings and preoperative test results (e.g., BE, contrast-enhanced CT, radiological enteroclysis). The endoscope was inserted under general anesthesia with pethidine hydrochloride or diazepam.

Table 1. Characteristics of the Study Patients

Characteristic	Total	CE	SBE	*p*-value
Patients with OGIB	194	103	91 (oral/rectal, 43/48)	
Sex, male/female	100/94	55/48	45/46	
Age, yr	67±17	63±16	68±17	
Lowest hemoglobin level, g/dL	7.7±2.0	7.8±2.1	7.6±1.9	<0.01[a]
Transfusion, yes/no	70/124	30/73	40/54	<0.01[b]
Comorbidity, yes/no[c]	114/80	61/42	53/38	NS[b]
Anticoagulation, yes/no	68/126	37/66	31/60	NS[b]

Values are presented as number or mean±SD.

CE, capsule endoscopy; SBE, single balloon-assisted enteroscopy; OGIB, obscure gastrointestinal bleeding; NS, not significant.

[a]Student *t*-test; [b]Chi-square test; [c]Including cardiovascular, renal, pulmonary, autoimmune (e.g., rheumatoid arthritis), and endocrine diseases.

</br>

If an approach failed to detect the bleeding source, tattooing to mark the extent of examination was performed at the deepest point during the session. An experienced gastroenterologist performed all examinations. Argon plasma coagulation or clip placement was performed when the bleeding source was identified, and a standard polypectomy snare (Olympus) was used for endoscopic management of vascular lesions, ulcerative lesions, polyps, and diverticula.

Statistical analysis

We compared continuous variables using Student t-test and frequencies using the chi-square test and Fisher exact test. All statistical analyses were performed using SPSS version 18 (SPSS Inc., Chicago, IL, USA). The significance level was set at $p<0.05$.

RESULTS

Patients

The study included 194 patients who underwent CE and/or BE to detect the source of OGIB. CE and SBE were performed in 103 and 91 patients, respectively, and 26 patients underwent both examinations. The patient characteristics are presented in Table 1.

Capsule endoscopy results

All 103 patients (65 overt and 38 occult bleeding cases) who underwent CE successfully swallowed the capsules, and there was no complaint or abnormality during the examination.

The mean times to pass through the stomach and small bowel were 47.6±47.0 minutes and 390±150 minutes, respectively. The capsule reached the cecum within the capsule recording time in 81 patients (79%), while evaluation of the entire small bowel failed in 22 patients (21%). All the patients successfully egested the capsule. Positive findings were noted in 49 patients (47.5%) (Table 2), and the findings were vascular lesions in 34 patients (69.4%), ulcers in 10 (20.4%), tumors in three (6.1%), and diverticula in two (4.1%) (Table 3).

Single balloon-assisted enteroscopy results

SBE was performed in 91 patients. The enteroscope was orally and rectally inserted in 43 and 48 patients, respectively. The mean procedure time was 89 minutes (range, 18 to 197). Mild pancreatitis was observed as an accidental symptom in three patients after oral enteroscopy. No perforation of the digestive tract was observed. Positive findings were noted in 67 patients (73%) (Table 2), and the findings were vascular lesions in 34 patients (50.7%), ulcers in 28 (41.8%), tumors in two (3%), and diverticula in three (4.5%) (Table 3). The rate of positive findings was higher using SBE (73.6%) than using CE (47.5%; $p<0.01$, chi-square test) (Table 2).

Endoscopic management was performed in 51 patients (76.1%), and clip placement, argon plasma coagulation, local injection of hypertonic saline-epinephrine, and polypectomy were performed in 28, 16, 6, and 1 patient, respectively (Table 4). No accidental symptom caused by endoscopy was observed.

The rate of positive findings was higher in overt bleeding cases than in occult bleeding cases for both CE and SBE.

Table 2. Rates of Positive Findings on CE and SBE according to the Bleeding Type

Variable	CE (n=103)	SBE (n=91)	p-value
Total	49 (47.5)	67 (73.6)	<0.01[a]
Overt	38/65 (58.4)	55/68 (80.8)	
Occult	11/38 (23.9)	12/23 (52.2)	<0.01[a]

Values are presented as number (%).
CE, capsule endoscopy; SBE, single balloon-assisted enteroscopy.
[a]Chi-square test.

Table 3. Rates of Positive Findings on CE and SBE according to the Finding

Variable	CE (n=49)	SBE (n=67)	p-value
Vascular lesion	34 (69.4)	34 (50.7)	NS[a]
Ulcer	10 (20.4)	28 (41.8)	NS[a]
Tumor	3 (6.1)	2 (3.0)	NS[a]
Diverticulum	2 (4.1)	3 (4.5)	NS[a]

Values are presented as number (%).
CE, capsule endoscopy; SBE, single balloon-assisted enteroscopy; NS, not significant.
[a]Chi-square test.

Among the overt bleeding cases, the rate of positive findings was higher in ongoing bleeding cases than in previous bleeding cases (Table 5). CE had been performed before SBE in 26 patients, and positive findings were observed in 20 (76.9%) of these patients. CE had not been performed before SBE in 65 patients, and positive findings were observed in 41 (63.1%) of these patients. These results indicated that CE performed before SBE significantly contributed to the rate of positive findings (*p*<0.01).

DISCUSSION

The rates of positive findings on CE and SBE in the diagnostic evaluation of OGIB were 47.5% and 73.6%, respectively, indicating the superiority of SBE in the detecting of the source of OGIB. Furthermore, the rate of positive findings was higher in overt bleeding cases than in occult bleeding cases for both CE and SBE, and among the overt bleeding cases, the rate of positive findings was higher in ongoing bleeding cases than in previous bleeding cases.

CE and SBE were developed in 2000 as novel approaches allowing detailed examination of the small bowel. These methods may overcome the drawbacks of conventional methods for small-bowel examination, such as push endoscopy and endoscopic surgery, which are traditionally the most common methods for evaluating the small bowel. Similar to esophagogastroduodenoscopy, push endoscopy enables endoscopic management; however, its working area is limited to the jejunum. Intraoperative endoscopy is most commonly used to evaluate the entire small bowel but it is the most invasive among all the methods. On the other hand, CE is less invasive and enables evaluation of the entire small bowel.[7] In the present study, using CE, the successful evaluation rate of the entire small bowel was 79%, and the rate of positive findings was 47.5%. The diagnostic yield of CE has been reported to be 38% to 75%,[8-10] and we speculate that differences in the diagnostic accuracy of various causes of OGIB may explain this wide range.

The diagnostic yield for OGIB was 60.5% in a recent pooled analysis of 227 studies on OGIB; however, we believe that this rate may be too high, as some studies considered minor redness or small erosions as the bleeding source.[11] Our results indicate that CE, with a diagnostic yield of 47.5%, may represent an appropriate diagnostic examination for OGIB.

In Western countries, vascular lesions are most commonly identified as the source of OGIB.[1] Detection of vascular lesions is challenging using modalities other than CE, because they are small and flat.[11] In this study, vascular lesions were found in 34 of 49 patients (69.4%), accounting for more than half of the positive findings. Detection of large tumor lesions or submucosal tumors without mucosal change is challenging when using CE; therefore, CE should be used in combination with other examinations. The presence of massive lesions, such as neoplastic lesions, should be confirmed using CT or radiological enteroclysis before performing CE, if possible.[3]

Some algorithms on the management of small-bowel bleeding have been previously reported. Because the burden on patients is higher with BE than with CE, CE is the first choice for the diagnosis of bleeding in most cases.[5,12,13] However, many questions remain regarding the most appropriate evaluation strategy in terms of using medical resources effectively in the short-term.[14] Importantly, CE can be used for diagnosis but not for treatment, whereas with BE, endoscopic diagnosis and treatment can be completed simultaneously, and a biopsy can be obtained for definitive diagnosis. Performing these examinations during bleeding contributes greatly to the detection of the bleeding source and to the selection of the method for the diagnostic evaluation of OGIB.[15]

In a previous study, in patients with OGIB, the diagnostic

Table 4. Rates of Positive Findings according to Endoscopic Management

Variable	Value
Total no. (%)	51/67 (76.1)
Clip placement	28
Argon plasma coagulation	16
Hypertonic saline-epinephrine	6
Polypectomy	1

Table 5. Rates of Bleeding on CE and SBE

Variable	Overt (ongoing)	Overt (previous)	Occult	*p*-value
CE	10/11 (90.9)	28/54 (51.8)	11/38 (23.9)	<0.01[a]
SBE	27/27 (100)	28/41 (68.2)	12/23 (52.2)	<0.01[a]

Values are presented as number (%).
CE, capsule endoscopy; SBE, single balloon-assisted enteroscopy.
[a]Chi-square test.

yield of emergent SBE (93.3%) performed within 24 hours after overt bleeding was significantly higher than that of elective SBE (64.3%) performed 24 hours or more after bleeding (Fisher exact test, $p<0.038$).[16] Although both CE and SBE may be useful for the diagnosis of OGIB, the rate of positive findings was higher with SBE (73.6%) than with CE (47.5%) in this study. Additionally, the rate of positive findings was higher in overt bleeding cases than in occult bleeding cases for both CE and SBE. Moreover, among overt bleeding cases, the rate of positive findings was significantly higher in ongoing bleeding cases than in previous bleeding cases. Thus, when overt bleeding is observed, especially during the acute phase, SBE should be considered, because endoscopic diagnosis and treatment can be completed simultaneously. CE may be more appropriate than SBE for occult bleeding cases or cases in which the SBE route cannot be determined based on the clinical symptoms or the results of other examinations. Additionally, performing CE before SBE significantly contributes to the rate of positive findings.

The development of CE and BE has resulted in progressive improvements in the diagnostic imaging of the small bowel in patients with OGIB. The timing of performing the examination and the selection of the method are important for a successful diagnosis; however, there are currently no clear criteria for determining these factors.

The present study has some limitations. First, this study was a retrospective study. Second, the study was performed at a single institution. Our findings should be interpreted keeping these limitations in mind.

In conclusion, both CE and SBE are useful to diagnose OGIB. For overt bleeding cases and ongoing bleeding cases, SBE may be more appropriate that CE, as endoscopic diagnosis and treatment can be completed simultaneously.

Conflicts of Interest

The authors have no financial conflicts of interest.

REFERENCES

1. Pasha SF, Hara AK, Leighton JA. Diagnostic evaluation and management of obscure gastrointestinal bleeding: a changing paradigm. Gastroenterol Hepatol (N Y) 2009;5:839-850.
2. Lewis BS. The history of enteroscopy. Gastrointest Endosc Clin N Am 1999;9:1-11.
3. Iddan G, Meron G, Glukhovsky A, Swain P. Wireless capsule endoscopy. Nature 2000;405:417.
4. Tsujikawa T, Saitoh Y, Andoh A, et al. Novel single-balloon enteroscopy for diagnosis and treatment of the small intestine: preliminary experiences. Endoscopy 2008;40:11-15.
5. Raju GS, Gerson L, Das A, Lewis B; American Gastroenterological Association. American Gastroenterological Association (AGA) Institute technical review on obscure gastrointestinal bleeding. Gastroenterology 2007;133:1697-1717.
6. Leighton JA, Goldstein J, Hirota W, et al. Obscure gastrointestinal bleeding. Gastrointest Endosc 2003;58:650-655.
7. Mylonaki M, Fritscher-Ravens A, Swain P. Wireless capsule endoscopy: a comparison with push enteroscopy in patients with gastroscopy and colonoscopy negative gastrointestinal bleeding. Gut 2003;52:1122-1126.
8. Scapa E, Jacob H, Lewkowicz S, et al. Initial experience of wireless-capsule endoscopy for evaluating occult gastrointestinal bleeding and suspected small bowel pathology. Am J Gastroenterol 2002;97:2776-2779.
9. Tang SJ, Haber GB. Capsule endoscopy in obscure gastrointestinal bleeding. Gastrointest Endosc Clin N Am 2004;14:87-100.
10. Carey EJ, Leighton JA, Heigh RI, et al. A single-center experience of 260 consecutive patients undergoing capsule endoscopy for obscure gastrointestinal bleeding. Am J Gastroenterol 2007;102:89-95.
11. Liao Z, Gao R, Xu C, Li ZS. Indications and detection, completion, and retention rates of small-bowel capsule endoscopy: a systematic review. Gastrointest Endosc 2010;71:280-286.
12. Raju GS, Gerson L, Das A, Lewis B; American Gastroenterological Association. American Gastroenterological Association (AGA) Institute medical position statement on obscure gastrointestinal bleeding. Gastroenterology 2007;133:1694-1696.
13. Pennazio M, Spada C, Eliakim R, et al. Small-bowel capsule endoscopy and device-assisted enteroscopy for diagnosis and treatment of small-bowel disorders: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy 2015;47:352-376.
14. Mensink PB. Acute obscure-overt gastrointestinal bleeding: capsule endoscopy first? Endoscopy 2012;44:335-336.
15. Aniwan S, Viriyautsahakul V, Angsuwatcharakon P, et al. Comparison of urgent video capsule endoscopy and urgent double-balloon endoscopy in massive obscure gastrointestinal bleeding. Hepatogastroenterology 2014;61:1990-1994.
16. Pinto-Pais T, Pinho R, Rodrigues A, et al. Emergency single-balloon enteroscopy in overt obscure gastrointestinal bleeding: efficacy and safety. United European Gastroenterol J 2014;2:490-496.