

# Combined Use of Capsule Endoscopy and Double-balloon Enteroscopy in Patients with Obscure Gastrointestinal Bleeding

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**Background:** Most of the sources of bleeding in patients with obscure gastrointestinal bleeding are located in the small bowel. Capsule endoscopy (CE) and double-balloon enteroscopy (DBE) are innovative modalities to examine the small intestine. This study evaluated the combined use of CE and DBE in patients with obscure gastrointestinal bleeding.

**Methods:** From October 2005 to November 2006, ten patients with obscure gastrointestinal bleeding who underwent CE followed by DBE were included in this study. The insertion route for DBE was determined according to the site of obscure gastrointestinal bleeding detected by CE in nine patients. The antegrade route was selected when the estimated location of the lesion was in the proximal two-thirds of the small bowel and the retrograde route was chosen when the estimated location was after the proximal two-thirds. In one patient without a definite lesion detected by CE, the route of insertion was determined according to clinical judgment.

**Results:** Eleven capsule endoscopies were performed in ten patients. Significant or suspicious small bowel lesions were discovered by CE in nine (90%; 9/10) patients, including angiodysplasia (n = 3), active bleeding (n = 3), a polypoid lesion (n = 1), suspected enteritis (n = 1) and gastric antral vascular ectasia with small bowel bleeding (n = 1). Eleven DBE were performed in ten patients. Significant small bowel lesions were detected by DBE in eight patients (80%), including angiodysplasias (n = 3), lymphangioectasias (n = 2), varices (n = 1), polypoid lesion (n = 1) and Dieulafoy's lesion (n = 1). Endoscopic treatments were performed successfully in 7 patients, including argon plasma coagulation in four, heat probe coagulation in one, endoscopic mucosal resection in one and sclerotherapy in one.

**Conclusions:** CE can provide useful information on the indications for DBE and the selection of the route of DBE. DBE can verify the findings of CE and provide therapeutic intervention. Combined use of CE and DBE is effective in the diagnosis and management of patients with obscure gastrointestinal bleeding. (*Chang Gung Med J* 2008;31:450-6)

**Key words:** capsule endoscopy, double-balloon enteroscopy, obscure gastrointestinal bleeding

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Received: May 10, 2007; Accepted: Oct. 5, 2007

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Obscure gastrointestinal bleeding refers to recurrent overt or occult gastrointestinal bleeding in which the source cannot be determined by conventional endoscopy examination (esophagogastroduodenoscopy and colonoscopy).<sup>(1)</sup> Small bowel lesions are presumed to be responsible for obscure gastrointestinal bleeding in most patients. However, the small bowel is difficult to thoroughly examine by conventional endoscopic methods given its length, free intraperitoneal location and rigorous contractility.<sup>(2)</sup> Other examination methods such as small bowel radiography and radionuclide bleeding scan are not satisfactory for detecting small bowel lesions.<sup>(1,3)</sup> Capsule endoscopy (CE) has been used to examine patients for suspected small bowel bleeding and has proven superior to other diagnostic modalities such as push enteroscopy and small bowel series.<sup>(4,5)</sup> Although CE is considered a noninvasive first line diagnostic modality for small bowel diseases, it is limited by its inability to provide to-and-fro observation, air inflation, water irrigation and therapeutic intervention.<sup>(6)</sup>

Double-balloon enteroscopy (DBE), recently developed by Yamamoto *et al.*, offers an excellent new endoscopic method for small bowel examination and overcomes the limitations of CE.<sup>(6,7)</sup> A total small bowel examination can be achieved with a high success rate with the combined use of anterograde and retrograde DBE.<sup>(7)</sup> However, the invasiveness of the procedure may require sedation or general anesthesia, fluoroscopic monitoring of the advancing scope, and the participation of two experienced endoscopists.<sup>(8)</sup> Therefore, the indications and insertion route for double-balloon enteroscopy should be carefully determined to reduce the time and number of examinations using DBE. The purpose of this study is to evaluate combined CE and DBE in patients with obscure gastrointestinal bleeding.

## METHODS

From October 2005 to November 2006, ten patients (three males and seven females; mean age  $63.5 \pm 22.7$  years, range 11~87 years) with obscure gastrointestinal bleeding who underwent CE followed by DBE were evaluated. The median lowest hemoglobin level was 7.3 g/dL (range, 3.8~11.2 g/dL). The mean duration of obscure gastrointestinal bleeding prior to DBE was  $5.4 \pm 7.5$  months.

Multiple diagnostic procedures were performed in the ten patients before CE and DBE in our hospital, with an average of 3.6 examinations per patient. The conventional diagnostic imaging procedures performed in these patients included esophagogastroduodenoscopy (n = 11), sigmoidoscopy (n = 2), colonoscopy (n = 5), small bowel follow-through (n = 6), visceral angiography (n = 1), technetium-99m-labeled radionuclide bleeding scanning (n = 5), abdominal computed tomography (n = 5), and Meckel scan (n = 1). A bleeding tendency was observed in 3 (30%) patients, who had end-stage renal disease (n = 1) and decompensated liver cirrhosis (n = 2). CE anteceded DBE by a median of 7 days (range, 3-57 days).

### Capsule endoscopy

All patients underwent Pill Cam SB capsule (Given Imaging, Yoqneam, Israel) examination with informed consent. Patients were instructed to fast overnight for 8-12 hours prior to the procedure. In the morning, they swallowed the capsule with a full glass of water after a sensor array was applied to their abdomen and connected to the data recorder which they wore on a belt. They were allowed to drink fluid two hours and to eat a meal four hours after ingesting the capsule. The capsule passed naturally through the gastrointestinal tract and took images of the intestine at a speed of two frames per second. The images were transmitted to the sensor array and saved to the data recorder. The data recorder was removed 8 hours later and the images were downloaded to the workstation computer. All of the CE examinations were interpreted by one endoscopist. The location of any lesion detected by CE in the small bowel was determined by the time ratio, which was calculated by the transit time from the pylorus to the lesion divided by the transit time from the pylorus to the cecum.

### Double-balloon enteroscopy

The DBE system (Fujinon Inc., Japan) consists of a high-resolution video endoscope with a balloon attached at the tip, a flexible overtube with another balloon, and a pump for inflation and deflation of the balloons. There are two types of endoscopes, the EN-450P5 type for general use and the EN-450T5 type for treatment. The general-use type is thinner with an external diameter of 8.5 mm and a forceps channel

diameter of 2.2 mm. The therapeutic endoscope has an external diameter of 9.4 mm and a forceps channel of 2.8 mm. The video endoscope has a working length of 200 cm while the flexible overtube is 140 cm long. Antegrade DBE was performed by mouth and retrograde DBE by rectum. The techniques of insertion of DBE have been described elsewhere.<sup>(3,9)</sup>

The insertion route was determined based on the estimated location of the lesions from CE. Antegrade DBE was selected when time ratio of the lesion was less than 2/3 and retrograde DBE was selected when time ratio of the lesion exceeded 2/3. In patients without a definite lesion detected by CE, the route of insertion was determined according to clinical presentation.

No specific preparation was required for the antegrade DBE besides fasting for 6-8 hours before the procedure. The retrograde route required bowel cleansing as in a colonoscopy. DBE was performed under minor conscious sedation (n = 7) or general anesthesia (n = 3) with informed consent. For minor conscious sedation, premedications including intravenously injected meperidine (0.5~1.0 mg/kg) and midazolam (0.05 mg/kg) were given before the procedure.

## RESULTS

Eleven CE were performed in ten patients. Complete visualization of the small intestine was

achieved in seven (70%; 7/10) patients. Significant or suspicious intestinal lesions were discovered by CE in nine (90%; 9/10) patients (Table 1). Small intestinal angiodysplasias (Fig. 1) were suspected in three patients, small intestinal active bleeding was observed in three patients, one small intestinal polypoid lesion with bleeding (Fig. 2) was found in one patient, enteritis was suspected in one patient, and gastric antral vascular ectasia with a small intestinal blood clot was identified in one patient. No definite lesion or source of bleeding was found in one (10%). The overall diagnostic yield of CE was 90%. The median time ratio to the lesion site was 0.14 (range, 0.02~0.66). In two cases, suspected small bowel angiodysplasia and active small bowel bleeding were observed, despite an incomplete CE study due to battery depletion before arrival at the cecum.

Eleven DBE examinations were performed in ten patients. The median examination time was 90 minutes (range, 22~104 minutes). Nine (90%) of the ten patients underwent DBE based on the results of CE. The indications included active small bowel bleeding of an unidentified nature (n = 4), angiodysplasia for endoscopic treatment (n = 3), suspicion of intestinal tumor (n = 1), and suspicion of enteritis for verification and biopsy (n = 1). Retrograde DBE was selected in one (10%) patient who presented with hematochezia with a negative CE study. Significant small bowel lesions were detected by DBE in eight patients (80%), including angiodysplasias (n = 3)

**Table 1.** Data on Patients with Obscure Intestinal Bleeding Who Had Capsule Endoscopy and Double-balloon Enteroscopy

No.	Age	Gender	CE findings	Time ratio to lesion site	DBE route	DBE findings	Treatment
1	69	F	GAVE/SB blood	< 0.03*	PO	Jejunal angiodysplasia	Tattooing followed by surgery
2	11	F	angiodysplasia	0.35	PO	jejunal angiodysplasia	Heat probe coagulation
3	50	F	polypoid lesion	0.14	PO	jejunal polypoid lesion	EMR
4	87	M	negative	–	PR	negative	–
5	52	M	SB bleeding	0.34	PO	jejunal varices	Sclerotherapy
6	73	F	jejunitis	0.15	PO	jejunal lymphagioectasia	Biopsy + APC
7	69	F	SB bleeding	0.02	PO	jejunal lymphagioectasia	Biopsy + APC
8	82	F	angiodysplasia	0.03	PO	Jejunal angiodysplasia	APC
9	87	F	SB bleeding	0.66	PO	Dieulafoy's lesion	APC
10	55	M	angiodysplasia	< 0.15*	PO	duodenal ulcer	–

**Abbreviations:** APC: argon plasma coagulation; CE: capsule endoscopy; DBE: double-balloon enteroscopy; EMR: endoscopic mucosal resection; GAVE: gastric antral vascular ectasia; PO: per oral route; PR: per rectal route; SB: small bowel; \*: CE did not reach cecum.



**Fig. 1** One of multiple angiodysplasia in the small bowel detected by capsule endoscopy in a patient with obscure gastrointestinal bleeding.



**Fig. 2** A polypoid lesion with a reddish surrounding surface in the small bowel discovered by capsule endoscopy.

(Fig. 3), lymphangioectasias (n = 2), varices (n = 1), polypoid lesion (n = 1) (Fig. 4) and Dieulafoy's lesion (n = 1) (Table 1). A duodenal ulcer in the healing stage was found in one patient. No definite lesion was found in one patient with a prior negative CE



**Fig. 3** One of multiple angiodysplasia in the small bowel observed by double-balloon endoscopy.



**Fig. 4** A somewhat nodular polypoid lesion with a pink surrounding surface in the small bowel detected by double-balloon endoscopy.

examination.

Endoscopic treatments were performed in eight patients. Two patients with small intestinal angiodysplasias were treated, one by argon plasma coagulation and one by heat probe coagulation. Two patients with small intestinal lymphangioectasias underwent biopsy followed by treatment with argon plasma coagulation. Endoscopic mucosal resection was performed for a granulating polypoid lesion in one patient. One patient with small intestinal varices was treated with sclerotherapy by histoacryl injection. One patient with small bowel Dieulafoy's lesion was treated with heat probe coagulation. Furthermore,

one patient with actively bleeding angiodysplasias in the small bowel in whom endoscopic treatment failed to achieve hemostasis was tattooed at the bleeding sites and subsequently underwent laparoscopic surgical intervention. All the procedures were well-tolerated and no complications occurred.

## DISCUSSION

CE is a useful tool for diagnosing small bowel lesions in patients with obscure gastrointestinal bleeding, with a yield rate of 38%~93%.<sup>(10)</sup> The diagnostic yield of CE was 92.3% in patients with ongoing overt bleeding, 44.2% in patients with obscure occult bleeding, and 12.9% in patients with previous obscure overt bleeding in one multicenter study of 100 patients.<sup>(11)</sup> In the present series, CE identified positive findings in nine (90%) of ten patients.

The diagnostic yield of DBE for patients with obscure gastrointestinal bleeding has been reported to reach 72%~80%.<sup>(3,7,12-15)</sup> In this study, eight patients (80%) were diagnosed by DBE. Comparisons of CE and DBE in detecting the causes of obscure gastrointestinal bleeding have not shown consistent results in the literature. In one prospective study, the detection rate for CE exceeded that of DBE (80% vs 60%,  $p = 0.01$ ) in patients with obscure GI bleeding.<sup>(16)</sup> Other studies showed that CE and DBE were equally effective in identifying intestinal lesions responsible for obscure gastrointestinal bleeding.<sup>(17,18)</sup> Our results showed that the diagnostic yields of both procedures were similar.

Although CE is a highly sensitive examination for the detection of small intestinal lesions in patients with obscure gastrointestinal bleeding, it is limited by its inability to provide to-and-fro observation, water washing, tissue biopsy, and therapeutic intervention. DBE overcomes the limitations of CE and can be used for endoscopic intervention. In our series, four bleeding small bowel lesions detected by CE were verified as angiodysplasia, varices, lymphangiectasia, and Dieulafoy's lesion by DBE. Seven therapeutic procedures were successfully performed in this study, including argon plasma coagulation in four patients, heat probe coagulation in one, endoscopic mucosal resection in one, and sclerotherapy in one. Balloon dilatation, stent placement, snare polypectomy, and foreign body removal have also been performed successfully using the DBE sys-

tem.<sup>(3,7,12,13,19)</sup> Therefore, DBE is an excellent modality for endoscopic intervention in the small intestine.

Total small bowel examination by DBE usually requires a combination of the antegrade route and retrograde routes with a success rate of 42%~86%.<sup>(7,12,14)</sup> If no definite lesion is detected in the initial DBE examination in patients with obscure gastrointestinal bleeding, DBE from the opposite direction may be required. However, DBE is an invasive procedure that demands sedation or general anesthesia, fluoroscopic monitoring, the participation of two experienced endoscopists, and a prolonged examination time. Accurate localization of the lesion in the small intestine may facilitate the selection of the insertion route for DBE and decrease the number and time of examinations in patients with obscure gastrointestinal bleeding. In this study, we used the time ratio of the lesion detected by CE to estimate the site of the lesion in the small bowel under the assumption that CE travels at a constant velocity in the small bowel. Furthermore, the estimated average insertion length by DBE is one-half to two-thirds the length of the entire small bowel.<sup>(7)</sup> Retrograde DBE is more difficult than antegrade DBE with more radiation exposure and greater discomfort for the patient.<sup>(8,12)</sup> Therefore, it is reasonable to select the antegrade route if the estimated site of the lesion is within the proximal two-thirds of the entire small bowel, i.e. time ratio of the lesion is less than 2/3. In the present series, all small bowel lesions detected by CE were approached with single route DBE using this method for selection of the insertion route.

In previous reports, patients with obscure gastrointestinal bleeding underwent an average of 5~7.4 procedures before detection or treatment of the source of bleeding by CE or DBE.<sup>(3,5,11,15)</sup> Acute small bowel bleeding was associated with a higher number of diagnostic procedures and blood transfusions, longer hospital stay, and higher health care expenditures than colonic bleeding and upper gastrointestinal bleeding in a comparative study.<sup>(20)</sup> Although CE and DBE are expensive examinations, early use of these two procedures in patients with obscure gastrointestinal bleeding may be cost-effective.

In conclusion, CE and DBE are good modalities with high diagnostic yields for detection of small bowel lesions. CE is a noninvasive procedure and could be used as the first choice for diagnostic investigation in patients with obscure gastrointestinal

bleeding. DBE can verify the findings of CE and provide therapeutic intervention in the small bowel. Combined use of CE and DBE is effective in the diagnosis and management of patients with obscure gastrointestinal bleeding.

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## 合併使用小腸膠囊內視鏡與雙氣囊小腸內視鏡 於原因不明的消化道出血病患

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**背景：** 大部分原因不明消化道出血的源頭位於小腸，而小腸膠囊內視鏡與雙氣囊小腸內視鏡被視為診斷與治療小腸疾病的新方法。此研究目的為評估合併小腸膠囊內視鏡與雙氣囊小腸內視鏡應用於原因不明消化道出血病患的實用性。

**方法：** 從民國 94 年 10 月至民國 95 年 11 月，一共有 10 位原因不明的消化道出血病患接受小腸膠囊內視鏡與雙氣囊小腸內視鏡檢查。9 位患者先接受小腸膠囊內視鏡檢查後，再依據小腸膠囊內視鏡的診斷選擇經口或經肛門的雙氣囊小腸內視鏡檢查。若評估病灶的位置位於近端前三分之二小腸時，則選擇經口雙氣囊小腸內視鏡檢查，反之亦然。1 位膠囊內視鏡檢查無異常患者則依據臨床判斷診斷選擇雙氣囊小腸內視鏡的插入途徑。

**結果：** 10 位病患接受 11 次小腸膠囊內視鏡檢查。9 (90%) 位病患膠囊內視鏡檢查有顯著或是疑似腸道異常病灶，包括 3 位疑似小腸血管發育不良，3 位小腸活動性出血，1 位小腸息肉樣病灶併活動性出血，1 位疑似小腸炎症，與 1 位胃竇部血管擴張併小腸血塊。10 位病患共接受 11 次雙氣囊小腸內視鏡檢查。8 (80%) 位病患雙氣囊小腸內視鏡檢查有顯著腸道病灶，包括 3 位小腸血管發育不良，2 位小腸淋巴管擴張，1 位小腸靜脈瘤，1 位小腸肉芽性息肉樣病灶，與 1 位小腸 Dieulafoy 氏潰瘍。7 位病患成功的接受小腸內視鏡治療，包括 4 位接受氫電漿凝固治療，1 位接受熱探子燒灼治療，1 位接受內視鏡黏膜切除術，1 位接受血管硬化劑注射治療。

**結論：** 小腸膠囊內視鏡能提供有價值的資料來選擇雙氣囊小腸內視鏡檢查的適應症與插入途徑。雙氣囊小腸內視鏡能證實小腸膠囊內視鏡的發現並提供內視鏡介入性處置。合併小腸膠囊內視鏡與雙氣囊小腸內視鏡能有效的診斷與治療原因不明的消化道出血。

(長庚醫誌 2008;31:450-6)

**關鍵詞：** 小腸膠囊內視鏡，雙氣囊小腸內視鏡，原因不明的消化道出血

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受文日期：民國96年5月10日；接受刊載：民國96年10月5日

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