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Original Article

Is a bleeding scan prior to single-balloon enteroscopy necessary in patients with obscure gastrointestinal bleeding?

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KEYWORDS

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Background/purpose: To evaluate the efficacy and accuracy of bleeder localization in a pre-enteroscopic bleeding scan in patients with obscure gastrointestinal bleeding (OGIB).

Methods: From January 2009 to December 2014, 98 patients with OGIB undergoing single-balloon enteroscopy (SBE) were enrolled. These patients were classified based on their history of a previous bleeding scan; 56 patients had undergone a previous bleeding scan, whereas 42 had not. The clinical characteristics, endoscopic findings, and rebleeding rate were compared between these two groups. The ability of the bleeding scan to localize the bleeding site was analyzed.

Results: The mean age of patients was 56 ± 22 years; final diagnostic yield, 65.3%; and the most common etiology of OGIB, angiodysplasia (29.6%). There was no significant difference in demographic characteristics, OGIB etiologies, and final diagnostic yields (67.9% vs. 61.2%, bleeding scan vs. control group) between groups. In the bleeding scan group, the rate of positive detection was approximately 80.4%. However, only 26.7% patients with a positive bleeding scan showed correct localization of bleeding. Moreover, the bleeding scan delayed SBE (8.9 days vs. 3.0 days, $p < 0.001$). During the 24 months of follow-up, 15 patients (15.3%) exhibited rebleeding and needed to be hospitalized, but there was no significant difference between the groups.

Conclusion: In our study, bleeding scans in patients with OGIB revealed poor localization of the bleeder and delay in performing SBE. Thus, a bleeding scan prior to SBE showed a limited role for patients with OGIB.

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Introduction

Obscure gastrointestinal bleeding (OGIB) or blood loss, the cause of which cannot be identified by upper endoscopy, colonoscopy, or radiology, accounts for 5%–10% of gastrointestinal bleeding events.¹ The diagnosis and treatment of OGIB were revolutionized in the past decade by the introduction of capsule endoscopy and enteroscopy. Previous studies have shown that in patients with OGIB, double-balloon enteroscopy (DBE) can provide a correct diagnosis in 60%–70% cases and can be used to administer endoscopic therapy in many cases.^{2,3} Thus, enteroscopy appears to have an important role in the diagnosis and treatment of OGIB. In 2008, a single-balloon enteroscopy (SBE) system was introduced as an alternative deep enteroscopy technique and has been considered a powerful tool in the diagnosis and treatment of small-bowel diseases. In addition, the technique is less time consuming and easier to perform compared with DBE.^{4,5}

Before patients with OGIB undergo enteroscopic intervention, physicians often use less-invasive methods, e.g., computed tomography angiography (CTA), capsule endoscopy, or scintigraphy with ^{99m}Tc (bleeding scan), to attempt pre-endoscopic localization of the bleeding. Based on past literature, capsule endoscopy prior to enteroscopy can increase the diagnostic yield of SBE in patients with small bowel diseases.⁶ Furthermore, CTA increases the detection rate of bleeders prior to SBE in patients with overt OGIB.⁷ A bleeding scan is commonly used in clinical practice, because it is non-invasive and can detect both arterial and venous bleeding sites. However, the efficacy of pre-endoscopic bleeding scans in localizing the site of bleeding in patients with OGIB is unknown. According to the findings by Brännler et al., a bleeding scan can only reliably localize approximately 50% of gastrointestinal bleeding cases.⁸ Furthermore, the benefits of this examination in patients with OGIB undergoing enteroscopy need further determination. The purpose of this study was to evaluate the efficacy and accuracy of bleeder localization by a pre-enteroscopic bleeding scan in patients with OGIB.

Methods

Patients

In all, 98 consecutive patients who underwent SBE at Tri-Service General Hospital for the evaluation of OGIB between January 2009 and December 2014 were identified from our institutional database for study inclusion. All patients in this study underwent esophagogastroduodenoscopy and colonoscopy before SBE. The need for patient consent in this study was waived because patient information was de-identified and anonymized prior to analysis.

The institutional review board of Tri-Service General Hospital approved this study (TSGHIRB: 1-106-05-154).

OGIB

OGIB was defined as occult or overt gastrointestinal bleeding that persists or recurs without an obvious etiology after standard endoscopic examination (routine esophagogastroduodenoscopy and colonoscopy).⁹ Overt OGIB was defined as clinically perceptible bleeding and occult OGIB was defined as iron-deficiency anemia, with a positive fecal occult blood test. In our study, patients with overt or occult OGIB were included.

SBE procedure

All procedures were performed with an Olympus single-balloon enteroscope (SIF-Q260; Olympus Optical, Tokyo, Japan) by an experienced endoscopist specialized in SBE. The initial insertion route for SBE was decided based on the judgment of the patient's clinical presentation and images; another routine SBE may be considered if the initial SBE showed negative findings. Bowel preparation was conducted using an oral electrolyte lavage solution administered 6 h prior to SBE via an anal approach; all patients fasted overnight prior to SBE. Before SBE, hyoscine-N-butylbromide, midazolam, and meperidine were administered to patients for sedation and pain control on demand. A cap was attached to the tip of the enteroscope. The enteroscope was inserted using the "hook-tip" procedure, as described by Tsujikawa et al.¹⁰ The time to perform SBE was defined as the days from the initial admission to the time of SBE.

Bleeding scan

Examination by scintigraphy was performed using the radionuclide ^{99m}Tc. Patients with OGIB underwent a bleeding scan before the enteroscopic intervention based on clinical decision-making. While performing the bleeding scan, the images were acquired immediately and 5, 10, 15, and 30 min and 1, 3, 5, and 24 h after radiopharmaceutical injection. The scintigraphic findings were reported by experienced attending nuclear medicine physicians.

Data collection

Demographic data as well as history of anti-platelet and anti-coagulant use, bleeding scan data, and endoscopic findings were obtained from electronic medical records.

Post-SBE follow-up

Patients underwent follow-up evaluations for at least 24 months and were excluded if they were lost to follow-up after undergoing SBE. Follow-up information was obtained from our institution's electronic medical records. In our study, enrolled patients with recurrent bleeding requiring hospitalization were considered to have recurrent OGIB.

Statistical analysis

Statistical analyses were performed using SPSS 12.0 statistical software (SPSS Inc., Chicago, IL). Values are shown as total numbers, averages, or percentages, where necessary. Statistical comparisons between groups were computed using the Student's *t* test or chi-square test, according to the type of data. The Kaplan–Meier method and log-rank test were also performed via SPSS. All reported *p* values were two-tailed. A *p* < 0.05 was considered to be statistically significant for all tests.

Results

Between January 2009 and December 2014, 98 patients underwent SBE for the evaluation of OGIB. The baseline data of these patients, including age, sex, underlying disease, history of anti-platelet or anti-coagulant use, and approach policies from the anal or oral cavities, are shown in Table 1. Ninety-four patients presented with overt gastrointestinal bleeding (96%), wherein melena was the

most common symptom (66.3%). Twenty-nine patients presented with hematochezia (29.6%). Only four patients undergoing SBE presented with occult gastrointestinal bleeding. The age of patients ranged from 14 to 94 years. Approximately 37.8%, 30.6%, and 31.2% of patients underwent SBE by antegrade, retrograde, and bilateral approaches, respectively (Table 1).

In OGIB patients undergoing SBE, the endoscopic diagnostic rate was 65.3%. The most common etiology was angiodysplasia (29.6%), followed by non-specific ulcers (16.3%) (Table 2). Four patients presented with anemia and occult OGIB. One of them was diagnosed with angiodysplasia, and three of them had negative results in SBE. Among the patients with a positive finding on SBE, the lesion was found in the duodenum in 7 patients (7.1%), jejunum in 27 patients (27.6%), ileum in 26 patients (26.5%), and colon in 4 patients (4.1%) (Table 2). After SBE, 5 patients underwent surgery and 48 underwent endoscopic treatment (Table 1).

Fifty-six patients underwent a bleeding scan before SBE (bleeding scan group), whereas 42 patients did not undergo a bleeding scan (control group). There was no significant difference in the baseline demographic characteristics (age, sex, history of vascular heart disease and anti-platelet or anti-coagulant use, hemoglobin level, and diagnosis) between the two groups. With regard to the diagnostic rate, patients who underwent a bleeding scan showed a higher detection rate (67.9% versus 61.2%); however, this finding was not significant. Importantly, patients who underwent a bleeding scan revealed a delay in SBE compared with those who did not undergo a bleeding scan (8.9 days vs. 3.0 days, *p* < 0.001) among patients with overt OGIB (Table 3).

In the bleeding scan group, 45 patients (45/56, 80.4%) exhibited positive findings during the bleeding scan, and the accuracy rate of bleeder localization was only 26.7% (12/45) (Table 4). Endoscopic intervention confirmed the findings reported in the bleeding scan, which indicated that

Table 1 Clinical characteristics of all enrolled patients (n = 98).

Characteristics	No. (%)
Age (years)	56 (14–94)
Male	45 (45.9%)
Without underlying disease	69 (70.4%)
With underlying disease	31 (31.6%)
Gastrointestinal tract malignancy	5 (5.1%)
Vascular heart disease	21 (21.4%)
Liver cirrhosis	3 (3.0%)
Chronic renal insufficiency	5 (5.1%)
Initial presentation	
Melena	65 (66.3%)
Hematochezia	29 (29.6%)
Occult bleeding	4 (4.0%)
Anti-coagulant use	5 (5.1%)
Antiplatelet use	26 (26.5%)
Bleeding scan	56 (57.1%)
Antegrade enteroscopy	37 (37.8%)
Retrograde enteroscopy	30 (30.6%)
Bi-directional enteroscopy	31 (31.2%)
Final diagnostic yield	64 (65.3%)
Surgical intervention	5 (5.1%)
Endoscopic hemostasis	48 (48.9%)
Argon plasma coagulation	26 (26.5%)
Adrenaline injection	9 (9.2%)
Hemoclipping	13 (13.3%)

Table 2 Endoscopic findings of all OGIB patients undergoing SBE (n = 98).

Lesion and bleeder site	No. (%)
Etiology	
Angiodysplasia	29 (29.6%)
Tumor	6 (6.1%)
Diverticulum	10 (10.2%)
Non-specific ulcer	16 (16.3%)
IBD	2 (2.0%)
Radiation enteritis	1 (1.0%)
Others	2 (2.0%)
Negative	34 (34.7%)
Localization	
Duodenum	7 (7.1%)
Jejunum	27 (27.6%)
Ileum	26 (26.5%)
Colon	4 (4.1%)
Negative	34 (34.7%)

OGIB: obscure gastrointestinal bleeding; SBE: single-balloon enteroscopy; IBD: inflammatory bowel disease.

Table 3 Demographics of patients with OGIB undergoing SBE.

	With bleeding scan (n = 56)	Without bleeding scan (n = 42)	p value
Age	57.2	54.8	0.24
Gender (male)	27 (48.2%)	18 (42.8%)	0.32
Vascular heart disease	7 (12.5%)	8 (19.0%)	0.18
Aspirin or clopidogrel	12 (21.5%)	14 (26.4%)	0.27
Warfarin	3 (5.4%)	2 (4.7%)	0.13
Diagnostic rate	38 (67.9%)	26 (61.2%)	0.65
Nadir hemoglobin (g/dL)	8.5	7.7	0.16
Diagnosis			
Angiodysplasia	18 (32.1%)	11 (26.2%)	0.84
Malignant tumor	3 (5.4%)	2 (4.8%)	0.13
Benign tumor	0 (0%)	1 (2.4%)	0.32
Diverticulum	6 (10.7%)	4 (9.5%)	0.57
Ulcer	10 (17.9%)	6 (14.3%)	0.79
IBD	1 (1.8%)	1 (2.4%)	0.34
Radiation enteritis	0 (0%)	1 (2.4%)	0.32
Others	1 (1.8%)	1 (2.4%)	0.22
Negative	18 (32.1%)	16 (38.1%)	0.57
Time to perform SBE since admission (days) ^a	8.9 ± 4.9	3.0 ± 2.8	<0.001
Post-SBE surgery	2 (3.5%)	3 (7.1%)	0.66

OGIB: obscure gastrointestinal bleeding; SBE: single-balloon enteroscopy; IBD: inflammatory bowel disease.

^a Four patients with occult gastrointestinal bleeding were excluded.

Table 4 Correlation between localization of positive bleeding scans and endoscopic findings in SBE.

Location on bleeding scan	Number	Match for endoscopic diagnosis (%)
Duodenum	4	1 (25.0)
Jejunum	12	6 (50.0)
Ileum	7	2 (28.6)
Colon	22	3 (13.6)
Total	45	12 (26.7)

SBE: single-balloon enteroscopy.

one, six, two, and three patients were bleeding from the duodenum, jejunum, ileum, and colon, respectively (Table 4).

Up to 84% patients with OGIB did not have rebleeding, requiring hospitalization, after SBE during the observation period. Among the 15 patients who experienced rebleeding and had to be hospitalized, three were diagnosed with angiodysplasia, two with ulcer bleeding, and one with a diverticulum. In patients with rebleeding, ten and six patients had previous negative and positive endoscopic findings, respectively. There was a significant difference in rebleeding-free survival between the patients with positive and negative enteroscopic findings ($p = 0.007$) (Fig. 1A). However, there was no significant difference in rebleeding-free survival between patients with positive and negative findings on the bleeding scan ($p = 0.691$) (Fig. 1B).

Discussion

Gastrointestinal bleeding is frequently encountered by endoscopists; however, in 5% of patients experiencing this

symptom, the location of bleeding cannot be identified even after repeating conventional upper endoscopy or colonoscopy. Such cases are termed as OGIB cases. Enteroscopy can help us identify the location of the lesion in the small intestine and offer the possibility of proper therapeutic hemostasis. Endoscopists conventionally obtain pre-procedure imaging data, including a bleeding scan or abdominal computed tomography. We designed our study with the intent to discuss the role of these pre-enteroscopic bleeding scans.

In this retrospective cohort study, the final diagnostic yield was 65.3% (67.9% and 61.2% in the bleeding scan and control groups, respectively), which is similar to that reported in previous studies.⁸ Between the two groups, we found that pre-enteroscopic bleeding scans may lead to a higher detection rate, but there was no significant difference (Table 3). Given that SBE is a time-consuming procedure that is performed carefully and allows clinicians to view the mucosa of small bowel directly, the diagnostic yield of SBE could reach nearly 70%.¹¹ This may account for the insignificant difference. Further analysis of bleeding detection revealed that the sensitivity and specificity of bleeding scans were 82.0% and 23.5%, respectively. Intermittent bleeding, less blood extravasation, and timing delay for performing a bleeding scan might contribute to the low specificity. Patients in the bleeding scan group were noted to have less severe anemia (8.3 g/dL versus 7.8 g/dL), probably owing to the physicians' preference in arranging additional studies prior to endoscopic intervention for patients with less severe anemia. Angiodysplasia was the cause of bleeding in most cases in both groups, which is similar to our previous study¹² and the study by Kushnir et al.¹³ Furthermore, there were two patients who underwent surgery in the bleeding scan group and three in the control group. There was no significant difference in

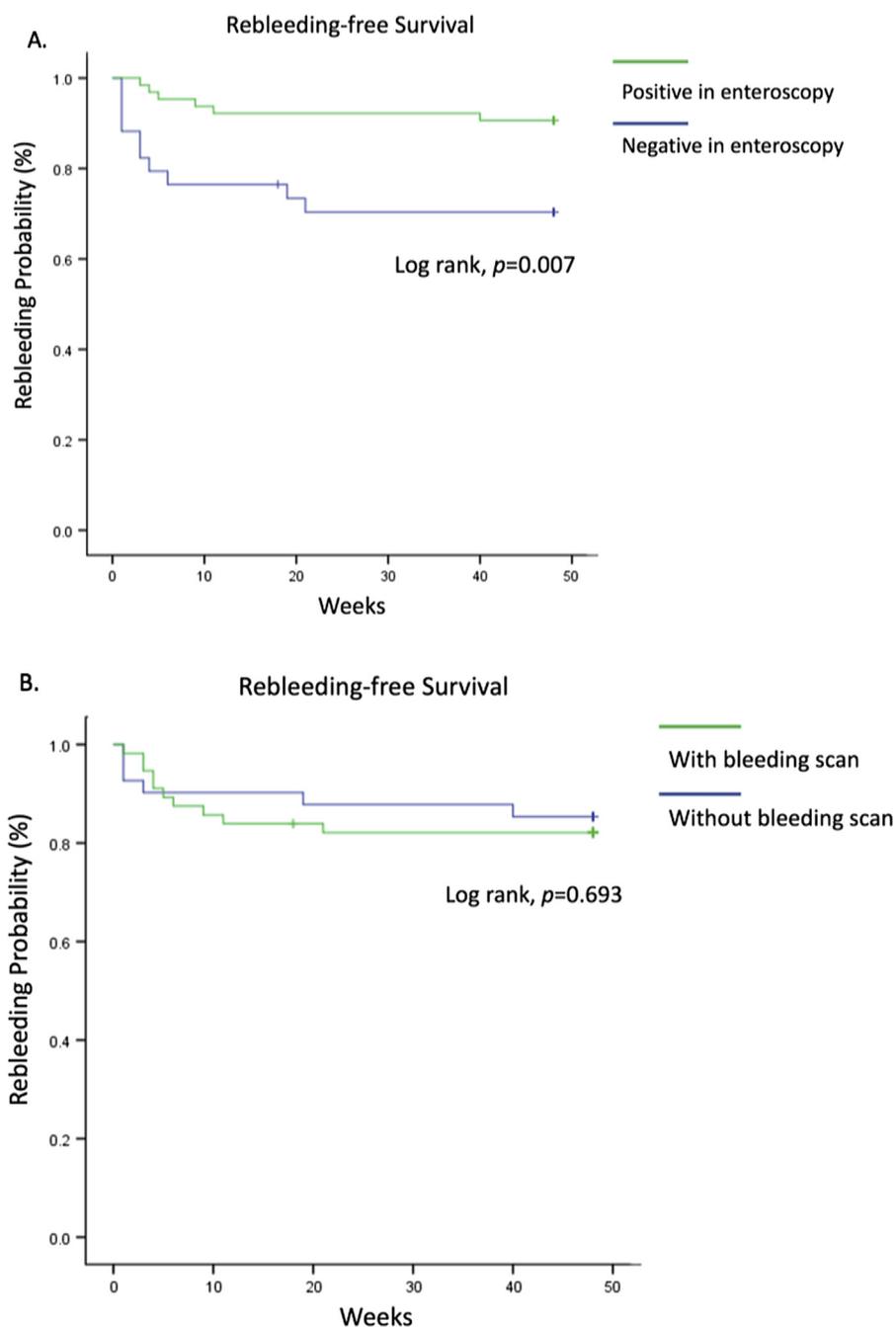


Fig. 1 Rebleeding-free survival between the patients with positive and negative enteroscopic findings (A). Rebleeding-free survival on bleeding scan between the positive and negative groups (B).

surgical treatment between the bleeding scan and control groups (Table 3).

In the current study, positive bleeding scans were localized in the duodenum, jejunum, ileum, and colon in 4, 12, 7, and 22 patients, respectively (Table 4). However, among the patients with positive bleeding scans, the accuracy of bleeder localization in jejunum (6/12, 50.0%) was higher than that in colon (3/22, 13.6%) on matching with the findings reported by SBE. This may be related to the fact that the jejunum is the most common location of bleeders (e.g., angiodysplasia) in patients with OGIB and the colon could be mistaken as the location of a bleeder

because of blood accumulation in the colon. The overall accuracy of positive bleeding scans in bleeder localization was only 26.7% (Table 4). These results could be compared with those of previous reports, where bleeding scans were able to correctly identify the location of gastrointestinal bleeding in 19%–96% of cases.^{14–16} Given that the major etiology of OGIB is small intestinal bleeding, accurate localization of a small bowel bleeder via a bleeding scan might be more difficult than that of bleeders in other sites. This examination often requires other diagnostic procedures for further confirmation. Furthermore, because a bleeding scan can only provide information on the site of

bleeding and not its etiology, patients must still undergo endoscopic intervention to more accurately diagnose and treat bleeding. Furthermore, a bleeding scan might delay the time to perform SBE in patient with overt OGIB owing to the long waiting time for the bleeding scan procedure (8.9 days vs. 3.0 days, $p < 0.001$). From the past literature, urgent enteroscopy (within 72 h) is better than non-urgent enteroscopy in terms of diagnostic and therapeutic impacts in patients with overt OGIB.¹⁷ Therefore, before patients with OGIB undergo SBE, a bleeding scan may be regarded as the screening tool to confirm whether small bowel bleeding exists or not. It helps clinicians decide if further examinations, such as capsule endoscopy or SBE, are required. However, the accuracy of bleeder localization by bleeding scans is unsatisfactory, and the procedure would delay the time to perform SBE; thus, arranging a bleeding scan before performing enteroscopy should be individualized when making clinical decisions.

The rebleeding rate after SBE in our study was 15.3%, which is less than that reported previously,^{18–20} probably because rebleeding in our study was defined as recurrent OGIB in patients needing hospitalization. The etiologies of rebleeding observed in our study were mainly from patients with negative endoscopic findings (9/15, 60.0%), angiodysplasia (3/15, 20.0%), non-specific ulcers (2/15, 13.3%), and diverticulum (1/15, 6.7%). We found that neoplastic lesions were less likely to result in rebleeding, which is similar to the findings by Kushnir et al.¹⁸ Rebleeding probability in the negative finding group of SBE was higher than that in the positive finding group of SBE, with a significant difference ($p = 0.007$) (Fig. 1A). However, there was no significant difference between the positive and negative finding groups for bleeding scans (Fig. 1B). SBE can not only reveal the bleeding lesion but also treat the lesion with endoscopic hemostasis.

This study had the following limitations. First, because this study was a retrospective analysis that was conducted at a single hospital, there may have been loss of patient data or inaccuracies in data entry, collection, and reporting. Second, only one experienced endoscopist performed SBE, and patients with OGIB underwent a bleeding scan or SBE depending on individualized clinical conditions. Third, with regard to rebleeding, only patients with recurrent OGIB that required hospital admission were considered to have rebleeding. Therefore, the rebleeding rate reported in the study should be lower than the actual rebleeding rate. Fourth, not all patients underwent bilateral SBE with complete small bowel examination and none of the patients underwent capsule endoscopy before SBE in our study; thus, the endoscopic diagnosis is not completely identical with the true diagnosis. Finally, the time to perform the bleeding scan or SBE was correlated with a positive rate, but the time to perform these procedures varied because of clinical decision-making and limited availability of facilities. Hence, a larger, prospective study may be necessary to validate our findings.

In our study, pre-enteroscopic bleeding scans in patients with OGIB revealed poor localization of bleeders and delay of time to perform SBE. In addition, there was no significant difference in the diagnostic rate. Thus, compared with the clinical impact of capsule endoscopy and CTA prior to enteroscopy, bleeding scan prior to SBE showed a limited

role for patients with OGIB. However, the high sensitivity of bleeding scans may help clinicians decide the next procedure to perform for managing bleeding in clinical practice. Therefore, the decision of performing a bleeding scan in patients with OGIB prior to SBE should be individualized for each patient.

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Declarations of interest

The authors have no conflicts of interest relevant to this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jfma.2018.11.002>.

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