

Risk factors for early rebleeding after endoscopic band ligation for colonic diverticular hemorrhage

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Background and study aims: Endoscopic band ligation (EBL) has been used for hemostasis of colonic diverticular hemorrhage. However, early rebleeding (<30 days after EBL) has been reported in some cases. The aim of this study was to elucidate risk factors for early rebleeding after EBL in treatment of colonic diverticular hemorrhage.

Patients and methods: A total of 101 patients with definite diverticular hemorrhage treated using EBL from June 2009 to October 2014 were included in the retrospective cohort study and divided into rebleeding and non-rebleeding groups, depending on the presence or absence of early rebleeding. Patients' ages, comorbid diseases, stigmata of recent hemorrhage (SRH) [active bleeding (AB), non-bleeding visible vessel (NBVV), or adherent clot (AC)], locations of bleeding diverticula, and eversion of the diverticula

after EBL were retrospectively evaluated in each group.

Results: Early rebleeding occurred in 15 cases. The median time (range) of early rebleeding occurrence was 5 days (range, 2 h to 26 days). Early rebleeding could be managed conservatively and/or endoscopically, except in one case in which surgery was done. Multivariate analysis revealed that age under 50 (adjusted OR, 8.7; 95% CI 1.6–52.5; $P=0.014$) and AB (adjusted OR, 4.21; 95% CI 1.15–18.1; $P=0.03$) were shown to be significant risk factors. The right side of the colon carried less risk than did the left side (adjusted OR, 0.21; 95% CI 0.04–0.84; $P=0.028$).

Conclusions: Younger age, AB of SRH, and left-sided lesions were identified as the risk factors for early rebleeding after EBL in the treatment of colonic diverticular hemorrhage.

Introduction

Colonic diverticular hemorrhage is the most common cause of acute lower gastrointestinal bleeding (LGIB), and therapeutic intervention is needed in severe bleeding cases [1–5]. Several types of endoscopic treatments such as coagulation therapy, epinephrine injection, and endoscopic clipping have been performed to achieve hemostasis of colonic diverticular hemorrhage [6–11].

Endoscopic variceal ligation (EVL) is widely used as a treatment for esophageal variceal bleeding. Recently, endoscopic band ligation (EBL), which uses devices and techniques similar to those for EVL, has been used for hemostasis of colonic diverticular hemorrhage and has been reported as a safe and effective endoscopic treatment for that indication [12–18]. However, rebleeding after EBL was reported in some cases, and the risk factors for it remain to be identified [16, 17].

The aim of this retrospective study was to elucidate the risk factors for early rebleeding after EBL

following treatment of colonic diverticular hemorrhage.

Patients and methods

Study population

Endoscopy records for patients with acute LGIB treated at St. Luke's International Hospital in Tokyo from June 2009 to October 2014 were retrospectively reviewed.

During that period, 108 patients with definite diverticular hemorrhage with stigmata of recent hemorrhage (SRH) [active bleeding (AB), non-bleeding visible vessel (NBVV), or adherent clot (AC)] [6] were treated. Patients treated with transcatheter arterial embolization (TAE), epinephrine injection, or endoscopic clipping as a first-line therapy were excluded, and a total of 101 patients with definite diverticular hemorrhage successfully treated using EBL were ultimately included in the retrospective cohort study.

License terms



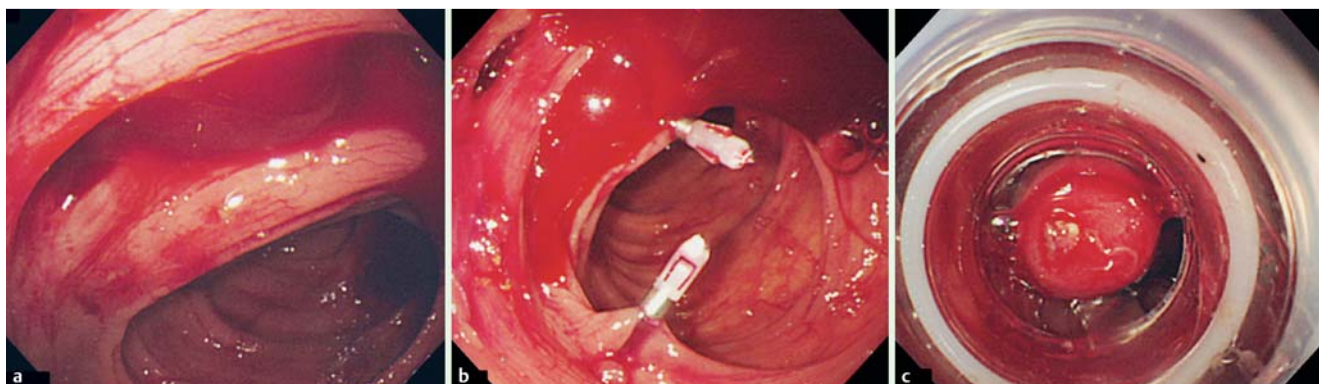


Fig. 1 **a** Endoscopic view of the colonic diverticulum with active bleeding. **b** Marking with the hemoclips was done near the diverticulum. **c** The colonoscope was pulled off and reinserted after attachment of the band ligator. The elastic O-band was released and successful hemostasis was obtained.

EBL methods and repeat colonoscopy for rebleeding

The method of EBL for colonic diverticular hemorrhage was the same as that reported in the previous literature [14–17]. Well-trained endoscopists and a trainee supervised by the experts performed EBL in the current study. After fluid resuscitation, bowel purge was done with polyethylene glycol and colonoscopy was performed. When the diverticulum with SRH was detected, the area was marked with (▶ Fig. 1 a and 1 b). Epinephrine injection was not performed for the diverticula with AB before EBL. The colonoscope was removed, the band-ligator device was attached to the tip, and the colonoscope was reinserted. The diverticulum was sucked into the band-ligator and the O-band was released (▶ Fig. 1 c).

Patients consumed a liquid meal the day after EBL and were usually discharged a few days after the procedure. Antiplatelet agents or nonsteroidal anti-inflammatory drugs (NSAIDs) were reintroduced the day after EBL, if required. Patients were basically followed on an outpatient basis at St. Luke's International Hospital for at least 30 days after EBL. In patients who had been taking regular meals and experienced rebleeding, a bowel purge with polyethylene glycol was done and repeat colonoscopy was performed using a water-jet scope (PCF-Q260AZI, PCF-Q260JI, or GIF-Q260J; Olympus Medical Systems) to rule out other bleeding sources. In some patients, repeat colonoscopy was performed without a bowel purge. The same gastroenterologists or on-call gastroenterologists performed the repeat colonoscopy. Further treatments were administered based on the judgments of the attending gastroenterologists. Patients who were not followed up at St. Luke's International Hospital were contacted by telephone. This study was approved by the ethics committee of St. Luke's International Hospital, and written informed consent was obtained from all patients.

Comparison between rebleeding and non-rebleeding groups

The 101 enrolled patients were divided into rebleeding and non-rebleeding groups based on the presence or absence of early rebleeding, which was defined as rebleeding within 30 days after initial treatment [6]. Comorbid diseases (hypertension, hyperlipidemia, and diabetes mellitus), use of antiplatelet agents or NSAIDs, SRH (AB vs. NBVV and AC), location of bleeding diverticula [right colon (cecum, ascending colon, and transverse colon) vs. left colon (descending colon and sigmoid colon)], and the eversion of the diverticula after EBL were retrospectively evaluated in each group.

Statistical analysis

Statistical analysis was performed using JMP version 9 (SAS Institute Inc., USA). The patients' ages were reported as mean [standard deviation (SD)]. Student's t-test and Fisher's exact test were applied for continuous and categorical variables, respectively, and a *P* value less than 0.05 was considered statistically significant. Odds ratios (ORs) and their 95% confidence intervals (CI) were calculated by multiple logistic regression analysis.

Results

Characteristics of rebleeding cases after EBL

The characteristics of 15 early rebleeding patients are listed in ▶ Table 1. Early rebleeding occurred in 15% of the patients (cecum, *n*=4; ascending colon, *n*=3; transverse colon, *n*=1; descending colon, *n*=1; sigmoid colon, *n*=6). The median time (range) of early rebleeding occurrence was 5 days (range, 2 h to 26 days).

In two cases (cases 1 and 2) where rebleeding occurred at 2 h and 11 h after initial EBL, dislodgement of the O-band was observed in repeat colonoscopy, and EBL was repeated (▶ Fig. 2). Complete eversion of the banded diverticula had not been achieved during the first EBL sessions in either case.

Ulceration was observed at the banded site in repeat colonoscopy in four early rebleeding cases. Two of those patients (cases 3 and 4) underwent endoscopic clipping at the visible vessel on the ulcer base (▶ Fig. 3). No interventions were required in the other two patients (cases 5 and 6), owing to the absence of visible vessels.

The banded diverticula transformed into yellowish or black balls on repeat colonoscopy performed in five early rebleeding cases (cases 7–11) (▶ Fig. 4), which had no other demonstrable bleeding sources. Eversion of the diverticula after EBL had been observed during the first EBL in five cases. In one of these five cases (case 7), right hemicolectomy was performed as the patient's preference, whereas the other four cases were managed conservatively without any interventions.

In two early rebleeding cases (cases 13 and 14), repeat colonoscopy 11 h and 24 days after the initial EBL demonstrated active bleeding from the diverticula that differed from the bleeding seen previously, and EBL was repeated. Hemostasis was obtained, and rebleeding did not occur during the follow-up periods of 59 and 37 months, respectively. In case 15, repeat colonoscopy showed scar formation at the previously banded site. However,

Table 1 Characteristics of 15 early rebleeding cases after EBL.

No.	Age	Gender	Location	Eversion after initial EBL	Time to rebleeding after EBL (hours or days)	Time to repeat endoscopy (hours or days)	Endoscopic feature at the initial EBL sites	Additional treatments
1	69	M	S	(-)	2	20	Dislodgement of O-ring	Repeat EBL
2	75	M	S	(-)	11	17	Dislodgement of O-ring	Repeat EBL
3	46	M	A	(+)	10	56	Ulcer with visible vessel	Clip
4	34	M	C	(+)	44	53	Ulcer with visible vessel	Clip
5	67	M	C	(-)	66	75	Ulcer without visible vessel	Conservative management
6	93	M	S	(+)	12 days	12 days	Ulcer without visible vessel	Conservative management
7	37	M	A	(+)	13	17	Yellowish tissue	Surgery
8	70	M	A	(+)	22	24	Yellowish tissue	Conservative management
9	77	M	T	(+)	32	35	Black tissue	Conservative management
10	46	M	C	(+)	33	49	Yellowish tissue	Conservative management
11	66	F	S	(+)	90	99	Yellowish tissue	Conservative management
12	55	M	C/A ¹	(+)	11	20	Black tissue (Bleeding from other diverticulum)	EBL
13	78	F	D/S ²	(+)	21 days	24 days	Ulcer with no vessel (Bleeding from other diverticulum)	EBL
14	55	M	S	(+)	26 days	27 days	Scar formation (Bleeding from other diverticulum)	Conservative management
15	94	F	S	(+)	60	(-)	No repeat endoscopy	Conservative management

C, cecum; A, ascending colon; T, transverse colon; D, Descending colon; S, sigmoid colon

¹ Initial bleeding sites and early rebleeding site were cecum and ascending, respectively.

² Initial bleeding sites and early rebleeding site were descending and sigmoid, respectively.

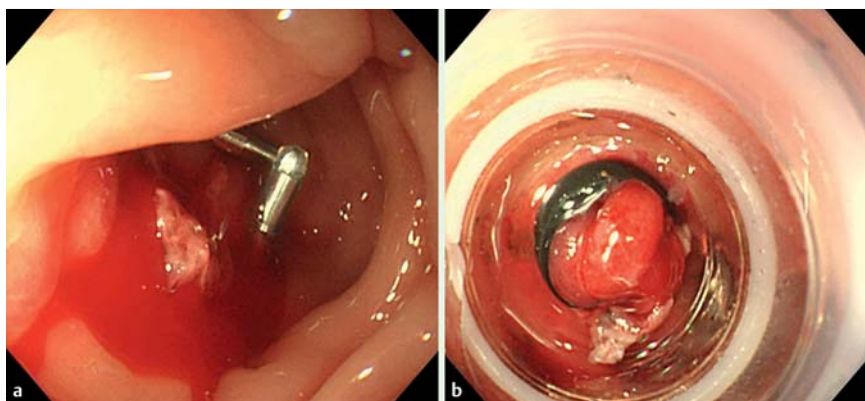


Fig. 2 a Early rebleeding was observed from the previously banded diverticulum, owing to early dislodgement of the O-band (case 1). b Repeat EBL was performed and bleeding stopped.

the rebleeding source was not identified. In case 16, repeat colonoscopy was not performed, owing to severe cardiopulmonary diseases, and rebleeding was managed conservatively.

Comparison between rebleeding and non-rebleeding groups

A comparison between 15 rebleeding and 86 non-rebleeding cases is presented in **Table 2**. No significant differences were noted for the parameters. However, left-sided location and AB of SRH were more common in the rebleeding group than in the non-rebleeding group, and these differences were considered marginally significant ($P=0.05$ and $P=0.08$, respectively).

Table 3 presents results of multivariate analysis of the risk factors of early rebleeding after EBL. This analysis revealed that age younger than 50 (adjusted OR, 8.7; 95% CI 1.6–52.5; $P=0.014$) and AB (adjusted OR, 4.21; 95% CI 1.15–18.1; $P=0.03$) were significant risk factors. The right side of the colon carried lesser risk than did the left side (adjusted OR, 0.21; 95% CI 0.04–0.84; $P=0.028$).

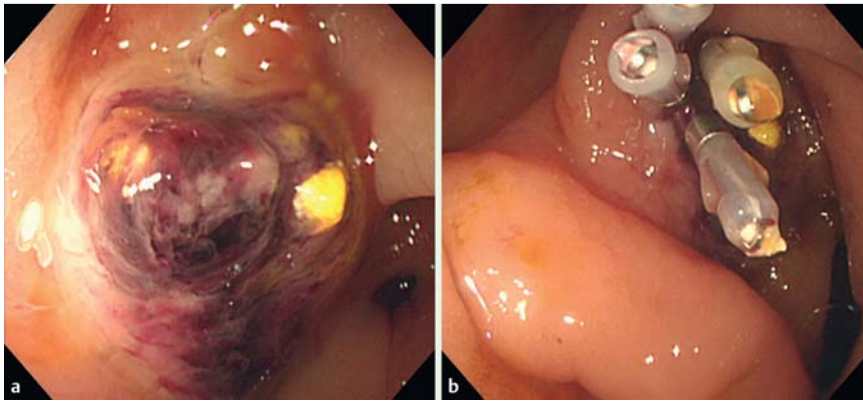


Fig. 3 a A non-bleeding visible vessel was observed at the post-EBL ulcer (case 4). b Endoscopic clipping was performed.

Discussion

The aim of this retrospective cohort study of EBL for colonic diverticular hemorrhage was to determine the risk factors for rebleeding after EBL. In the current study, repeat colonoscopy was performed for early rebleeding after EBL, and further treatments for early rebleeding were selected according to the endoscopic features of post-EBL sites as follows: repeat EBL for early dislodgement of the O-band, endoscopic clipping for visible vessels at the post-EBL ulcer, no intervention in ulcer cases with no visible vessels or in the cases of yellow or black tissues, and EBL for different bleeding diverticula. Importantly, the yellowish or black tissues are considered necrotic tissues after EBL and should not be removed because the muscularis propria may be banded by the O-band and the yellowish or black tissues can contain muscularis propria [17]. Given the results, which indicate that early rebleeding can be managed conservatively and/or by endoscopic treatment (except in one ascending case), repeat colonoscopy can be considered useful for determining information about the banded sites after EBL and for selecting further endoscopic procedures that would obviate the need for more invasive treatments such as surgery.

On repeat colonoscopy, another lesion was identified as the source of bleeding in cases 13 and 14, which might lead to the conclusion that EBL was performed mistakenly on the first lesions targeted. That was not the case, however, because SRH were evident in the diverticula initially treated with EBL. In addition, in this study, early rebleeding was defined as rebleeding within 30 days after initial EBL. Therefore, cases 13 and 14 were not excluded from the analysis.

The vascular anatomy at the diverticulum consists of arcades of arteries from the neck that join and form the artery in the base

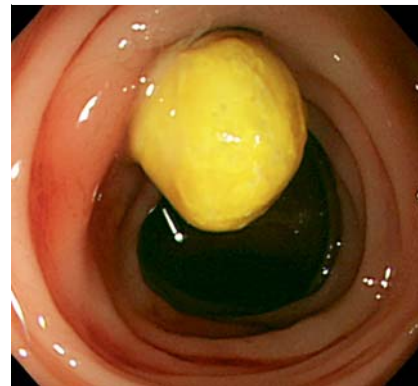


Fig. 4 The banded diverticulum became yellowish on repeat colonoscopy (case 11).

of the diverticulum, and bleeding from the ruptured vasa recta occurs in colonic diverticular hemorrhage [19]. Although the diameter of the vessel at the diverticula and the extent of significant hemorrhage could not be assessed in this study, these factors may contribute to early rebleeding after EBL, given that AB was a significant risk factor for early rebleeding.

Colonic diverticulosis and diverticular bleeding are more common in the right colon of patients from eastern countries including Japan, and a location in the right colon – especially the ascending colon – was reported as a predictor of refractory colonic diverticular hemorrhage after endoscopic clipping [11]. However, left-sided location was a significant risk factor for early rebleeding after EBL in this study. Ex-vivo study of EBL of the colon using a fresh surgical specimen revealed inclusion by the band ligator of the muscularis propria in the right colon and the submucosa in the left colon [20]. The surgical specimen from the banded diverticulum in the ascending colon also contained the muscularis propria [17]. Given these results, inclusion of the muscularis pro-

	Rebleeding group (n = 15)	Non-rebleeding group (n = 86)	P value
Male gender, n (%)	11 (73)	63 (73)	1.00
Age, mean ± SD (years)	63 ± 17	65 ± 13	0.46
History of HT, n (%)	8 (53)	46 (53)	1.00
History of DM, n (%)	2 (13)	11 (13)	1.00
History of HL, n (%)	6 (40)	18 (20)	0.18
Antiplatelet agents or NSAIDs, n (%)	5 (33)	34 (39)	0.77
Location in colon (C/A/T/D/S)	4/3/1/1/6	3/57/8/7/11	
Right side (C/A/T), n (%)	8 (53%)	68 (79%)	0.05
SRH:AB, n (%)	9 (60)	29 (33)	0.08
Complete eversion, n (%)	11 (73)	76 (88)	0.22

HT, hypertension; DM, diabetes mellitus; HL, hyperlipidemia; NSAIDs, nonsteroidal anti-inflammatory drugs; C, cecum; A, ascending colon; T, transverse colon; D, descending colon; S, sigmoid colon; SRH, stigmata of recent hemorrhage; AB, active bleeding. Statistical significance was defined as $P < 0.05$.

Table 2 Characteristics of rebleeding and non-rebleeding groups.

	Crude OR (95% CI)	P value	Adjusted OR (95%CI)	P value
Age under 50	3.11 (0.74–11.5)	0.11	8.7 (1.6–52.5)	0.014
Male gender	1.00 (0.3–3.9)	1.00		
History of HT	0.99 (0.33–3.01)	1.00		
History of DM	1.05 (0.15–4.52)	0.95		
History of HL	2.51 (0.76–7.95)	0.13	2.97 (0.78–11.4)	0.11
Antiplatelet agents or NSAIDs	0.76 (0.22–2.35)	0.67		
Right side (C/A/T)	0.30 (0.1–0.97)	0.04	0.21 (0.04–0.84)	0.028
SRH:AB	2.94 (1.38–18.7)	0.05	4.21 (1.15–18.1)	0.03
Complete eversion	0.36 (0.10–1.49)	0.15	0.34 (0.07–1.74)	0.19

Table 3 Multivariate analysis of risk factors of early rebleeding after EBL.

HT, hypertension; DM, diabetes mellitus; HL, hyperlipidemia; NSAIDs, nonsteroidal anti-inflammatory drugs; C, cecum; A, ascending colon; T, transverse colon; D, descending colon; S, sigmoid colon; SRH, stigmata of recent hemorrhage; AB, active bleeding; Statistical significance was defined as $P < 0.05$; OR, odds ratio; CI, confidence intervals.

pria in the O-band may be necessary to prevent early rebleeding when using EBL to treat colonic diverticular hemorrhage. Therefore, a diverticular location in the left colon should be considered as a risk factor specific to EBL rather than an overall risk factor for diverticular rebleeding.

Non-eversion of the diverticula after EBL, on the other hand, was not a risk factor for early rebleeding after EBL. As a consequence, EBL may be useful for treatment of stigmata regardless of eversion of the banded diverticular, if reliable banding is obtained and EBL can occlude either the major SRH or the underlying artery.

Hypertension, arteriosclerosis, and regular use of anti-platelet agents or NSAIDs have been reported to be risk factors for colonic diverticular hemorrhage [21–24]. In general, younger patients are considered to have fewer comorbidities, but in this study, younger age was a risk factor for early rebleeding after EBL. The reason for this association could not be identified, and further studies are necessary to clarify the relationship of age to risk of rebleeding after EBL.

The rebleeding from the diverticula seen in this study differed from outcomes with previously banded diverticula in three rebleeding cases, and in some rebleeding cases, bleeding sources other than the banded site were not identified with certainty in repeat colonoscopy. Specifically, the three cases reported here may not be “early rebleeding cases,” as the latter cases were. However, the sources of early rebleeding after endoscopic treatments were considered to be from the same diverticula treated endoscopically, although that was not fully established.

Establishing risk factors for recurrent bleeding after EBL may not change the treatment strategy and another endoscopic treatment or surgery may be desirable in patients who have risk factors. With the exception of one case in which surgery was performed because of patient preference, neither surgery nor TAE was not needed to control early rebleeding because management was possible with conservative therapy and/or endoscopic clipping in this study. Previously banded diverticula also may resolve after EBL, preventing late rebleeding from the same diverticula [17]. Therefore, if there are no particular concerns, EBL is considered the first priority. It may be useful to identify risk factors for

early rebleeding after EBL so that patients with colonic diverticular hemorrhage who those risk factors can be closely followed.

In conclusion, although the number of patients was limited and the study design was retrospective, younger age, AB of SRH, and left-sided lesions were identified as the risk factors of early rebleeding after EBL in the treatment of colonic diverticular hemorrhage.

Competing interests: None

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