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A new device for endoscopic band ligation for colorectal diverticular bleeding

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ABSTRACT

Background and study aims Endoscopic band ligation (EBL) has been reported to be effective for colorectal diverticular bleeding. However, current EBL devices have some limitations, and we have developed a novel EBL device.

Methods This novel EBL device has a tapered hood attached to the tip of the endoscope and an outer cylinder that loads two EBL bands. Twelve EBL procedures were performed in a live porcine model alternately using a conventional EBL device (Group C) and the novel EBL device (Group N).

Results EBL was successful in all cases in both groups. There were no cases of perforation in the 10 days after EBL. After ligation, the mean major axis of the ridge was significantly larger in Group N than Group C (9.7 ± 1.4 mm vs 7.2 ± 1.4 mm, $P = 0.011$). Pathological examination revealed disruption of the muscularis propria at four of the six ligation sites in Group C and at five of the six ligation sites in Group N.

Conclusions Using this novel EBL device, it was possible to perform multiple ligation procedures in succession with a good field of view. No perforation was observed, but disruption of the muscularis propria was observed at approximately three-quarters of the ligation sites pathologically.

Introduction

Colorectal diverticular bleeding is now being encountered with increasing frequency in daily clinical practice, mainly because of population aging and the increasing use of antithrombotic agents. However, the endoscopic field of view is poor due to large amounts of bloody stool, and it is sometimes difficult to identify the bleeding source. Even if a bleeding diverticulum can be found, the exposed blood vessels cannot always be observed directly. Therefore, it is difficult to stop bleeding using a clip, and rebleeding after hemostasis remains a major problem [1–3].

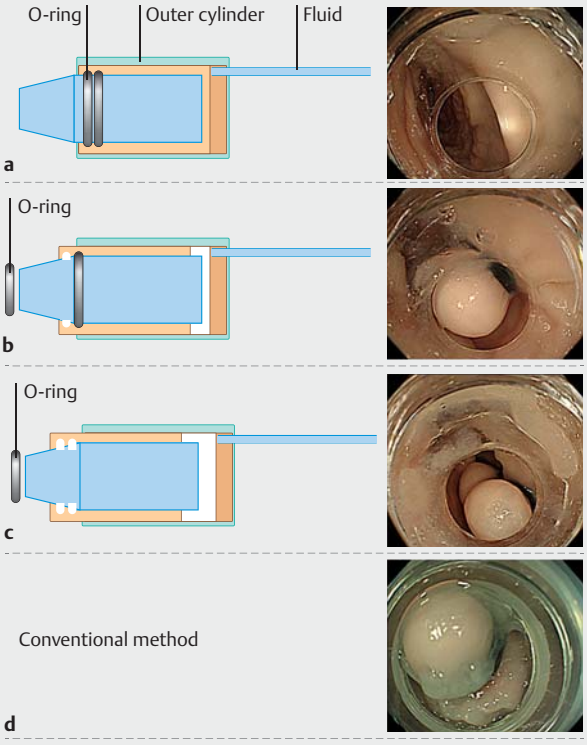
Various hemostatic methods have been developed for diverticular bleeding, and endoscopic ligation, which has been used for hemostasis in patients with esophageal varices, has been reported to be effective [4]. Unlike when using a clip, bleeding can be stopped by suctioning, reversing, and ligating the bleeding diverticulum even if the exposed blood vessels cannot be observed directly. However, the field of view is poor when a conventional EBL device is used. Furthermore, the current EBL devices are single-use, and if ligation fails, it is necessary to remove the endoscope and attach an O-ring to the tip. Moreover, complete aspiration is not always possible when ligating a bleeding diverticulum. In collaboration with Asahi Intecc Co. Ltd (Aichi, Japan), we have developed a novel EBL device that allows multiple ligations to be performed in succession with a better field of view and a stronger suction force.

Methods

Description

The novel EBL device (Endoligar) consists of a tapered conical hood and an outer cylinder with an O-ring for ligation on the outside (▶ **Fig. 1**). The tip of the hood is tapered for easier suction. Two O-rings are loaded, and it is possible to fire them separately depending on the amount of fluid injected from the outside (▶ **Fig. 2**). The outer cylinder loaded with the O-ring is located behind the hood, so it does not interfere with the endoscopic field of view. The maximum diameter of this novel EBL device is 19 mm, and the tip diameter is 9 mm.

▶ **Fig. 1** Appearance of the new device.



▶ **Fig. 2** Schematic diagram of the novel EBL device and endoscopic images. **a** Before endoscopic band ligation (EBL). Two O-ring are mounted on the outer cylinder. The O-ring is behind the tip of the endoscope and dose not interfere with the endoscopic view. **b** After the first EBL. After suctioning of the colonic mucosa, the first O-ring is fired. No particular change of the endoscopic view was observed after first EBL. **c** After the second EBL. The second EBL can be performed immediately after the first EBL. No particular change of the endoscopic view was observed after the second EBL. **d** Endoscopic view after EBL by conventional EBL device.

Experimental method

We investigated the feasibility of this novel EBL device in a porcine model at the Fukushima Medical Device Development Center. A 40-kg female pig was used. After intramuscular injection of a mixed solution of midazolam and medetomidine, tracheal intubation was performed and the experiment was conducted under general anesthesia. The experiment was approved by the Animal Experiment Committee of Toranomon Hospital.

Twelve ligation procedures were performed in the normal colonic mucosa alternately using the novel EBL device (Group N) and a conventional EBL device (Group C) (Sumitomo Bakelite Co. Ltd., Tokyo, Japan) between 30 cm and 16 cm from the anal margin. The distance from the anal margin to the ligation site was the same in both groups. Six ligation procedures were performed using three novel EBL devices (▶ **Video 1**). In both groups, the ligation was performed after fully aspirating the target colonic mucosa. In Group N, a 10-mL syringe was used to perform a first injection of 5 mL of distilled water and a second injection of 10 mL of distilled water. In Group C, air was injected using a 5-mL syringe. A successful procedure was defined as swelling of the aspirated colonic mucosa and the residue of an O-ring at its base.

The pig was fasted on the day of the experiment with resumption of a normal diet on the following day. Ten days after the ligation procedure, the pig was euthanized after endoscopic observation under general anesthesia. The abdomen was then opened and the large intestine was removed for pathological examination. Each ligation site in the resected specimen was identified, and a residual O-ring was confirmed. Next, the size of the ridge at each ligation site was measured using a caliper. After fixing with 10 % formalin solution, hema-

VIDEO

▶ **Video 1** Endoscopic view of the experiment. During insertion of the colonoscope, a good endoscopic field of view can be maintained. Two EBL procedures can be performed consecutively.

toxylin-eosin staining and Masson's trichrome staining were performed (▶ **Fig. 3**). Two pathologists determined the presence or absence of disruption of the muscularis mucosae, submucosal fibrosis, and disruption of the muscularis propria.

Statistical analysis

Data were analyzed using the Fisher's test and Mann-Whitney U-test. A $P<0.05$ was considered significant. All statistical analyses were performed using SPSS version 20 (SPSS IBM statistics).

Results

The 12 EBL procedures were performed without any complications. In Group N, it was possible to fire the two O-rings separately, and all procedures were successful. No adverse events, such as fever or signs of abdominal pain, were observed during the 10-day observation, and food intake was good. The body weight was 42.2 kg on the day of ligation and 43.8 kg at the time of necropsy.

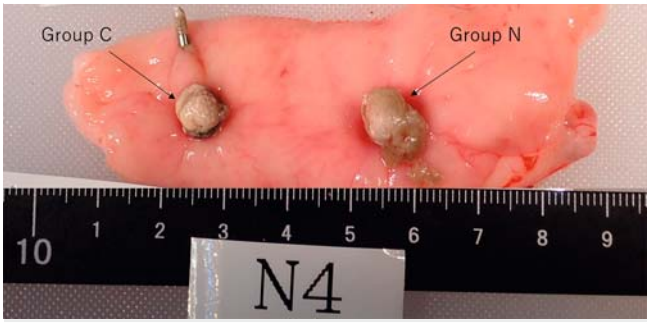
Endoscopic observation of the EBL site revealed that all O-rings remained (▶ **Table 1**). No perforation was observed. The average major axis of the ridge was significantly larger in Group N than in Group C (9.7 ± 1.4 mm vs 7.2 ± 1.4 mm) ($P=0.011$).

Pathological examination revealed disruption of the muscularis mucosae at all ligation sites (▶ **Table 2**). Fibrosis of the submucosal layer was also observed at all sites. Disruption of the muscularis propria was observed at five of six sites in Group N and at four of six sites in Group C. And the length of the disruption of the muscularis propria was 6.8 ± 3.5 mm in Group N and was 3.9 ± 3.6 mm in Group C (▶ **Fig. 4**). Average length of the disruption of the muscularis propria did not significantly differ between the groups ($P=0.18$).

Discussion

We developed a novel EBL device for diverticular bleeding, and conducted a comparative experiment with a conventional EBL device. Using this novel EBL device, ligation procedures can be performed in succession with a good field of view. And the mucosal ridge after ligation by the novel EBL device was significantly larger compared to the conventional EBL device.

Diverticular bleeding is a common cause of acute lower gastrointestinal hemorrhage. It typically has a rapid onset without abdominal pain and can be distinguished from other acute lower gastrointestinal bleeding disorders, such as ischemic colitis and rectal ulcer. Diagnosis is more reliable when enhanced computed tomography (CT) is performed and outflow of contrast medium is observed from the blood vessel. Enhanced CT is useful for not only diagnosing diverticular bleeding but also identifying the bleeding site, which is usually in the ascending or sigmoid colon. An endoscopic finding of stigmata of recent hemorrhage involving a diverticulum is an indication for endoscopic treatment. However, it may be difficult to identify the diverticulum that is the source of the bleeding endoscopically because of the presence of blood and residual stool [5].



▶ **Fig. 3** Excised specimen. All O-rings remained in the colonic mucosa. The size of the ridge is significantly larger in group N than in group C.

▶ **Table 1** Technical results of the study.

	Group C	Group N	
n	6	6	
Success rate of ligation (%, n/n)	100 (6/6)	100 (6/6)	N.S.
Perforation (%, n/n)	0 (0/6)	0 (0/6)	N.S.
Residue of the O-ring 10 days after EBL (%, n/n)	100 (6/6)	100 (6/6)	N.S.
Average size of the ridge (mm ± SD)	7.2 ± 1.4	9.7 ± 1.4	$P=0.011$

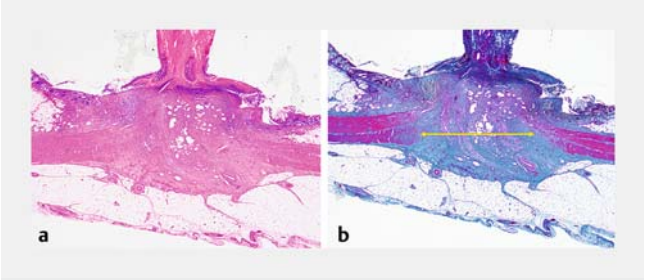
EBL, endoscopic band ligation; SD, standard deviation.

▶ **Table 2** Pathological results of the study.

	Group C	Group N	
n	6	6	
Disruption of the muscularis mucosae (%, n/n)	100 (6/6)	100 (6/6)	N.S.
Fibrosis of the submucosal layer (%, n/n)	100 (6/6)	100 (6/6)	N.S,
Disruption of the muscularis propria (%, n/n)	66.7 (4/6)	83.3 (5/6)	N.S.
Length of the disruption of the muscularis propria (mm ± SD)	3.9 ± 3.6	6.8 ± 3.5	$P=0.18$

SD, standard deviation.

Various treatments have been used for diverticular bleeding. In the past, clipping was often performed but the rebleeding rate was high because of the difficulties involved in identifying the exposed blood vessels in the diverticulum [6–8]. More recently, EBL that ligates the entire diverticulum has been preferred, but its effectiveness varies depending on the site. It has been reported that EBL has a higher success rate with less risk of rebleeding in the ascending colon than in the sigmoid colon



▶ **Fig. 4** Histopathological image of group N. **a** Hematoxylin-eosin staining. Inflammatory cell infiltration and fibrosis are observed from the submucosal layer to the subserosal layer. **b** Masson's trichrome staining. The muscularis propria was completely ruptured and the length of disruption was 9.2 mm (yellow arrow).

[9]. There has also been a report of a similar ligation method that uses a detachable snare [10]. When using that method, the detachable snare is inserted as soon as a bleeding source is found; the diverticulum is then aspirated and the detachable snare is ligated. The major advantage of using this method is that there is no need to remove and reinsert the endoscope. Recently, the usefulness of the over-the-scope clip system for diverticular bleeding has also been reported [11]. Non-endoscopic treatment methods include embolization, surgery, and barium filling, each of which has its strengths and weaknesses [12].

The rebleeding rate is an indicator of the effectiveness of treatment for diverticular bleeding. The short- and long-term rebleeding rates are reported to be lower for EBL than for the clipping [13]. In our experiment, extensive fibrosis of the submucosal layer was observed at the EBL site. One possible reason for this finding is that blood flow to the diverticulum had been blocked for a lengthy period due to widespread fibrosis. Perforation is one of the safety indicators of hemostasis for colonic diverticular bleeding. According to Sato et al. [14], perforation can occur after EBL. In our study, no signs of perforation were observed in the 10 days following the EBL procedure; however, disruption of the muscularis propria was observed at nine of 12 EBL sites, suggesting that safety needs to be verified in the future.

When a bleeding diverticulum is found, a clip is placed in the vicinity and the endoscope is removed for attachment of the EBL and then reinserted. Next, the diverticular bleeding source near the clip is identified and aspirated, after which the entire diverticulum is ligated. However, removal and reinsertion of an endoscope is a time-consuming and labor-intensive procedure, and ideally ligation would be performed immediately when a bleeding diverticulum is found on endoscopy. Moreover, reinsertion of the endoscope into the ascending colon is painful, so treatment immediately after discovery is desirable for lessening the burden on patients. Conventional EBL devices have an O-ring attached to the tip of the hood, which obstructs the field of view. This problem is avoided when using the novel EBL device because the O-ring is placed at the base of the hood instead of at its tip. Therefore, the field of view is not obstructed when the endoscope is inserted.

The diverticulum may not be reversed even if the diverticulum is aspirated during EBL. If the O-ring is fired without the diverticulum being inverted by firm suction, ligation might fail. When ligation is inadequate using a conventional device, the endoscope needs to be removed and then reinserted after attachment of the O-ring. However, when using the novel EBL device, two O-rings are loaded and it is possible to attempt ligation again even if the first attempt has failed. Moreover, unlike a conventional EBL device, the tip of the hood is longer and tapered, so the suction power may be higher. In this experiment, the mucosal ridge after ligation was larger in Group N, suggesting that it may be effective for diverticula that cannot be aspirated by a conventional EBL device. A device that can be used to perform multiple ligation procedures for esophageal varices is available. Shiratori et al. have compared that device with the EBL device we used in our conventional group and have reported a similar postoperative course and pathological findings [15]. However, Shiratori et al. encountered problems, including a poor field of view and a lengthy insertion time.

This research and the device used have some limitations. First, the outer diameter of this novel EBL device is 19 mm, which is relatively large, and resistance may be encountered when it is inserted deep into the sigmoid colon. The sigmoid colon with diverticula can be stiff and this can be a major clinical problem. Therefore, further studies are needed to assess its safety in clinical practice. Second, the EBL procedures were performed in normal mucosa between the rectum and sigmoid colon, and the results may be different when performed for a bleeding diverticulum. Even in a normal colon wall, we confirmed disruption of the muscularis propria at five of six ligation sites in Group N and at four of six sites in Group C. In the experiment by Shiratori et al., the muscle layer was ligated at a high rate, but no perforation was observed. However, these studies were small, and large-scale prospective studies of the safety of these devices are needed in the future.

Conclusions

In conclusion, we developed a novel EBL device for diverticular bleeding. Our experimental findings suggest that the suction power of the novel EBL device may be superior to that of a conventional EBL system. Despite a high rate of disruption of the muscularis propria, there were no complications, such as perforation or fever. This novel device has the potential to be useful for treatment of diverticular bleeding.

Acknowledgment

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Competing interests

The prototype of the device described in this paper was manufactured by Asahi Intecc Co. Ltd. Drs. Kikuchi and Hayasaka and Asahi Intecc have signed a consulting contract for development of the device.

References

[1] Kaise M, Nagata N, Ishii N et al. Epidemiology of colonic diverticula and recent advances in the management of colonic diverticular bleeding. Dig Endosc 2020; 32: 240–250

[2] Nagata N, Ishii N, Manabe N et al. Guidelines for Colonic Diverticular Bleeding and Colonic Diverticulitis: Japan Gastroenterological Association. Digestion 2019; 99: 1–26

[3] Schultz JK, Azhar N, Binda GA et al. European Society of Coloproctology: guidelines for the management of diverticular disease of the colon. Colorectal Dis 2020; 22: 5–28

[4] Ishii N, Setoyama T, Deshpande GA et al. Endoscopic band ligation for colonic diverticular hemorrhage. Gastrointest Endosc 2012; 75: 382–387

[5] Nagata N, Niikura R, Sakurai T et al. Safety and effectiveness of early colonoscopy in management of acute lower gastrointestinal bleeding on the basis of propensity score matching analysis. Clin Gastroenterol Hepatol 2016; 14: 558–564

[6] Hayasaka J, Kikuchi D, Odagiri H et al. Effectiveness of clipping for definitive colonic diverticular bleeding in preventing early recurrent bleeding. Intern Med 2022; 61: 451–460

[7] Ishii N, Hirata N, Omata F et al. Location in the ascending colon is a predictor of refractory colonic diverticular hemorrhage after endoscopic clipping. Gastrointest Endosc 2012; 76: 1175–1181

[8] Kawanishi K, Kato J, Kakimoto T et al. Risk of colonic diverticular rebleeding according to endoscopic appearance. Endosc Int Open 2018; 6: E36–E42

[9] Ikeya T, Ishii N, Nakano K et al. Risk factors for early rebleeding after endoscopic band ligation for colonic diverticular hemorrhage. Endosc Int Open 2015; 3: E523–E528

[10] Akutsu D, Narasaka T, Wakayama M et al. Endoscopic detachable snare ligation: a new treatment method for colonic diverticular hemorrhage. Endoscopy 2015; 47: 1039–1042

[11] Kawano K, Kawano R, Moriguchi T et al. Over-the-scope clipping and detachable snare ligation as a novel combination hemostatic therapy for diverticular bleeding. Endoscopy 2022; 54: 218–219

[12] Fujimoto A, Sato S, Kurakata S et al. Effectiveness of high-dose barium enema filling for colonic diverticular bleeding. Colorectal Dis 2011; 13: 896–898

[13] Nagata N, Niikura R, Ishii N et al. Cumulative evidence for reducing recurrence of colonic diverticular bleeding using endoscopic clipping versus band ligation: systematic review and meta-analysis. J Gastroenterol Hepatol 2021; 36: 1738–1743

[14] Sato Y, Yasuda H, Fukuoka A et al. Delayed perforation after endoscopic band ligation for colonic diverticular hemorrhage. Clin J Gastroenterol 2020; 13: 6–10

[15] Shiratori Y, Ikeya T, Suzuki K et al. Comparison of endoscopic band ligation devices used for colonic diverticular bleeding: in vivo animal study. JGH Open 2020; 5: 50–55