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*FIELD OF VISION*

# Endoscopic band ligation: Beyond prevention and management of gastroesophageal varices

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## Abstract

Endoscopic band ligation (EBL) is the preferred endoscopic technique for the endoscopic treatment of acute esophageal variceal bleeding. EBL has also been used to treat nonvariceal bleeding. Recently, Han *et al* demonstrated that EBL can be a feasible and safe alternate technique for the management of iatrogenic gastric perforation especially in cases in which closure with endoclips is difficult. EBL is technically simpler to perform than other methods and provides a good view of the lesions under direct pressure and suction from the transparent ligation cap. EBL can be used even if the diameter of the perforation is greater than 10 mm or if there is a severe tangential angle. In this commentary, we discuss the efficacy and safety of EBL for the closure of iatrogenic gastrointestinal perforation. We also discuss the advantages and disadvantages of EBL for the treatment of nonvariceal bleeding.



**Key words:** Band ligation; Endoscopy; Intestinal perforation; Gastrointestinal hemorrhage

**Core tip:** Recently, Endoscopic band ligation (EBL) has been widely used in the treatment of nonvariceal bleeding from angiodysplasia, Dieulafoy's lesion, Mallory-Weiss tears, polypectomy bleeding and colonic diverticular bleeding. In this commentary, we describe EBL may be useful for the endoscopic closure in iatrogenic gastrointestinal perforation in which endoclip closure failed. In addition, the advantages and disadvantages of EBL for the treatment of nonvariceal bleeding are discussed.

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## COMMENTARY ON HOT TOPICS

Elastic band ligation was introduced in the United States in 1951[1], and has been used for decades to treat bleeding and/or prolapsed internal hemorrhoids[2]. In the late 1980s, Stiegmann *et al*[3] demonstrated that the results of an initial endoscopic band ligation (EBL) trial were equal to or superior to those obtained with endoscopic sclerotherapy for the treatment of active bleeding, the prevention of recurrences, and survival. Currently, EBL is the most useful and accepted treatment for acute esophageal variceal bleeding[4]. Recently, EBL has been widely used in the treatment of nonvariceal bleeding from angiodysplasia, Dieulafoy's lesion, Mallory-Weiss tears, polypectomy bleeding and colonic diverticular bleeding[5]. This

technique is equally as useful as the standard methods, such as endoclipping, epinephrine injections, and thermal therapy.

In a recent case report series, Han *et al*[6] have shown successful endoscopic closure using band ligation in iatrogenic gastric wall perforations in which primary endoclip closure failed. In this commentary, we describe the clinical efficacy and safety of EBL for the closure of iatrogenic gastrointestinal (GI) perforation. In addition, the advantages and disadvantages of EBL for the treatment of nonvariceal bleeding will be discussed.

### *Iatrogenic GI perforation*

Although iatrogenic perforations occurring during endoscopic procedures are typically managed surgically, the successful endoscopic management of iatrogenic perforation has been increasingly reported. Surgery is required in patients in whom the endoscopic closure of a perforation failed or in whom the recognition of an endoscopic perforation was delayed. The endoscopic devices approved by the United States Food and Drug Administration for the closure of perforations include endoclips, stents, and endoscopic suturing devices[7]. Several case reports or series have described iatrogenic GI perforation managed by endoscopic clip placement[8-11]. Clipping is currently the standard method for closing perforations. Several through-the-scope (TTS) clips have been developed, including the QuickClip2 (Olympus Inc.), the Resolution clip (Boston Scientific Inc.), and the Tri-Clip and Instinct clip (Cook Medical). However, there still are no comparative studies evaluating one type of clip as superior to another for the closure of perforations[7]. The decision to close an iatrogenic perforation with clips is made on the basis of the duration of the procedure; the cause, location, and size of the perforation; the patient's age and general health; and the endoscopist's experience[12]. The most common causes of iatrogenic acute perforation in the GI tract are endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD)[9,10,13]. Perforation can also occur during the process of diagnostic endoscopy. The endoscopic closure of a perforation caused by EMR or ESD is simpler to perform than the endoscopic closure of a perforation caused by a blunt instrument because of the smaller size of the perforation caused by therapeutic endoscopy. Fujishiro *et al*[14] suggested that there are four prerequisites for a successful outcome after closing an iatrogenic perforation with endoscopic clips and using conservative management: (1) the perforation must be small (less than 1 cm); (2) the content of the GI tract must be as clean as possible and the amount of material escaping into the abdomen or mediastinum must be minimized; (3) the closure must be performed by experienced endoscopists'; and (4) there should be no deterioration in the clinical symptoms and laboratory indices, which should be closely monitored by experienced surgeons. The risk factors associated with the need for early surgery within 24 h after endoscopic closure were reported to be a large perforation, leukocytosis, severe abdominal pain, and a large amount of peritoneal free air[15].

The over-the-scope clip (OTSC; Ovesco Endoscopy AG, Tübingen, Germany) has a higher compression force and the capacity to capture a larger volume of tissue than the TTS clip[7]. In a recent prospective multicenter study the CLIPPER study group[16] showed that 32 of 36 consecutive patients with acute iatrogenic perforations (5 esophageal, 6 gastric, 12 duodenal, and 13 colonic perforations) had successful closures without adverse events. Newly developed endoscopic suturing devices for NOTES and antireflux and bariatric surgery may also be suitable for the closure of iatrogenic perforation[17].

Although clipping devices are relatively inexpensive and easy to use, endoscopic clip closure may be difficult in cases that involve large perforations, tangential angles, and/or fibrotic tissue. OTSC and endoscopic suturing devices are not readily available in many countries and require experience in their use for the closure of iatrogenic perforations. Recently several case reports or series of iatrogenic perforations treated by EBL have been described in the literature, involving the stomach, duodenum[18], and colon-rectum[19-21]. Moon *et al*[19] reported the first successful endoluminal closure of a 3 mm rectal perforation with one band following the ESD of a lateral spreading tumor. Two case reports showed that EBL was used to successfully close three iatrogenic colonic perforations in which closure with endoclips initially failed because there were two large perforations and a severe tangential angle[20,21]. Perforations occurring in the process of diagnostic endoscopy, as in these cases, are generally large because of the strong pressure of the endoscope on the wall of the gut over a large area[12]. In these cases, EBL may be applied successfully despite a large perforation. Duodenal perforations are complicated by the leakage of contaminated intestinal fluid and digestive enzymes and require early surgical repair[8]. Even when using a transparent cap on the tip of the endoscope, the application of clips to close perforations is still difficult in the posterior wall of the duodenal bulb because of the limited space and the tangential angle[22]. The deployment of band ligation is simpler than clipping, but displacement of the band poses another problem. Fan *et al*[18] reported the successful repair of a polypectomy-induced duodenal perforation with a combination of hemoclips and band ligation. The perforation was located on the posterior wall of the duodenal bulb and measured 10 mm in diameter. Although the endoscopic closure of large perforations (larger than 20 mm in diameter) is difficult, the successful endoscopic closure of a large duodenal perforation using endoloops and endoclips has been reported[23]. The perforation was located in the duodenal second portion and measured 30 mm in diameter. Two endoloop snare-endoclip sutures achieved complete closure.

In case reports by Han *et al*[6] rescue EBLs were performed in five patients in whom primary endoclip closure either failed or was technically difficult. The common causes of closure failure with clips in four of the

iatrogenic perforations were difficulties in approximating the location of the adjacent gastric mucosa due to wall tension and a tangential angle. In a case of ulcer base perforation, the fibrotic tissue on the base made clipping difficult. Successful endoscopic closure was achieved in all five patients, with no complications occurring. Based on these results, EBL may be a safe and effective alternate therapy for the closure of acute gastric perforations, especially when repairs using endoclips are problematic. Prospective clinical trials are required to demonstrate the efficacy and safety of EBL for the treatment of iatrogenic GI perforations.

### Nonvariceal bleeding

The Dieulafoy lesion (DL), a rare vascular abnormality consisting of a large and tortuous artery that is located in the submucosa, can cause potentially life-threatening gastrointestinal bleeding. With advances in endoscopic techniques, endoscopic treatment has become the treatment of choice for many endoscopists because of its effectiveness in the majority of bleeding DLs. Endoscopic treatments include injection, thermal therapy, and mechanical methods such as endoscopic hemoclip placement (EHP) or EBL. These methods have been used with high rates of successful hemostasis[24-26]. Of the endoscopic treatments available, mechanical methods demonstrated good hemostatic efficacy and long-term outcomes, primarily for lesions located in the upper GI tract[27]. In a prospective study, Park *et al*[28] reported that EBL ($n$ = 13) and EHP ($n$ = 13) were equally effective and safe methods for the treatment of bleeding gastric DLs. In a recent large retrospective study that compared EHP with EBL, Ahn *et al*[29] showed that both EHP and EBL were effective for the treatment of bleeding DLs, although recurrent bleeding occurred in 6 of the 66 cases; 5 (15%) and 1 (3%) in the EHP and EBL groups, respectively. This result suggests that EBL may be used as an initial endoscopic treatment for bleeding DLs due to a more favorable clinical outcome than EHP and a shorter procedure time. Although DLs are usually located in the stomach, esophageal, duodenal, and rectal DLs have been successfully treated with EBL[30-32]. However, EBL entails some risks and disadvantages including recurrent bleeding due to ulcer formation, perforation, delay in overtube preparation, and technical difficulties (particularly in retroflexion)[33]. We have previous experience with six patients with acute lower gastrointestinal bleeding due to rectal DL who were treated with thermal therapy, EHP, and EBL[34]. Of the four patients who were treated with EBL, two experienced rebleeding after EBL. Using additional injections and hemoclipping to achieve hemostasis failed, and transanal suture ligations of the vessel were performed. Our cases suggest that residual vessels at the base of a necrotic ulcer may cause delayed bleeding, and it may be difficult to predict this complication on the basis of an endoscopic examination.

Some patients with Mallory-Weiss syndrome (MWS), a vomiting-induced mucosal laceration in the region of the gastroesophageal junction, may require intensive care, especially those with active bleeding, unstable vital signs, and associated comorbid diseases. Although endoscopic injection may be incomplete for a patient with a large and/or long plexuses of vessels, the results of hemostasis using epinephrine injection only are controversial. Chung *et al*[35] reported that rebleeding was more common in hemostasis with hypertonic saline-epinephrine (HSE) injection treatment than in mechanical hemostasis. However, Park *et al*[36] reported that EBL and HSE injections had the same efficacy with a primary hemostasis of 100% *vs* 94%, respectively, without recurrent bleeding or major complications in either group. In addition, Huang *et al*[37] reported that EHP and HSE were equally effective with respect to achieving hemostasis and reducing the rebleeding rate. A prospective, randomized study that compared EBL with EHP in our group showed that the two procedures were equivalent with respect to primary hemostasis (100%) and rebleeding rate (6% *vs* 10%, respectively)[38]. Recently, Lecleire *et al*[39] compared the efficacy of EBL with hemoclips plus epinephrine (H and E) in bleeding MWS. They showed that rebleeding occurred in 0% in the EBL group *vs* 18% in the H and E group and that hemostasis by H and E was an independent predictive factor of early rebleeding. Although a further large prospective study is required, this result suggests that EBL may be the first choice of endoscopic treatments for actively bleeding MWS. Although these studies have shown promising results for the treatment of nonvariceal bleeding, few of these reports were prospective controlled design, and sample sizes of randomized trials were small. Further prospective studies with a large number of patients are necessary to demonstrate the hemostatic efficacy of EBL.

Recently, EBL has been applied to the management of other types of nonvariceal bleeding, including post-polypectomy bleeding[40-43], vascular malformation[44,45], gastric antral vascular ectasia (GAVE)[46-50], blue rubber bleb nevus syndrome[51], and chronic hemorrhagic radiation proctitis[52]. Akahishi *et al*[43] showed that band ligation after endoscopic resection with an HSE injection was effective for the prevention of polypectomy-related bleeding in 20 pedunculated or semipedunculated polyps that were larger than 1 cm. Although the resection margin was histologically affected by the non-neoplastic components in 6 of 20 lesions, all 20 polyps were completely resected. In a prospective study, Junquera *et al*[45] reported that EBL achieved hemostasis in a single endoscopic session in 14 patients with angiodysplasia located in the duodenum (bulb, $n$ = 5; 2$^{nd}$ portion, $n$ = 8; 3$^{rd}$ portion, $n$ = 1), and no patients had further bleeding at 40 days of follow-up. In a recent retrospective study, Sato *et al*[50] demonstrated that the recurrence rate of argon plasma coagulation (68%) was higher than that of EBL (8%) after treatment in patients with GAVE in association with liver disease.

More recently, EBL has been used in the treatment of colonic diverticular bleeding[53-57]. In a large retrospective

study, Ishii *et al*[57] reported that EBL was successful in 27 of 31 cases of colonic diverticular bleeding with the stigmata of a recent hemorrhage, except in 3 diverticula with a small orifice and a large dome and in 1 diverticulum with a large orifice. There were no perforation or penetration complications. Early rebleeding after EBL occurred in 3 cases (11%), which were managed conservatively by a repeat EBL or by a right hemicolectomy. Although the ruptured vasa recta were not identified, the histopathological examination of the surgical specimen showed that the muscularis propria was banded by an O ring. Considering that the direct placement of endoclips is difficult in cases of dome location, massive hemorrhage, or small diverticular orifice, EBL could be an alternative endoscopic treatment for colonic diverticular bleeding.

### Endoscopic banding devices

Currently available EBL devices include single-band and multiband ligation devices. While the single-band ligator needs overtube for repeated intubation to place multiple bands, multiband ligator doesn't require use of an overtube. For the treatment of nonvariceal bleeding and GI perforation, single-band ligator has been usually used. For the variceal ligation, the use of multiband device was associated with a significant reduction in sedation requirement, endoscopic time, and patient discomfort compared to single-band ligator[58]. The multiband ligators include the Saeed Multi-band Ligator (Cook Endoscopy, Winston-Salem, North Carolina), the Auto-band Ligator (Scandimed International, Glostrup, Denmark), and the Speedband Superview Super 7 Multiple Band Ligator (Boston Scientific Corp, Natick, Mass)[59]. All EBL devices have a short transparent cylindrical cap that carries 1, 4, 5, 6, 7, or 10 bands, a tripwire that runs from the cap through the accessory channel to the control handle, and a control handle with a retracting spool that is fixed to the biopsy port for attachment and firing of the trip wire[59].

### Safety of EBL

Stiegmann *et al*[3] showed that band ligation in the esophagus, when used for variceal bleeding, affected only the mucosa and submucosa. However, the safety of EBL in the anatomically thinner bowel (the colon and small intestine) has not been established. In an *ex vivo* study of EBL for the small bowel and colon using fresh surgical specimens, the histologic evaluation revealed the inclusion by the band ligator of the muscularis propria and serosa on the small bowel, the muscularis propria in the right colon, and the submucosa in the left colon[60]. This result suggests that EBL may not be safe in the small bowel and the right colon but is likely to be safe in the thicker left colon. Recently, Kakutani *et al*[61] showed that the full thickness of the duodenal wall after EBL was captured in the duodenum using *ex vivo* porcine models, and routine EBL is not recommended in the duodenum because of the high risk of perforation. However, Farrell *et al*[54] reported that none of the 11 band ligated colonic diverticula in surgical resected specimens contained either muscularis propria or serosal involvement, and there was no perforation in patients with actively bleeding colonic diverticula controlled by EBL. Further studies are needed to define the appropriate indications and locations for EBL.

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