Endoscopic mechanical hemostasis of GI arterial bleeding (with videos)

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An increasing body of evidence is available on the use of endoscopic clips, loops, and bands in the treatment of GI bleeding. This review provides a summary of the mechanical endoscopic hemostatic devices and the techniques used in the management of GI arterial bleeding.

REVIEW METHOD

A MEDLINE search of English language publications was performed from 1966 to October 2006 related to endoscopic mechanical hemostasis by using the key words ''endoclip,'' ''hemoclip,'' ''band ligation,'' and ''endoloop.'' Additionally, a manual search of *Gastrointestinal Endoscopy* and *Endoscopy* from 1994 to October 2006 for published articles on this subject was performed. Reference lists from relevant articles were also inspected to identify additional applicable articles missed with the above search strategy. An overall quality assessment of the available publications was done according to ''Evidence based gastroenterology and hepatology'' (see Appendix). Recommendation grades for the use of endoscopic hemostatic devices appear within the text as follows: (**Recommendation [R]** grade A, B, or C) depending on the quality of evidence.[1]

MECHANICAL HEMOSTASIS DEVICES

Endoscopic clips

History. Initially used in the neurosurgical field, clips were first applied in the GI tract through a rigid endoscope to mark a gastric lesion 4 decades ago.[2] Since then, flexible devices were developed that are inserted through the instrument channel in flexible endoscopes. Further developments in clip technology, such as the ability to rotate (HX-5LR-1 Hemoclip MD 850, Olympus, America, Allentown, Pa), to reopen and close multiple times before deployment (Resolution clip, Microvasive Endoscopy, Boston Scientific, Natick, Mass; InScope, Ethicon Endosurgical, Cincinnati, Ohio), to flush water through the clip device (TriClip, Wilson-Cook Medical, Winston-Salem, NC), or to deploy 4 clips in one application session (InScope MultiClip Applier, InScope) have made the devices simpler and more user friendly.

Technology. Five endoscopic clips are available, each with distinctive features: (1) the Rotating clip, (2) the QuickClip2, (3) the TriClip, (4) the Resolution clip, and (5) InScope MultiClip Applier. Most of the literature on endoscopic hemostasis published so far is based on the experience with clips manufactured by Olympus.[3]

Technique. Familiarity with the devices, application, and limitations of the clips are critical for the appropriate choice of devices and successful endoscopic mechanical hemostasis of GI bleeding. The proper application of endoscopic clips involves a general multistep process, as shown in Videos 1 to 5 (available online at www.giejournal.org) and Figures 1 and 2. Practical tips to optimize the endoscopic clip application technique are outlined in Table 1.

Detachable snare (endoloop)

History. In the mid-1980s, Pontecorvo and Pesce[4] developed the first detachable snare, the ''safety snare.'' Hachisu[5] developed the first commercially available detachable snare for endoscopic use.

Technology. Two forms of detachable nylon loop snares (Olympus Medical, Tokyo, Japan) are available: (1) Endo-Loop is a reusable device with a 30-, 20- (in the United States), and 11-mm (in Japan) opening diameter and (2) Poly-Loop is a preassembled ready-to-use version of the Endo-Loop with a 30-mm opening diameter. In addition, a smaller Endo-Loop (11 mm) can be used for variceal ligation in conjunction with a transparent ligation chamber (Olympus MH-593) attached to the end of an endoscope.

The loop device has an outer plastic sheath and an inner metal coil around a central cable with a hook that houses the nylon loop. The elliptically shaped nylon loop has a silicone rubber stopper that permits customized tightening.

Technique. Detachable snares are predominantly used in the prevention of immediate and delayed polypectomy bleeding. Several practical tips to optimize the use of detachable snares are outlined in Table 2.

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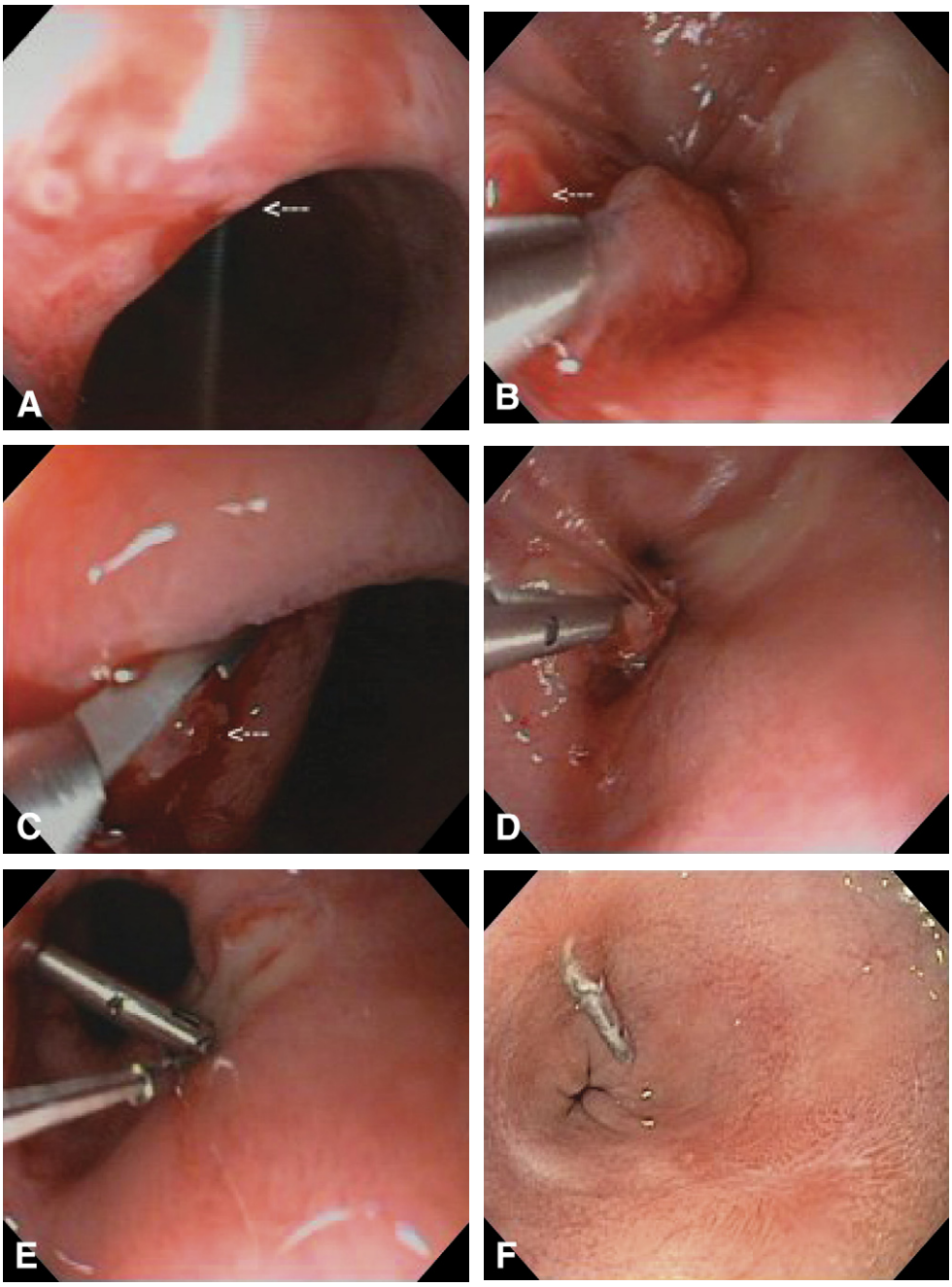

Figure 1. Endoscopic clip application of actively bleeding esophageal ulcer: the principles of using of an endoscopic clip to treat an actively bleeding visible vessel. In this example, an actively bleeding artery was localized within an esophageal ulcer. **A**, Clipping requires precision. A water-jet equipped therapeutic endoscope is important to maintain visualization of the target site. In addition, the head of the bed was elevated to improve visualization. The arterial bleeding vessel had been localized (*arrow*). **B**, The location of the bleeding site, posterior to the heart, posed a challenge due to the continuous movement from rapid heart beat. Thus, it was important to optimize clip handling by bringing it close to the tip of the endoscope. Before deployment, care was taken to ensure that the vessel was captured. The position of the clip, however, was too distal. Thus, as can be expected, the closed clip did not include the entire bleeding vessel and the surrounding tissue to the vessel. Bleeding did not stop. **C**, The clip was reopened and repositioned to be slightly more proximal to the bleeding vessel. Placing it slightly proximal to the vessel and pushing it leftward toward the wall (while the lumen was suctioned) allowed capture of as much underlying tissue to the vessel as possible, thus ensuring its efficacy. **D** and **E**, The clip was closed and slowly released. There was no further bleeding. The patient was prescribed oral proton-pump inhibitor medication twice daily. **F**, Two months later the ulcer healed. The clip remained in place.

Endoscopic band ligation

History. Van Stiegmann et al[6] developed the band ligation technology for esophageal varices management. With subsequent developments, the transparent endoscopic elastic band ligating device,[7] pneumatic release of bands,[8] and multiple band application in one session,[9]

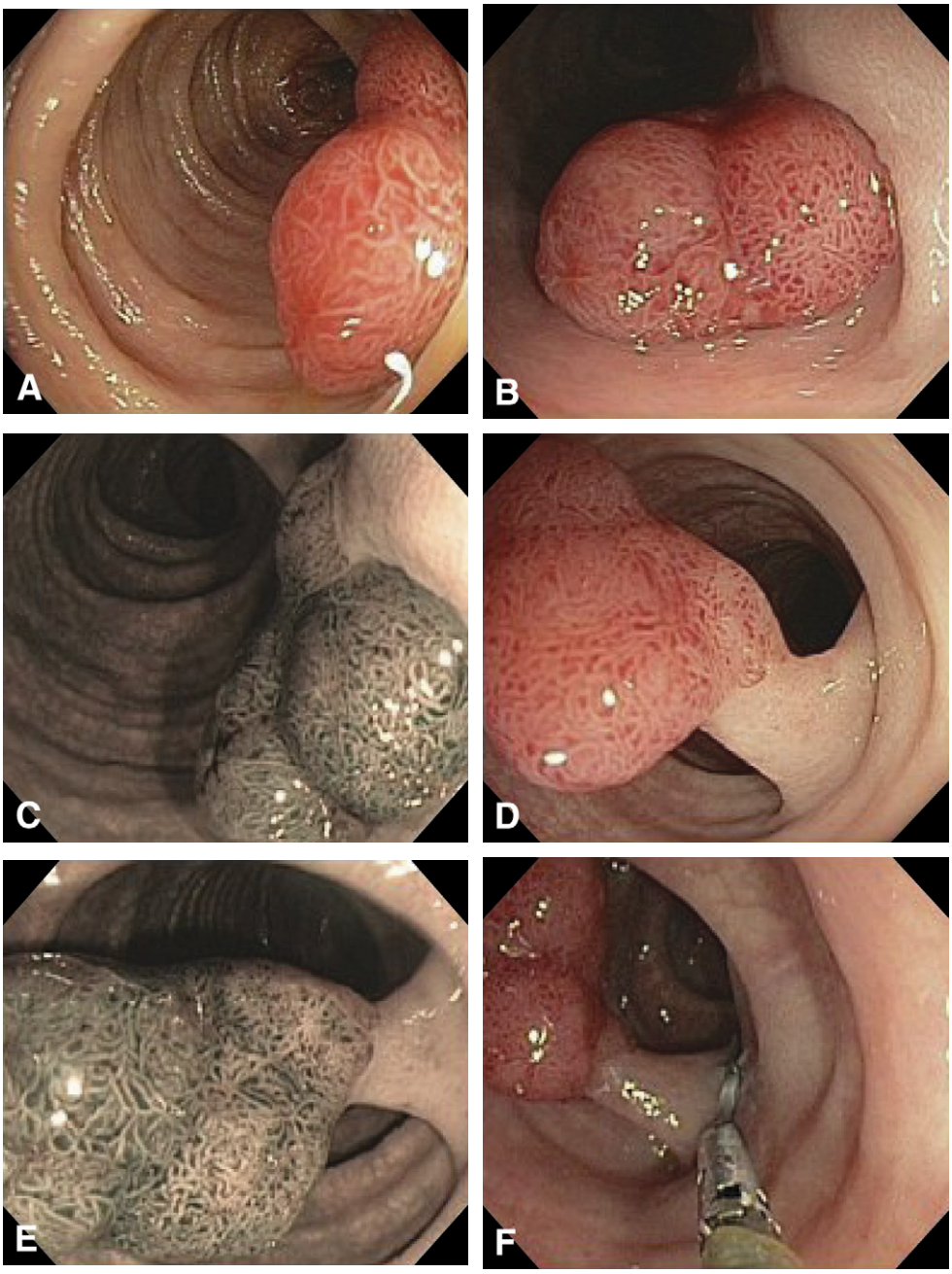

Figure 2. Endoscopic clip ligation of polyp stalk to prevent bleeding after snare polypectomy. **A**, This patient was referred for endoscopic mucosal resection of a 2-cm descending colon polyp. **B**, On the left lateral decubitus position, the polyp was thought to be sessile. **C**, The surface pattern of the mucosa was studied by using the narrow band imaging. The polyp had a sulci appearing mucosal pattern, and there was no area without pattern, which signified the possibility of invasive carcinoma. **D** and **E**, The importance of patient position is shown. The long stalk of the polyp was exposed by rotating the patient's position. **F**, Prevention of postpolypectomy bleeding was accomplished by placement of a clip at the base of the polyp.

band ligation became the standard of care for variceal bleeding.

Technology. Multiple variceal band ligation devices are currently available for endoscopic mechanical hemostasis of arterial bleeding from the esophagus, stomach, left colon, and rectum.[10] The potential risk of full-thickness entrapment and perforation of the right colon and small intestine is noteworthy.[11]

Technique. Device operation is similar to the technique used in variceal ligation, although it is suggested to minimize the amount of tissue sucked into the cap before the application of a band to prevent serosal entrapment. Release of the bands to leave only 1 or 2 bands on the ligator before insertion of the endoscope improves the field of view through the cap (Table 3, Video 6, available online at www.giejournal.org).

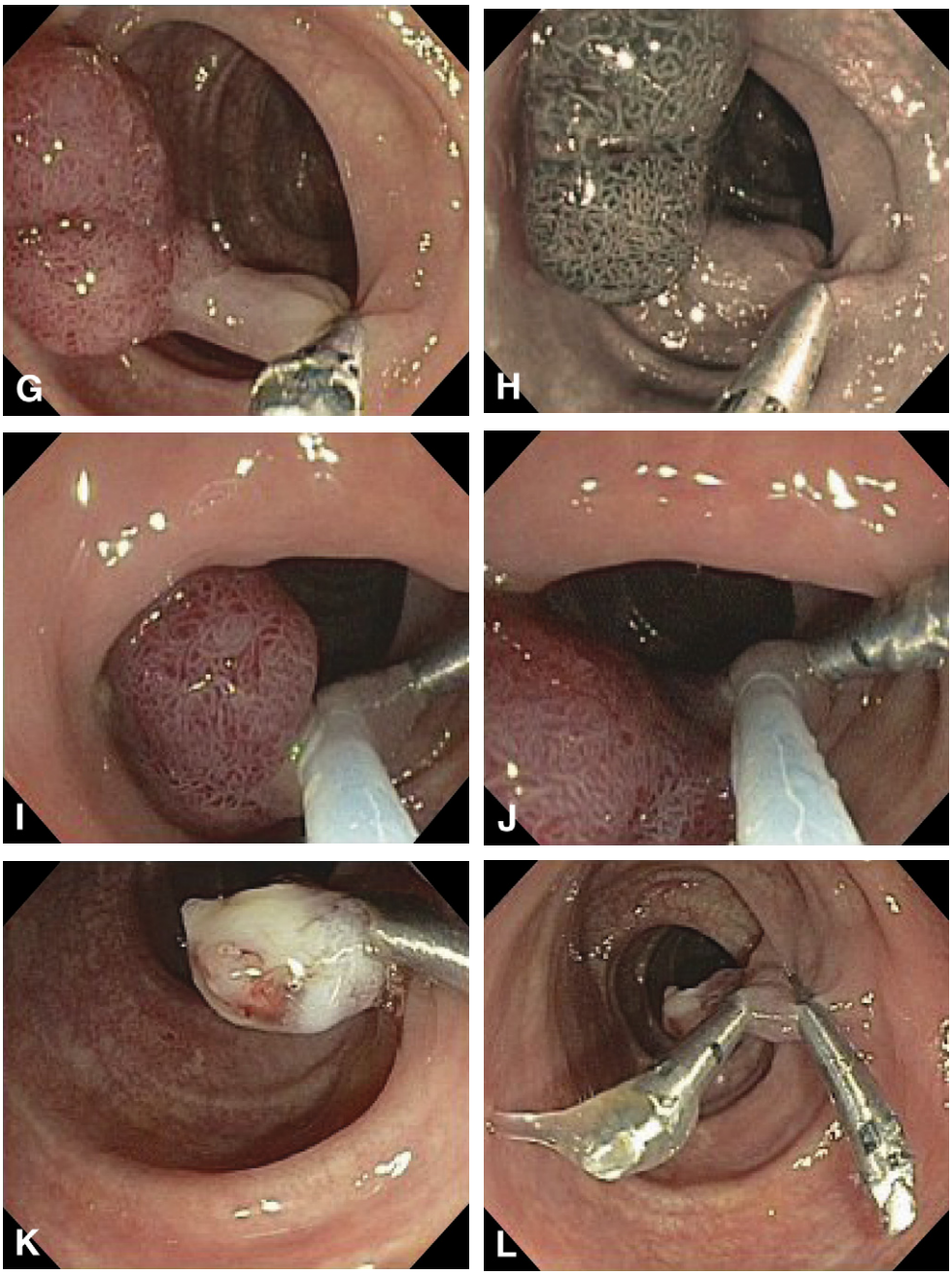

Figure 2 (*continued*) **G**, The polyp became ischemic, indicating that the blood supply of the polyp had been strangulated adequately. **H**, The congested mucosal microvessels as seen by using the narrow band imaging. **I**, A snare loop was carefully placed above the clip. The snare was positioned a few mm above the clip. **J**, A rapid cut current was applied to prevent burning at the clip site. **K**, The cut surface after resection. A possible vessel was seen at the center of the stalk. **L**, Another clip was placed below the first clip.

STANDARD MANAGEMENT OF GI BLEEDING

After initial resuscitation of patients with GI bleeding, urgent endoscopy is the standard of care to diagnose the etiology of bleeding, to stratify the risk of rebleeding, and to deliver appropriate therapy. Peptic ulcer is the most common cause of GI bleeding. Less common causes include varices, Mallory-Weiss tears (MWT), Dieulafoy's lesion, tumors, diverticulosis, and angiomas.

A number of factors influence the outcome of endoscopic hemostasis, irrespective of the method used to control bleeding. Clearing the stomach of blood clots by the intravenous injection of 250 mg of erythromycin 20 minutes before endoscopy improves visualization and minimizes the need for a second-look endoscopy.[12,13] A large-channel therapeutic endoscope, especially the 6-mm channel endoscope with a water pump attachment, allows suction of blood clots easily.[14] Connecting a 3-way

TABLE 1. Practical tips for endoscopic clip application*

1. **Precision.** Keeping the clip and the target close to the endoscope allows controlled deployment of the clip.
2. **Approach.** We prefer the tangential approach because it allows more tissue to be captured during the clip deployment. If a tangential approach cannot be achieved through endoscope repositioning or clip rotation, the en face approach is used. In the en face approach, the first clip typically causes the clipped tissue to tent up. The second clip can then be placed tangentially under the first clip.
3. **Capture.** Slight suction to collapse the lumen before the deployment of the endoclip permits maximal capture of tissue surrounding the vessel.
4. **Placement.** Although a single clip may be sufficient for adequate clamping of a protruding vessel, we typically place 2 additional clips to ligate the feeding vessel proximal and distal to the bleeding point.
5. **Use of epinephrine.** We avoid epinephrine injection around a visible vessel or bleeding site because the injection alone may provide temporary cessation of bleeding and thus give an inaccurate assessment of hemostasis created by endoclip application, except in cases of peptic ulcer with an adherent clot (when we use epinephrine injection and the guillotine snare technique[104].
6. **Overcome limitations inherent in clip technology**

   a. Use of a distal attachment cap. Some sites may be difficult to access, such as those in the proximal lesser curvature and posterior duodenal bulb or inside a diverticulum. The use of a translucent (band ligator cap or an endoscopic mucosal resection) cap on the distal tip of the endoscope can facilitate clip application by permitting the endoscope to be placed in a stable position and allowing the target to be oriented properly.

   b. Use of Resolution clip without its sheath (the "naked clip"). Removal of the outer plastic sheath allows for insertion the clip device through a diagnostic side-viewing and double-balloon endoscopes. It improves suction ability and permits the endoscopist to rotate the clip in a one-to-one fashion.

*Soetikno R, Gotoda T, Barro J, et al. Endoscopic clipping technique. ASGE Learning Video Library. Chicago: American Society for Gastrointestinal Endoscopy; 2003.

TABLE 2. Practical tips for endoscopic detachable snare (Endo-Loop) application*

1. **Polyp position.** Orient the polyp in the 5 to 7 o'clock position to facilitate endolooping of the polyp.
2. **Use tactile and visual cues for controlled ligation.** Close the loop snug around the polyp stalk. Tight ligation may result in the transaction of stalk and bleeding, whereas loose ligation may be ineffective in strangulating the feeding vessel. Placing a mark on the loop tightening silicon stopper provides the endoscopist withthe benefit of visual confirmation in addition to tactile sensation of stalk ligation.
3. **Avoid ligation of thin stalked polyps (<5 mm), inflammatory, and short-stalked polyps.** The use of the detachable snare may actually precipitate bleeding in some settings because it tends to transect a thin or soft stalked polyp during ligation or dislodge in short-stalked polyps after polypectomy.
4. **Avoid entanglement of the detachable snare with the polypectomy snare.** Removal of the snare may be difficult and could precipitate bleeding.
5. **"Lift and ligate" large polyps.** A 2-channel endoscope allows the use of a grasping forceps through the second channel to maneuver a large polyp into the Endo-Loop. A 2-channel colonoscope can alternatively be prepared by taping a plastic tube along the shaft of a single-channel colonoscope.
6. **"Ligate and let go" of benign pedunculated lesions.**† In this technique, endoscopic looping of polypoid lesions to induce ischemic necrosis is perfomed. Thus, polypectomy is achieved by self-amputation.

*Soetikno R, Barro J, Friedland S. Endoscopic looping technique. ASGE Learning Video Library. Chicago: American Society for Gastrointestinal Endoscopy; 2004.
†Friedland S, Kahng LS, Torosis J, et al. Ligate and let go. Gastrointest Endosc 2003;58:473-4.

stopcock for suction and water input to the 6-mm channel at the biopsy port bypasses the umbilical cord and suction valve to permit clearance of large blood clots within 5 minutes.[15] Large-diameter orogastric lavage may be required occasionally in massive bleeding.

Endoscopic therapy has been shown to be effective to control active bleeding, prevent rebleeding, reduce transfusion requirement, decrease hospitalization, limit the need for surgery and angiography, and decrease the mortality rate in patients with peptic ulcers with active bleeding, nonbleeding vessels, or adherent clot.[16-19] In the United States, a combination of epinephrine injection and cautery is widely used in the endoscopic hemostasis of arterial bleeding. Endoscopic therapy has not proved necessary in patients with minor stigmata (flat spot) or clean-based ulcer hemorrhage; these patients could be fed early, triaged to a nonintensive care bed, or even be discharged home earlier.[20] High-dose proton pump inhibitor has been shown to improve the outcome in patients with peptic ulcer with a high risk of rebleeding.[21,22] Eradication of *Helicobacter pylori*, long-term antisecretory maintenance therapy, and counseling about the risks of aspirin or nonsteroidal anti-inflammatory drug use are highly recommended.[23]

Despite significant advances, rebleeding occurs in up to 20% of patients who undergo endoscopic therapy.[24] A potential drawback of thermal methods and injection of sclerosing agents is the risk of tissue necrosis and perforation.[18,25] In contrast, mechanical endoscopic hemostasis is not associated with significant tissue injury and thus is an attractive treatment modality.

MANAGEMENT OF GI BLEEDING WITH ENDOSCOPIC MECHANICAL HEMOSTASIS

The use and efficacy of mechanical hemostasis has been reported in a variety of diseases.

Bleeding peptic ulcer

Endoscopic clips. Outcomes after endoscopic clip application of bleeding peptic ulcers have proved similar, if not better, than other endoscopic treatment modalities and should be considered instead of other approaches when local expertise is available (**R** grade A). Primary hemostasis rates have been high (85%-100%), rebleeding rates have been low (2%-20%), and the safety record has been excellent (Table 4). Of the published randomized controlled trials (RCTs), endoscopic clip application was compared with injection therapy of various agents (distilled water injection, hypertonic saline solution–epinephrine, and epinephrine-polidocanol) in 3 studies,[26-28] with heater probe therapy in 2 studies,[29,30] and with combination epinephrine injection and multipolar electrocoagulation in another study. In 4 trials, the hemostasis results of the clip application group and the control group were comparable.[27-30] In 2 studies, the use of endoscopic clips was favorable.[26,29] Four case-controlled studies similarly showed clips to be excellent in controlling the bleeding, with significantly lower rebleeding rates compared with ethanol injection (15% vs 29%, $P = .023$),[31] epinephrine injection (4.4% vs 17%, $P < .05$),[32] and a combination of epinephrine injection and heater probe cautery (5% vs 33%, $P < .05$) (Video 5).[33]

Recently, the combination of endoscopic injection of epinephrine and clip application has been shown to be superior to epinephrine injection alone in the treatment of high-risk bleeding ulcers in a study of 105 patients with active spurting, oozing, nonbleeding visible vessels or adherent clots in ulcer bases; in another study of 293 patients with bleeding peptic ulcer there was no benefit.[34,35] In the former study, less rebleeding (3.8% vs 21%, $P = .008$), a higher percentage of permanent hemostasis (100% vs 33%, $P = .02$), and less need for emergency surgery (0% vs 9%, $P = .023$) were observed, whereas in the latter study there was no difference at all between the 2 treatments.[34,35] A randomized trial comparing endoscopic hemoclip application (n = 42), ethanol injection (n = 42), and a combination of both (n = 42) for bleeding gastric ulcer demonstrated the efficacy of endoscopic hemostasis with hemoclips; a combination of ethanol injection and hemoclips did not improve the results of hemostasis over either method alone.[36] In a randomized comparative study of combination therapy of epinephrine injection and multipolar electrocoagulation with hemoclips in 47 patients with acute nonvariceal upper GI bleeding, primary hemostasis was successful 100% of patients receiving hemoclips and 95.2% of patients receiving combination therapy ($P = .450$) and the rebleeding rates were 15.4% in the hemoclip patients and 23.8% in the combination therapy patients ($P = .49$). There was no difference in duration of hospitalization, units of blood transfused, surgery rates, and mortality rates.[37]

TABLE 3. Practical tips for endoscopic band ligation

1. **Preparation:** Removing the bands from a variceal multiband ligator except for the last 2 bands before the insertion of the endoscope improves the field of view through the cap.
2. **Band ligation:** Operation of the band ligator for arterial band ligation in the esophagus and stomach is similar to the technique used in variceal ligation: suction followed by application of band. Caution: It is safer to minimize the amount of tissue sucked into the cap before the application of a band to prevent serosal entrapment of colon and small intestine.
3. **Special consideration:** Band ligation provides quick mechanical tamponade of arterial bleeding, which may be useful in situations where the target is mobile such as the gastroesophageal junction bleeding and bleeding sites that are difficult to access such as high lesser curve or cardia of the stomach.

Band ligation. Experience with endoscopic band ligation of peptic ulcer is limited.[38-41] The RCT by Park et al[40] demonstrated lower peptic ulcer rebleeding after combination therapy with a clip or band ligation plus epinephrine injection compared with epinephrine injection alone (2/44 [4.5%] vs 9/44 [20.5%], $P < .05$). His group subsequently showed the safe and effective use of band ligation in the treatment of bleeding from small-sized nonfibrotic acute peptic ulcer of the stomach, duodenum, and Billroth II anastomosis.[39] Case series have reported the benefit of endoscopic band ligation in controlling peptic ulcer bleeding in settings where prior attempts to control bleeding with standard techniques had failed.[38,41] Further studies are needed to determine which bleeding situations may best be managed with clips or bands versus other hemostasis approaches. The familiarity of the endoscopist with each approach should be taken into account when selecting a therapy because studies of outcomes with endoscopic therapy typically are performed at centers with expertise in these devices. Therefore, until further evidence is available, endoscopic band ligation (EBL) should be reserved for those situations where other standard endoscopic approaches have failed or are unavailable (**R** grade B).

Endoloop. There is no literature to date on the use of endoscopic looping to treat peptic ulcer bleeding.

MWT

Endoscopic therapy with clips or band should be considered in patients with a MWT with active bleeding, a nonbleeding visible vessel, or an adherent clot (**R** grade A).[42-44]

Clips. An RCT comparing endoscopic hemoclip application (n = 18) with epinephrine injection (n = 17) in

TABLE 4. Endoclipping of bleeding peptic ulcers: RCTs

Study	Treatment	Primary hemostasis	Rebleeding	Transfusion (units)	Hospital stay (d)	Surgery/ embolization	Mortality rate
Chung et al, 1999[27]	Clip (n = 41)	98%	2%	7	NA	5%	2%
	Injection (n = 41)	95%	15%	8	NA	15%	2%
	Combination (n = 42)	98%	10%	11	NA	2%	2%
		NS	NS	NS		NS	NS
Cipolletta et al, 2001[29]	Clip (n = 56)	85%	1.80%	3	6	4%	4%
	Heater probe (n = 57)	85%	21%	4	7	7%	4%
		NS	$P < .05$	$P < .05$	$P < .05$	NS	NS
Lin et al, 2002[30]	Clip (n = 40)	85%	8.8%	3	8	5%	5%
	Heater probe (n = 40)	100%	5%	3	9	3%	3%
		$P < .05$	NS	NS	NS	NS	NS
Gevers et al, 2002[28]	Clip (n = 35)	85%	20%	5	NA	NA	0%
	Injection (n = 34)	85%	6%	5	NA	NA	0%
	Combination (n = 32)	90%	15%	4	NA	NA	9%
		NS	NS	NS			NS
Chou et al, 2003[26]	Clip (n = 39)	100%	10%	NA	9	5%	3%
	Injection (n = 40)	98%	28%	NA	8	13%	5%
		NS	$P < .05$		NS	NS	NS
Shimoda et al, 2003[36]	Clip (n = 42)	90.5%	9.5%	274 ± 54 mL	NA	0%	7.1%
	Alcohol injection (n = 42)	85.7%	14.3%	331 ± 77 mL	NA	0%	2.4%
	Combination (n = 42)	92.9%	7.1%	163 ± 42	NA	0%	2.4%
		NS	NS	$P = .05$	NS	NS	NS
Chua et al 2005[35]	Injection + clip (n = 91)	100%	11%	NA	NA	1.1%	6.6%
	Injection (n = 202)	99%	4%	NA	NA	1.5%	5.4%
		NS	NS			NS	NA
Saltzman et al, 2005[37]	Clips (n = 26)	100%	15.4%	4	4	11.5%	0%
	Injection + coagulation (n = 21)	95.2%	23.8%	5	4	4.7%	9.5%
		NS	NS	NS	NS	NS	NS
Lo et al, 2006[34]	Injection + clip (n = 52)	98%	3.8%	NA	7.1	0%	2%
	Injection (n = 53)	92%	21%	NA	11	9%	0%
		NS	$P = .008$		NS	$P = .02$	NS

NA, Not available; *NS*, not significant.

35 patients with actively bleeding MWT demonstrated similar outcomes in terms of primary hemostasis (94%), rebleeding rates (6%), transfusion requirements, duration of hospital stay, and mortality rates.[45] Another small study of MWT showed superiority of mechanical hemostasis with clip or EBL over hypertonic saline solution and epinephrine injection (n = 14) in prevention of rebleeding (0% vs 28%, $P < .05$).[46] In a case-series, clip application resulted in successful primary hemostasis in all 26 patients with actively bleeding MWT, and with no rebleeding, complications, or death.[47]

Band ligation. EBL has been shown to be effective in achieving hemostasis and preventing rebleeding in patients with actively bleeding MWT (**R** grade A).[48,49] In an RCT of 34 patients with actively bleeding MWT, primary hemostasis was achieved in all 17 patients who were

treated with EBL compared with 16 of 17 patients (94.1%) in the epinephrine injection group; there was no recurrence of bleeding or major complication in either group.[50] Higuchi et al[51] reported successful hemostasis in 36 of 37 patients with MWT who had active bleeding, exposed vessels, or both. Except for one patient who had severe liver failure, there was no rebleeding, perforation, or other complications during a follow-up of 1 to 24 months. Gunay et al[48] reported successful control of bleeding with EBL in 4 patients with MWT.

Dieulafoy's lesion

Bleeding from Dieulafoy's lesion can be controlled by endoscopic clip placement, EBL, injection therapy, and cauterization (**R** grade B). Epinephrine injection alone has been associated with a high risk of rebleeding.[52]

Clips. Endoscopic clip application has been shown to provide complete hemostasis of Dieulafoy's bleeding. In a prospective study of 34 patients with a Dieulafoy's lesion treated by clip application alone, initial hemostasis was successful in 94% of patients, and rebleeding was seen in 9% of patients. None of the patients required surgery, with a 3% 30-day mortality rate and 1 unrelated death.[53] In lesions in the proximal stomach or those with a protruding vessel, clip application has been shown to be superior to injection therapy to control the rebleeding rate (0%-8.3% vs 33.3%-35.7%).[52,54]

Band ligation. EBL has been used to control bleeding from the Dieulafoy's lesions of the esophagus, stomach, small intestine, colon, and rectum.[48-61] A retrospective study of bleeding gastroduodenal Dieulafoy's lesions treated with EBL (n = 14) or injection therapy with or without thermal therapy (n = 9) showed similar hemostasis characteristics.[55] Use of clips and EBL has been reported to be successful in the control of bleeding from esophageal Dieulafoy's lesion in 2 cases.[56]

Endoloop. Endoloop ligation to the base of previously placed clips has been used to control bleeding from a patient with a colonic Dieulafoy's lesion.[57]

Postpolypectomy bleeding

Postpolypectomy bleeding occurs in approximately 1% of the procedures and results in higher patient morbidity and mortality rates and treatment costs.[58-61] Immediate bleeding from the polypectomy site can be controlled by resnaring the stalk and applying tamponade. Injection of epinephrine, cauterization, band ligation, clip application, or use of a detachable snare can be used to control both immediate and delayed bleeding.

Clips. After the initial report of Hachisu,[62] Binmoeller et al[63] reported successful management of 42 cases of postpolypectomy hemorrhage with endoclip application.[63] A combination of epinephrine injection and application of clips may be useful in the management of bleeding after endoscopic snare excision of giant colorectal polyps.[64] Later studies have confirmed that clips are successful to control immediate and delayed postpolyectomy bleeding and to prevent rebleeding and surgery (**R** grade B).[65] Figure 2 shows the use of endoscopic clips to prevent postpolypectomy bleeding. A detachable snare in addition to clips may be beneficial to control delayed postpolypectomy bleeding.

Clip application to close the mucosal defect after endoscopic mucosal resection has not been shown to prevent delayed bleeding (0.98% vs 0.96%) in a randomized trial of an average-risk population of 413 patients (**R** grade A).[66] Patients at high risk of rebleeding, such as those with a bleeding diathesis, or patients who live far away from a medical facility, may benefit from empiric prophylactic clip application. In a retrospective study of patients on long-term anticoagulation (international normalized ratio = 2.3 [range 1.4-4.9]), 1 to 2 clips were applied after snare resection of polyps ranging from 3 to 10 mm in size. In the 41 cases, there were no episodes of postpolypectomy bleeding (**R** grade B).[67] Formal evaluation of the potential role of empiric clip therapy in patients at high risk of rebleeding is warranted.

EBL. EBL has been used to control postpolypectomy bleeding.[10,68,69] Seventeen patients with 20 pedunculated or semipedunculated gastric polyps with heads 1 cm or greater in diameter were treated with hypertonic saline solution and epinephrine injection, followed by snare resection and band ligation of the resection site. None of the patients had any bleeding or perforation (**R** grade C).[70]

Endoloop. Endoloop has been shown to be useful in the prevention of postpolypectomy bleeding, control of postpolypectomy bleeding, and induction of ischemic necrosis of polyps.[4,5,71-79] It has been shown to be useful in the prevention of immediate or delayed hemorrhage after snare polypectomy in patients with bleeding diathesis and in patients with large pedunculated polyps.[4,5,72,79-82] Therefore, endoloop placement should be considered when the risk of postpolypectomy bleeding is high (patients with a large polyp [>1 cm]) (**R** grade A).

In a RCT of 89 patients, Iishi et al[71] demonstrated a significant reduction of postpolypectomy bleeding (0% vs 12%, $P < .05$) and duration of hospitalization in patients undergoing endoloop ligation of the polyp stalk before its resection. In an RCT of 488 patients with large pedunculated colorectal polyps (>1 cm), postpolypectomy bleeding was reported in 1.8% of patients undergoing ligation before polypectomy, 3.1% of patients undergoing epinephrine injection before polypectomy, and 7.9% of patients undergoing polypectomy alone. There was no difference in rebleeding rates in patients with polyps smaller than 2 cm, whereas in those with larger polyps ($\geq$ 2 cm), postpolypectomy bleeding occurred in 2.7% of patients in the detachable snare group and in 2.9% of patients in the epinephrine injection group compared with 15.1% of patients in the control group ($P < .05$).[79] Use of clips to

achieve initial hemostasis followed by the application of a detachable snare has been used to manage bleeding from lesions that cannot be controlled with the use of a detachable snare alone.[83] Recently, a combination of epinephrine injection and detachable snare in 84 patients with a large colonic polyp (>2 cm) has been shown to significantly decrease the number of early postpolypectomy bleeding episodes compared with injection of epinephrine alone in 75 patients (2.3% vs 10.6%, $P = .04$). The number of early bleeding episodes was significantly less in the combination therapy group compared with the group treated with epinephrine injection alone (1% vs 9%, $P = .02$). In contrast, there was no significant difference between the 2 groups as far as the delayed bleeding is concerned.[84]

Other uses of detachable snares to decrease bleeding include (1) hemostasis before biopsy to confirm the diagnosis of a large lesion with potential for bleeding, such as a large polypoid arteriovenous malformation in the colon,[85] (2) prevention of bleeding and perforation by placing a detachable snare ligation below a band ligation followed by snare resection above the band for removal of rectal carcinoids,[86] and (3) removing lipomas with or without electrocautery snare resection.[87-89]

Colonic diverticular bleeding

Endoscopic injection of epinephrine, cautery, or both have been shown to control diverticular bleeding, prevent rebleeding, and reduce the need for surgery.[90] Recently, clip application to the bleeding vessel in the diverticulum has been shown to control diverticular bleeding.[91-93] Clip application is safe (avoids the risk of perforation from cautery) and serves as a fluoroscopic marker to guide the interventional radiologist in embolization of the vessel. Because the clips may fall off and migrate, one should be cautious about relying on a single clip as a marker. Use of multiple clips in addition to the use of a tattoo may be reassuring. Therefore, clips should be considered as an alternative to other approaches for hemostasis in the setting of colonic diverticular bleeding (**R** grade B). Although endoscopic band ligation is effective in controlling colonic diverticular bleeding, it requires removal of the endoscope after the site of bleeding marked and loading of the band ligator before band ligation (**R** grade C).[94,95]

Duodenal diverticular bleeding

Experience with endoscopic management of duodenal diverticular bleeding is limited to a few cases.[96] Treatment options attempted include administration of antacids and sucralfate,[97] prompt surgery,[98] epinephrine injection,[99] and epinephrine injection and multipolar coagulation.[100] Clip application can control bleeding while avoiding the risk of perforation associated with cautery[101] and may require application through a side-viewing endoscope.[102] Further studies are needed to help define the role of endoscopic mechanical hemostasis approaches.

CLIPS AS MARKERS FOR ANGIOGRAPHIC CONTROL OF BLEEDING

Clips serve as excellent radiographic markers.[103] When bleeding cannot be controlled by endoscopic therapy, marking the bleeding ulcer with a clip enhances the possibility of embolization of the correct vessel by the interventional radiologist. In one study, clips helped direct therapy in half of the 13 patients who stopped bleeding during angiography.[104]

CONCLUSIONS

Clips, loops, and bands are useful endoscopic accessories in the management of GI bleeding as alternatives to current endoscopic therapies or as a preferred modality, depending on the etiology of bleeding and the underlying condition of the patient. Given the relatively uncommon incidence of many of the bleeding situations being considered, most existing studies are relatively small in size, leading to concerns about type II statistical errors. Further studies are needed to determine which bleeding situations may best be managed with clips or bands versus other hemostasis approaches. The familiarity of the endoscopist with each approach should be taken into account when selecting a therapy because studies of outcomes with endoscopic therapy typically are performed at centers with expertise in these devices.

DISCLOSURE

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Abbreviations: EBL, endoscopic band ligation; MWT, Mallory-Weiss tears; RCT, randomized controlled trial.

REFERENCES

1. McDonald J, Burroughs A, Feagan B. Evidence based gastroenterology and hepatology. BMJ 1999.
2. Hachisu T, Miyazaki S, Hamaguchi K. Endoscopic clip-marking of lesions using the newly developed HX-3L clip. Surg Endosc 1989;3:142-7.
3. Raju GS, Gajula L. Endoclips for GI endoscopy. Gastrointest Endosc 2004;59:267-79.
4. Pontecorvo C, Pesce G. The "safety snare"—a ligature-placing snare to prevent haemorrhage after transection of large pedunculated polyps. Endoscopy 1986;18:55-6.
5. Hachisu T. A new detachable snare for hemostasis in the removal of large polyps or other elevated lesions. Surg Endosc 1991;5:70-4.
6. Van Stiegmann G, Cambre T, Sun JH. A new endoscopic elastic band ligating device. Gastrointest Endosc 1986;32:230-3.

7. Hashizume M, Ohta M, Ueno K, et al. A transparent endoscopic elastic band ligating device. Gastrointest Endosc 1993;39:686-8.
8. Frimberger E. Endoscopic elastic band ligating device, pneumatically released. Gastrointest Endosc 1987;33:129-30.
9. Saeed ZA. The Saeed Six-Shooter: a prospective study of a new endoscopic multiple rubber-band ligator for the treatment of varices. Endoscopy 1996;28:559-64.
10. Witte JT. Band ligation for colonic bleeding: modification of multiband ligating devices for use with a colonoscope. Gastrointest Endosc 2000;52:762-5.
11. Barker KB, Arnold HL, Fillman EP, et al. Safety of band ligator use in the small bowel and the colon. Gastrointest Endosc 2005;62:224-7.
12. Frossard JL, Spahr L, Queneau PE, et al. Erythromycin intravenous bolus infusion in acute upper gastrointestinal bleeding: a randomized, controlled, double-blind trial. Gastroenterology 2002;123:17-23.
13. Spahr L, Queneau PE, Giostra E, et al. Erythromycin intravenous bolus infusion in acute upper gastrointestinal bleeding: a randomized, controlled, double-blind trial. Gastroenterology 2002;123:2162.
14. Kodali VP, Petersen BT, Miller CA, et al. A new jumbo-channel therapeutic gastroscope for acute upper gastrointestinal bleeding. Gastrointest Endosc 1997;45:409-11.
15. Hintze RE, Adler A, Veltzke W. The wide-channel endoscope optimizes the success of emergency endoscopy. Acta Gastroenterol Belg 1996;59:237-9.
16. Laine L, Peterson W. Bleeding peptic ulcers. N Engl J Med 1994;331: 717-27.
17. Sacks HS, Chalmers TC, Blum AL, et al. Endoscopic hemostasis: an effective therapy for bleeding peptic ulcers. JAMA 1990;264: 494-9.
18. Cook D, Guyatt G, Salena B, et al. Endoscopic therapy for acute nonvariceal upper gastrointestinal hemorrhage: a meta-analysis. Gastroenterology 1992;102:139-48.
19. Jensen DM. Endoscopic control of non-variceal upper gastrointestinal hemorrhage. In: Yamada T, Alpers D, Owyand C, et al, editors. Textbook of gastroenterology, 2nd ed. Philadelphia: Lippincott; 1995. p. 2991-3011.
20. Laine L, Cohen H, Brodhead J, et al. Prospective evaluation of immediate versus delayed refeeding and prognostic value of endoscopy in patients with upper gastrointestinal hemorrhage. Gastroenterology 1992;102:314-6.
21. Lau JY, Sung JJ, Lee KK, et al. Effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment of bleeding peptic ulcers. N Engl J Med 2000;343:310-6.
22. Javid G, Masoodi I, Zargar SA, et al. Omeprazole as adjuvant therapy to endoscopic combination injection sclerotherapy for treating bleeding peptic ulcer. Am J Med 2001;111:280-4.
23. Jensen DM. Management of severe ulcer rebleeding. N Engl J Med 1999;340:799-801.
24. Stiegmann GV. Endoscopic approaches to upper gastrointestinal bleeding. Am Surg 2006;72:111-5.
25. Kumar P, Fleischer DE. Thermal therapy for gastrointestinal bleeding. Gastrointest Endosc Clin North Am 1997;7:593-609.
26. Chou Y-C, Hsu P-I, Lai K-H, et al. A prospective, randomized trial of endoscopic hemoclip placement and distilled water injection for treatment of high-risk bleeding ulcers. Gastrointest Endosc 2003;57: 324-8.
27. Chung IK, Ham JS, Kim HS, et al. Comparison of the hemostatic efficacy of the endoscopic hemoclip method with hypertonic saline-epinephrine injection and a combination of the two for the management of bleeding peptic ulcers. Gastrointest Endosc 1999;49:13-8.
28. Gevers AM, De Goede E, Simoens M, et al. A randomized trial comparing injection therapy with hemoclip and with injection combined with hemoclip for bleeding ulcers. Gastrointest Endosc 2002;55: 466-9.
29. Cipolletta L, Bianco MA, Marmo R, et al. Endoclips versus heater probe in preventing early recurrent bleeding from peptic ulcer: a prospective and randomized trial. Gastrointest Endosc 2001;53:147-51.
30. Lin HJ, Hsieh YH, Tseng GY, et al. A prospective, randomized trial of endoscopic hemoclip versus heater probe thermocoagulation for peptic ulcer bleeding. Am J Gastroenterol 2002;97:2250-4.
31. Nagayama K, Tazawa J, Sakai Y, et al. Efficacy of endoscopic clipping for bleeding gastroduodenal ulcer: comparison with topical ethanol injection. Am J Gastroenterol 1999;94:2897-901.
32. Buffoli F, Graffeo M, Nicosia F, et al. Peptic ulcer bleeding: comparison of two hemostatic procedures. Am J Gastroenterol 2001;96: 89-94.
33. Lee YC, Wang HP, Yang CS, et al. Endoscopic hemostasis of a bleeding marginal ulcer: hemoclipping or dual therapy with epinephrine injection and heater probe thermocoagulation. J Gastroenterol Hepatol 2002;17:1220-5.
34. Lo CC, Hsu PI, Lo GH, et al. Comparison of hemostatic efficacy for epinephrine injection alone and injection combined with hemoclip therapy in treating high-risk bleeding ulcers. Gastrointest Endosc 2006; 63:767-73.
35. Chua TS, Fock KM, Ng TM, et al. Epinephrine injection therapy versus a combination of epinephrine injection and endoscopic hemoclip in the treatment of bleeding ulcers. World J Gastroenterol 2005;11: 1044-7.
36. Shimoda R, Iwakiri R, Sakata H, et al. Evaluation of endoscopic hemostasis with metallic hemoclips for bleeding gastric ulcer: comparison with endoscopic injection of absolute ethanol in a prospective, randomized study. Am J Gastroenterol 2003;98:2198-202.
37. Saltzman JR, Strate LL, Di Sena V, et al. Prospective trial of endoscopic clips versus combination therapy in upper GI bleeding (PROTECCT—UGI bleeding). Am J Gastroenterol 2005;100:1503-8.
38. Misra SP, Dwivedi M, Misra V, et al. Endoscopic band ligation as salvage therapy in patients with bleeding peptic ulcers not responding to injection therapy. Endoscopy 2005;37:626-9.
39. Park CH, Lee WS, Joo YE, et al. Endoscopic band ligation for control of acute peptic ulcer bleeding. Endoscopy 2004;36:79-82.
40. Park CH, Joo YE, Kim HS, et al. A prospective, randomized trial comparing mechanical methods of hemostasis plus epinephrine injection to epinephrine injection alone for bleeding peptic ulcer. Gastrointest Endosc 2004;60:173-9.
41. Banerjee B, Trivedi MH, Swied AM. Endoscopic band ligation for gastric ulcer bleeding. Surg Laparosc Endosc Percutan Tech 2000;10: 246-8.
42. Bataller R, Llach J, Salmeron JM, et al. Endoscopic sclerotherapy in upper gastrointestinal bleeding due to the Mallory-Weiss syndrome. Am J Gastroenterol 1994;89:2147-50.
43. Peng YC, Tung CF, Chow WK, et al. Efficacy of endoscopic isotonic saline-epinephrine injection for the management of active Mallory-Weiss tears. J Clin Gastroenterol 2001;32:119-22.
44. Kim JW, Kim HS, Byun JW, et al. Predictive factors of recurrent bleeding in Mallory-Weiss syndrome. Korean J Gastroenterol 2005;46: 447-54.
45. Huang SP, Wang HP, Lee YC, et al. Endoscopic hemoclip placement and epinephrine injection for Mallory-Weiss syndrome with active bleeding. Gastrointest Endosc 2002;55:842-6.
46. Chung IK, Kim EJ, Hwang KY, et al. Evaluation of endoscopic hemostasis in upper gastrointestinal bleeding related to Mallory-Weiss syndrome. Endoscopy 2002;34:474-9.
47. Yamaguchi Y, Yamato T, Katsumi N, et al. Endoscopic hemoclipping for upper GI bleeding due to Mallory-Weiss syndrome. Gastrointest Endosc 2001;53:427-30.
48. Gunay K, Cabioglu N, Barbaros U, et al. Endoscopic ligation for patients with active bleeding Mallory-Weiss tears. Surg Endosc 2001; 15:1305-7.
49. Myung SJ, Kim HR, Moon YS. Severe Mallory-Weiss tear after endoscopy treated by endoscopic band ligation. Gastrointest Endosc 2000; 52:99-101.
50. Park CH, Min SW, Sohn YH, et al. A prospective, randomized trial of endoscopic band ligation vs epinephrine injection for actively bleeding Mallory-Weiss syndrome. Gastrointest Endosc 2004;60:22-7.

51. Higuchi N, Akahoshi K, Sumida Y, et al. Endoscopic band ligation therapy for upper gastrointestinal bleeding related to Mallory-Weiss syndrome. Surg Endosc 2006;20:1431-4.
52. Chung IK, Kim EJ, Lee MS, et al. Bleeding Dieulafoy's lesions and the choice of endoscopic method: comparing the hemostatic efficacy of mechanical and injection methods. Gastrointest Endosc 2000;52: 721-4.
53. Yamaguchi Y, Yamato T, Katsumi N, et al. Short-term and long-term benefits of endoscopic hemoclip application for Dieulafoy's lesion in the upper GI tract. Gastrointest Endosc 2003;57:653-6.
54. Park CH, Sohn YH, Lee WS, et al. The usefulness of endoscopic hemoclipping for bleeding Dieulafoy lesions. Endoscopy 2003;35:388-92.
55. Mumtaz R, Shaukat M, Ramirez FC. Outcomes of endoscopic treatment of gastroduodenal Dieulafoy's lesion with rubber band ligation and thermal/injection therapy. J Clin Gastroenterol 2003; 36:310-4.
56. Khurana V. Tandem utilization of a hemostatic clip and a banding device in the esophagus: a novel hemostatic technique. Gastrointest Endosc 2006;63:517-9.
57. Gimeno-Garcia AZ, Parra-Blanco A, Nicolas-Perez D, et al. Management of colonic Dieulafoy lesions with endoscopic mechanical techniques: report of two cases. Dis Colon Rectum 2004;47:1539-43.
58. Macrae FA, Tan KG, Williams CB. Towards safer colonoscopy: a report on the complications of 5000 diagnostic or therapeutic colonoscopies. Gut 1983;24:376-83.
59. Waye JD, Lewis BS, Yessayan S. Colonoscopy: a prospective report of complications. J Clin Gastroenterol 1992;15:347-51.
60. Rosen L, Bub DS, Reed JFI, et al. Hemorrhage following colonoscopic polypectomy. Dis Colon Rectum 1993;36:1126-31.
61. Gibbs DH, Opelka FG, Beck DE, et al. Postpolypectomy colonic hemorrhage. Dis Colon Rectum 1996;39:806-10.
62. Hachisu T. Evaluation of endoscopic hemostasis using an improved clipping apparatus. Surg Endosc 1988;2:13-7.
63. Binmoeller KF, Thonke F, Soehendra N. Endoscopic hemoclip treatment for gastrointestinal bleeding. Endoscopy 1993;25:167-70.
64. Binmoeller KF, Bohnacker S, Seifert H, et al. Endoscopic snare resection of ''giant'' colorectal polyps. Gastrointest Endosc 1996;43:183-8.
65. Parra-Blanco A, Kaminaga N, Kojima T, et al. Hemoclipping for postpolypectomy and postbiopsy colonic bleeding. Gastrointest Endosc 2000;51:37-41.
66. Shioji K, Suzuki Y, Kobayashi M, et al. Prophylactic clip application does not decrease delayed bleeding after colonoscopic polypectomy. Gastrointest Endosc 2003;57:691-4.
67. Friedland S, Soetikno R. Colonoscopy with polypectomy in anticoagulated patients. Gastrointest Endosc 2006;64:98-100.
68. Slivka A, Parsons WG, Carr-Locke DL. Endoscopic band ligation for treatment of post-polypectomy hemorrhage. Gastrointest Endosc 1994;40:230-2.
69. Smith RE, Doull J. Treatment of post-polypectomy bleeding site by endoscopic band ligation. Gastrointest Endosc 1994;40:499-500.
70. Akahoshi K, Yoshinaga S, Fujimaru T, et al. Endoscopic resection with hypertonic saline-solution-epinephrine injection plus band ligation for large pedunculated or semipedunculated gastric polyp. Gastrointest Endosc 2006;63:312-6.
71. Iishi H, Tatsuta M, Narahara H, et al. Endoscopic resection of large pedunculated colorectal polyps using a detachable snare. Gastrointest Endosc 1996;44:594-7.
72. Rey JF, Marek TA. Endo-loop in the prevention of the post-polypectomy bleeding: preliminary results. Gastrointest Endosc 1997;46:387-9.
73. Matsushita M, Hajiro K, Takakuwa H, et al. Ineffective use of a detachable snare for colonoscopic polypectomy of large polyps. Gastrointest Endosc 1998;47:496-9.
74. Soetikno RM, Friedland S, Lewit V, et al. Lift and ligate: a new technique to treat a bleeding polypectomy stump. Gastrointest Endosc 2000;52:681-3.
75. Friedland S, Kahng LS, Torosis J, et al. Ligate and let go. Gastrointest Endosc 2003;58:473-4.
76. Friedland S, Benaron D, Parachikov I, et al. Measurement of mucosal capillary hemoglobin oxygen saturation in the colon by reflectance spectrophotometry. Gastrointest Endosc 2003;57:492-7.
77. Matsushita M, Hajiro K, Okazaki K, et al. A large juvenile polyp in a 1-year-old child safely removed by colonoscopic polypectomy with a detachable snare. Gastrointest Endosc 2000;52:118-20.
78. Matsushita M, Takakuwa H, Matsubayashi Y, et al. Handcrafted two-channel colonoscope for grasping-forceps-assisted resection of giant pedunculated polyps. Gastrointest Endosc 2005;62:132-6.
79. Di Giorgio P, De Luca L, Calcagno G, et al. Detachable snare versus epinephrine injection in the prevention of postpolypectomy bleeding: a randomized and controlled study. Endoscopy 2004;36:860-3.
80. Pai KP, Morgan RH. Endoloop: a helpful new device for transanal rectal polypectomy. Br J Surg 1995;82:748.
81. Waye JD. New methods of polypectomy. Gastrointest Endosc Clin North Am 1997;7:413-22.
82. Pietropaolo V, Bogliolo G, Lande A, et al. Endoscopic ligation in the prevention of hemorrhage after polypectomy: our experience [Italian]. G Chir 1999;20:51-2.
83. Uno Y, Satoh K, Tuji K, et al. Endoscopic ligation by means of clip and detachable snare for management of colonic postpolypectomy hemorrhage. Gastrointest Endosc 1999;49:113-5.
84. Paspatis GA, Paraskeva K, Theodoropoulou A, et al. A prospective, randomized comparison of adrenaline injection in combination with detachable snare versus adrenaline injection alone in the prevention of postpolypectomy bleeding in large colonic polyps. Am J Gastroenterol 2006;101:2805.
85. Ji JS, Choi KY, Lee BI, et al. A large polypoid arteriovenous malformation of the colon treated with a detachable snare: case report and review of literature. Gastrointest Endosc 2005;62:172-5.
86. Moon JH, Kim JH, Park CH, et al. Endoscopic submucosal resection with double ligation technique for treatment of small rectal carcinoid tumors. Endoscopy 2006;38:511-4.
87. Raju GS, Gomez G. Endoloop ligation of a large colonic lipoma: a novel technique. Gastrointest Endosc 2005;62:988-90.
88. Vardas EM, Theodoropoulou AP, Zois ES, et al. Detachable snare in the removal of large colonic lipomas. Gastrointest Endosc 2005;62: 648-9.
89. Murray MA, Kwan V, Williams SJ, et al. Detachable nylon loop assisted removal of large clinically significant colonic lipomas. Gastrointest Endosc 2005;61:756-9.
90. Jensen DM, Machicado GA, Jutabha R, et al. Urgent colonoscopy for the diagnosis and treatment of severe diverticular hemorrhage. N Engl J Med 2000;342:78-82.
91. Hokama A, Uehara T, Nakayoshi T, et al. Utility of endoscopic hemoclipping for colonic diverticular bleeding. Am J Gastroenterol 1997; 92:543-4.
92. Yoshikane H, Sakakibara A, Ayakawa T, et al. Hemostasis by capping bleeding diverticulum of the colon with clips. Endoscopy 1997; 29(Suppl):S33-4.
93. Simpson PW, Nguyen MH, Lim JK, et al. Use of endoclips in the treatment of massive colonic diverticular bleeding. Gastrointest Endosc 2004;59:433-7.
94. Tucker LE. Diverticular bleeding: novel treatment with band ligation. Mo Med 2004;101:61-3.
95. Farrell JJ, Graeme-Cook F, Kelsey PB. Treatment of bleeding colonic diverticula by endoscopic band ligation: an in-vivo and ex-vivo pilot study. Endoscopy 2003;35:823-9.
96. Rioux L, Des Groseilliers S, Fortin M, et al. Massive upper gastrointestinal bleeding originating from a fourth stage duodenal diverticulum: a case report and review of the literature. Can J Surg 1996; 39:510-2.
97. Ryan ME, Hamilton JW, Morrissey JF. Gastrointestinal hemorrhage from a duodenal diverticulum. Gastrointest Endosc 1984;30:84-6.
98. Francheschi D, Castillo W, Yuh J, et al. Endoscopic diagnosis of upper gastrointestinal tract bleeding from a duodenal diverticulum. Gastrointest Endosc 1987;33:383-4.

99. Choudari CP, Luman W, Eastwood MA, et al. Bleeding duodenal diverticulum. Endoscopy 1995;27:284.
100. Khandelwal M, Akerman PA, Jones WF, et al. Endoscopic therapy of a bleeding duodenal diverticulum. Am J Gastroenterol 1995;90: 1328-9.
101. Raju GS, Nath S, Zhao X, et al. Duodenal diverticular hemostasis with hemoclip placement on the bleeding and feeder vessels: a case report. Gastrointest Endosc 2003;57:116-7.
102. Wu NH, Wang HP, Yang CS, et al. Endoscopic hemoclip therapy of a bleeding duodenal diverticulum. Gastrointest Endosc 2000;51: 489-91.
103. Golder S, Strotzer M, Grune S, et al. Combination of colonoscopy and clip application with angiography to mark vascular malformation in the small intestine. Endoscopy 2003;35:551.
104. Eriksson LG, Sundbom M, Gustavsson S, et al. Endoscopic marking with a metallic clip facilitates transcatheter arterial embolization in upper peptic ulcer bleeding. J Vasc Interv Radiol 2006;17:959-64.

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APPENDIX

Grading of recommendations and levels of evidence used in ''Evidence based gastroenterology and hepatology''

Grade A

- Evidence from large randomized clinical trials or systematic reviews (including meta-analyses) of multiple randomized trials that collectively have at least as much data as a single well-defined trial
- Evidence from at least one ''all or none'' high-quality cohort study; in which ALL patients died/failed with conventional therapy and some survived/succeeded with the new therapy (eg, chemotherapy for tuberculosis, meningitis, or defibrillation for ventricular fibrillation) or in which many died/failed with conventional therapy and NONE died/failed with the new therapy (eg, penicillin for pneumococcal infections)
- Evidence from at least one moderate-sized randomized controlled trial (RCT) or meta-analysis of small trials that collectively only have a moderate number of patients
- Evidence from at least one RCT

Grade B

- Evidence from at least one high-quality study of nonrandomized cohorts that did and did not receive the new therapy
- Evidence from at least one high-quality case-control study
- Evidence from at least one high-quality case series

Grade C

- Opinions from experts without reference or access to any of the foregoing (eg, argument from physiology, bench research, or first principles)

Adapted and modified from McDonald et al.[1]