

Endoscopic clipping

Michael J GRUPKA & Jay BENSON

Department of Medicine, University of Connecticut Health Center, Farmington, Connecticut, USA

Endoscopic clips are relatively new devices that have been shown to be effective for the control of acute gastrointestinal hemorrhage. Various different models are available and offer simplicity of use with relatively few

complications. Recently, endoscopic clips have been used for a variety of non-hemorrhagic conditions. In this article we review the literature and present current thinking about the indications, efficacy and safety of these devices.

KEY WORDS: endoscope devices, fistula, hemorrhage, hemostasis, perforation.

INTRODUCTION

Endoscopic clips were first introduced in 1975 by Hayashi *et al.*¹ to treat gastrointestinal bleeding. Over the past 30 years the clips have undergone a significant improvement in design and are now being used for a wide variety of indications. Here we review the literature regarding the indications, efficacy and safety of clipping devices. Most extensively studied is the use of clips in non-variceal upper gastrointestinal (GI) bleeding. Most trials deal with peptic ulcers that are actively bleeding or that demonstrate a non-bleeding visible vessel. We also review other indications for clip placement including treatment of fistulas, perforations, markers for radiology, biliary cannulation and anchoring stents.

Peptic ulcers and Dieulafoy's lesions

Most of the studies on clip use, efficacy and safety have been performed with the endoclip (or hemoclip) from Olympus, Tokyo. There are two forms: a reusable device in which clips are reloaded after each use or a preloaded

single use device (Quickclip, Olympus, Tokyo). This device has two prongs and the newer models can be rotated. The TriClip made by Cook Endoscopy, Winston-Salem, NC is a three-pronged device with a 12-mm opening span. The Resolution Clip (Boston Scientific, Natick, MA), has the ability to rotate as well as to be reopened and closed multiple times to facilitate proper placement. The newest clip in development is the Multi-Clip by InScope, Ethicon Endosurgery, Cincinnati, OH. It can apply four clips sequentially without having to exchange the deployment device down the endoscope between each clip placement.²

Peptic ulcer bleeding is one of the main indications for clip use. The bleeding stops spontaneously in most patients (approximately 70–80%).³ In the subset of ulcers that do not stop bleeding, there is a significant mortality of 12–18%.^{4,5} Ulcers at risk for continued or recurrent bleeding are identified by the presence of active spurting or oozing blood, or the appearance of a non-bleeding visible vessel at the time of endoscopy.^{6–8} Endoscopic intervention has reduced mortality in this group to 3–6%.^{9–11} Different technologies have been used to treat peptic ulcers, including injection therapy and thermal ablation. They may be used separately or in combination. Injecting agents include epinephrine, hypertonic saline or alcohol. Thermal ablation is performed by a bicap, heater probe or argon plasma beam coagulation.

Clips were originally designed as an alternative treatment to control bleeding by direct mechanical pressure. The

Correspondence to: Michael J GRUPKA, Department of Medicine, Division of Gastroenterology-Hepatology, University of Connecticut Health Center, Rm. AM-044, 263 Farmington Ave., Farmington, CT 06030. Email: Grupka@hotmail.com

© 2008 The Authors

Journal compilation © 2008 Chinese Medical Association Shanghai Branch, Chinese Society of Gastroenterology and Blackwell Publishing Asia Pty Ltd.

clip is used to grasp and compress a bleeding vessel similar to surgical ligation.¹² The appeal of this method is that it minimizes injury to surrounding tissues as opposed to injection or thermal therapy.¹³ This may reduce the risk of necrosis and perforation. In an animal model, mechanical ligation methods were superior to injection or thermal injury methods in the treatment of mesenteric vessels greater than 2 mm in diameter.¹⁴ To achieve hemostasis with a clip requires locating the vessel, which may be difficult in patients who are actively bleeding. Therefore, pretreatment with injection therapy to reduce bleeding may be required before clip placement, negating the theoretical advantage of using the clip to cause no tissue injury.¹²

Multiple trials have been conducted to assess the efficacy of clipping versus other modalities. All these studies have been performed using the Olympus endo-clip. The main outcomes evaluated have been initial hemostasis (at the time of first endoscopy), re-bleeding rate (any bleeding after first endoscopy), permanent hemostasis (no further bleeding for a defined follow-up period), need for surgery (the failure of endoscopic therapy) and mortality. The first uncontrolled study of 88 patients showed a 100% initial hemostasis rate, with five patients re-bleeding, one of whom ultimately required surgery. This study included both lower and upper gastrointestinal bleeds.¹⁵ A prospective look at endoclips specifically for peptic ulcer bleeding found an initial hemostasis rate of 95%, a re-bleeding rate of 8%, a permanent hemostasis rate of 93% and a mortality rate of 3% in a series of 40 patients.¹¹

The endoclip has been compared to various injection therapies. A retrospective review of 113 patients found the permanent hemostasis rate for an injection using either ethanol, ethanol plus epinephrine or aethoxysclerol plus ethanol was 84% as compared to a 100% hemostasis rate for clipping. Injection complications included increasing the size of the ulcer bed and one case of perforation. No complications were noted with clipping.¹⁶ A prospective study comparing an injection of ethanol to an endoclip application and to combination therapy (an injection followed by clip placement) did not reach statistical significance for finding a difference in a re-bleeding rate or permanent hemostasis. The only finding of statistical significance was that less blood was transfused in the combination therapy group.¹⁷ In a retrospective review of endoclips compared to hypertonic saline there was a trend towards improved initial hemostasis and lower re-bleeding rates with the clip. However, the results did not reach statistical significance.¹⁸ Chou *et al.* evaluated 79 patients, comparing the endoclip to a distilled water injection. Initial

hemostasis was excellent in both groups (100 vs 97.5%, for the clip and distilled water, respectively), but there was a much higher re-bleeding rate in the distilled water group (10.3% for the clip vs 28.2% for distilled water, $P = 0.04$).¹³ Park *et al.* also saw a significantly higher re-bleeding rate for injection therapy alone (20%) versus injection therapy in combination with mechanical hemostasis (banding or clipping) (4%). Re-bleeding difference was most notable in ulcers greater than 2 cm in diameter.¹⁹ Evaluating an epinephrine injection alone versus one used in combination with clips, a prospective study found a significantly higher re-bleed rate (21 vs 3.8%) and need for emergency surgery (9 vs 0%) in the group using injection therapy alone.²⁰

Two studies found the results of endoscopic clipping to be inferior. In comparing an epinephrine injection used alone vs one used in combination with the endoclip, no difference was found in primary or delayed hemostasis, surgery or mortality. The re-bleeding rate was higher for combination therapy (4% for epinephrine vs 11% for epinephrine plus clip). However, the endoclip group was older with a higher incidence of comorbidities, including chronic renal insufficiency.⁹ Gevers *et al.* found endoscopic hemoclip placement significantly less effective than injection therapy for achieving hemostasis in patients with a bleeding ulcer. The reduced efficacy of the clips was due to difficulty in deploying the clipping device on ulcers that required a tangential approach, especially in the duodenal bulb. There was a 34% failure rate in control of bleeding with a clip versus only 6% for injection therapy.²¹

Clip placement has also been compared to a heater probe. Cipolletta *et al.* studied 113 patients and found recurrent bleeding in 21% of patients treated with a heater probe versus 1.8% in cases using endoclips. The difference was felt to be due to cases with spurting blood which dissipated the heat from the probe. Most re-bleeding was managed endoscopically. There was no mortality difference.¹⁰ Lin *et al.* prospectively treated 80 patients and achieved 85% initial hemostasis for an endoclip versus 100% for heater probe. The posterior wall of the duodenum and the lesser curvature of the stomach were areas where clip placement was difficult and this accounted for the failures. Permanent hemostasis was only 77% for the clip versus 97.5% for the heater probe. There was no difference in the need for surgery, mortality or length of hospital stay between the two techniques. The heater probe offered an advantage in these ulcers that are difficult to approach.²² In the PROTECCT_UGI Bleeding trial endoscopic clipping was compared to the combination

therapy of an epinephrine injection and bipolar probe ablation, and non-statistically significant differences were found in initial hemostasis, the time taken to achieve initial hemostasis, re-bleeding, permanent hemostasis, the need for surgery, length of stay in hospital and mortality.²³

Dieulafoy's lesions are another source of upper GI bleeding that is amenable to clip therapy. They account for a small percentage of all upper gastrointestinal bleeding. Prospective studies found initial hemostasis rates at 94–95%, with re-bleeding rates of between 9 and 10%.^{24,25} Clipping is superior to injection therapy alone for achieving initial hemostasis, recurrent bleeding and the need for surgery.^{26,27} Heater probes also have excellent rates for hemostasis, but there is no comparative data between these and clips.

In a recent meta-analysis of the above trials for peptic ulcer bleeding and Dieulafoy's lesions, clip placement was found to reduce the re-bleed rate (9.5% for the clip *vs* 19% for the injection) and the need for surgery when compared to various injection therapies. Similar results were found for combination therapy *vs* an injection on its own. There are no data to compare clipping alone to combination therapy (an injection plus clip application). Endoclippping versus thermocoagulation did not reveal any statistically significant differences in initial or definitive hemostasis, re-bleeding, the need for surgery or mortality.²⁸ Many of the trials did not use high-dose proton pump inhibitor therapy, which has been shown to reduce the re-bleeding rate.²⁹

Other causes of GI bleeding

Mallory–Weiss tears are often managed conservatively, but a small percentage of cases with active bleeding may require endoscopic therapy. The advantage of clip therapy is that it can treat deeper tears and perforations at the same time as controlling bleeding.³⁰ Huang *et al.* prospectively examined 35 active bleeders and randomized them to epinephrine injection therapy or to clip placement. Each case averaged 2.5 clips. They achieved a 100% initial hemostasis with a 6% re-bleed rate in each arm. All cases stabilized using the same repeat therapy. Both the epinephrine and the clips were equally safe and effective.³¹ Yamaguchi *et al.* successfully clipped 26 cases of Mallory–Weiss tears using an average of 2.8 clips per case.³²

Other sources of bleeding in the GI tract can also be managed with clipping devices. Endoscopic clips have been used on gastric tumors, post-sphincterotomies, arterio–venous malformations and diverticular bleeds.^{33,34} The clip has been placed across the mouth of the

bleeding diverticulum as well as on the vessel in the diverticulum. The clip can also serve as a marker for angiography, should bleeding continue.

Post-polypectomy bleeding occurs in less than 1% of cases and is often managed conservatively. Cases with continued bleeding may require endoscopic intervention. Clips were successful in providing hemostasis in a series of 42 patients.¹⁵ In a large review of over 9000 colonoscopies, the authors found endoclips to be 100% successful in controlling 45 immediate post-polypectomy and post-biopsy bleeds. They reported one failure in controlling 18 delayed post-polypectomy bleeds.³⁵

Endoscopic clips are used to prevent post-polypectomy bleeding³⁶ especially in cases with large polyps, using a cutting current, and patients on anticoagulation. Due to the low incidence of this type of bleeding, it is difficult to power a study high enough to prove a difference prospectively. For patients who must remain on anticoagulants such as warfarin, clips have been proposed as a way to perform a polypectomy while keeping the incidence of bleeding to a minimum. A case report described the removal of a 6-cm duodenal polyp from a patient on Coumadin therapy, and with the use of a hemoclip on the stalk there was no bleeding.³⁷ Friedland and Soetikno reported on a series of 41 polypectomies on patients with an average international normalized ratio of 2.3. All the polyps were less than 1 cm in diameter. With prophylactic clip placement they reported zero post-polypectomy bleeds.³⁸ There is conflicting evidence on the prevention of bleeding after the resection of large polyps. Sobrino-Faya *et al.* retrospectively studied 223 polypectomies, of which only large polyps (>15 mm) were routinely clipped. Thirty cases were clipped before the polypectomy and four cases were clipped after the polypectomy. They had only one case of mild immediate bleeding, which was stopped with the placement of a second clip.³⁹ In comparison, Shioji *et al.* found a 0.98% delayed bleeding rate in patients who had an endoscopic mucosal resection with a prophylactic clip placement versus a 0.96% delayed bleeding rate in patients without a clip placement.⁴⁰ It has been argued that this study may have been underpowered.⁴¹ Another retrospective look at 152 flat lesion polypectomies using pure cutting current with a prophylactic clip placement experienced no perforations or delayed bleeds. But there was no comparison group to determine an outcome without the clips.⁴¹

Non-bleeding indications

Endoscopic clips have been used to close a variety of small perforations and fistulas throughout the gastrointestinal tract. Closing anastomotic leaks and fistulas

has been demonstrated in various case reports. Favorable outcomes depend on rapid clip deployment to minimize bacterial contamination.¹² Successful clipping of esophageal perforations due to pneumatic dilation,^{42,43} traumatic nasogastric tube placement⁴⁴ and an acute perforation from ingesting a fish bone⁴⁵ has been described. A gastric perforation secondary to the snare excision of a gastric leiomyoma⁴⁶ and an EMR excision of a dysplastic lesion⁴⁷ have been successfully clipped. Clips have been used in duodenal perforations caused by a sphincterotomy⁴⁸ a biliary stent⁴⁹ and a polypectomy.^{50–52} Fan *et al.* were able to close a 1-cm posterior duodenal wall perforation after a polypectomy using a combination of clippings followed by a band ligation.⁵⁰ Post-colonoscopy perforations have been treated as well.^{53,54} Anastomotic leakages in esophagogastric surgery⁵⁵ and esophagopleural fistulas⁵⁶ have been closed. Clips have been used in conjunction with Argon plasma beam coagulation.⁵⁷ Closures of a percutaneous endoscopic gastrostomy tube fistula created by the inadvertent removal of the tube⁵⁸ and a colcutaneous fistula⁵⁹ have been reported. In the colon, case reports show the closure of a colovesical fistula⁶⁰ and closure of a fecal fistula after appendectomy using clips.⁶¹

Jejunal feeding tube placement can often be difficult and the tube refluxing back into the stomach occurs frequently. A clip-assisted jejunal feeding-tube (J-tube) placement has been utilized to prevent this occurrence.⁶² In a report of two cases, Frizzell *et al.* described placing a loop of suture string at the end of a J-tube, and using a Resolution Clip to snare it. Withdrawing the clip within the endoscope, the scope is then advanced distally to the proximal jejunum. There the Resolution Clip is extended and then deployed to the mucosa, thereby anchoring the distal end of the J-tube. This method prevents retracting the tube along with the endoscope, and provides a short-term anchor for it.⁶³

Clips have been used in radiology. An interventional radiology series of 13 patients found that the placement of a metallic clip facilitated arterial embolization of peptic ulcer bleeds. In six of the patients this was believed to be essential.⁶⁴ As compared to India ink for marking lesions such as tumors, the short time span of clip adherence makes it a less effective marker.⁶⁵

Endoscopic clips can anchor esophageal stents. Sriram *et al.* describe a case of a patient with a bronchoesophageal fistula secondary to cancer. A stent was placed to wall off this fistula. However, due to a lack of esophageal luminal involvement there was a high risk

of stent migration. A clip was placed to anchor the stent, and X-ray demonstrated that the stent location at 4 weeks post-procedure was appropriate.⁶⁶

One case report described clip placement to alter the biliary anatomy to help in biliary cannulation. Careful placement was necessary, as errant clip placement can obstruct duct outflow. The traction applied can also alter the anatomy and make interpretation of the cholangiogram difficult.⁶⁷

Comparison and safety

Few studies have been performed to compare one type of clip with another. In an animal model comparing the TriClip, Quickclip and the Resolution Clip, hemostasis rates were 100% for all models. All these devices required a similar learning curve for successful placement, and none interfered with the ulcer healing. The grasp and release mechanism was important for repositioning and resulted in less clips being lost. At times the thin prongs of the TriClip sliced through the sides of ulcers. Short-term retention rates were significantly lower for the TriClip (less than 1 week). The Quickclip retention time averaged 2 weeks versus 4 weeks for the Resolution Clip.⁶⁸ In humans, the endoclip was compared to TriClip placement in peptic ulcer bleeds. Primary hemostasis was 94% for the endoclip versus 76% for the TriClip. Of the 12 TriClip patient failures, 10 were successfully clipped using the endoclip, an 83% salvage rate. The differences between these clips in the re-bleeding rate, the need for surgery, hospital stay and mortality did not reach statistical significance.⁶⁹

The use of endoscopic clips has been safe. There are very few reports of adverse events. There are only two case reports of perforation, one occurring after clipping a post-polypectomy bleed site⁷⁰ and the other occurring after clipping a Dieulafoy's lesion inside of a duodenal diverticulum.⁷¹ The clips have been found to grasp only the mucosal and submucosal layers, and will dislodge after a short retention period. The clips are metal, and will conduct a current after application.

The duodenal bulb, lesser curvature of the stomach and posterior wall of the proximal body and cardia can be difficult for clip placement. The necessary tangential approach may make clip placement a blind procedure.^{10,13,21} In a prospective study of 77 patients, there was a 16.9% failure rate in bulb and posterior antrum lesions.⁷² The misfire rate is as high as 42% of cases.¹⁰ The average number of clips used per case is between 2.8 and 3.0.^{10,15,20,23} Stronger ligating forceps are needed to hold onto chronic ulcers with fibrotic bases.²³ The size of the defects that can be treated is limited by the

size of the clip.^{10,21} These figures are based on studies using endoclips. Further study with newer clip technology, such as those that can grasp and release, and have improved rotation ability, may show reduced rates of misfiring, of failed hemostasis and of the number of clips used per case.

CONCLUSION

In summary, clips have been proved to be a valuable alternative method of controlling hemostasis by using mechanical pressure. There is no injury to surrounding tissue with this method, and the clips do not interfere with healing. Prospective studies have shown that clips are superior to injection therapy in controlling ulcer bleeding. In comparison to thermal ablations they appear to be of similar efficacy. However, in areas that are difficult to approach and where clip placement is tangential, thermal methods may be preferred. Clips have also been successfully used in treating many other forms of GI tract bleeding including Dieulafoy's, Mallory-Weiss tears, diverticular and post-polypectomy bleeding. Many endoscopists also use clips to prevent post-polypectomy bleeding, especially in cases involving coagulation issues or large polyps. But the evidence has not been conclusive in determining the benefit of this. Case reports have shown the wide variety of uses, ranging from anchoring stents, catheters and feeding tubes to closing fistulas and small perforations. The clips are very safe to use and learning how to use them is rapid. Further study is needed to define the role of clips used on their own versus clips used in combination therapy, the efficacy of the newer clips and the efficacy of different clips compared to each other.

REFERENCES

- Hayashi I, Yonezawa TM, Kuwabara T, Kudoh I. The study on staunch clip for the treatment by endoscopy. *Gastroenterol Endoscopy* 1975; 17: 92–101.
- Chuttani R, Barkun A, Carpenter S *et al.* Endoscopic clip application devices. *Gastrointest Endosc* 2006; 63: 746–50.
- Sugawa C, Joseph AL. Endoscopic interventional management of bleeding duodenal and gastric ulcers. *Surg Clin North Am* 1992; 72: 317–34.
- Lin HJ, Perng CL, Lee FY. Clinical courses and predictors for rebleeding in patients with peptic ulcers and non-bleeding visible vessels: A prospective study. *Gut* 1994; 35: 1389–93.
- Hsu PI, Lai KH, Lin XZ. When to discharge patients with bleeding peptic ulcers: A prospective study of residual risk of rebleeding. *Gastrointest Endosc* 1996; 44: 382–7.
- Lin HJ, Chan FY, Lee ZC. Endoscopic injection to arrest peptic ulcer hemorrhage: A prospective, randomized controlled trial; preliminary results. *Hepatogastroenterology* 1991; 38: 291–4.
- Hsu PI, Lin XZ, Chan SH. Bleeding peptic ulcer-risk factors for rebleeding and sequential changes in endoscopic findings. *Gut* 1994; 35: 746–9.
- Wara P. Endoscopic prediction of major rebleeding – a prospective study of stigmata of hemorrhage in bleeding ulcer. *Gastroenterology* 1985; 88: 1209–14.
- Chua TS, Fock KM, Ng TM, Teo EK, Tan JY, Ang TL. 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.
- 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.
- Lai YC, Yang SS, Chi HW, Chen TK. Endoscopic hemoclip treatment for bleeding peptic ulcer. *World J Gastroenterol* 2000; 6: 53–6.
- Devereaux CE, Binmoeller KF. Endoclip: Closing the surgical gap. *Gastrointest Endosc* 1999 Sep; 50: 440–2.
- Chou YC, Hsu PI, Lai KH *et al.* A prospective, randomized trial of endoscopic hemoclip placement and distilled water injection for treatment of high-risk bleeding ulcers. *Gastrointest Endosc* 2003 Mar; 57: 324–8.
- Hepworth CC, Kadirkamanathan SS, Gong F, Swain CP. A randomised controlled comparison of injection, thermal and mechanical endoscopic methods of haemostasis on mesenteric vessels. *Gut* 1998; 42: 462–9.
- Binmoeller KF, Thonke F, Soehendra N. Endoscopic hemoclip treatment for gastrointestinal bleeding. *Endoscopy* 1993; 25: 167–70.
- Nagasu N, DiPalma JA. Bleeding ulcer: inject or clip? *Am J Gastroenterol* 1998; 93: 1998.
- Shimoda R, Iwakiri R, Sakata H *et al.* Evaluation of endoscopic hemostasis with metallic hemoclips for bleeding gastric ulcer: Comparison with endoscopic injection for absolute ethanol in a prospective, randomized study. *Am J Gastroenterol* 2003; 98: 2198–202.
- Chung IK, Ham JS, Kim HS, Park SH, Lee MH, Kim SJ. 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.
- Park CH, Joo YE, Kim HS, Choi SK, Rew JS, Kim SJ. 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.
- 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.
- Gevers AM, De Goede E, Simoons M, Hiele M, Rutgeerts P. A randomized trial comparing injection therapy with hemoclip and with injection combined with hemoclip for bleeding ulcers. *Gastrointest Endosc* 2002 Apr; 55: 466–9.
- Lin HJ, Hsieh YH, Tseng GY, Perng CL, Chang FY, Lee SD. A prospective, randomized trial of endoscopic hemoclip versus heater probe thermocoagulation for peptic ulcer bleeding. *Am J Gastroenterol* 2002; 97: 2250–4.
- 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.
- Ljubicic N. Efficacy of endoscopic clipping and long-term follow-up of bleeding Dieulafoy's lesions in the upper gastrointestinal tract. *Hepatogastroenterology* 2006 Mar–Apr; 53: 224–7.

- 25 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.
- 26 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.
- 27 Park CH, Sohn YH, Lee WS *et al*. The usefulness of endoscopic hemoclippping for bleeding Dieulafoy lesions. *Endoscopy* 2003; 35: 388–92.
- 28 Sung JJ, Tsoi KK, Lai LH, Wu JC, Lau JY. Endoscopic clipping versus injection and thermocoagulation in the treatment of bleeding non-variceal upper gastrointestinal bleeding: A meta-analysis. *Gut*. epub ahead of print.
- 29 Lau JY, Sung JJ, Lee KK. Effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment of bleeding peptic ulcers. *N Engl J Med* 2000; 343: 310–16.
- 30 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.
- 31 Huang SP, Wang HP, Lee YC *et al*. Endoscopic hemoclip placement and epinephrine injection for Mallory–Weiss syndrome with active bleeding. *Gastrointest Endosc* 2002 Jun; 55 (7): 842–6.
- 32 Yamaguchi Y, Yamato T, Katsumi N *et al*. Endoscopic hemoclippping for upper GI bleeding due to Mallory–Weiss syndrome. *Gastrointest Endosc* 2001; 53: 427–30.
- 33 Yoshikane H, Sakakibara A, Ayakawa T *et al*. Hemostasis by capping bleeding diverticulum of the colon with clips. *Endoscopy* 1997; 29: S33–4.
- 34 Hokama A, Uehara T, Nakayoshi T *et al*. Utility of endoscopic hemoclippping for colonic diverticular bleeding. *Am J Gastroenterol* 1997; 92: 543–4.
- 35 Parra-Blanco A, Kaminaga N, Kojima T *et al*. Hemoclippping for postpolypectomy and postbiopsy colonic bleeding. *Gastrointest Endosc* 2000 Jan; 51 (1): 37–41.
- 36 Iida Y, Miura S, Munemoto Y *et al*. Endoscopic resection of large colorectal polyps using a clipping method. *Dis Colon Rectum* 1994; 37: 179–80.
- 37 Chen YY, Su WW, Soon MS, Yen HH. Hemoclip-assisted polypectomy of large duodenal Brunner's gland hamartoma. *Dig Dis Sci* 2006; 51: 1670–2.
- 38 Friedland S, Soetikno R. Colonoscopy with polypectomy in anticoagulated patients. *Gastrointest Endosc* 2006; 64: 98–100.
- 39 Sobrino-Faya M, Martínez S, Gomez Balado M *et al*. Clips for the prevention and treatment of postpolypectomy bleeding (hemoclips in polypectomy). *Rev Esp Enferm Dig* 2002 Aug; 94 (8): 457–62.
- 40 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.
- 41 Su MY, Hsu CM, Ho YP *et al*. Endoscopic mucosal resection for colonic non-polypoid neoplasms. *Am J Gastroenterol* 2005; 100: 2174–9.
- 42 Wewalka FW, Clodi PH, Haidinger D. Endoscopic clipping of esophageal perforation after pneumatic dilation for achalasia. *Endoscopy*, 1995; 27: 608–11.
- 43 Cipolletta L, Bianco MA, Rotondano G, Marmo R, Piscopo R, Meucci C. Endoscopic clipping of perforation following pneumatic dilation of esophagojejunal anastomotic strictures. *Endoscopy* 2000; 32: 720–2.
- 44 Blocksom JM, Sugawa C, Tokioka S, Williams M. The hemoclip: A novel approach to endoscopic therapy for esophageal perforation. *Dig Dis Sci* 2004 Aug; 49: 1136–8.
- 45 Shimamoto C, Hirata I, Umegaki E, Katsu K. Closure of an esophageal perforation due to fish bone ingestion by endoscopic clip application. *Gastrointest Endosc* 2000; 51: 736–9.
- 46 Binmoeller KF, Grimm H, Soehendra N. Endoscopic closure of a perforation using metallic clips after snare excision of a gastric leiomyoma. *Gastrointest Endosc* 1993; 39: 172–4.
- 47 Kim HS, Lee DK, Jeong YS *et al*. Successful endoscopic management of a perforated gastric dysplastic lesion after endoscopic mucosal resection. *Gastrointest Endosc* 2000; 51: 613–15.
- 48 Baron TH, Gostout CJ, Herman L. Hemoclip repair of a sphincterotomy-induced duodenal perforation. *Gastrointest Endosc* 2000; 52: 566–8.
- 49 Rose's LL, Ramirez AG, Seco AL *et al*. Clip closure of a duodenal perforation secondary to a biliary stent. *Gastrointest Endosc* 2000; 51: 487–9.
- 50 Fan CS, Soon MS. Repair of a polypectomy-induced duodenal perforation with a combination of hemoclip and band ligation. *Gastrointest Endosc* 2007; 66: 203–5.
- 51 Kaneko T, Akamatsu T, Shimodaira K *et al*. Non-surgical treatment of duodenal perforation by endoscopic repair using a clipping device. *Gastrointest Endosc* 1999; 50: 410–14.
- 52 Seibert DG. Use of an endoscopic clipping device to repair duodenal perforation. *Endoscopy* 2003; 35: 189.
- 53 Yoshikane H, Hidano H, Sakakibara A *et al*. Endoscopic repair by clipping of iatrogenic colonic perforation. *Gastrointest Endosc* 1997; 46: 464–6.
- 54 Mana F, Vogelaere KD, Urban D. Iatrogenic perforation of the colon during diagnostic colonoscopy: endoscopic treatment with clips. *Gastrointest Endosc* 2001; 54: 258–9.
- 55 Rodella L, Laterza E, De Manzoni G *et al*. Endoscopic clipping of anastomotic leakages in esophagogastric surgery. *Endoscopy* 1998; 30: 453–6.
- 56 Raymer GS, Sadana A, Campbell DB, Rowe WA. Endoscopic clip application as an adjunct to closure of mature esophageal perforation with fistulae. *Clin Gastroenterol Hepatol* 2003; 1: 44–50.
- 57 Bodegraven AK van, Kuipers EJ, Bonenkamp HJ, Meuwissen SGM. Esophagopleural fistula treated endoscopically with argon beam electrocoagulation and clips. *Gastrointest Endosc* 1999; 50: 407–10.
- 58 Blocksom JM, Sugawa C, Tokioka S, Field E. Endoscopic repair of gastrostomy after inadvertent removal of percutaneous endoscopic gastrostomy tube. *Surg Endosc* 2004; 18: 868–70.
- 59 Kim HS, Lee DK, Baik SK, Kwon SO. Endoscopic management of colocutaneous fistula after percutaneous endoscopic gastrostomy. *Endoscopy* 2002; 34: 430.
- 60 Jacobson BC, Briggs DR, Carr-Locke DL. Endoscopic closure of a colovesical fistula. *Gastrointest Endosc* 2001; 54: 248–50.
- 61 Lee SO, Jeong YJ. Colonoscopic clipping of fecal fistula that occurred as a postoperative complication in patients with perforated appendicitis: Two case reports. *Gastrointest Endosc* 2001; 54: 245–7.
- 62 Ginsberg GG, Lipman TO, Fleischer DE. Endoscopic clip-assisted placement of enteral feeding tubes. *Gastrointest Endosc* 1994; 40: 220–2.
- 63 Frizzell E, Darwin P. Endoscopic placement of jejunal feeding tubes by using the Resolution Clip: Report of 2 cases. *Gastrointest Endosc* 2006; 64: 454–6.
- 64 Eriksson LG, Sundborn M, Gustavson S, Nyman R. Endoscopic marking with a metallic clip facilitates transcatheter arterial embolization in upper peptic ulcer bleeding. *J Vasc Interv Radiol* 2006; 17: 959–64.
- 65 Raju GS, Gajula R. Technological review. Endoclips for GI endoscopy. *Gastrointest Endosc* 2004; 59: 267–79.

- 66 Sriram PVJ, Das G, Rao GV, Reddy DN. A novel use of endoscopic clipping: to anchor an esophageal endoprosthesis. *Endoscopy*, 2001; 33: 724–6.
- 67 Scotiniotis I, Ginsberg GG. Endoscopic clip-assisted biliary cannulation. externalization and fixation of the major papilla from within a duodenal diverticulum using the endoscopic clip fixing device. *Gastrointest Endosc* 1999; 50: 431–3.
- 68 Jensen DM, Machicado GA, Hirabayashi K. Randomized controlled study of 3 different types of hemoclips for hemostasis of bleeding canine acute gastric ulcers. *Gastrointest Endosc* 2006; 64: 768–73.
- 69 Lin HJ, Lo WC, Cheng YC, Perng CL. Endoscopic hemoclip versus TriClip placement in patients with high-risk peptic ulcer bleeding. *Am J Gastroenterol* 2007; 102: 539–43.
- 70 Tominaga K, Yoshinori S, Fujinuma S, Tanaka H, Saida Y, Sakai Y. Colonic perforation after endoclip placement for delayed post-endoscopic-resection bleeding. *Gastrointest Endosc* 2006; 64 (5): 839–40.
- 71 Ko KH, Lee SY, Hong SP, Hwang SK, Park PW. Duodenal perforation after endoscopic hemoclip application for bleeding from Dieulafoy's lesion in a duodenal diverticulum. *Gastrointest Endosc* 2005; 62: 781–2.
- 72 Peng YC, Chen SY, Tung CF, Chou WK, Hu WH, Yang DY. Factors associated with failure of initial endoscopic hemoclip hemostasis for upper gastrointestinal bleeding. *J Clin Gastroenterol* 2006; 40: 25–8.