

# Endoscopic treatment of non-variceal gastrointestinal bleeding: hemoclips and other hemostatic techniques

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Although the number of hospitalizations for non-variceal gastrointestinal bleeding has decreased in recent years, acute upper gastrointestinal hemorrhage continues to be a common reason for hospital admission, and peptic ulcers account for at least fifty percent of all cases. Despite the fact that bleeding from ulcer scases spontaneously in approximately 80% of patients, it is still a diagnosis associated with substantial medical costs and significant morbidity and mortality, the latter ranging between 8 and 14%<sup>[1]</sup>, especially in the elderly.

The most common risk factors associated with upper gastrointestinal bleeding are *Helicobacter pylori* infection and the use of nonsteroidal anti-inflammatory drugs and alcohol. The eradication of *H. pylori* decreases the rate of rebleeding in peptic ulcer disease with absolute reductions that range from 2.5% to 33% according to different studies<sup>[2]</sup>. The eradication of *H. pylori*, the increased awareness of potential dangers of nonsteroidal anti-inflammatory drugs and the widespread use of H2 receptor blockers and proton pump inhibitors in recent years account for the reduction in the number of patients hospitalized for upper gastrointestinal bleeding from ulcers<sup>[3]</sup>.

Nonetheless, no proven effective medical therapy exists for treatment of active peptic ulcer bleeding. In randomized trials, patients have demonstrated better outcomes from endoscopic therapies than from medical therapies. Emergency endoscopy should be performed as soon as safely possible after resuscitation to detect the bleeding lesion, to define stigmata of recent hemorrhage and

to perform endoscopic therapy when required. The value of endoscopic hemostatic therapy in patients with active arterial bleeding and non bleeding visible vessel has been firmly established with 75% decrease in rebleeding and operation rates and a 40% reduction in mortality<sup>[4]</sup>. It has been shown that shock on presentation, bright red blood in the nasogastric aspirate or in the stomach that fails to clear with lavage, the number and severity of concomitant illnesses, and the age of the patient as well as the presence of rebleeding after successful endoscopic therapy all can predict rebleeding and mortality.

Lau *et al* showed that the stigmata of hemorrhage in bleeding peptic ulcers are prognostic, and that they allow the risk of rebleeding to be quantified<sup>[5]</sup>. As a basis for the diagnosis of endoscopic appearance of lesions, the Forrest's classification is commonly used:

FIA: active bleeding (spurting)

FIB: active bleeding (oozing)

FIIA: non-bleeding visible vessel

FIIB: adherent clot

FIIC: presence of many brown or red, flat pigmentations or only one large dark area on the ulcer surface (black base)

FIIL: white flat base without any signs of recent bleeding.

Unfortunately, the disagreement on the classification of ulcer features may happen in more than 25% of cases, as shown by Laine *et al*<sup>[6]</sup>. Mondardini *et al* showed that good agreement was obtained on bleeding ulcers, both spurting and oozing<sup>[7]</sup>. In Lau *et al* study, good agreement among international experts was obtained only on active spurters, but agreement was poor for visible vessels<sup>[8]</sup>.

Endoscopy is advocated for the treatment of active bleeding ( spurting and oozing ) and nonbleeding visible vessels and, in some cases, non bleeding adherent clots. Endoscopic treatment controls bleeding in up to 90% and reduces significantly the rates of further bleeding, the need for blood transfusions, hospital costs and emergency surgery. A second endoscopic treatment can be attempted in patients with further hemorrhage after the initial endoscopic therapy, and permanent hemostasis can be achieved in half of these cases.

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A variety of endoscopic treatment methods for bleeding peptic ulcers have been tested in trials. These methods include thermal application (laser, heater probe and bicap), local injection (hypertonic saline, epinephrine or various sclerosing agents such as absolute alcohol and polidocanol) and mechanical hemostasis. Each method has both merits and problems related to the hemostatic mechanism and technical procedure itself, and which one of these methods is superior remains controversial, since comparative studies have in general failed to show any superiority of one technique over another.

Although laser photocoagulation was one of the earliest forms of effective endoscopic hemostasis, currently it is being used mainly for treatment of vascular lesions or tumors, given its limitations of high cost, lack of portability and technical difficulty<sup>[9]</sup>.

Injection therapy is a low cost effective and safe procedure that is easy to implement in a variety of clinical settings. No one hemostatic agent has been shown to be clearly superior and the main difference between the available agents is probably the safety profile. Complications are less common after epinephrine injection than a sclerosant injection, the latter being associated with transmural tissue necrosis and perforation.

Heater probe and bicap achieve hemostasis through direct coaptive application of the thermal probe to the bleeding site. Thermocoagulation probes can seal arteries as large as 2mm in diameter and contain irrigation devices, which are helpful during hemostasis. Limitations include the requirement of a therapeutic endoscope, probe sticking and precipitation of treatment induced bleeding from a nonbleeding visible vessel. Repeat therapy increases the risk of perforation<sup>[9]</sup>.

Argon plasma coagulation (APC) results in evenly applied uniform surface coagulation and the noncontact mode is an advantage since there is no adhesion to the tissue. The probe can be used tangentially on lesions and the depth of tissue injury is quite superficial, minimizing the risk of perforation. Cipolletta *et al* demonstrated faster hemostasis with APC when compared to heater probe<sup>[10]</sup>, but at this time there is not enough literature to justify its routine use.

Recent studies have reported that the use of a combination of epinephrine injections and thermocoagulation for initial endoscopic control of bleeding ulcers yields significantly better results than the use of either treatment alone<sup>[11-14]</sup>.

The use of metallic endoscopic clips for hemostasis was developed in the mid 1970s. Until recently, however, due to cumbersome application of the technique, there has been limited use in the hemoclip. Improvements in design of the device

have led to increased ease of use. The bleeding vessel is ligated, achieving immediate hemostatic effect, which is definitive if the vessel is properly ligated. When compared to thermal methods and injection of sclerosing agents, both of which may cause excessive tissue injury leading to necrosis and perforation, injury to the surrounding tissue is minimized with hemoclips. Hachisu reported permanent hemostasis of upper gastrointestinal bleeding in 84.3% of 51 patient treated with hemoclips<sup>[15]</sup>. A prospective study from Binmoeller *et al* confirmed the efficacy and safety of hemoclips (clip application device HX- 3L Olympus Corp.) to a wide range of bleeding sources. Initial hemostasis was achieved in all 88 patients, and rebleeding rate was 5%<sup>[16]</sup>. Lee *et al* applied the hemoclip in 139 patients with a variety of bleeding sources. Recurrent bleeding was seen in 24% of patients presenting with active spurting, 4% of those with oozing and 6% of those with nonbleeding visible vessels. Permanent hemostasis was obtained in over 85% of patients with no major complications<sup>[17]</sup>. Ohta *et al* achieved hemostasis in all 10 critically ill patients with severe gastrointestinal bleeding from spurting and oozing gastric ulcers<sup>[18]</sup>.

In this present uncontrolled prospective study, Lai *et al* used a new rotatable clip device (HX-5LR-1, Olympus) for the application of hemoclip (MD 850, Olympus) to 40 patients with active bleeding (spurting or oozing) from peptic ulcers. The overall hemostatic rate was 93%, hemostasis failed in two patients due mainly to the location of the bleeding source, which made clipping difficult to perform. Rebleeding after hemoclip treatment occurred in three cases secondary to dislodging of clips associated with difficult to approach location when applying the clips in two patients and use of anticoagulants in the other. Hemoclip treatment reduced the rates of rebleeding to 15% in the spurting group and 4% in the oozing group. The study did not include non bleeding visible vessels and did not compare the efficacy of this new improved hemoclip device to other forms of endoscopic therapy.

Villanueva *et al* compared injection with epinephrine alone versus injection combined with hemoclip in a randomized study with 78 patients with peptic ulcer bleeding. Rebleeding occurred in only 5% of patients with hemoclip and injection compared with 19% in the group with injection therapy alone<sup>[19]</sup>.

Takahashi *et al* have reported that hemoclip is as effective as the pure ethanol injection or heater probe methods in controlling the bleeding from primary gastric lesions<sup>[20]</sup>.

Nagayama *et al* recently compared the efficacy of endoscopic clipping with topical ethanol injection

in a retrospective study. Endoscopic clipping was performed using the clipping devices Olympus HX-3L or HX-5LR and clips Olympus MD-750. Endoscopic clipping improved therapeutic outcome as determined by rebleeding rates, need for blood transfusion and duration of hospital stay<sup>[21]</sup>.

These studies demonstrate the efficacy and safety of hemoclips. The advantage of clips is that they do not result in chemical or electrical damage to the surrounding tissue, do not appear to impair healing of ulcers, the hemostatic rate is good and similar to other methods and recurrent bleeding and complication rates are low. There are virtually no limitations to the number of clips to be applied, and therefore, the technique can be used repeatedly.

Because hemoclippping is a local form of mechanical hemostasis, it cannot be performed without identification of the bleeding point. Loading of the clip onto the application device is cumbersome and time consuming. It is usually technically more difficult to clip a vessel when the angle of approach is tangential (upper two thirds of the posterior wall or the lesser curvature of the gastric body and the posterior wall of the duodenal bulb). This technical difficulty persisted even in the rotatable clip device used by Lai *et al.*

Besides hemostasis of peptic ulcers, clips can also be applied to Dieulafoy's lesions<sup>[22]</sup>, colonoscopic diverticular bleeding<sup>[23]</sup>, Mallory-Weiss tears, postpolypectomy bleeding, post sphincterotomy bleed<sup>[16]</sup> and gastric cancers. Radiopaque clipping serves as a good landmark for radiologists to identify the bleeding point during angiography when clipping fails in hemostasis. The clips can also serve as markers for proper esophageal stent placement.

In summary, endoscopic hemoclip treatment provides an effective and safe modality for hemostasis in gastrointestinal bleeding. Controlled prospective studies comparing hemoclip with other endoscopic methods are still required before this modality becomes widely used.

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