# Endoscopic Treatment of Ulcer Bleeding

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**Current Treatment Options in Gastroenterology** 2007, **10:**143–148
Current Medicine Group LLC ISSN 1092-8472


## Opinion statement

Upper gastrointestinal (UGI) bleeding secondary to ulcer disease occurs commonly and results in significant patient morbidity and medical expense. After initial resuscitation, carefully performed endoscopy provides an accurate diagnosis of the source of the UGI hemorrhage and can reliably identify those high-risk subgroups that may benefit most from endoscopic hemostasis. Large-channel therapeutic endoscopes are recommended. Endoscopists should be very experienced in management of patients with UGI hemorrhage, including the use of various hemostatic devices. For patients with major stigmata of ulcer hemorrhage—active arterial bleeding, nonbleeding visible vessel, and adherent clot—combination therapy with epinephrine injection and either thermal coaptive coagulation (with multipolar or heater probe) or endoclips is recommended. High-dose intravenous proton-pump inhibitors are recommended as concomitant therapy with endoscopic hemostasis of major stigmata. Patients with minor stigmata or clean-based ulcers will not benefit from endoscopic therapy and should be triaged to less intensive care and be considered for early discharge. Effective endoscopic hemostasis of ulcer bleeding can significantly improve outcomes by reducing rebleeding, transfusion requirement, and need for surgery, as well as reduce cost of medical care.

## Introduction

Upper gastrointestinal (UGI) bleeding secondary to ulcers occurs frequently and is a common cause of hospitalization or inpatient bleeding. Such bleeding results in substantial patient mortality and medical care expense. Ulcer disease is the most common cause of UGI hemorrhage, and UGI bleeding is the most common complication of peptic ulcer disease [1].

After initial resuscitation of patients with severe UGI hemorrhage and initiation of medical therapy, urgent endoscopy is the preferred procedure for diagnosis and treatment because of its high accuracy and low complication rate. Endoscopy is diagnostic in approximately 95% of patients with severe UGI bleeding. Endoscopy also may reveal stigmata of recent hemorrhage on ulcers that have important prognostic value, helping to triage patients into low and high risk. Whereas some stigmata are associated with increased rebleeding, patients without stigmata of hemorrhage rarely rebleed. By consensus, stigmata are divided into either 1) active bleeding (arterial spurting or oozing) or 2) recent hemorrhage (nonbleeding visible vessel [NBVV]; overlying clot without oozing; or flat, dark slough or spots) [1,2]. From analysis of the Center for Ulcer Research and Education (CURE) randomized controlled trials, medically treated patients have different rebleeding rates according to their stigmata of ulcer hemorrhage. Without endoscopic therapy, the rebleeding rate of ulcers with active arterial bleeding is 90%, whereas with NBVV, it is 50%, and 33% with nonbleeding adherent clots [1,2]. Ulcers with oozing, flat spots, or clean bases have much lower rebleeding rates (10%, 7%, and 3%, respectively). Based on the high rebleeding rates with medical treatment alone, we recommend endoscopic therapy for all patients with active arterial bleeding, NBVV, and adherent clots. Although rebleeding occurs less frequently, persistent oozing also may be treated endoscopically. A large US multicenter

trial illustrates the prevalence of these stigmata. Of 4090 hospitalized patients (duodenal ulcer 2033, gastric ulcer 2057), 10.3% had active bleeding (arterial or oozing), 12.2% had NBVV, 8.3% had adherent clot, 9.9% had flat spot, and 58.4% had clean ulcer base [3].

Newer techniques such as endoscopic Doppler ultrasound may provide more objective findings in ulcer bleeding patients to better predict the likelihood of rebleeding and to determine persistence of blood flow after endoscopic therapy [4]. Endoscopic ultrasound also may be utilized as a guide to the endoscopist for completion of endoscopic hemostasis if treatment is continued until the underlying blood flow disappears. After successful endoscopic hemostasis of ulcer bleeding, proton-pump inhibitors (PPIs) are the medical therapy of choice. For high-risk patients with major stigmata treated with endoscopic hemostasis, most favor a high-dose, intravenous PPI, such as pantoprazole (80 mg bolus + 8 mg/h for 72 hours, or equivalent intravenous dose), based upon randomized controlled trials [5,6]. For the less high-risk patient, particularly non-European or Asian patients, there is a controversy over optimal dose and route of administration [7,8]. PPI treatment may be stopped after 8 weeks unless the patient is *Helicobacter pylori* positive, requires low-dose aspirin maintenance, or uses a nonselective NSAID. *Helicobacter pylori*-positive patients should receive eradication therapy and should be retested to document *H. pylori* eradication. Patients needing long-term aspirin or NSAIDs should receive PPI maintenance therapy to reduce ulcer recurrence [1].

### ENDOSCOPIC THERAPY FOR ULCER HEMOSTASIS

Several different techniques have been developed for endoscopic treatment of ulcer bleeding. An ideal endoscopic hemostasis technique should posses the following features: 1) reproducible effectiveness, 2) easy and rapid application, 3) low complications rate, 4) low cost, 5) portability to the bedside, and 6) widespread availability. Endoscopic techniques have been grouped into three general types of methods and are categorized according to whether or not tissue contact is necessary to achieve hemostasis. A combined therapy group (dilute epinephrine injection + thermal or mechanical treatment) is considered separately.

The major thermal endoscopic therapies include multipolar probes (MPECs), heater probe, and argon plasma coagulator (APC). The contact probes (heater probes and MPECs) can be applied en face or tangentially in peptic ulcers with major stigmata of hemorrhage. Target irrigation, suctioning using therapeutic endoscopes, and tamponade of the bleeding point allow the localization of the ulcer stigma and permit endoscopic treatment. Large-diameter probes (3.2 mm) and slow coagulation provide the most effective hemostasis and prevention of rebleeding by coaptive coagulation of the underlying artery in the ulcer base [1,2]. APC coagulates poorly through blood and provides only superficial coagulation (≤ 1 mm unless it touches the mucosa and becomes a monopolar coagulator) and thus is ineffective for the treatment of larger underlying vessels [2].

Injection techniques use epinephrine (usually 1:10,000 or 1:20,000), sclerosants, or clotting factors (non-United States) and are probably the most frequently used techniques either alone or in combination with thermal or mechanical modalities for emergency hemostasis. Hemoclips may provide hemostasis by grasping underlying vessels and/or closing acute lesions.

### RETREATMENT

Rebleeding after endoscopic therapy of UGI ulcers occurs in 10% to 25% of patients and represents a challenging problem [9]. One large randomized trial showed a significant reduction in complication rates in patients retreated endoscopically with epinephrine injection and heater probe compared with emergency surgery. These results, together with our own experience, suggest that repeat endoscopic therapy is warranted for rebleeding after initial hemostasis for ulcer hemorrhage. We recommend endoscopic combination treatments for retreatment of ulcer bleeding.

### ENDOSCOPIC HEMOSTASIS COMPLICATIONS

Potential complications include perforation or precipitation of bleeding from NBVV. In a meta-analysis of injection or thermal probe coagulation, hemorrhage was induced in 0.4% of patients, and perforation in 0.7%. Perforations are more common after endoscopic retreatments [1].

# Treatment

## Endoscopic therapy

### Overview of emergency endoscopy

- Prior to endoscopy for ulcer bleeding, all resuscitative measures should be started, and the patient should be hemodynamically stable.
- There should be adequate intravenous access, careful monitoring of the patient, and correction of severe coagulopathies. Endotracheal intubation should be strongly considered to prevent aspiration in patients with ongoing hematemesis, altered mental status or respiratory status, or severe

neuromuscular disorders. Large single- or double-channel therapeutic endoscopes and hemostasis devices should be available at the bedside.

### *Injection treatment*

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|---|---|
| | Injection therapy for ulcer bleeding has been advocated because it is easy to use, inexpensive, and widely available, and many endoscopists have had prior experience sclerosing esophageal varices [1,2]. |
| **Mechanism of action** | Epinephrine at a concentration of 1:10,000 to 1:20,000 in saline provides local tamponade and vasoconstriction and improves platelet aggregation. Saline injection causes local vessel compression or tamponade. Sclerosants such as alcohol, ethanolamine, and polidocanol cause tissue necrosis. Alcohol may predispose to ulceration and possible perforation. |
| **Technique** | Injection through a sclerotherapy catheter with a 25-gauge retractable needle in four quadrants around actively bleeding point or nonbleeding vessel. Dilute epinephrine/saline solution (1:10,000 to 1:20,000) is injected in 0.5- to 1.5-mL increments up to a total of 25 to 30 mL. Alcohol is injected in 0.1- to 0.2-mL increments up to a maximum of 1 mL. Caution is recommended to avoid tissue damage, necrosis, and perforation with alcohol. |
| **Effective for** | Active ulcer bleeding (arterial or oozing) and prevention of NBVV rebleeding. Addition of a second endoscopic treatment after epinephrine injection significantly reduces rate of recurrent bleeding, surgery, and mortality [10•]. |
| **Special points** | Volume of alcohol injection should be limited to less than 1 mL. This treatment should not be repeated if rebleeding occurs [1]. Alcohol injection should not be combined with thermal modalities. |

### *Electrocoagulation*

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|---|---|
| | Electrical current generates heat that can coagulate tissue, including arteries. |
| **Mechanism of action** | In bipolar or multipolar electrocoagulation (MPEC), the current flows between two or more electrodes separated by 1 to 2 mm at the probe tip. Current flow is concentrated closer to the tip than with a monopolar probe, providing less depth of tissue injury and lesser potential for perforation [11]. |
| **Technique** | Large-diameter probe (3.2-mm diameter) should be applied directly on the ulcer stigmata or bleeding site to compress the underlying vessel with moderate appositional (tamponade) pressure before coagulation. The pressure on the stigmata temporarily interrupts blood flow through the underlying vessel, reduces the heat sink effect, and, with application of heat, can coaptively seal arteries up to 2 mm in diameter. Low-energy (12 to 16 W on a BICAP II generator [ACMI Corp., Southborough, MA]), long-duration (10 seconds) electrocoagulation can weld the walls of arteries up to 2 mm in diameter (Table 1). |
| **Effective for** | Actively bleeding ulcer, NBVV, or adherent clot. |
| **Special points** | Coaptive coagulation with low-power settings and long duration provides deeper coagulation that is especially useful for therapy of large, chronic ulcers or large arteries [11]. |

### *Heater probe*

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|---|---|
| **Mechanism of action** | Probe effectively transfers heat from its end or sides to tissues, allowing heat transfer whether applied perpendicularly or tangentially. Teflon (DuPont, Wilmington, DE) coating of heater probes lessens sticking. |
| **Technique** | Large (3.2-mm) heater probes and firm tamponade should be used directly on the bleeding point or visible vessel and coagulated with energy setting of 25 to 30 J, using four to five pulses (total of 125 to 150 J) per tamponade station (before changing the probe position) [11] (Table 1). |
| **Effective for** | Actively bleeding ulcer, NBVV, and adherent clot. |

**Table 1. Comparison of thermal coagulation and hemoclipping for nonvariceal UGI hemorrhage**

| | Thermal coagulation | Hemoclipping |
|---|---|---|
| Ease of emergency use | Easy | Relatively easy |
| Tangential treatment | Easy | More difficult |
| Irrigation with device | Yes | No |
| Different sizes of probes or clips | Yes | Yes |
| Different brands of devices | Yes | Yes |
| Increase tissue injury (lesion size/depth) | Yes | No |
| Time to lesion healing | Longer | Shorter |

UGI—upper gastrointestinal

## *Endoclips*

Several devices, including metallic clips, endoloops, and rubber band ligation, have been described for the mechanical endoscopic treatment of bleeding ulcers. Endoclips have been the most extensively studied [12–14].

**Mechanism of action** Clipping devices are designed to grasp into the submucosa, seal bleeding vessels, or approximate the sides of lesions during endoscopy. The clips produce hemostasis similar to surgical ligation. They do not interfere with ulcer healing [12–14].

**Technique** Precise deployment is critical. En face approach allows for optimal capture of the target site and surrounding tissue. A single clip may be sufficient to grasp NBVV; however, we suggest placing two additional clips to ligate proximally and distally from the bleeding point (Table 1).

**Effective for** Active arterial bleeding, NBVV, and adherent clot [15]. Failure of hemostasis associated with duodenal bulbar and gastric fundic lesions [16].

**Special points** Size of the vessel (< 2 mm in diameter), difficulty in accessing ulcers (proximal lesser curve and posterior duodenal bulb), fibrotic lesions, and single-clip deployment (although multiple clips often are needed) are potential limitations [12–14]. However, not all clips are alike. They differ in size, shape, deployment characteristics, ability to grasp and release bleeding point and to rotate, and in long-term clip retention [17•], as well as in clinical efficacy [18]. All hemoclips appear to be safe and do not cause significant tissue inflammation or injury.

## *Combination therapy*

Combination treatment with epinephrine injection and thermal therapy (MPEC or heater probe) or endoclips has theoretical advantages, as each technique has different mechanism of action for hemostasis.

**Mechanism of action** Combination therapy combines the mechanisms of action of each hemostasis technique. Both epinephrine injection and thermal devices activate platelet coagulation and produce tamponade of the vessel. Epinephrine also produces vessel constriction, and thermal probes cause coaptive coagulation. Endoclips cause vessel ligation and can be used to close lesions [1].

**Technique** Epinephrine injection into four quadrants around stigmata in the ulcer base, followed by thermal coagulation with heater probe or MPEC or deployment of endoclips.

**Effective for** Standard treatment for actively bleeding ulcers and nonbleeding adherent clots.

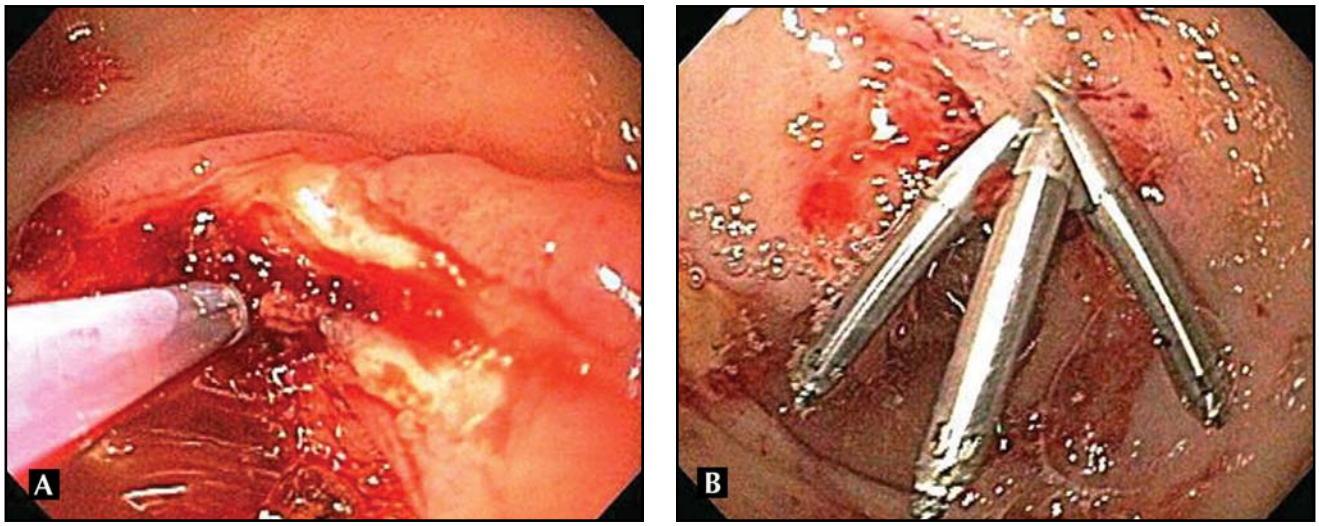


**Figure 1.** Hemostasis of an actively bleeding gastric ulcer with endoscopic combination therapy including epinephrine injection (**A**) and hemoclipping (**B**). Cessation of bleeding occurred after endoscopic treatment.

## Recommendations for endoscopic therapy based on stigmata of ulcer hemorrhage

### Active arterial bleeding

- Combination therapy with epinephrine injection (1:10,000 or 1:20,000) and thermal coagulation (either with MPEC or heater probe) is recommended. Coaptive coagulation is the goal. Successful endoscopic hemostasis occurs in nearly 100% of lesions. Rebleeding occurs in less than 10% to 20%, compared with continued bleeding or rebleeding of 85% to 95% on medical therapy [1,11]. Combination therapy with epinephrine and hemoclipping is a newer alternative [10•,19,20••] (Figs. 1A and 1B).

### Ulcer oozing without other stigmata of hemorrhage

- If oozing from an ulcer base persists despite irrigation and observation, any monotherapy (thermal probes, injection, or mechanical method) is effective. Rebleeding rates are less than 5%, compared with rebleeding rates varying from 10% to 27% on medical therapy alone [1,2].

### NBVV

- Monotherapy with thermal coagulation (heater probe or MPEC) is effective. With large-diameter probes (3.2 mm in diameter), firm tamponade, slow coagulation with low-power setting to flatten the visible vessel is recommended, as rebleeding rates are less than 5% to 10%, compared with 50% rebleeding rate with medical therapy alone [11].

### Nonbleeding adherent clot

- Combination therapy including the following is recommended:
  - Four-quadrant epinephrine injection around the base of the clot.
  - A rotatable polypectomy snare is used to shave down the clot using a cold-guillotine technique.
  - The residual clot or NBVV is treated with thermal coaptive coagulation or hemoclipping.

- The rebleeding rate after combination therapy in a CURE trial was less than 5%, compared with 35% rebleeding rate with medical therapy alone [21]. A recent meta-analysis confirmed the benefit of endoscopic combination therapy for adherent clot overlying an ulcer [22••].

### Flat spots or clean-based ulcers

- No benefit from endoscopic hemostasis is seen because outcomes do not improve, as patients with these endoscopic findings have a very low rebleeding rate—7% and 3%, respectively—on medical therapy alone.

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