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HIGH RISK BLEEDING, PART II

THERAPEUTIC ENDOSCOPY FOR NONVARICEAL GASTROINTESTINAL BLEEDING

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During the past 20 years, endoscopy has developed as the modality of choice for determining diagnosis, prognosis, and therapy for severe gastrointestinal bleeding. When endoscopy was first introduced to evaluate gastrointestinal bleeding in the late 1970s, early diagnostic endoscopy did not affect patient outcome. [46] Subsequently, improvements in endoscopes and endoscopic accessories allowed development of therapeutic techniques. Experienced endoscopists now can diagnose a source of upper gastrointestinal bleeding in greater than 90% of cases, which facilitates simultaneous treatment via endoscopy. [14] There are now standardized techniques for endoscopy, consensus for high-risk stigmata of hemorrhage, and effective endoscopic hemostasis treatments. This article reviews the indications, technique, and efficacy of therapeutic endoscopy.

EVALUATION AND MANAGEMENT BEFORE ENDOSCOPY

Patients with acute bleeding should be asked about prior gastrointestinal bleeds, history of ulcers or liver disease, recent gastrointestinal symptoms, nonsteroidal anti-inflammatory drugs (NSAIDs) or alcohol use, and weight loss. All patients should be questioned carefully about over-the-counter medications, particularly about aspirin, NSAIDs, histamine-2 (H₂)-receptor antagonists, and antacids. The physical examination should include evaluation for orthostatic hypotension, stigmata of liver disease, rectal examination to assess for melena or red blood, and nasogastric lavage to assess for blood in the stomach. Blood samples should be sent to determine hematocrit, platelets, and prothrombin time (PT) as well as for type and crossmatch for possible transfusion. Patients older than age 60 or with risk factors for coronary

artery disease should also have an electrocardiogram to determine whether any cardiac ischemic changes are present.

The initial evaluation focuses on determining whether the bleeding is from an upper or lower gastrointestinal source. Hematemesis or nasogastric lavage showing blood or *coffee grounds* indicates an upper gastrointestinal bleeding source. Melena usually indicates an upper gastrointestinal source but can occasionally come from a small intestinal or right colonic bleed. A clear nasogastric lavage does not always imply a lower gastrointestinal source because 16% of patients with duodenal ulcer bleeds have negative nasogastric lavage. [14] If bile is present in a nonbloody nasogastric lavage, an upper gastrointestinal bleed is unlikely. Bright red blood per rectum nearly always indicates a lower gastrointestinal source, unless it is accompanied by hypotension from a severe upper gastrointestinal or small bowel bleed with rapid transit of blood. [62] Guaiac card testing of nasogastric aspirates is unnecessary because of poor accuracy, and other clinical indicators of the bleeding site are more accurate. [38]

Endoscopy should be performed when it can be done safely and when the information may influence patient care. General recommendations for care of severe nonvariceal upper gastrointestinal bleeders before endoscopy include the following:

1. Protect the airway. Intubate for active bleeding or altered mental status.
2. Perform medical resuscitation with fluids and blood products (goals: heart rate <100 beats/min; systolic blood pressure >100 mmHg).
3. Correct coagulopathies (goals: PT, <15 seconds; platelets, > 50,000/mm³).
4. Lavage with large-bore orogastric tube if red blood or blood clots obscure much of stomach.
5. Use therapeutic double-channel videoendoscope.
6. Have thermal probes, sclerotherapy needle, epinephrine, snare, and other accessories for therapeutic endoscopy ready before endoscopy.
7. Have nurse assistant trained in therapeutic endoscopy available at therapeutic endoscopy.

Patients should be medically resuscitated before endoscopy. Ideally the patient should be hemodynamically stable, with a heart rate of less than 100 beats/min and systolic blood pressure greater than 100 mmHg. Most patients require medical resuscitation with intravenous saline, and many patients require transfusion of packed erythrocytes. In the actively bleeding patient, severe thrombocytopenia (platelet count < 50,000/mm³) should be corrected with platelet transfusions before emergency endoscopy, and a markedly prolonged PT should be corrected with fresh frozen plasma. Patients with active hematemesis should have their airway protected with an overtube or undergo endotracheal intubation before endoscopy to prevent aspiration of blood. Patients who have an altered mental status or who are difficult to sedate may sometimes require intubation. Resuscitation code status (e.g., do not resuscitate [DNR]) should be clarified before endoscopy, especially in patients with terminal and severe medical problems.

Patients with active upper gastrointestinal hemorrhage should undergo emergency endoscopy after medical resuscitation. In patients with massive bleeding and shock, endoscopy is best performed in the operating room. Patients with acute self-limited blood loss with no evidence of ongoing bleeding can undergo endoscopy within 24 hours except for patients with cirrhosis, possible aortoenteric fistula, or evidence of rebleeding. Middle-of-the-night endoscopy should be avoided if well-trained endoscopy nurses, appropriate endoscopy equipment, and surgical backup are unavailable.

In severe upper gastrointestinal bleeding, nasogastric lavage with a large (34F) orogastric tube is performed to evacuate blood from the stomach to prevent aspiration and to clear the stomach of blood and clots before endoscopy. Iced-saline lavage does not prevent or decrease upper gastrointestinal bleeding. [2] Gastric lavage with lukewarm tap water is as safe as lavage with saline and considerably cheaper. [49]

Large therapeutic endoscopes are recommended in patients with severe upper gastrointestinal bleeding. A double-channel therapeutic videoendoscope, with 3.8 and 2.8 mm diameter suction channels, is most desirable because this instrument permits large therapeutic probes and simultaneous suctioning. A prototype endoscope with a 6-mm-wide working channel has been reported to be effective in removing large blood clots in patients with severe upper gastrointestinal bleeding. [18] [29]

The capability of forceful water irrigation should also be available via a separate (third) irrigation channel or a suction channel with a water pump or a large syringe. Rarely a therapeutic side-viewing duodenoscope is helpful to visualize bleeding duodenal lesions not well visualized with a forward-viewing endoscope. Useful endoscopic accessories depend on the endoscopist's experience but at a minimum should include some type of coagulation probe, a sclerotherapy needle or band ligation kit, epinephrine, and a sclerosant. Additional accessories include a biopsy forceps and snare.

Well-trained, experienced endoscopic assistants are critical because emergency endoscopies for severe upper gastrointestinal hemorrhage can be the most challenging cases of endoscopy. Most emergency endoscopies performed in an intensive care unit require two nurses or assistants. One nurse is responsible for administering drugs for

conscious sedation and monitoring the patient. The other nurse functions as the gastrointestinal assistant and needs to be well trained in setting up and using various endoscopic accessories, which may be required for hemostasis. Most patients receive conscious sedation with midazolam and meperidine, although patients who have been intubated for airway control and are receiving mechanically assisted ventilation may receive propofol.

During endoscopy, the patient may need to be turned to move blood and clots to a dependent position away from the bleeding site. During endoscopy, the patient should not be in restraints, and the patient's stretcher should be functioning properly. The patient's head may be elevated to help clear the esophagus of blood and to prevent aspiration. Turning the patient from the left lateral decubitus to the back or even the right lateral decubitus position can help visualize the gastric cardia, but care must be taken to avoid aspiration. Preliminary reports have suggested that 3% hydrogen peroxide can help dissolve small clots and cause blood to become translucent, which can improve the ability to visualize and treat underlying lesions. [27]

Patients with severe lower gastrointestinal bleeding should undergo a rapid colonic purge before urgent colonoscopy. [24]

This rapid purge allows colonoscopy to be performed safely and can allow identification of a small bleeding site, such as a diverticulum or angiodysplasia. This purge is generally performed using 4 L of polyethylene sulfate (e.g., GoLYTELY) either orally or via nasogastric tube over a several-hour period (administered as 1 L every 30 to 60 minutes) until the effluent is clear. Metoclopramide may facilitate gastric emptying and reduce nausea. Other purge agents, such as oral phosphosoda solution, may also be used in some cases, such as ambulatory patients who appear to have stopped bleeding and are stable.

Surgical consultation should be performed on admission for patients who appear to be at high risk for continued bleeding or rebleeding, such as those who are in shock, have bright red blood in the nasogastric tube, or require numerous transfusions (≥ 5 units) of packed erythrocytes. A surgeon should also be notified after endoscopy if endoscopic hemostasis was unsuccessful or if a lesion at high risk of rebleeding was diagnosed, such as a Dieulafoy's lesion or a large, pulsating artery in the base of an ulcer.

RISKS OF ENDOSCOPY IN SEVERE GASTROINTESTINAL BLEEDING

In the older literature, complications related to emergency endoscopy were reported in 1% of patients. [28] The commonest complications include gastrointestinal perforation, pulmonary aspiration, induced hemorrhage, medication reactions, hypotension, and hypoxia. [28]

Patients with large amounts of red blood in their stomach should undergo prophylactic airway protection before endoscopy, with a large overtube or endotracheal intubation.

The occasional patient with severe upper gastrointestinal bleeding and recent myocardial infarction may require urgent endoscopy. The risks of cardiopulmonary complications in the setting of an acute myocardial infarction are significantly increased in patients who are medically unstable before endoscopy, as compared with peri-myocardial infarction patients who are relatively stable. [5]

ENDOSCOPIC HEMOSTASIS MODALITIES

Techniques of endoscopic hemostasis are as follows:

Thermal

- Bipolar probe

- Monopolar probe

- Argon plasma coagulation

- Laser

Heater probe

Microwave

Injection

Epinephrine

Alcohol

Ethanolamine

Cyanoacrylate

Polidocanol

Thrombin

Fibrin

Cyanoacrylate glue

Mechanical

Hemoclips

Sewing

Band ligation

Endoloop

Many of these techniques are extensively used in the United States, whereas others are not approved by the U.S. Food and Drug Administration (FDA) and have mainly been used in European and Asian countries.

Thermal Modalities

Thermal coagulation is used to heat and seal the bleeding blood vessel. In coaptive coagulation, a probe (such as the heater or bipolar probe) is used to compress physically and tamponade the vessel, followed by thermal sealing of the vessel. Coaptive thermal endoscopic treatments include bipolar coagulation and heater probe. Noncoaptive thermal techniques include argon and neodymium-yttrium aluminum garnet (Nd:YAG) laser, argon plasma coagulation, and microwave.

Electrocoagulation can be performed with monopolar or bipolar current. Monopolar current passes through the probe and is conducted through the patient's body into a grounding pad. This current produces increased temperature at the point of tissue contact, leading to tissue coagulation. Monopolar coagulation can, however, produce excessive heat, resulting in deep tissue penetration and a risk of perforation.

Bipolar or multipolar probes are the most popular thermal coaptive hemostasis devices. In these devices, the positive and negative electrodes are near each other, resulting in current flow between them over a short distance. The advantage of these probes is a reduced risk of deep thermal injury and perforation as well as the capability to apply mechanical pressure and tangential coagulation. Animal studies have shown that bipolar probes can coagulate arteries 2.5 mm in diameter, which is the upper limit of the diameter of arteries in resected human peptic ulcers. [\[17\]](#) [\[26\]](#) [\[58\]](#) Bipolar probes do not stop bleeding from vessels larger than 2.5 mm in diameter, however. [\[17\]](#)

The heater probe has an inner heating coil with a thermocouple, which maintains a constant temperature at the tip. A preset amount of energy is delivered with each pulse, and no electric current passes through the tissue. Laser therapy, either Nd:YAG or argon, can be used for endoscopic hemostasis but is uncommonly used because of greater expense, difficulty in transporting to the bedside, and an increased risk of perforation. Argon plasma coagulation is a noncontact form of electrocoagulation in which monopolar current is transmitted from a probe by ionized, electrically conductive

argon plasma gas. The gas flows at a constant rate of 0.5 L/min, and power outputs of 40 to 60 watts are used. [\[55\]](#)

Injection Therapy

In injection therapy, a 23- to 25-gauge sclerotherapy needle is used to inject a liquid compound into or around the bleeding lesion. Epinephrine at a concentration of 1:10,000 or 1:20,000 is the most commonly injected compound. Epinephrine injection causes local tamponade, vasoconstriction, and possibly enhanced platelet aggregation. [\[7\]](#) Several studies suggest that the mechanism of action may be tamponade because saline injection may be as effective as epinephrine for endoscopic hemostasis of bleeding ulcers. [\[31\]](#) [\[39\]](#) Potential adverse effects of injecting epinephrine include systemic absorption of epinephrine, which is rarely clinically significant. [\[57\]](#) Epinephrine is generally injected into the submucosa in 1-mL increments in all four quadrants around the bleeding site. This injection often results in blanching of the surrounding mucosa because of epinephrine diffusion and vasoconstriction. Despite clinical use, injection sclerosis with epinephrine followed by ethanolamine was unable to stop bleeding from either 1 or 2 mm diameter mesenteric vessels in an animal study. [\[17\]](#)

Sclerosants, such as polidocanol, ethanolamine, and sodium tetradecyl sulfate, cause tissue necrosis. They have been used for endoscopic hemostasis alone or in combination with epinephrine. Alcohol injection produces dehydration and fixation of tissue, with subsequent necrosis and ulceration. Because of a high risk of ulceration and perforation, only small amounts of alcohol are recommended, with a maximum volume of 2 mL. Injection of fibrinogen and thrombin works by reacting together to form an active fibrin sealant. *N*-butyl-2-cyanoacrylate is a liquid glue that polymerizes on contact with blood. Although studied in variceal bleeding, few studies have analyzed the use of this glue for arterial ulcer bleeding.

Mechanical Methods

Probes can tamponade mechanically and stop active arterial bleeding but must be followed with thermal coagulation to seal the vessel permanently. Devices for potentially permanent mechanical treatment of bleeding include metal clips, rubber band ligation, endoloops, and sewing devices.

Endoscopic metallic clips, which resemble those used in surgery, have been used to ligate bleeding vessels. In a randomized trial that compared endoscopic hemoclips versus hypertonic saline-epinephrine injection versus the combination of both for peptic ulcers with active bleeding or visible vessels, all three methods achieved a greater than 95% rate of initial hemostasis. Hemoclip therapy tended to produce less rebleeding and fewer emergency surgeries, but these differences were not statistically significant. [\[6\]](#)

Hemoclips are limited by technical and practical considerations, including difficulty of device setup, need for a well-trained assistant to manipulate the deployment device, need to reload after each deployment, possibility of the clip tearing the vessel, inability to treat from a tangential approach, and clips that may attach improperly or that immediately fall off a fibrotic ulcer base. An animal study found that hemoclips could not stop bleeding from 1- or 2-mm arteries, apparently because they could not generate sufficient compressive force. [\[17\]](#) The same clips did stop bleeding if they were more tightly squeezed manually. This study suggests that with technical refinement a clipping device could be useful in the future.

Other means of mechanical ligation include rubber band ligation, as performed for hemorrhoid and variceal ligation. Endoloops are detachable nylon snares. Band ligation and endoloops are useful to treat varices but are difficult to apply to a fibrotic ulcer base. An investigational endoscopic sewing device has been developed that has the potential to provide suture ligation of underlying vessels, as is performed surgically. [\[58\]](#)

CAUSES OF SEVERE NONVARICEAL UPPER GASTROINTESTINAL BLEEDING

Table 1

shows the causes of severe upper gastrointestinal bleeding in the Center for Ulcer Research (CURE) hemostasis studies. Peptic ulcers are the commonest cause. The relative frequency of variceal bleeding at an institution varies according to the patient population and the presence of a liver transplant center. The independent clinical and laboratory risk factors associated with poor outcomes from nonvariceal upper gastrointestinal bleeding include the following:

Age greater than 60

Comorbid medical illnesses

Persistent hypotension

Severe coagulopathy

Onset of bleeding in the hospital (secondary bleeding)

Transfusion of 6 units or more of packed erythrocytes for a single bleed

Red blood in stomach

Rebleeding from the same lesion during hospitalization

TABLE 1 -- CAUSES OF SEVERE UPPER GASTROINTESTINAL BLEEDING IN CURE HEMOSTASIS STUDIES ($n = 948$)

Cause	%
Peptic ulcer	55
Gastric or esophageal varices	14
Angioma	6
Mallory-Weiss tear	5
Tumor	4
Erosions	4
Dieulafoy's lesion	1

Data from Savides TJ, Jensen DM, Cohen J, et al: Severe upper gastrointestinal tumor bleeding: Endoscopic findings, treatment, and outcome. *Endoscopy* 28:244-248, 1996.

PEPTIC ULCER BLEEDING

Prognostic Value of Endoscopic Stigmata of Ulcer Hemorrhage

The endoscopic appearance of ulcer bases associated with recent bleeding helps predict the risk of rebleeding and guide endoscopic therapy. Active arterial bleeding is spurting or pulsatile and arises from the ulcer base. A nonbleeding visible vessel is usually only 1 to 2 mm in diameter and appears as a discrete *pigmented protuberance*. What is denoted a *visible vessel*

may represent a small clot covering a side hole in an underlying vessel, a pseudoaneurysm, or an actual vessel. [59] It has been proposed that translucent visible vessels are actually the underlying vessel and have an increased risk of rebleeding. [12] *Adherent clots*

are defined as greater than 5 mm in diameter, red, and amorphous in shape. To be considered an adherent clot, the clot should persist despite several minutes of vigorous irrigation.

Table 2

shows the prevalence of these endoscopic stigmata of ulcer hemorrhage and their relative risks of bleeding. In CURE hemostasis studies of high-risk, elderly patients with ulcer hemorrhage, active arterial bleeding has a 90% rebleeding rate without endoscopic therapy, as compared with 50% for visible vessel, 33% for adherent clot, 10% for oozing without stigmata, 7% for flat spot, and 3% for clean-based ulcer. [30] Laine et al [36] reported lower rebleeding rates with adherent clots in low-risk patients (12%). Chung et al [8] reported higher rates of rebleeding (27%) in patients with oozing in the absence of other stigmata.

TABLE 2

-- ENDOSCOPIC STIGMATA OF ULCER HEMORRHAGE: PREVALENCE, RISKS OF REBLEEDING, AND REDUCED RISK OF REBLEEDING AFTER ENDOSCOPIC HEMOSTASIS

Endoscopic Appearance	Prevalence (%)	Rebleed Rate Without Endo Tx (%)	Rebleed Rate With Endo Tx (%)
Active arterial bleeding	12	90	15-30
Visible vessel	22	50	15-30
Adherent clot	10	12 [*] -33	5
Oozing without stigmata	14	10-27 [†]	N/A
Flat spot	10	7	N/A
Clean ulcer base	32	3	N/A

Data based on UCLA-CURE [19A] studies except as indicated.

End = Endoscopic; Tx = treatment; N/A = not available.

*Laine et al [37] data on clots in low-risk patients.

† Chung et al [8] data from Hong Kong.

Endoscopic stigmata of a high risk of rebleeding, including active bleeding, nonbleeding visible vessels, and adherent clots, are the targets for endoscopic hemostasis to try to reduce the rebleeding rates. Patients with ulcers with a clean base or flat spots do not benefit from endoscopic hemostasis. [34] They may be able to be directly discharged if they are reliable and able to return immediately if medical care is needed. [41]

Endoscopic Hemostasis Techniques for Endoscopic Stigmata

Various techniques have been used for endoscopic hemostasis of peptic ulcers. The best studies are comparative, prospective, and randomized, with well-defined criteria for inclusion and outcomes. Some studies combine high-risk groups, such as active bleeding and nonbleeding visible vessels.

The endoscopic stigmata of active bleeding and nonbleeding visible vessels have the highest rates of rebleeding on solely medical therapies. Randomized controlled trials have found that multipolar probe electrocoagulation, heater probe, and injection therapy are all significantly better than medical therapy alone for treating ulcers with active bleeding or visible vessels, in terms of fewer transfusions, shorter length of hospital stay, and less frequent emergency surgery. [23] [32] [33]

A meta-analysis of 30 randomized studies of endoscopic therapy for acute nonvariceal hemorrhage reported that endoscopic hemostasis with thermal probes, laser, or injection therapy significantly reduced rebleeding and surgery rates. [10]

Subgroup analysis showed that only patients with high-risk endoscopic stigmata for rebleeding (active bleeding and nonbleeding visible vessels) had decreased rates of rebleeding, surgery, and mortality but not patients with lower-risk endoscopic stigmata for rebleeding (flat spots or adherent clots). [10] The results of University of California at Los Angeles (UCLA)/CURE data for reducing rebleed rate for peptic ulcers are shown in [Table 2](#).

Choices of Techniques for Endoscopic Hemostasis of Peptic Ulcers

The endoscopic technique depends on the endoscopic stigmata and the experience of the endoscopist. The authors' experience is mostly with monotherapy (thermal bipolar probe therapy or epinephrine injection) or the combination of these, and this is the focus of review here. These techniques are the most studied in terms of well-designed, prospective, controlled trials and are summarized in [Table 3](#).

TABLE 3 -- UCLA-CURE ENDOSCOPIC TECHNICAL PARAMETERS FOR BIPOLAR COAGULATION*

	Peptic Ulcer			Mallory-Weiss Tear	Dieulafoy's Lesion	Gastric AVM	Colon Diverticula Visible Vessel	Colon AVM
	Active Bleed	Nonbleeding Visible Vessel	Adherent Clot					
Epinephrine injection	Yes †	No	Yes ‡	Maybe	Yes	No	Maybe §	No
Probe size ¶	Large	Large	Large	Large/small	Large	Large	Large/small	Large/small
Pressure ¶¶	Very firm	Very firm	Very firm	Moderate	Firm	Light	Light	Light
Power setting **	15-20 W	15-20 W	15-20 W	15-20 W	15-20 W	10-15 W	10-15 W	10-15 W
Pulse duration	8-10 s	8-10 s	8-10 s	4 s	8-10 s	2 s	2 s	2 s
Endpoint	Bleed stops	Vessel flattens	Flat stigma	Bleed stops	Vessel flattens	Blanches	Vessel flattens	Blanches

AVM = Arteriovenous malformation; W = watts.

*These are general guidelines that have been standardized from laboratory and randomized endoscopic studies. Power, pressure, and duration settings must be reduced for small, acute, or very deep bleeding lesions. Probes should be checked before endoscopic application.

† Epinephrine (1:10,000) injected in four quadrants of 1-mL aliquot each should be used to control bleeding initially, followed by coagulation.

‡ Epinephrine (1:10,000) injected in four quadrants of 1-mL aliquot each should be initially injected around clot, followed by piecemeal snare resection and treatment of underlying stigmata.

§Colonic diverticula with active bleeding can be treated with epinephrine injection in the neck or base. If a visible vessel is seen at the neck, it can be treated with bipolar coagulation.

¶

Large probe is 10F (3.2 mm diameter) and fits through a 3.8-mm endoscope channel. Small probe is 7F (2.4 mm) and fits through a 2.8-mm endoscope channel.

¶¶Pressure is the tamponade pressure exerted en face or tangentially via the contact probe, directly on the lesion.

**Power setting using BICAP II (Circon Acmi, Stamford, CT) generator.

Active Arterial Bleeding

Two well-designed studies have shown that active arterial bleeding is best controlled by a combination of epinephrine injection and thermal coagulation, rather than either modality alone. [9] [23] The authors' technique for active spurting is to inject via a sclerotherapy needle 0.5- to 1.0-mL aliquots of 1:10,000 epinephrine in four quadrants within 1 to 2 mm of the bleeding site. For combination therapy, coagulation is then performed with a large 10F Gold Probe (Microvasive-Boston Scientific, Natuck, MA). After epinephrine injection, the probe is placed directly on the bleeding site to tamponade the bleeding, then slow coagulation is applied with long (10-second) pulses and firm pressure at a low (15 to 20 watt) power setting (Color Fig. 1)

. The probe is then slowly removed from the ulcer (sometimes with gentle irrigation to prevent pulling coagulated tissue), and thermal coagulation is repeated as necessary to stop bleeding and flatten any underlying visible vessel.

Epinephrine injection can also be repeated if rebleeding persists. With successful endoscopic hemostasis, the rebleed rate can be decreased to 15% (combination therapy) to 30% (monotherapy) (see Table 2).

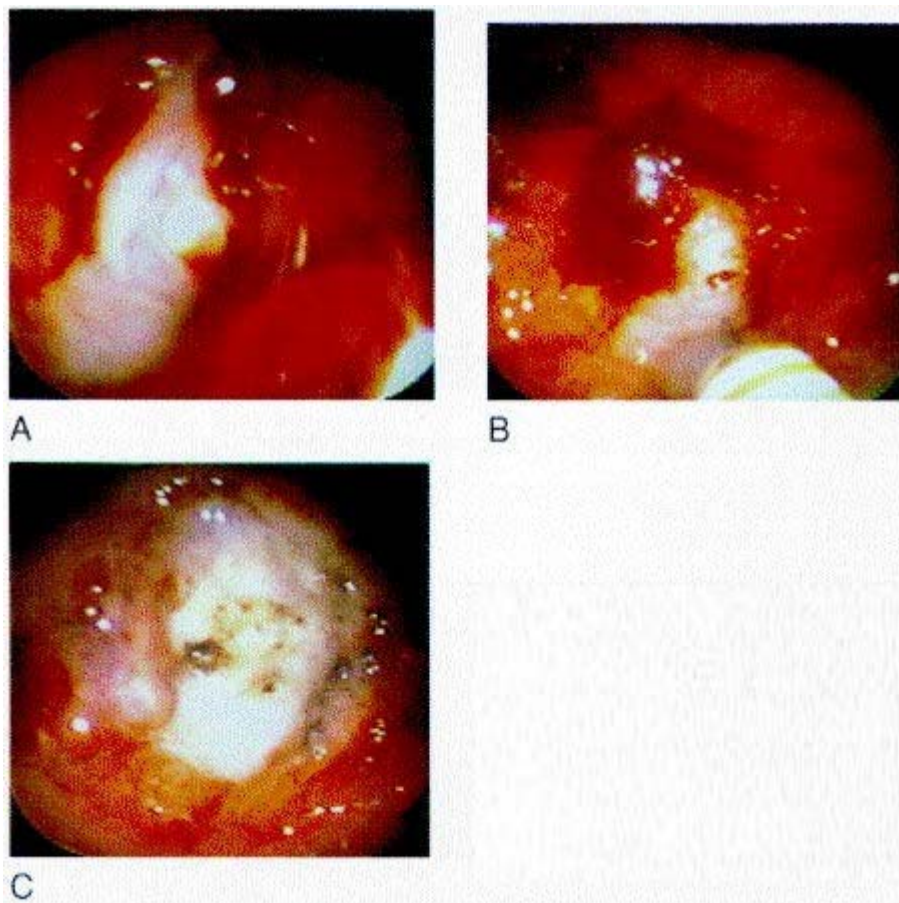


Figure 1. Actively bleeding duodenal ulcer treated with epinephrine injection and Gold Probe. *A*, An actively bleeding duodenal ulcer being irrigated with water. *B*, Ulcer appearance after epinephrine injection. *C*, Ulcer base after epinephrine and Gold Probe coagulation.

Nonbleeding Visible Vessel

In contrast to active arterial bleeding, current studies find no statistically significant difference between thermal therapy alone versus combination (thermal plus epinephrine injection) for nonbleeding visible vessels. [9] [23] The same technique as described for active bleeding is used to flatten visible vessels, using a large probe, firm pressure, and a low power setting (Color Fig. 2). With therapy, the rebleeding rate is reduced to 15% to 30% (see Table 2).

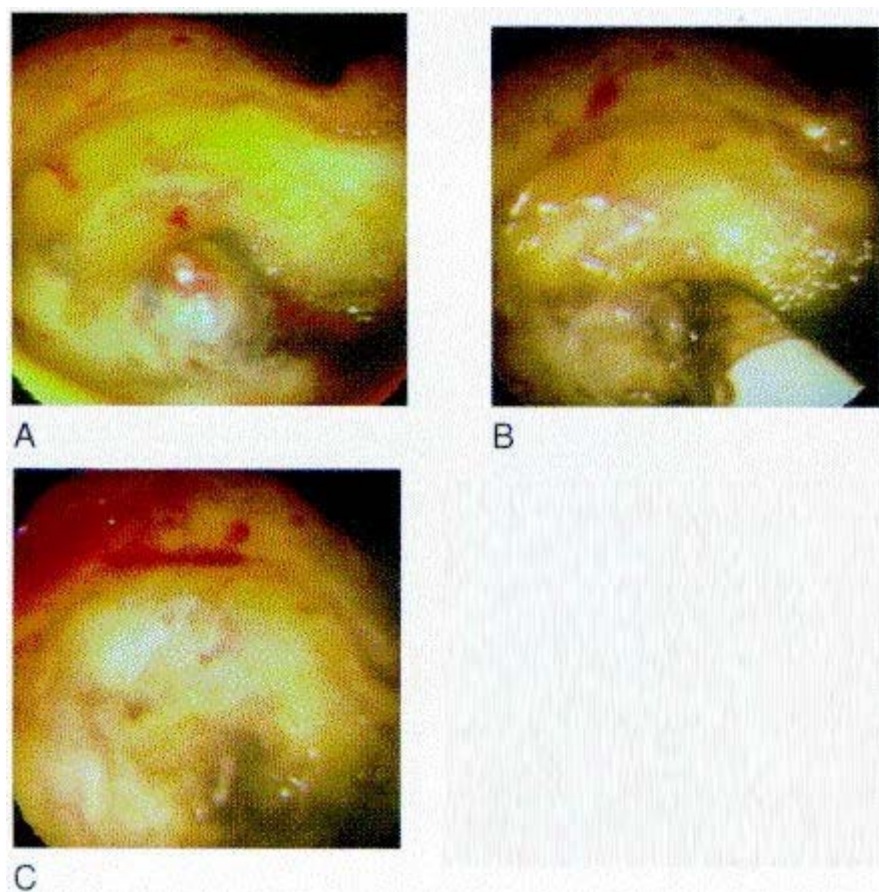


Figure 2. Nonbleeding visible vessel in a gastric ulcer treated with Gold Probe. *A*, The visible vessel before treatment. *B*, Gold Probe coagulation of the visible vessel. *C*, Ulcer after Gold Probe coagulation, with flattening of the visible vessel and cessation of bleeding.

Nonbleeding Adherent Clot

The rebleed rate for nonbleeding adherent clots is 8% to 36% (Color [Fig. 3](#)).^{[35] [36]} Clot removal can theoretically help identify the underlying lesion and apply endoscopic hemostasis if appropriate (i.e., for active bleeding or adherent clot). Clot removal, however, entails the risk of inducing severe bleeding after the body's own coagulation system has been successful.



Figure 3. Adherent clot on a duodenal ulcer.

Several studies, published in abstract form, suggest that combination endoscopic treatment of adherent clots reduces rebleeding risk. A multicenter trial coordinated by the Mayo Clinic reported that adherent clots treated with combination therapy (heater probe and epinephrine injection) had a statistically significant reduction of the rebleeding rate to 5% from the 34% rate in patients treated medically.^[4]

A retrospective study of 192 patients with adherent clots reported that patients who had endoscopic treatment of adherent clots had a rebleed rate of 6% compared with 25% in the group of patients who did not have endoscopic treatment ($P < .001$).^[3] There was no significant difference in 30-day surgery or mortality rates.

Randomized, controlled studies from the UCLA/CURE group showed that treating adherent clots with a combination of epinephrine injection and Gold Probe coagulation was effective, whereas monotherapy (heater probe or injection) was ineffective no better than medical treatment. The authors currently recommend first to treat an adherent clot on an ulcer by injecting epinephrine 1:10,000 in 1-mL increments in four quadrants around the clot. Then a cold snare is used to

piecemeal guillotine the clot, without pulling it off the base, until any underlying bleeding stigmata in the ulcer base are identified. Coagulation is performed if a visible vessel or active bleeding is seen. In the ongoing CURE multicenter study, the rate of rebleeding in patients with adherent clots treated with clot guillotining, as described earlier, is 5%, compared with 29% in the medically treated group. [21]

Ulcer Oozing Without Other Stigmata

Minor bleeding from the edge or base of an ulcer, without other stigmata, which continues despite water irrigation and observation, suggests the need for endoscopic treatment. The rebleeding rate for ulcers with persistent oozing treated medically varies from 10% (CURE) to 27% (Hong Kong). [8] Monotherapy with either probes or injection reduces the rebleed rate to less than 5%.

Clean-Based Ulcers

Patients with clean-based ulcers at endoscopy have a rebleed rate of less than 5%. Laine et al [34] showed that outcome was not affected by immediate feeding of these patients as compared with waiting several days to start eating. Longstreth and Feitelberg [41] have shown that selected compliant and low-risk patients with mild upper gastrointestinal bleeds and clean-based ulcers can be discharged safely to home with a significant cost savings.

Determination of *Helicobacter pylori* Status in Bleeding Ulcer Patients

Biopsy specimens from the antrum and body for *Helicobacter pylori* are recommended for the rapid urease test at the initial endoscopy, after any endoscopic hemostasis. Biopsy specimens are also taken for histopathology for Giemsa staining or *H. pylori* selective examination if the rapid urease test is negative. If the rapid urease test and histopathology are negative, the patient should undergo either a serologic blood test or urea breath test, in case the rapid urease test result was falsely negative.

Second-Look Endoscopy

Some studies have reported that repeat or *second-look* endoscopy 24 hours after the initial endoscopic hemostasis with repeat endoscopic hemostasis with heater probe or fibrin glue for persistent high-risk endoscopic stigmata significantly decreases the rebleeding rate. [50] [51] This repeat endoscopy is expensive, difficult to justify, and impractical, and routine second-look endoscopy is not usually recommended. Patients should undergo repeat endoscopy if there is recurrent, clinically significant gastrointestinal bleeding.

Rebleeding After Endoscopic Hemostasis

The rebleed rate after successful endoscopic hemostasis for active bleeding or nonbleeding visible vessels is 9% to 25%. [37]

With severe rebleeding, the clinician is faced with the options of repeat endoscopic hemostasis or surgical treatment. A large, well-designed, randomized study from Hong Kong found that repeat endoscopic hemostasis for patients with significant rebleeding, after initial endoscopic hemostasis, of bleeding ulcers reduced the rate of surgery and complications. [37]

They reported an initial rebleed rate of 8.7% using endoscopic hemostasis with combination epinephrine injection and heater probe. After endoscopic retreatment, 27% required surgery--23% for treatment failure and 4% for gastrointestinal perforation. Multivariate analysis identified hypotension during rebleeding and ulcer diameter greater than 2 cm as independent risk factors for endoscopic retreatment failure. Patients who rebleed after a second session of endoscopic hemostasis should be treated with either surgery or embolization for hemostasis.

Medical Treatment After Successful Endoscopic Hemostasis for Peptic Ulcers

The authors recommend a high-dose proton-pump inhibitor, such as omeprazole 20 mg orally twice daily or lansoprazole 30 mg orally twice daily for 1 month, followed by one per day for the next month. Patients infected with *H. pylori* should receive triple therapy of some form and subsequently undergo a breath test to confirm *H. pylori*

eradication. A large CURE study is underway to determine if *H. pylori* eradication alone is sufficient to prevent future bleeds, although other short-term studies suggest the rebleed rate within 1 year is low if *H. pylori* is eradicated. High-risk patients may also be treated with a maintenance dose H₂-receptor antagonist, such as ranitidine 300 mg orally once daily or famotidine 40 mg orally once daily, which has been shown to reduce rebleed rates significantly compared with placebo. [\[20\]](#)

Patients with ulcer bleeding as a result of aspirin or NSAIDs should ideally stop these drugs. Patients who still need NSAIDs may benefit from the new selective cyclooxygenase-2-inhibitor drugs, which are reported to cause fewer ulcers. Otherwise, patients who had a severe ulcer bleed and continue NSAIDs or aspirin should receive cotherapy with misoprostol or a proton-pump inhibitor to reduce ulcer recurrence. [\[15\]](#) Gastrointestinal bleeding associated with NSAIDs is considered in detail in another article.

Discharge After Endoscopic Hemostasis

As discussed earlier, reliable patients without high-risk endoscopic stigmata in their ulcer bases can usually be discharged immediately. A study from Hong Kong in which daily endoscopies were performed reported that visible vessels take approximately 4 days to resolve after an initial bleed. [\[60\]](#) The same group found the risk of rebleeding after endoscopic hemostasis decreased to less than 3% after 4 days for nonbleeding visible vessels and after 3 days for active bleeding. [\[19\]](#)

It is recommended that patients who undergo endoscopic hemostasis for major stigmata of ulcer hemorrhage be observed in the hospital for 48 to 72 hours for any signs of rebleeding. Implementation of clinical guidelines that include endoscopy findings, time from bleed, hemodynamic status, and medical comorbidities has resulted in a significant decrease in hospital days for upper gastrointestinal bleeding from 4.6 to 2.9 days and no difference in complication rates or patient satisfaction. [\[16\]](#)

NONVARICEAL, NONULCER CAUSES OF SEVERE UPPER GASTROINTESTINAL BLEEDING

Dieulafoy's Lesions

A Dieulafoy's lesion is a large, submucosal artery that protrudes through the mucosa, is not associated with a peptic ulcer, and can cause massive bleeding. It is usually located in the gastric fundus, within 6 cm of the gastroesophageal junction, although lesions can occur in other parts of the gastrointestinal tract. Endoscopic hemostasis has been described with injection therapy, thermal probes, clipping devices, and band ligation. [\[1\]](#) [\[13\]](#) [\[43\]](#) [\[45\]](#) [\[54\]](#) [\[56\]](#) Several studies suggest low rebleed rates after endoscopic therapy, although a CURE study with single-modality therapy had a 50% rebleed rate. [\[44\]](#)

The authors currently recommend treatment of Dieulafoy's lesion with combination therapy (epinephrine injection and Gold Probe), with the same technique as ulcers with active bleeding or adherent clots. This treatment reduces the rebleeding rate to less than 20%. India ink tattooing around the bleeding site is also recommended so that if the patient requires surgery, the bleeding site can be easily detected intraoperatively from the serosal side.

Mallory-Weiss Tears

Mallory-Weiss tears are mucosal lacerations that occur at the gastroesophageal junction, often just within a hiatal hernia. They are usually related to vomiting and result in mild, self-limited bleeding. Laine [\[32\]](#) found that patients with actively bleeding Mallory-Weiss tears treated with bipolar electrocoagulation had lower rates of continued bleeding, transfusions, and emergency surgery compared with a medically treated group. A UCLA-CURE study found that endoscopic treatment for actively bleeding Mallory-Weiss tears, without portal hypertension, had a 100% hemostasis rate as compared with 40% for medical treatment. [\[22\]](#) Only 20% of patients with nonbleeding visible vessels or adherent clots rebled. The authors recommend treating only actively bleeding Mallory-Weiss tears, in patients without portal hypertension, with low power setting, light touch bipolar coagulation, or epinephrine injection. Patients with portal hypertension and an actively bleeding Mallory-Weiss tear should have endoscopic treatment of the adjacent varices, with sclerotherapy or rubber band ligation and not bipolar coagulation.

Upper Gastrointestinal Malignancy

Malignancy accounts for 1% of severe upper gastrointestinal bleeds. Malignancies that bleed are usually large, ulcerated masses in the esophagus, stomach, or duodenum. Endoscopic hemostasis with bipolar electrocautery, laser, or injection therapy can control acute bleeding and allow for medical stabilization while determining the long-term treatment strategy. [53]

Despite medical, endoscopic, or surgical therapy, UCLA-CURE patients with severe bleeding from upper gastrointestinal tumors had a 90% 1-year mortality. [53]

Upper Gastrointestinal Angiodysplasia

Upper gastrointestinal angiodysplasia or angiomas are mostly idiopathic but may be found as part of *watermelon stomach*, Osler-Weber-Rendu syndrome, chronic renal failure, and blue rubber bleb syndrome. Bleeding is usually occult or mild. Endoscopic therapy with thermal probes or lasers can reduce bleeding and transfusion rates (Color Fig. 4). [42]

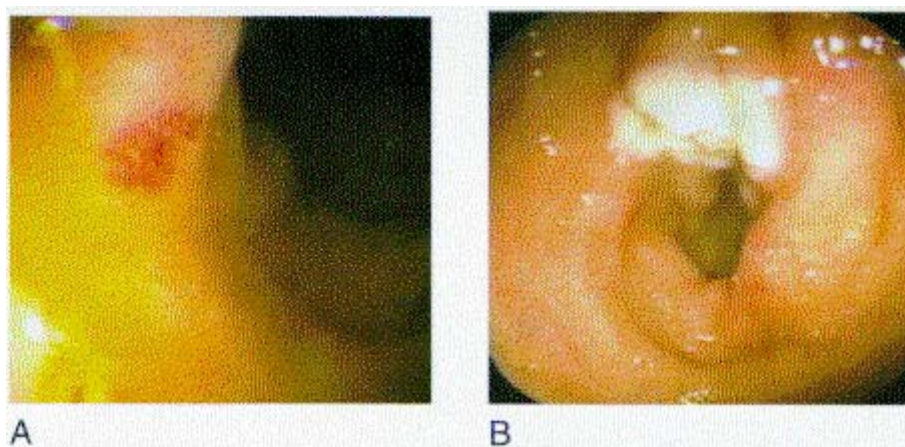


Figure 4. Duodenal bulb angiodysplasia treatment with Gold Probe in a patient with recurrent melena. A, A nonbleeding duodenal angiodysplasia. B, Coagulated angiodysplasia after Gold Probe coagulation.

Aortoenteric Fistula

Aortoenteric fistulas usually occur in patients who have undergone surgical repair of abdominal aortic aneurysms. The upper portion of the aortic graft impacts against the second or third portion of the duodenum and can result in a fistulous communication. Aortic graft infection appears to be important in fistulization. Patients may have an initial self-limited (*herald*)

bleed, followed by massive hemorrhage. Patients with an upper gastrointestinal bleed and prior aortic aneurysm repair should have urgent vascular surgery consultation as well as an upper endoscopy to identify possible duodenal erosion by the graft or blood in the duodenum. Computed tomography may show inflammation around the graft. Surgery is required for aortoenteric fistulas, during which the infected graft is removed. There is no role for therapeutic endoscopy in managing bleeding from aortoenteric fistulas.

SEVERE LOWER GASTROINTESTINAL BLEEDING

Acute lower gastrointestinal bleeding has an annual hospitalization rate of 22 per 100,000. [40] Most ambulatory patients with hematochezia stop bleeding spontaneously, allowing for elective diagnostic evaluation in most cases. Urgent colonoscopy using a rapid lavage purge is required for patients with severe, ongoing, or recurrent hematochezia. [25] A 1988 CURE study found that angiodysplasia and diverticula were the commonest causes of severe hematochezia in the elderly. [24]

Of patients with severe hematochezia, 64% required therapeutic intervention for control of bleeding, including endoscopic hemostasis in 39%, surgery in 24%, and therapeutic angiographic in 1%. In the authors' experience, diverticular bleeding is the commonest cause of mild-to-moderate hematochezia in ambulatory patients. Diverticular

bleeding was the commonest cause of acute lower gastrointestinal bleeding in studies from Kaiser in San Diego [\[40\]](#) and from an American College of Gastroenterology survey. [\[47\]](#)

Colonic Diverticular Hemorrhage

Colonoscopic hemostasis of actively bleeding diverticula has been reported using bipolar probe coagulation, epinephrine injection, and metallic clips. [\[11\]](#) [\[48\]](#) [\[52\]](#) [\[61\]](#) In some studies, a pigmented protuberance was seen at the edge of the suspected bleeding diverticulum. [\[11\]](#) [\[52\]](#)

Surgical resection of this area in one patient revealed the pigmented protuberance to be a sentinel clot adherent to a medium-sized artery. [\[11\]](#)

This protuberance may be stigmata for recurrent bleeding. No large studies have analyzed different endoscopic modalities for treating diverticular bleeding because of the rarity of identifying a diverticulum with active bleeding or a pigmented protuberance.

The authors perform a rapid colonic purge followed by urgent colonoscopy for suspected diverticular bleeding. If active bleeding is seen from a single diverticulum, the authors try to define the bleeding site precisely. If the bleeding is coming from the edge of the diverticulum or there is a pigmented protuberance on the edge, the authors apply a bipolar probe for a 2-second pulse duration at a low power setting (10 to 15 watts) and with light pressure to cauterize the edge. The authors have also coagulated the base of a diverticulum with this technique without causing perforation, but their experience with this technique is limited. Epinephrine injection can also be performed at the edge and even within the base of a diverticulum.

Colonic Angiodysplasia

Colonic angiodysplasias are usually found in the right colon. As with upper gastrointestinal angiodysplasia, they may be associated with chronic renal failure or Osler-Weber-Rendu syndrome. Bleeding from angiodysplasia is usually self-limited and intermittent and often presents as chronic iron deficiency anemia. The CURE group has extensive experience treating angiodysplasia with bipolar probe coagulation. [\[25\]](#) Patients generally require more than one session of endoscopic hemostasis. The main risks to colonoscopic bipolar coagulation of angiodysplasia are severe, delayed bleeding in 5% of patients and postcoagulation syndrome in 1.7% of patients. [\[25\]](#)

Colonic Tumors

Colonic tumors rarely present with severe bleeding. Endoscopic treatment may be applied for a focal bleeding site. Long-term management, however, usually involves surgical resection.

Colitis

Lower gastrointestinal bleeding can be due to inflammatory bowel disease, infectious colitis, or ischemic colitis. If severe colitis is encountered during urgent colonoscopy for hematochezia, the colonoscope should not be advanced more than 10 to 20 cm into the inflammatory area to avoid perforation. Biopsy specimens should be obtained to help determine the diagnosis. Most patients with ischemic colitis and inflammatory bowel disease should subsequently undergo elective outpatient colonoscopy to assess healing and exclude other pathology.

CONCLUSIONS

Endoscopy has emerged as the initial diagnostic and therapeutic tool in the evaluation and treatment of severe gastrointestinal hemorrhage. Research continues in improving technologies (i.e., clips and sewing devices) as well as outcomes research (determine optimal timing of endoscopy and criteria for hospitalization). Therapeutic endoscopy will continue to have a pivotal role in high-risk gastrointestinal bleeding in the future.

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