



Current therapy for nonvariceal upper gastrointestinal bleeding

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Received: 5 March 2003/Accepted: 29 May 2003/Online publication: 21 November 2003

Abstract. Upper gastrointestinal bleeding continues to plague physicians despite the discovery of *Helicobacter pylori* and advances in medical therapy for peptic ulcer disease. Medical therapy with new nonsteroidal anti-inflammatory medications and somatostatin/octreotide and intravenous proton pump inhibitors provides hope for reducing the incidence of and treating bleeding peptic ulcer disease. Endoscopic therapy remains the mainstay for diagnosis and treatment of upper gastrointestinal bleeding. Many methods of endoscopic hemostasis have proven useful in upper gastrointestinal hemorrhage. Currently, combination therapy with epinephrine injection and bicap or heater probe therapy is most commonly employed in the United States. Angiography and embolization play a role primarily when endoscopic therapy is unsuccessful.

Key words: Endoscopic therapy — Nonvariceal bleeding — Upper gastrointestinal hemorrhage

The magnitude of the problem

Upper gastrointestinal bleeding continues to be a vexing problem for physicians. The association of *Helicobacter pylori* with gastric ulceration by Warren and Marshall in 1984 changed the therapy of peptic ulcer disease. The incidence of hospitalization for peptic ulcer disease has diminished with the advent of medical therapy of *H. pylori* [10]. This has not lessened the incidence of admission for upper gastrointestinal bleeding, which is approximately 0.1% of the population in several large studies [27, 32]. There are 200,000–300,000 admissions of upper gastrointestinal bleeding per year in the United States. Terdiman [46] estimates the hospital costs of therapy in the United States to exceed 1 billion a year.

Despite improvement in the understanding of the etiology of peptic ulcer disease, the incidence of bleeding from peptic ulcer disease, the most common complication, has not changed. Hemorrhage occurs in 20–30% of patients with peptic ulcer disease [45]. The mortality of bleeding peptic ulcer disease has not improved with a better understanding of the pathophysiology of its development. Mortality rates of 5–15% have not changed for the past 30 years. The lack of improvement in mortality rates despite improvements in diagnosis, endoscopic treatment, and critical care therapeutics has been attributed to a combination of the increased age of the population of patients presenting with nonvariceal gastrointestinal bleeding and an increase in the use of medications predisposing to gastrointestinal bleeding.

Age is a major risk factor for mortality in patients bleeding from peptic ulcer disease, along with rebleeding and comorbid conditions. In Rockall et al.'s [32] survey, in a patient population of 15.5 million people with acute upper gastrointestinal hemorrhage, 27% were older than age 80. Mortality from gastrointestinal bleeding varies from 3% in patients younger than age 60 to 20% in those older than age 80 [5]. The majority of these deaths are attributed to cardiovascular complications or other comorbid conditions. Fewer than 20% of these deaths involve uncontrolled gastrointestinal hemorrhage [46]. The importance of this trend of increasing patient age and lack of improvement in mortality is heightened by demographic predictions. Census figures from 1990 indicated a population of 31 million people aged 65 or older. This age group is projected to increase to 52 million by 2020 and to 68 million by the year 2040, representing more than 20% of the U.S. population [37].

Nonsteroidal antiinflammatory drugs (NSAIDs) have been used in more than half of patients admitted for upper gastrointestinal bleeding [46]. Twenty million Americans routinely take NSAIDs. Lanza [20] noted that patients on chronic NSAID therapy for rheumatoid arthritis and osteoarthritis have a 15–20% incidence of ulceration with significantly higher complication rates than those patients not using NSAIDs. Lanza also reported a 4.5-fold increase in the relative risk of death from gastrointestinal causes for elderly patients using NSAIDs.

Medical therapy for nonvariceal upper gastrointestinal bleeding

Medical therapy has proven efficacious in the prevention of peptic ulceration in patients taking long-term NSAIDs for chronic illnesses. In randomized controlled trials, prophylaxis with misoprostol, the prostaglandin E analog, and the proton pump inhibitor omeprazole were proven effective in preventing gastric and duodenal ulcers. In contrast, histamine (H₂) receptor antagonists have been shown to prevent duodenal but not gastric ulceration. Sucralfate has not been proven effective in preventing peptic ulcer disease in patients using chronic NSAID therapy. Therefore, Lanza and colleagues [20] recommend misoprostol for patients using NSAIDs who are at high risk of developing hemorrhage, including patients with prior hemorrhage, patients older than 60 years, use of a high dosage of aspirin or other NSAID, or concurrent use of corticosteroids or anticoagulation. They allow that omeprazole is an acceptable alternative to misoprostol therapy. They further recommend that patients with known peptic ulcer disease who require continued NSAID therapy should be maintained on a proton pump inhibitor [20]. Several studies have shown the efficacy of therapy for *H. pylori* in preventing future bleeding episodes in patients with bleeding peptic ulcer with proven *H. pylori* infection [29, 31, 36, 44].

For many years, medical therapy was not effective in the acute management of nonvariceal bleeding. Several authors have shown that antacids and H₂ receptor antagonists are not useful in decreasing the transfusion requirements or lowering rates of rebleeding in peptic ulcer patients [10, 12, 20, 34, 48]. Recently, the use of somatostatin or octreotide and intravenous proton pump inhibitors has changed this paradigm.

In 1997, Imperiale and Birgisson [15] performed a meta-analysis of 14 randomized controlled trials involving the use of somatostatin or octreotide versus H₂ antagonists or placebo in patients with acute nonvariceal upper gastrointestinal bleeding. Somatostatin is a peptide known to diminish splanchnic blood flow and inhibit gastric acid secretion. Both somatostatin and its long-acting synthetic analog, octreotide, had previously proven effective in the management of episodes of acute variceal bleeding. Somatostatin/octreotide was found to reduce the risk of rebleeding to 0.53, a risk reduction of 47%. Subgroup analysis revealed that somatostatin/octreotide was more effective in the treatment of peptic ulcer bleeding than non-peptic ulcer bleeding. The majority of patients with non-peptic ulcer bleeding suffered from hemorrhagic gastritis. The authors concluded that intravenous therapy with somatostatin or octreotide may reduce the risk of persistent nonvariceal upper gastrointestinal hemorrhage caused by peptic ulcer disease and suggested this therapy might have a therapeutic role in the initial management of this problem or in situations in which endoscopy is either not available or not successful [15].

In 1997, Khuroo and associates [18] first described the effectiveness of proton pump inhibitors in the acute management of nonvariceal upper gastrointestinal bleeding. This randomized, blinded, placebo-controlled

study of 220 patients examined the effects of 40 mg omeprazole given orally twice daily on bleeding peptic ulcers. The study revealed a significant improvement in rates of rebleeding, need for blood transfusions, and need for surgery. However, the mortality rate was not significantly affected. An important qualifier of this study is that none of the patients underwent endoscopic methods of hemostasis.

After this initial study, several others showed the effectiveness of proton pump inhibitor therapy. Lau and colleagues [21] performed a randomized, double-blind, placebo-controlled study of 240 patients after endoscopic hemostasis using intravenous omeprazole. Bleeding recurred within 30 days in 6.7% of the omeprazole-treated patients and 23% of those receiving placebo. The need for repeat endoscopic therapy and blood transfusions was decreased with omeprazole, and hospital stays were shortened. Other studies have corroborated the finding that intravenous proton pump inhibitor therapy can be beneficial in nonvariceal upper gastrointestinal hemorrhage even after endoscopic therapy has been used [2, 12, 24].

Endoscopic therapy for upper gastrointestinal bleeding

Upper gastrointestinal endoscopy is of paramount importance in the management of upper gastrointestinal bleeding. Early endoscopy provides the most accurate means for diagnosis of the source of upper gastrointestinal bleeding. Furthermore, early endoscopy allows for risk stratification and triage of patients with upper gastrointestinal bleeding. Endoscopic therapy has become the treatment of choice for upper gastrointestinal bleeding. Although there are few data to support endoscopy within the first 12–24 h of presentation, early endoscopy is recommended for the reasons previously discussed [38, 46]. Lin and colleagues [26] found early endoscopy to be beneficial in the subset of patients with bloody nasogastric aspirates. In these patients, endoscopy within 12 h of presentation resulted in reduced rebleeding rates, transfusion requirements, hospital length of stay, and hospital costs.

Upper gastrointestinal endoscopy in the hands of an experienced endoscopist has a >90% diagnostic rate for the source of acute upper gastrointestinal hemorrhage [35]. The relative frequency of causes of upper gastrointestinal bleeding varies significantly with the patient population observed. However, peptic ulcer disease is consistently the most common source of nonvariceal upper gastrointestinal bleeding. Two methods have been described that may increase diagnostic accuracy of upper endoscopy in the setting of acute upper gastrointestinal bleeding.

In 1999, Kalloo and colleagues [17] described the use of 3% hydrogen peroxide during upper endoscopy for acute upper gastrointestinal bleeding to enhance visualization. The authors also noted the effectiveness of hydrogen peroxide in providing hemostasis in locations outside the gastrointestinal tract. Although the use of hydrogen peroxide subjectively improved visualization in their study, the safety and clinical effectiveness of

increased diagnostic accuracy and potential therapeutic benefits have yet to be proven. In a randomized controlled trial, Coffin and associates [7] described the use of the prokinetic agent erythromycin to increase the effectiveness of endoscopic exam. Given intravenously prior to esophagogastroduodenoscopy, erythromycin was found to improve the quality of the exam and tended to reduce the need for repeat endoscopy.

Endoscopic examination has proven useful as a means of risk assessment with regard to the likelihood of further bleeding from peptic ulcer disease. This not only provides guidance for triage purposes but also guides endoscopic therapy. The stigmata of recent hemorrhage have proven useful in predicting further bleeding. The presence of ongoing active bleeding at the time of endoscopy is the most important predictor of recurrent bleeding and is associated with a 90% risk of further bleeding without endoscopic therapy. A visible vessel on endoscopy results in a 50% rebleed rate. An adherent clot despite attempted washing results in a 20% rate of future bleeding. Clean-based ulcers and Mallory-Weiss tears have a less than 5% rate of further bleeding [35].

The use of these stigmata of recent hemorrhage has been combined with clinical factors to assist in triaging patients in a spectrum from outpatient therapy to intensive care units. Several clinical guidelines for the management of upper gastrointestinal bleeding have been proposed [1, 9, 11, 14, 28, 33]. In 1996, Rockall and colleagues [33] described a risk score system using age, shock, comorbidity, stigmata of recent hemorrhage, and rebleeding to predict mortality. This study of 4,185 patients admitted with acute upper gastrointestinal hemorrhage revealed that 29% of patients were found to be at low risk of further bleeding or mortality and therefore could potentially be triaged to earlier discharge.

In 1997, Hay and associates [14] described their clinical practice guidelines for management of acute upper gastrointestinal hemorrhage. They prospectively evaluated 299 patients using an alternate-month design to evaluate the effectiveness of their practice guidelines for early discharge of patients considered to be at low risk for complications. According to their guidelines, 70% of their patients were found to be at low risk. The implementation of the guidelines resulted in a decrease of mean hospital length of stay from 4.6 to 2.9 days ($p < 0.001$). No differences in complications, patient health status, or patient satisfaction were observed 1 month after discharge [14].

Blatchford and Murray [1] described a risk stratification system using only clinical factors. Their score uses admission hemoglobin, blood urea nitrogen, heart rate, systolic blood pressure, syncope, melena, and the presence of hepatic disease or cardiac failure to evaluate the risk of patients requiring blood transfusion or endoscopic or surgical intervention. They found that their score correlated better with the need for clinical intervention than did the Rockall score, with the area under the receiver operating characteristic curve of 0.92 versus 0.75 for the Rockall score. Despite these findings, we recommend endoscopy prior to early hospital discharge in the setting of acute gastrointestinal bleeding.

Endoscopic therapy for peptic ulcer disease

The stigmata of recent hemorrhage also provide guidance for the use of endoscopic therapy for upper gastrointestinal bleeding. Rebleeding is the leading cause of morbidity and mortality in patients with acute upper gastrointestinal hemorrhage. The use of the stigmata of recent hemorrhage allows selection of patients considered at greatest risk for further bleeding. These patients then undergo some form of endoscopic therapy. Patients with clean ulcer bases and Mallory-Weiss tears are considered to be at low risk for further bleeding and typically do not undergo endoscopic therapy.

The role of endoscopic therapy in the setting of adherent clots is still under consideration. Adherent clots are commonly associated with acute upper gastrointestinal hemorrhage. The 1989 National Institutes of Health [30] consensus conference on gastrointestinal bleeding recommended against aggressive attempts at removal of the clot. However, since that conference a more active approach to the management of adherent clot has been favored in several studies.

In 2002, Jensen and associates [16] described the results of a randomized controlled trial of combination endoscopic therapy versus medical therapy in a group of patients with nonbleeding adherent clot. Their study involved 32 patients who were randomized to medical therapy versus their technique for the management of adherent clots. This technique involves epinephrine injection in four quadrants around the clot followed by shaving the clot using a snare to cold guillotine the clot 3 or 4 mm above its base. If active bleeding occurs or a visible vessel is identified, these are treated with bipolar coagulation. By hospital discharge, 35% of medically treated patients had had a rebleeding episode compared with none of the patients in the endoscopically treated group. There were no complications of endoscopic therapy.

The management of a visible vessel or active bleeding provokes an entirely different controversy. Endoscopic therapy has been shown to have a clear benefit in these cases. The rate of rebleeding after endoscopic therapy is reduced to 13–30% compared to 90% in patients with ongoing active arterial bleeding and 50% in patients with a visible vessel [27]. Clearly, endoscopic therapy is beneficial in these patients. However, which therapy is preferable? There is a veritable cornucopia of modalities available for the endoscopic treatment of upper gastrointestinal bleeding, ranging from simple thermal devices (including electrocautery), injection therapy, and hemoclips to more exotic methods as well as combinations of therapies.

Devices using thermal therapy are among the most commonly employed. Monopolar electrocoagulation is one of the oldest methods of providing endoscopic hemostasis. A high-frequency (1 million Hertz) current flows from the tip of the electrode through the body tissue to a ground plate. This current produces heat, which results in collagen denaturation and vessel constriction leading to hemostasis. Although effective in providing endoscopic hemostasis, the monopolar electrode has fallen out of favor since the development of

multipolar electrodes, which result in less surrounding tissue damage with similar hemostatic efficacy [42].

One of the most common methods of thermal electrocoagulation is the multipolar endoscopic probe, also called bipolar electrocoagulation or bicap therapy. Microelectrodes are spaced around the sides and end of the probe tip of this device to allow for the approach of a bleeding site from any direction. Electric current flows between the adjacent electrodes, making a ground plate unnecessary. The probe head is applied to the site of bleeding until tamponade is obtained. Heat is then applied to allow for coaptive coagulation. Bipolar electrocoagulation has been associated with a reduced amount of thermal injury compared to the monopolar probe or YAG laser methods [39, 40]. In 1987, Laine [19] reported 44 patients with active ongoing upper gastrointestinal tract hemorrhage who were randomized to multipolar electrode therapy or sham electrocoagulation. Patients undergoing multipolar electrocoagulation had significantly less transfusion requirements, lower length of hospital stay, less need for emergency surgery, and lower cost of hospitalization. Mortality was lower in the treatment group as well; however, the difference was not statistically significant.

A different approach to thermal therapy is the use of a heater probe. The heater probe uses a Teflon-coated aluminum cylinder that houses an electrical heating element to produce thermal energy for hemostasis. Instead of electrical current, heat passes into the target tissue by conduction. Heater probes are designed to allow simultaneous application of thermal energy and pressure. This combination results in tissue edema, protein denaturation, vascular constriction, and tissue desiccation, resulting in subsequent hemostasis. The heater probe is applied to the bleeding vessel with firm pressure in an effort to coapt the vessel walls. While this pressure is applied, four sequential pulses of 30 J each are administered in tandem, without a cooling period between individual pulses. Larger diameter heater probes (3.2 mm) have proven more effective. The heater probe method of endoscopic hemostasis is very popular because of its effectiveness, low cost, and ease of use [40, 42]. Gralnek and associates [13] performed a randomized, controlled trial of heater probe therapy versus medical treatment for actively bleeding peptic ulcer in 31 patients. Heater probe therapy resulted in higher hemostasis rates, lower rates of rebleeding, lower rates of emergency surgery, lower blood transfusion requirements, and lower direct costs per patient.

Laser energy has been harnessed to allow for effective photocoagulation. Two devices are used for endoscopic therapy of upper gastrointestinal hemorrhage: the argon laser and the neodymium yttrium-aluminum-garnet (Nd:YAG) laser. Because the argon laser has little penetration power and only coagulates to a tissue depth of 1 mm, the YAG laser is more commonly employed. Controlled trials have proven the effectiveness of lasers in providing endoscopic hemostasis. Lasers are rarely used for endoscopic hemostasis because of their relatively high cost, lack of portability, and the high level of training necessary for the endoscopist and technician [40, 42, 43].

Injection sclerotherapy was initially proven effective in the treatment of esophageal varices. Recently, it has been found to be efficacious in the treatment of nonvariceal sources of upper gastrointestinal bleeding. Epinephrine has become the agent of choice in injection therapy. The injection of epinephrine results in local tamponade, vasoconstriction, and increased platelet aggregation. A 1:10,000 solution of epinephrine is injected in four areas around the bleeding vessel. This has been shown to provide hemostasis, decrease transfusion requirements, and reduce the need for surgical therapy. Injection therapy is very popular due to its low cost and ease of use [40]. Gralnek and associates [13] performed a randomized, controlled trial of injection sclerotherapy versus medical therapy for actively bleeding peptic ulcer in 31 patients. Injection therapy resulted in higher hemostasis rates, lower rates of emergency surgery, lower blood transfusion requirements, and lower direct costs per patient.

Absolute ethanol has also been used as an injection agent. Ninety-eight percent dehydrated ethanol is injected in 0.1- or 0.2-ml increments around the bleeding vessel for a total of 0.6–1.2 ml. This results in dehydration and thrombosis of the bleeding vessel. Success rates >90% for permanent hemostasis have been reported with alcohol sclerotherapy [41]. However, epinephrine therapy is associated with less overall tissue damage than ethanol injection, which has greater hemostatic effectiveness. Furthermore, epinephrine injection is technically much simpler than the precise low-dose injections required for ethanol sclerotherapy [40].

The combination of injection therapy and thermal therapy has become the most commonly employed method of endoscopic hemostasis at many institutions, including our own. First, a solution of 1:10,000 epinephrine is injected into the submucosa in four quadrants around the bleeding vessel for a total of 5–20 ml. Subsequently, the heater probe device is applied to the vessel to provide further hemostasis. A device currently on the market in the United States allows for both injection therapy and heater probe therapy using a single device (Injector Gold Probe; Boston Scientific, Natick, MA). Lin and colleagues [25] reported on the increased efficacy of combination therapy in bleeding peptic ulcer. They reported on 96 patients with actively bleeding ulcers or nonbleeding visible vessels who were randomized to epinephrine injection, bicap treatment, or combination therapy. Initial hemostasis was achieved in 31 of 32 patients undergoing epinephrine treatment, 30 of 32 patients undergoing bicap therapy, and 30 of 32 patients undergoing combination therapy. Rebleeding episodes were fewer in the combination therapy group (two patients) than in the bicap group (nine patients) or the injection alone group (11 patients). The volume of blood transfusion required was significantly lower for the combination therapy group than for the other two groups; however, hospital length of stay, patients requiring urgent surgery, and mortality rates were not significantly different among the three groups.

Hemoclips (miniature metal clips) have been popular for endoscopic hemostasis in Japan for many years.

Recently, a simple-to-use preloaded device has become available in the United States (Quickclip, Olympus). The applicator is inserted through the biopsy channel of the endoscope and clips are applied directly to the visible bleeding vessel. Recent studies have reported the hemoclip to be effective. Cipoletta and colleagues [6] reported 51 patients with major stigmata of ulcer hemorrhage randomized to heater probe therapy or endoscopic hemoclip placement. Hemostasis, rates of emergency surgery, and mortality were similar for both groups. However, recurrent bleeding was seen in 21% of patients undergoing heater probe therapy versus 1.8% of patients undergoing hemoclip therapy. Both the length of hospital stay and transfusion requirements were also significantly lower for those patients who underwent hemoclip therapy. Chung and associates [3] compared the use of the hypertonic saline epinephrine injection alone, hemoclip only, and hypertonic saline and epinephrine injection combined with hemoclip therapy and found no benefit to combination therapy. They also noted a higher complication rate for patients receiving epinephrine therapy. Lin and colleagues [23] randomized 80 patients with bleeding ulcers or nonbleeding visible vessels to either hemoclip therapy or heater probe therapy and found higher initial hemostasis rates in the heater probe group (100 vs 85% in the hemoclip group). They specifically noted that for difficult to approach bleeding sites hemostasis was easier to achieve with heater probe therapy. Length of hospital stay, blood transfusion requirements, patients requiring urgent surgery, and mortality were not statistically different between the two groups.

The argon plasma coagulator has proven very useful in hepatic surgery. It also has a role in endoscopic hemostasis. It is a noncontact thermal modality that delivers inert argon gas via a small catheter through the biopsy channel of the endoscope. Activating the wire at the tip of the catheter results in an electric current between the tip of the sheath and the gastric wall, causing a spray of ionized argon gas that provides coagulative hemostasis. Because it penetrates to only 2 or 3 mm in depth, the argon plasma coagulator is particularly effective for superficial lesions, such as arteriovascular malformations and bleeding tumors [8, 40].

Several techniques have proven useful in the therapy of bleeding peptic ulcer. Multipolar electrocoagulation, heater probe therapy, and injection therapy have been considered the most beneficial for some time in the United States. However, there has been a resurgence of interest in the hemoclip with the development of new and easier to use delivery devices. Although we have successfully used the hemoclip for bleeding peptic ulcer, this method is somewhat user dependent and success rates vary substantially with the experience of the endoscopist. It is difficult to recommend a single technique due to the wide variety of situations involving gastrointestinal bleeding and the skill and experience of endoscopists. For the majority of our patients presenting with upper gastrointestinal bleeding, we prefer the combination of epinephrine injection and bicap or heater probe therapy.

Endoscopic therapy for nonulcer upper gastrointestinal bleeding

Gastric arteriovenous malformations are much less common than peptic ulcer bleeding. Frequently, these lesions are small and do not require endoscopic therapy. When necessary, endoscopic heater probe treatment should aim at the submucosal level and avoid full-thickness burning. A small lesion can be easily treated directly by endoscopic hemostasis. For larger lesions, treatment proceeds from the periphery to the center of the lesion. Gentle pressure is applied with the heater probe and 10 J is used for one or two pulses to eventually cover the entire arteriovenous malformation [40]. Cohen and colleagues [8] described their experience with argon plasma coagulation in 32 patients with gastrointestinal angiomata. Rapid hemostasis was achieved in all patients, with one patient experiencing rebleeding and two patients reporting mild abdominal pain after the procedure.

Mallory-Weiss tears are a common cause of upper gastrointestinal hemorrhage. They frequently resolve spontaneously without the need for endoscopic therapy. When endoscopic therapy is administered, the heater probe is used with moderate pressure. The heater probe is set to 20 J and two or three pulses are typically required at the site of bleeding to render effective hemostasis [40]. Yamaguchi and associates [49] reported the use of the hemoclip in 58 patients with Mallory-Weiss syndrome, of which 28 had active bleeding, nonbleeding visible vessels, or fresh adhesive clot. These 28 patients underwent endoscopic therapy with the hemoclip device. There were no complications, episodes of recurrent bleeding, or deaths.

Dieulafoy's lesion is a bleeding or clot-bearing artery protruding into the lumen of the gastrointestinal tract without surrounding ulceration. Chung and colleagues [4] reported the relative effectiveness of mechanical endoscopic therapy versus injection therapy in 24 patients with Dieulafoy's lesion randomized to hemoclip therapy, band ligation, or hypertonic saline injection. Initial hemostasis was obtained in 91.7% of patients undergoing mechanical therapy versus 75% in patients undergoing injection therapy. The need for subsequent surgery and rate of recurrent bleeding were significantly lower in patients undergoing mechanical means of hemostasis.

Complications of endoscopic therapy

Complications related to endoscopic therapy of upper gastrointestinal bleeding are relatively rare. Studies suggest a 1 or 2% incidence of complications. The majority of complications are cardiorespiratory in nature. Gastrointestinal perforation, pulmonary aspiration, increased hemorrhage, medication reactions, hypotension, and hypoxia are the most commonly reported complications. Continuous monitoring of blood pressure and oxygen saturation is recommended to help diagnose and prevent these complications. Patients with a large amount of intragastric blood benefit from airway pro-

tection via elective endotracheal intubation prior to attempts at endoscopic hemostasis. Patients with a history of recent myocardial infarction should be stabilized hemodynamically prior to performing endoscopic hemostasis [35, 39].

The role of angiography in nonvariceal upper gastrointestinal bleeding

Although endoscopy plays the primary role in diagnosis and management of upper gastrointestinal bleeding, angiography also has a role. Angiography is indicated for patients with ongoing hemorrhage that endoscopy is unable to control. In this setting, Walsh and associates [47] demonstrated that 52% of patients were successfully embolized. They emphasize that patients who fail embolotherapy need urgent surgical intervention. Embolotherapy has been shown to be more effective than intraarterial vasopressin infusion for the control of gastrointestinal bleeding [22].

References

- Blatchford O, Murray WR (2000) A risk score to predict need for treatment for upper-gastrointestinal haemorrhage. *Lancet* 356: 1318–1321
- Bustamante M, Stollman N (2000) The efficacy of proton-pump inhibitors in acute ulcer bleeding: a qualitative review. *J Clin Gastroenterol* 30: 7–13
- Chung IK, Ham JS, Kim HS, et al. (1999) Comparison of the hemostatic efficiency 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* 49: 13–18
- Chung IK, Kim EJ, Lee MS, et al. (2000) Bleeding Dieulafoy's lesion and the choice of endoscopic method: comparing the hemostatic efficacy of mechanical and injection methods. *Gastrointest Endosc* 52: 721–724
- Chung SC (1997) Surgery and gastrointestinal bleeding. *Gastrointest Endosc Clin North Am* 7: 687–701
- Cipolleta L, Bianco MA, Marmo R, et al. (2001) Endoclips versus heater probe in preventing early recurrent bleeding from peptic ulcer: a prospective and randomized trial. *Gastrointest Endosc* 53: 147–151
- Coffin B, Pocard M, Riche F, et al. (2002) Erythromycin improves the quality of EGD in patients with acute upper GI bleeding: a randomized controlled study. *Gastrointest Endosc* 56: 174–179
- Cohen J, Abedi M, Haber G, et al. (1996) Argon plasma coagulation: a new effective technique of noncontact thermal coagulation. Experience in 44 cases of GI angiomata. *Gastrointest Endosc* 43: 293.
- Corley DA, Stefan AM, Wolf M, et al. (1998) Early indicators of prognosis in upper gastrointestinal hemorrhage. *Am J Gastroenterol* 93: 336–340
- Cowles RA, Mulholland MW (2000) Surgical management of peptic ulcer disease in the helicobacter era: management of bleeding peptic ulcer. *Surg Laparosc Endosc Percutan Tech* 11: 2–8
- Eisen GM, Dominitz JA, Faigel DO, et al. (2001) An annotated algorithmic approach to upper gastrointestinal bleeding. *Gastrointest Endosc* 53: 853–858
- Erstad BL (2001) Proton-pump inhibitors for acute peptic ulcer bleeding. *Ann Pharmacother* 35: 730–740
- Gralnek IM, Jensen DM, Kovacs TO, et al. (1997) An economic analysis of patients with active arterial peptic ulcer hemorrhage treated with endoscopic heater probe, injection sclerotherapy, or surgery in a prospective, randomized trial. *Gastrointest Endosc* 46: 105–112
- Hay JA, Maldonado L, Weingarten SR, et al. (1997) Prospective evaluation of a clinical guideline recommending hospital length of stay in upper gastrointestinal tract hemorrhage. *J Am Med Assoc* 278: 2151–2156
- Imperiale TF, Birgisson S (1997) Somatostatin or octreotide compared with H2 antagonists and placebo in the management of acute nonvariceal upper gastrointestinal hemorrhage. *Ann Int Med* 127: 1062–1071
- Jensen DM, Kovacs TO, Jutahba R, et al. (2002) Randomized trial of medical or endoscopic therapy to prevent recurrent ulcer hemorrhage in patients with adherent clots. *Gastroenterology* 123: 632–636
- Kalloor AN, Canto MI, Wadwa KS, et al. (1999) Clinical usefulness of 3% hydrogen peroxide in acute upper GI bleeding: a pilot study. *Gastrointest Endosc* 49: 518–521
- Khuroo MS, Yattoo GN, Javid G, et al. (1997) A comparison of omeprazole and placebo for bleeding peptic ulcer. *N Engl J Med* 336: 1054–1058
- Laine L (1987) Multipolar electrocoagulation in the treatment of active upper gastrointestinal tract hemorrhage: a prospective controlled trial. *N Engl J Med* 316: 1613–1617
- Lanza FL (1998) A guideline for the prevention and treatment of NSAID-induced ulcers. *Am J Gastroenterol* 93: 2037–2046
- Lau JY, Sung JJ, Lee KK, et al. (2000) Effect of intravenous omeprazole on recurrent bleeding after endoscopic treatment of bleeding peptic ulcers. *N Engl J Med* 343: 310–316
- Lefkowitz Z, Cappell MS, Kaplan M, et al. (2000) Radiology in the diagnosis and management of gastrointestinal bleeding. *Gastroenterol Clin North Am* 29: 489–512
- Lin HJ, Hsieh YH, Tseng GY, et al. (2002) A prospective, randomized trial of endoscopic hemoclip versus heater probe thermo-coagulation for peptic ulcer bleeding. *Am J Gastroenterol* 97: 2161–2165
- Lin HJ, Lo WC, Lee FY, et al. (1998) A prospective, randomized comparative trial showing that omeprazole prevents rebleeding in patients with bleeding peptic ulcer after successful endoscopic therapy. *Arch Intern Med* 158: 54–58
- Lin HJ, Tseng GY, Perng CL, et al. (1999) Comparison of adrenaline injection and bipolar electrocoagulation for the arrest of peptic ulcer bleeding. *Gut* 44: 715–719
- Lin HJ, Wang K, Perng CL, et al. (1996) Early or delayed endoscopy for patients with peptic ulcer bleeding: a prospective randomized study. *J Clin Gastroenterol* 22: 267–271
- Longstreth GF (1995) Epidemiology of hospitalization for acute upper gastrointestinal bleeding. *Am J Gastroenterol* 90: 206–210
- Longstreth GF, Feitelberg SP (1998) Successful outpatient management of acute upper gastrointestinal hemorrhage: use of practice guidelines in a large patient series. *Gastrointest Endosc* 47: 219–222
- Macri G, Milani S, Surrenti E, et al. (1999) Eradication of *Helicobacter pylori* reduces the rate of duodenal ulcer re-bleeding: a long term follow-up study. *Curr Surg* 56: 309–311
- National Institutes of Health Consensus Conference(1989) Therapeutic endoscopy and bleeding ulcers. *J Am Med Assoc* 262: 1369–1372
- Pellicano R, Peyre S, Leone N, et al. (2001) The effect of the eradication of *Helicobacter pylori* infection on hemorrhage because of duodenal ulcer. *J Clin Gastroenterol* 32: 222–224
- Rockall TA, Logan RF, Devlin HB, et al. (1995) Incidence of and mortality from acute upper gastrointestinal haemorrhage in the United Kingdom. *Br Med J* 311: 222–226
- Rockall TA, Logan RF, Devlin HB, et al. (1996) Risk assessment after acute upper GI hemorrhage. *Gut* 38: 316–321
- Rodriguez G, Cattaruzi C, Troncon MG, Agostinis L (1998) Risk of hospitalization for upper gastrointestinal tract bleeding associated with ketorolac, other nonsteroidal anti-inflammatory drugs, calcium antagonists and other antihypertensive drugs. *Arch Intern Med* 158: 33–39
- Savides TJ, Jensen DM (2000) Therapeutic endoscopy for non-variceal gastrointestinal bleeding. *Gastroenterol Clin North Am* 29: 465–487
- Sonnenberg A, Olson C, Zhang J (1999) The effect of antibiotic therapy on bleeding from duodenal ulcer. *Am J Gastroenterol* 94: 950–954

37. Spencer G (1989) Projections of the population of the United States—age, sex, and race: 1988 to 2080. U.S. Bureau of the Census, Washington, DC
38. Spiegel BM, Vakil NB, Ofman JJ (2001) Endoscopy for acute nonvariceal upper gastrointestinal tract hemorrhage: is sooner better? *Arch Intern Med* 161: 1393–1404
39. Steffes CP, Sugawa C (1992) Endoscopic management of nonvariceal gastrointestinal bleeding. *World J Surg* 16: 1025–1033
40. Sugawa C (1999) Control of nonvariceal upper GI bleeding. In: Scott-Conner CE (Ed) *The SAGES manual: fundamentals of laparoscopy and GI endoscopy*. Springer-Verlag, New York, pp 448–456
41. Sugawa C, Fujita Y, Ikeda T, Walt AJ (1986) Endoscopic hemostasis of bleeding of the upper gastrointestinal tract by local injection of ninety eight percent dehydrated ethanol. *Surg Gynecol Obstet* 162: 159–163
42. Sugawa C, Joseph AL (1992) Endoscopic interventional management of bleeding duodenal and gastric ulcers. *Surg Clin North Am* 72: 317–334
43. Sugawa C, Joseph AL (1994) Management of nonvariceal upper gastrointestinal bleeding. In: Greene FL, Ponsky JL (Eds) *Endoscopic surgery*. Saunders, Philadelphia, pp 125–140
44. Sung JJ, Leung WK, Suen R, et al. (1997) One-week antibiotics versus maintenance acid suppression therapy for *Helicobacter pylori*-associated peptic ulcer bleeding. *Dig Dis Sci* 42: 2524–2528
45. Swain CP (1992) Pathology of the bleeding lesions. In: Sugawa C, Schuman BM, Lucas CE (Eds) *Gastrointestinal bleeding*. Igaku-Shoin, New York
46. Terdiman JP (1998) Update on gastrointestinal bleeding. *Postgrad Med* 103: 43–64
47. Walsh RM, Amain P, Geisinger M, et al. (1999) Role of angiography and embolization for massive gastroduodenal hemorrhage. *J Gastrointest Surg* 3: 61–66
48. Wolfe MM, Lichtenstein DR, Singh G (1999) Gastrointestinal toxicity of nonsteroidal anti-inflammatory drugs. *N Engl J Med* 340: 1888–1899
49. Yamaguchi Y, Yamato T, Katsumi N, et al. (2001) Endoscopic hemoclippping for upper GI bleeding due to Mallory-Weiss syndrome. *Gastrointest Endosc* 53: 427–430