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CME CREDIT HOURS

Peptic ulcer bleeding: perspectives on some common dilemmas

KEY POINTS:

Upper gastrointestinal hemorrhage stops spontaneously in about 80% of patients who present with it.

The endoscopic appearance of the ulcer and presence of major stigmata are the most important predictors of rebleeding. Without endoscopic therapy, active arterial bleeding leads to continued bleeding or rebleeding in 85% of cases; a nonbleeding visible vessel has a 40% to 50% chance of rebleeding, especially if the patient is in shock.

Patients found to have active arterial bleeding at endoscopy should be treated and admitted to the ICU. Usually, such patients present with major bleeding and shock on admission and are admitted directly to the ICU before endoscopy.

Gastric acid secretion, *Helicobacter pylori*, and the use of nonsteroidal anti-inflammatory drugs should be addressed when drug therapy is being considered in patients with bleeding peptic ulcers.

ABSTRACT: Not all patients who present with peptic ulcer bleeding need endoscopic therapy, intensive care, or even hospital admission; clinical signs and endoscopic findings determine the need for various levels of care.

Gastrointestinal bleeding due to peptic ulcer requires a physician to make difficult clinical decisions. For instance, once the patient is hemodynamically stable, does he or she need to be admitted to the hospital, and if so, at what level of care? Is endoscopic therapy indicated? If the patient has been receiving anticoagulant therapy or nonsteroidal anti-inflammatory drugs, should these be discontinued? What antisecretory and antimicrobial drug therapy is most effective if *Helicobacter pylori* is present? This article presents some guidelines on how to manage this challenging problem.

DETERMINING THE PROGNOSIS

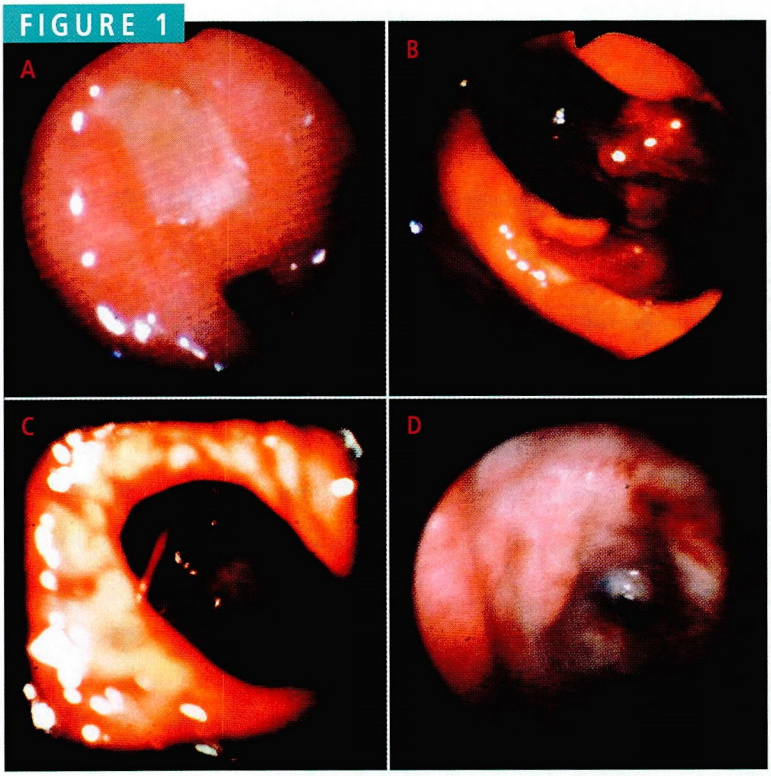
Peptic ulcer is the most common cause of bleeding from the upper gastrointestinal tract, accounting for about 50% of cases. Endoscopic therapy is now the first-line treatment in appropriate "high-risk" patients[1,2]; surgery is reserved for patients in whom endoscopic therapy fails.

Upper gastrointestinal hemorrhage stops spontaneously in about 80% of patients who present with it. The clinician should therefore try to identify patients at risk of further bleeding and death. Three factors define the risk of further bleeding:

Severity of the bleeding. Clinical features that indicate severe bleeding include shock on presentation or unstable hemodynamic signs (orthostatic changes in blood pressure and pulse rate, persistent tachycardia, hypotension), bright red hematemesis or hematochezia, and the need for blood transfusion.[3,4]

Concomitant conditions. Patients at higher risk are elderly (older

FIGURE 1



Appearance of ulcers during endoscopy:

A shows a clean-based ulcer;

B, adherent clot after irrigation;

C, active arterial bleeding; and

D, nonbleeding visible vessel.

From Schiller et al, reference 32

than 60 years), have concomitant medical diseases, began bleeding while in the hospital because of another condition, or have coagulopathy.[4–6]

Endoscopic findings. The appearance of the ulcer during endoscopy (**FIGURE 1**), especially the presence of major stigmata such as active arterial bleeding or a nonbleeding visible vessel, is the most important predictor of rebleeding.

Patients with active arterial bleeding or a nonbleeding vessel visible on endoscopy should undergo some form of endoscopic hemostatic therapy. In fact, according to a National Institutes of Health consensus panel and a recent meta-analysis, endoscopic therapy is beneficial only in these groups.[1,3] Without endoscopic intervention, active arterial bleeding leads to continued bleeding or rebleeding in 85% of cases[7]; a nonbleeding visible vessel has a 40% to 50% chance of rebleeding, especially if associated with shock.[8]

IS HOSPITALIZATION NECESSARY? AT WHAT LEVEL?

Before diagnostic endoscopy

Clinical prognostic features and the initial response to stabilization in the emergency room determine whether a patient should be hospitalized.

Policies regarding admitting a patient with gastrointestinal bleeding directly to the intensive care unit (ICU) vary, depending on the hospital's guidelines for emergency endoscopy, the severity of the bleeding, and the medical and ancillary resources available. Generally accepted criteria for ICU admission include signs of severe bleeding (hematemesis, hematochezia, shock on presentation), massive bleeding necessitating intubation to protect the airway before endoscopy, and ongoing active bleeding requiring emergency endoscopy.

Most other patients should be placed in an observation unit or clinical decision unit or remain in the emergency room while awaiting endoscopy, since the need for admission is usually determined by the endoscopic findings (**FIGURE 2**).

After diagnostic endoscopy

Patients with a clean-based ulcer or minor stigmata (**FIGURE 1A**) such as flat pigmented spots, irrespective of other clinical risk factors, almost invariably recover with conservative support and should not be given endoscopic hemostatic treatment. Once their condition has been stabilized in the emergency room or observation unit, they may be sent home with drug therapy.

Patients with an adherent clot (**FIGURE 1B**) are not treated endoscopically, but should be admitted to a regular ward for observation.

Patients with active arterial bleeding at endoscopy (**FIGURE 1C**) should be treated and admitted to the ICU. Usually, such patients present with major bleeding and shock on admission and are admitted directly to the ICU before endoscopy.

Patients with a nonbleeding visible vessel (**FIGURE 1D**) need endoscopic therapy followed

by hospitalization in either an ICU or a regular ward. Such patients do not need intensive care if the endoscopic examination is adequate and the endoscopic therapy optimal. However, they may need intensive care if they are elderly and have severe concomitant medical illnesses, or suffer complications from bleeding or from endoscopic therapy (aspiration, cardiac arrhythmia, ischemia), or have a technically difficult endoscopy resulting in suboptimal therapy.

Which patients need surgery?

Bleeding recurs after endoscopic treatment in approximately 20% of cases. Repeat treatment achieves permanent hemostasis in about 50% to 60% of cases. Therefore, fewer than 10% of patients initially given endoscopic treatment ultimately need surgery.

Most repeat bleeding episodes occur within 72 hours of presentation, most often within 48 hours[9]; this fact is the rationale for observing patients in the hospital for 2 to 3 days after endoscopic treatment.

BLEEDING DURING ANTICOAGULANT THERAPY

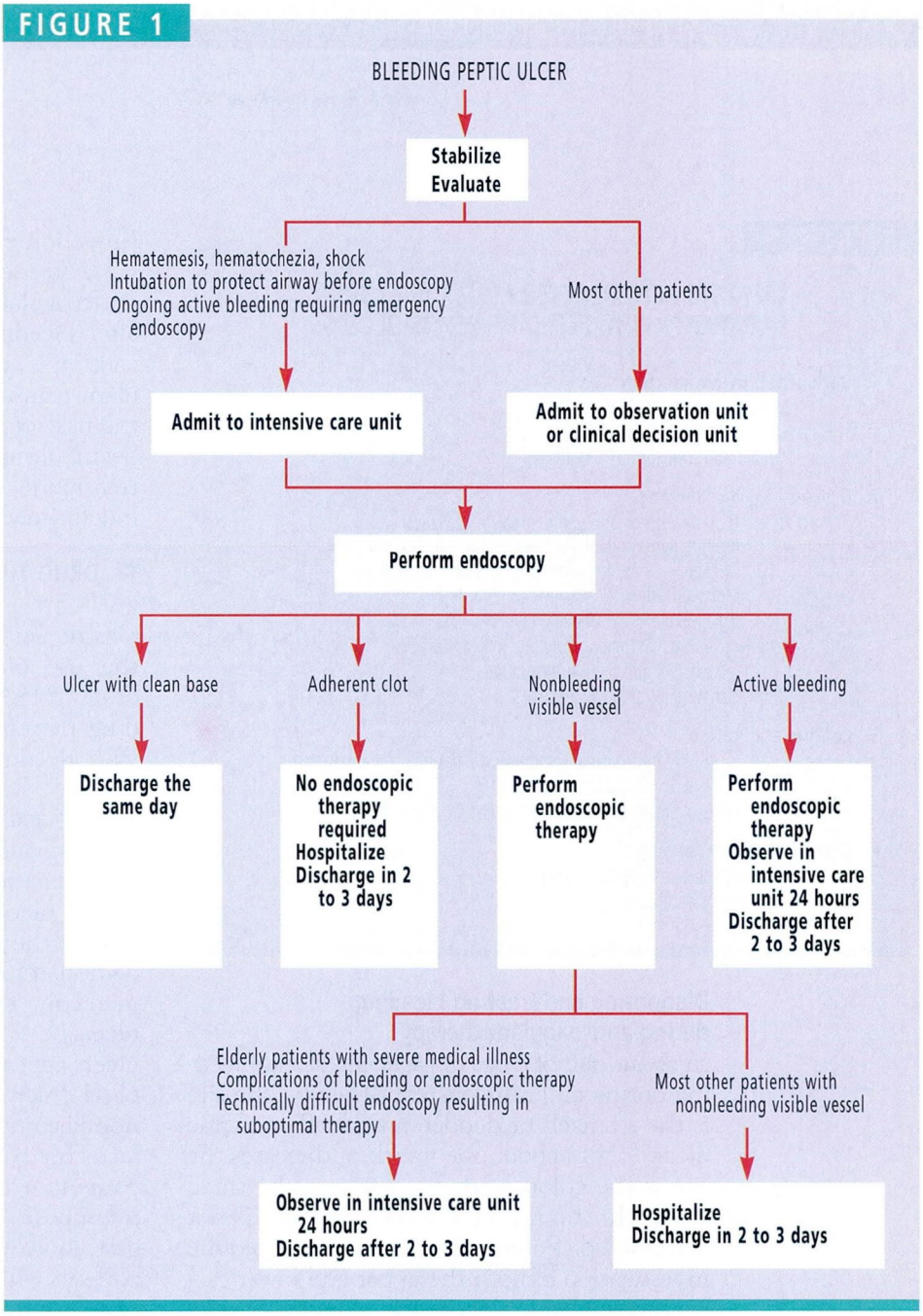
Massive gastrointestinal bleeding during anticoagulant therapy poses a dilemma. Anti-coagulant therapy is prescribed to reduce the risk of thromboembolism. Should the clinician reverse the anticoagulation and risk thromboembolism — or continue anticoagulation and risk exsanguination?

Risk of bleeding during anticoagulation

The risk of bleeding is highest during the first year of anticoagulation therapy. In a recent review of the risk of bleeding during anticoagulant therapy, the mean daily incidences of fatal, major, and major or minor bleeding during heparin therapy were 0.05%, 0.8%, and 2.0% respectively; the mean annual incidences of fatal, major, and major or minor bleeding during warfarin therapy were 0.6%, 3.0%, and 9.6% respectively.[10] The most common site of bleeding was the gastrointestinal tract.

Several factors increase the risk: a prolonged prothrombin time, concomitant aspirin consumption, advanced age, previous gastrointestinal bleeding, atrial fibrillation, and concomitant medical diseases such as renal failure and anemia.[11]

FIGURE 1



Admission criteria and recommended stay in hospital for patients with bleeding peptic ulcers.

TABLE 1

TREATING *HELICOBACTER PYLORI* INFECTION IN PATIENTS WITH BLEEDING PEPTIC ULCERS

1. **Document *H pylori* infection**
   - Urease testing or histologic analysis (at index endoscopy), or
   - Urea breath test (before discharge)
2. **Give anti-*H pylori* therapy**
   - Triple therapy with proton pump inhibitor (2 weeks)
     - Bismuth subsalicylate, two tablets four times a day
     - Tetracycline or amoxicillin 500 mg four times a day
     - Metronidazole 250 mg three times a day
     - Omeprazole 20 or 40 mg a day
   - Alternative regimen: omeprazole plus two antibiotics (amoxicillin and metronidazole, or clarithromycin and tinadazole)
3. **Confirm eradication**
   - (Currently not routine; should be standard when breath tests become available)
   - Assess 4 weeks after cessation of antimicrobial therapy
4. **Give maintenance therapy**
   - (Consider on a case-by-case basis)
   - H2 receptor antagonists

Diagnosing and treating bleeding during anticoagulant therapy

In about half of cases of gastrointestinal bleeding during oral anticoagulant therapy, the site is the stomach or duodenum, usually a peptic ulcer.[12–14] In about one fourth of the cases the site is the colon, and in a few it is the small bowel. In the rest of the cases the site is not determined. Some patients therefore require investigation of both the upper and lower gastrointestinal tract before the clinician can be confident of the bleeding source. This is best done endoscopically, after stabilization, during a single session if possible.

Until recently the safety and efficacy of endoscopic hemostasis had not been assessed in patients taking anticoagulants. Our experience suggests that the outcomes of hemostatic therapy in patients receiving anticoagulant therapy are similar to those in patients with normal coagulation.[14] We give fresh frozen plasma to partially correct the international normalized ratio to 1.5 to 2.5 in anticoagulated patients before endoscopic treatment (injection or heater probe).

After endoscopic treatment, continued anticoagulation is usually safe, starting 5 days after bleeding has been stopped.[14] However, caution is advised, and a less-intense anticoagulant regimen should be prescribed to balance the risks of rebleeding against those of thromboembolism. It is wise to give long-term drug treatment with H2 receptor antagonists indefinitely.

DRUG THERAPY

Gastric acid secretion, *Helicobacter pylori*, and the use of nonsteroidal anti-inflammatory drugs (NSAIDs) should be addressed when drug therapy is being considered in patients with bleeding peptic ulcers.

H pylori and bleeding ulcers

The prevalence of *H pylori* in patients with symptomatic duodenal ulcers (about 95%) or gastric ulcers (70% to 80%) is much higher than in the general population. Several studies demonstrated that eradicating *H pylori* markedly reduces the recurrence of peptic ulcers.[15,16] However, patients with bleeding ulcers appear to have a 15% to 20% lower rate of *H pylori* infection than do patients with nonbleeding ulcers.[17–19]

Thus, one cannot assume that almost all patients with duodenal ulcer bleeding are *H pylori*-positive. Preliminary evidence does suggest, however, that eradicating *H pylori* in patients with bleeding ulcers decreases the rate of recurrence.[20,21]

***Documenting* H pylori *infection*.** First, *H pylori* infection must be documented (**TABLE 1**). Urease testing and histologic examination of gastric biopsy samples are appropriate diagnostic techniques, because all patients with bleeding peptic ulcers should undergo endoscopy, during which a biopsy sample can be easily obtained. These tests have a sensitivity and specificity greater than 90%. Urea breath tests, which are now becoming available, will be another option and could be performed when the patient is more stable. Although serologic testing is an excellent noninvasive means of

detecting *H pylori*, it is unnecessary if the patient undergoes endoscopy and biopsy.

Treating H pylori infection. If *H pylori* infection is present, it should be eradicated. Consideration of the various therapeutic regimens should take into account their efficacy, cost, and side effects, and how well patients comply with them.[22]

"Triple therapy" is the gold standard.[22] It consists of 2 weeks of therapy with two bismuth subsalicylate tablets four times a day, tetracycline 500 mg four times a day, and metronidazole 250 mg three times a day with food. This regimen eradicates *H pylori* in approximately 90% of cases.[22] Amoxicillin 500 mg four times a day can be substituted for tetracycline with only a slight loss in efficacy (eradication rate > 80%).[22]

A National Institutes of Health consensus report advises also giving a drug to suppress gastric acid secretion.[22] Studies have shown that giving a proton pump inhibitor increases the efficacy of triple therapy and lessens its side effects.[23–25]

Although dual therapy with omeprazole and amoxicillin was initially reported to achieve eradication rates of more than 80%, pooled data from 36 studies showed an average cure rate of only 60%, and this regimen probably should no longer be used.[26] Preliminary data on shorter regimens consisting of a proton pump inhibitor plus two antibiotics (eg, omeprazole, amoxicillin, and metronidazole[27]; or omeprazole, clarithromycin, and tinidazole[28]) are encouraging but need to be compared to triple therapy.

Confirming H pylori eradication. Because eradication rates are not 100%, clinicians should confirm that *H pylori* has been eradicated in patients with bleeding ulcers, generally 4 weeks after cessation of antimicrobial therapy. This is not yet routinely done in clinical practice, as there is no readily available, inexpensive, and accurate noninvasive test. When urea breath tests become commercially available, they will become the most cost-effective way to confirm eradication. If *H pylori* persists (because of failure of therapy, noncompliance, or reinfection), another regimen should be tried.

Although it seems logical to stop treatment if eradication is confirmed, there is understandable caution among clinicians, as we do not yet have good long-term data as to whether to give maintenance therapy with H2 blockers or whether eradication of *H pylori* normalizes the subsequent risk of bleeding. A recent review suggested that antisecretory therapy be continued after *H pylori* eradication in elderly, frail patients with severe concomitant illness, in whom another episode of bleeding might be catastrophic.[29]

TABLE 2

TREATMENT OPTIONS FOR PATIENTS WITH BLEEDING PEPTIC ULCERS WHO TAKE NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

1. **Discontinue NSAIDs until ulcer heals**
2. **Check *Helicobacter pylori* status**
   - If positive, treat *H pylori* (see Table 1)
   - If negative, give H2 blockers or omeprazole for at least 8 weeks
3. **Check ulcer healing in gastric ulcer endoscopically**
4. **Give prophylactic therapy in patients in whom NSAID must be continued**
   - Misoprostil 100–200 µg four times a day
     (for gastric or duodenal ulcers; side effects limit its use)
   - H2 receptor blockers
     (eg, ranitidine 150 mg twice a day; for duodenal ulcers only)
   - Omeprazole (20 mg/day)
     (for gastric or duodenal ulcers)

NSAIDs and ulcer risk

NSAID use is linked to peptic ulcer complications (bleeding and perforation). Several factors affect the risk of adverse gastrointestinal effects during treatment with NSAIDs: the patient's age and hepatorenal function; the NSAID used and its dosage, route of administration, and duration of treatment; and concomitant use of aspirin, anticoagulants, or corticosteroids.[30]

If a patient presenting with a bleeding peptic ulcer has been taking NSAIDs, all NSAIDs should be stopped, if possible, until the ulcer has healed (**TABLE 2**). If *H pylori* is present as well, I recommend eradicating it. Traditionally, H2 blockers have been used to heal NSAID-related ulcers, but there is some evidence that omeprazole may be superior.[31] Regardless of which drug is used, endoscopy should be performed at the conclusion of therapy (at least 8 weeks) to confirm the ulcer has healed and, in the case of gastric ulcers, to exclude cancer.

If a patient must continue taking an NSAID, for example, for rheumatoid arthritis or osteoarthritis, most clinicians would prescribe some form of prophylaxis, particularly in an elderly patient with multiple medical illnesses who has had major bleeding. Misoprostol significantly decreases the devel-

opment of new gastric and duodenal ulcers in patients taking NSAIDs, but its tendency to cause diarrhea limits its use. H2 receptor antagonists are effective in preventing duodenal but not gastric ulcers. Omeprazole may prevent both gastric and duodenal ulcers caused by NSAIDs, although there is not enough evidence yet to prove this. However, none of these drugs have been shown to prevent ulcer bleeding or perforation in patients who continue to take NSAIDs. ■

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