Recommendations on the management of patients with upper gastrointestinal bleeding (UGIB) are needed to assist physicians in making informed decisions regarding optimal care of patients. In addition, national data has suggested that previous recommendations on the management of upper GI bleeding may lead to improved patient outcomes. This issue of CLIPS briefly summarizes an article that provides an update to the recommendations for the management of patients with an acute nonvariceal upper gastrointestinal bleed based on a review of the 2003 consensus guidelines and subsequent published literature. If you need further information, please contact the Samford University Drug Information Service at (205) 726-2659.


Epidemiology of Upper Gastrointestinal Bleeding
- The reported incidence of upper gastrointestinal bleeding (UGIB) ranges from 48 to 160 cases per 100,000 adults per year; the mortality incidence is 10% to 14%.
- Upper gastrointestinal bleeding also presents a large economic burden with the mean length of hospital stays between 2.7 and 4.4 days and costs between $3402 and $5632 in 2004.
- From 1998 to 2006, mortality from UGIB decreased by 23% in the United States.

Preendoscopy Recommendations
- Prognostic scales are suggested for early stratification of patients into low and high risk groups for rebleeding and mortality. Morbidity and mortality can be minimized if high risk patients are identified early.
- Early identification of high-risk patients (age >65 years, shock, poor overall health status, etc.) allows appropriate intervention, which minimizes morbidity and mortality.
- In patients receiving anticoagulants (e.g. warfarin), correction of coagulopathy is recommended, but should not delay endoscopy unless the patient’s INR is supratherapeutic.
- Promotility agents should not be used regularly before endoscopy to increase the diagnostic yield, but may be beneficial in patients who are suspected to have large amounts of blood or clots in their upper GI tract.
- Pre-endoscopic proton pump inhibitor (PPI) therapy (e.g. pantoprazole) may be useful to downstage the endoscopic lesion and reduce the need for endoscopic intervention, but should not cause a delay in endoscopy.

Endoscopic Management Recommendations
- Early endoscopy (2 to 24 hours after initial presentation) is recommended for most patients with acute upper GI bleeding.
- The role of endoscopic therapy for ulcers with clots is controversial. Intensive PPI therapy alone may be sufficient although endoscopy can be considered.
- Epinephrine injection alone does not provide maximal efficacy and is not recommended. Clips, thermocoagulation, or sclerosant injection can be used alone or in combination with epinephrine injection in patients with high risk lesions.
- The routine use of second-look endoscopy is not recommended.
- While older data suggests a benefit with second-look endoscopy, those trials did not use current management strategies associated with a decreased risk for rebleeding. In addition, cost-effectiveness data does not support the use of routine second-look endoscopy.
Pharmacologic Recommendations

- Histamine$_2$ receptor antagonists (e.g., famotidine, ranitidine, cimetidine, etc.) for patients with acute ulcer bleeding are not recommended.
- Somatostatin and octreotide are not routinely recommended for patients with acute upper GI bleeding.
- An intravenous bolus followed by continuous infusion PPI therapy is recommended to reduce rebleeding and mortality in high risk patients who have undergone successful endoscopic therapy.
- Recent data has linked hospital PPI use with *Clostridium difficile* infection; however, investigators felt the benefits of PPI therapy in patients with an UGIB outweigh the risk.
- Patients should be discharged with a prescription for a single daily dose oral PPI. The duration of treatment is dependent on the underlying etiology. Most randomized controlled clinical trials assessing postendoscopic PPI therapy, recommend a prescription for a once daily PPI starting 72 hours after endoscopic hemostasis.
- PPI therapy in the community is associated with potential adverse effects including *C. difficile* infection, pneumonia, and osteoporosis-related fracture. However, the benefits of PPI therapy for ulcer healing outweigh the risks; caution is warranted with long-term use.

Nonendoscopic and Nonpharmacologic In-Hospital Management Recommendations

- Most high-risk patients who have undergone endoscopic hemostasis should be hospitalized for 72 hours or more thereafter.
- Patients with bleeding peptic ulcers should be tested for *Helicobacter pylori* and receive eradication therapy if present. After completion of therapy, eradication of *H. pylori* will need to be confirmed.
- One meta-analysis indicated that PPI therapy alone was not as effective as the eradication of *H. pylori* in the prevention of rebleeding in peptic ulcer disease.
- *H. pylori* diagnostic tests that are reported as negative in the acute setting should be repeated.

Recommendations for Aspirin and NSAIDS at Discharge

- Patients requiring an NSAID (e.g., ibuprofen, naproxen, etc.) after acute upper GI bleeding should be aware that treatment with an NSAID plus PPI or a cyclooxygenase-2 (COX-2) inhibitor is still associated with an important risk for rebleeding.
- Treatment with a PPI plus a COX-2 inhibitor is recommended to reduce the risk of recurrent bleeding over a COX-2 inhibitor alone in patients requiring an NSAID after an acute UGIB.
- Two meta-analyses, conducted by Kearney et al and Rostom et al, have demonstrated an increased risk for serious cardiovascular events associated with COX-2 inhibitors compared with placebo. Therefore, optimal long-term NSAID therapy considers both gastrointestinal and cardiovascular risks.
- In patients requiring low dose aspirin (ASA) for cardiovascular protection and develop an acute bleed, ASA therapy should be reinitiated as soon as the risk for a cardiovascular complication outweighs the risk for bleeding.
- Results of one randomized clinical trial (RCT) included 156 patients with an ASA-induced ulcer bleed that underwent endoscopic therapy, reintroduced ASA immediately in the presence of oral and intravenous PPI therapy, and found a 2-fold increase in risk of recurrent bleeding. However, discontinuation of ASA therapy was associated with a significantly increased 8-week mortality rate.
- Another RCT reported no cases of rebleeding in patients with ASA-associated endoscopic ulcers who were treated with a PPI and restarted ASA or clopidogrel therapy within 1 day of endoscopy.
- Clopidogrel alone has a higher risk for rebleeding than ASA combined with a PPI in patients with a previous acute ulcer bleed requiring cardiovascular protection.
- Physicians should be aware of the interaction between PPIs and clopidogrel. PPIs may decrease the platelet inhibitory effect of clopidogrel through competing with clopidogrel for the cytochrome P450 enzyme CYP2C19 which is required to convert clopidogrel to its active metabolite.

Future Directions

- Even though many advances have been made in the area of management of upper GI bleeding, more data is still needed in many areas.
- As new data becomes available, these guidelines are anticipated to be updated.

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