Non-Variceal Upper Gastrointestinal Bleeding

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Acute Upper GI Bleeding: A Lethal Disease

Outcomes include
- Death
- Cardiac Arrest
- MI
- CVA
- Injury (E.G. Fx, Head)
- Seizures
- Surgery or angiography
- Rebleeding

ASA-associated DU eroding into artery
General Approach to the patient with Acute Upper GI Bleeding

• Guiding Principles
  – Restoration and/or maintenance of hemodynamic stability
    • Blood products if needed (Maintain Hgb >7)
  – Nasogastric lavage (varices are NOT a contraindication)
  – Antisecretory medications
  – Endoscopy with hemostasis (timing varies)
  – Surgery if necessary
Symptoms and Signs

Upper GI Bleed

- Hematemesis
- Melena/hematochezia
- Lightheadedness/Syncope
Physical Exam

- Vital signs: numbers and character
- Mucus membranes
- Stigmata of cirrhosis
- Digital rectal exam (DRE)
- Skin
- Mental status
Etiology of Upper GI Bleeding (UGIB): Changing Epidemiology

- **Peptic Ulcer Disease**: 21%
  - Gastric ulcer
  - Varices
  - Mallory-Weiss tear
  - Esophagitis
  - Erosive duodenitis
  - Neoplasm
  - Miscellaneous
  - Mucosal erosive disease
  - Duodenal ulcers
  - Gastric erosions

- **Varices**: 21%

**UCLA CURE Data**

- No diagnosis or >1 type of lesion: 11%
- Ulcers: 59%
- Gastroesophageal varices: 33%
- Other: 39%

- 1963–1992 (n = 945)
- 2000–2008 (n = 300)

**References**

- Boonponmanee S, Fleischer DE, and Benjamin SB *et al*; GI Endoscopy, 2004
- Jutabha R and Jensen D; UpToDate, 2013
## Medical Clues on Etiology of UGIB

<table>
<thead>
<tr>
<th>Bleeding etiology</th>
<th>Historical clues</th>
</tr>
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<tbody>
<tr>
<td>Mallory-Weiss tear</td>
<td>Emesis before hematemesis, alcoholism</td>
</tr>
<tr>
<td>Esophageal ulcer</td>
<td>Odynophagia, GERD, esophagotoxic pill ingestion</td>
</tr>
<tr>
<td>Peptic ulcer</td>
<td>Epigastric/RUQ pain, NSAID or aspirin use</td>
</tr>
<tr>
<td>Stress gastritis</td>
<td>Patient in an ICU, gastrointestinal bleeding occurring</td>
</tr>
<tr>
<td></td>
<td>after admission, respiratory failure, multiorgan failure</td>
</tr>
<tr>
<td>Varices, portal gastropathy</td>
<td>Alcoholism, cirrhosis</td>
</tr>
<tr>
<td>Gastric antral vascular ectasia</td>
<td>Renal failure, cirrhosis</td>
</tr>
<tr>
<td>Malignancy</td>
<td>Recent involuntary weight loss, dysphagia, cachexia, early satiety</td>
</tr>
<tr>
<td>Angiodysplasia</td>
<td>Chronic renal failure, hereditary hemorrhagic telangiectasia</td>
</tr>
<tr>
<td>Aortoenteric fistula</td>
<td>Known aortic aneurysm, prior abdominal aortic aneurysm repair</td>
</tr>
</tbody>
</table>

*Abbreviations:* GERD, gastroesophageal reflux disease; NSAID, nonsteroidal anti-inflammatory drug; RUQ, right upper quadrant.
GI Bleed: Prognostic Factors

- Initial assessment of an acute upper GI bleed can predict risk of mortality and complications:
  - Age >60 years
  - Transfusion requirement of >6 units of blood
  - Shock
  - Presence of comorbidity (hepatic, renal, pulmonary disease, cancer, CHF)
  - Ongoing bleeding
  - Low systolic BP
  - Elevated INR
  - Erratic mental status
  - Major stigmata of recent hemorrhage

Management of Acute GI Bleeding

Initial Management
- IV Access (2 Large bore IV)
- Hemodynamic Assessment
- CBC, PT/PTT; INR, LFTs, electrolytes/creatinine
- Type and Cross
- Resuscitation Measures
- NPO

Assess Initial Risk
- Age >60 years
- Comorbidity
- Low systolic blood pressure
- Shock
- Ongoing bleed
- Prolonged PT
- Erratic mental status

Endoscopy ± Hemostasis

High Risk
- ICU/Surgical consult

Low Risk
- Med./Surg. Ward

Management of Acute GI Bleeding (cont’d)

Endoscopy ± Hemostasis

Evaluate Risk for Rebleed

High Risk

- active bleed, adherent clot
- visible vessel

Therapeutic Endoscopy
- IV PPI
- ICU
- Surgical Consult

Low Risk

- clean base, flat spot

Treat Underlying Ulcer
- Oral PPI
- Ward (or even D/C)

Resuscitation - I

- Initiate ABC’s of Emergency Care

- Establish IV access:
  - 2 large bores (ideally at least 18-gauge peripheral IVs)
  - in MICU, may place triple-lumen or Cordis catheter

- Replace intravascular volume
  - if hypotensive and/or orthostatic, give NS/LR boluses
  - if anemic (Hgb ≤7 g/dL), give PRBCs
  - may need FFP (for coagulopathy) and/or platelets (for thrombocytopenia/<50K or dysfunction from chronic antiplatelet agents usage) if massive GI bleed
Resuscitation - II

Transfusion Strategies for Acute Upper Gastrointestinal Bleeding

Càndid Villanueva, M.D., Alan Colomo, M.D., Alba Bosch, M.D., Mar Concepción, M.D., Virginia Hernández-Gea, M.D., Carles Aracil, M.D., Isabel Graupera, M.D., María Poca, M.D., Cristina Álvarez-Urturi, M.D., Jordi Gordillo, M.D., Carlos Guarner-Arjente, M.D., Miquel Santaló, M.D., Eduardo Muñiz, M.D., and Carlos Guarner, M.D.


In summary, we found that a restrictive transfusion strategy, as compared with a liberal transfusion strategy, improved the outcomes among patients with acute upper gastrointestinal bleeding. The risk of further bleeding, the need for rescue therapy, and the rate of complications were all significantly reduced, and the rate of survival was increased, with the restrictive transfusion strategy. Our results suggest that in patients with acute gastrointestinal bleeding, a strategy of not performing transfusion until the hemoglobin concentration falls below 7 g per deciliter is a safe and effective approach.
Resuscitation - III

Key Points
Keep Hb ≤7 g/dL for low-risk patients
Keep Hb ≤10 g/dL for high-risk patients

Villanueva C and Guarner C et al; NEJM, 2013
Pre-endoscopy Management - I

- Nasogastric intubation and NG lavage (even if varices may be present)
- No role of occult blood testing of NG aspirate (or frankly bloody stool)
- Interpretation of aspirate:
  - bright red, clots = active UGIB
  - coffee grounds = slow bleeding, may have stopped, localizes to upper GI source
  - clear = indeterminate (NOT a guarantee that the bleeding has stopped); ~18% of patients with UGIB source
  - bilious = bleeding has stopped; ~18% of patients with UGIB source
- Contraindications
  - Facial trauma, nasal bone fracture
  - Known esophageal abnormalities (strictures, diverticuli)
  - Ingestion of caustic substances, esophageal burns
  - In general, esophageal varices are NOT a contraindication to NG tube placement
Pre-endoscopy Management - II

- IV Erythromycin 250 mg (or azithro) bolus 30-60 min before EGD
- Initiate PPI drip: 80 mg bolus followed by 8 mg/h infusion
- No role for H$_2$-receptor antagonists
- Initiate Octreotide drip (if suspecting variceal bleeding): 50 µg bolus followed by 50 µg/h infusion
  - Initiate Somatostatin drip (if octreotide not available): 250 µg bolus followed by 500 µg/h infusion
- Consider EGD within 6-12 h (or at least before 24 h)
Acute UGIB: Differential Diagnosis

- Peptic ulcer disease
  - Gastric ulcer
  - Duodenal ulcer
- Mallory-Weiss tear
- Portal hypertension
  - Esophagogastric varices
  - Gastropathy
- Esophagitis
- Dieulafoy’s lesion
- Vascular anomalies
- Hemobilia
- Hemorrhagic gastropathy
- Aortoenteric fistula
- Neoplasms
  - Gastric cancer
  - Kaposi’s sarcoma
Bleeding Peptic Ulcer

- 250,000-300,000 admissions / year
- $2.5 Billion in costs
- Re-bleeding rate after hemostasis about 20%
- Mortality remains 5 – 14%
Gastric ulcers presenting with acute upper GI bleeding

- Spurt
- Visible vessel
- Adherent clot
- Spots Dots
Gastro-Duodenal Ulcers - Various Stigmata
GI Bleed: Risk of Rebleeding

<table>
<thead>
<tr>
<th>Clean Base</th>
<th>Flat Spot</th>
<th>Adherent Clot</th>
<th>NBVV*</th>
<th>Active Bleed</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.jpg" alt="Image" /></td>
<td><img src="image2.jpg" alt="Image" /></td>
<td><img src="image3.jpg" alt="Image" /></td>
<td><img src="image4.jpg" alt="Image" /></td>
<td><img src="image5.jpg" alt="Image" /></td>
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<table>
<thead>
<tr>
<th>Prevalence (%)</th>
<th>42</th>
<th>20</th>
<th>17</th>
<th>17</th>
<th>18</th>
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</thead>
<tbody>
<tr>
<td>Rebleeding risk (%)</td>
<td>5</td>
<td>10</td>
<td>22 †</td>
<td>43 †</td>
<td>55†</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>2</td>
<td>3</td>
<td>7</td>
<td>7</td>
<td>11</td>
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</tbody>
</table>

*Nonbleeding visible vessel. † Endoscopic therapy recommended.

Medical Therapy for Non-Variceal UGI Bleeding

- Proton pump inhibitors (PPIs)
  - IV
  - PO
- Histamine-2 receptor antagonists
  - Minor benefit for GUs, ineffective for DUs
- Somatostatin or its analog, octreotide
  - Option when cause of bleeding is unclear prior to endoscopy (PPIs favored for PUD)

Levine et al, Aliment Pharmacol Ther 2002; 16: 1137

*P=0.02; †P=0.17; ‡P=0.98
IV PPI Therapy Alone is Insufficient

- **IV Omeprazole + Endo Rx**
- **IV Omeprazole**

*P < 0.05.*

Endoscopic hemostasis: Efficacy in nonvariceal UGI bleeding

• 30 RCTs reviewed
• Almost all patients had bleeding ulcers
• Thermal, laser and injection therapy all decreased
  - re-bleeding (OR 0.38)
  - surgery (OR 0.36)
  - mortality (OR 0.55)

in patients with active bleeding or visible vessels, but not those with flat spots or adherent clot.

Cook et al. Gastroenterology 1992;102:139
Randomized Placebo-Controlled Comparison of IV PPI in Bleeding Peptic Ulcer

• All patients had actively bleeding vessel or a non-bleeding visible vessel (NBVV) and received endoscopic therapy

![Bar chart showing re-bleeding in 3 days, re-bleeding in 30 days, surgery, and 30-day mortality percentages.]

- Omeprazole 80 mg I.V. bolus + 8 mg/hr infusion for 72 hours (n = 120)
- Placebo by I.V. infusion for 72 hours (n = 120)

* * p < 0.001 vs. placebo

Oral PPIs as an Adjunct to Endoscopic Therapy

- Treatment reduced rates of rebleeding (significantly) as well as surgery and mortality (not significantly)

*P < 0.05

Management of UGIB: Non-Variceal

- Syncope, shock, severe comorbidity, hematochezia, bright red blood per nasogastric tube, or inpatient start of upper gastrointestinal bleed
  - Yes: Resuscitation and treatment in an intensive care unit
  - No: Evaluate and resuscitate in step-down unit or ward

- Urgent upper endoscopy

Arterial bleed, nonbleeding visible vessel, or clot:
- Combination endoscopic hemostasis
- IV bolus and infusion PPI for 72 hours

Oozing without other stigmata:
- Hemoclip or thermal coagulation hemostasis
- Oral PPI twice daily

Flat spot or clean base ulcer:
- Oral PPI and early discharge

Discharge on oral PPI twice daily
Contraindications of Urgent Endoscopy in Acute UGIB

- When the risks to patient health or life are judged to outweigh the most favorable benefits of the procedure.

- When adequate patient cooperation or consent cannot be obtained.

- When a perforated viscus is known or suspected.
**Management of Patients with Ulcer Bleeding: ACG Practice Guidelines**

*Lists 30 recommendations* for pre and post endoscopic management of patients with ulcer bleeding including follow up to prevent recurrent bleeding

<table>
<thead>
<tr>
<th><strong>H. pylori</strong></th>
<th><strong>H. pylori Therapy</strong></th>
<th><strong>Document Cure</strong></th>
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<tbody>
<tr>
<td></td>
<td>Stop PPI/H2RA</td>
<td></td>
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<table>
<thead>
<tr>
<th><strong>NSAID</strong></th>
<th><strong>Stop NSAID</strong></th>
<th><strong>If NSAID required, use coxib+PPI</strong></th>
</tr>
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<table>
<thead>
<tr>
<th><strong>Low-dose aspirin</strong></th>
<th><strong>1. Primary CV Prevention</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Do not resume aspirin in most patients</td>
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</table>

| | **2. Secondary CV Prevention** |
| | Resume aspirin soon after hemostasis (e.g. 1-7 days) in most patients and start PPI |

<table>
<thead>
<tr>
<th><strong>Idiopathic</strong></th>
<th><strong>Maintenance PPI</strong></th>
</tr>
</thead>
</table>

Adapted from: Laine L and Jensen D. Am J Gastroenterol 2012, 107:345-60
Erosive Esophagitis
Mallory Weiss tears

- Painless upper GI bleeding due to mucosal tear(s) near EG junction, usually on the gastric side.
- Contrasted with intramural hematoma and esophageal rupture (Boorhaave’s)

Photographs Courtesy Brian Fennerty, MD
Upper GI Cancers: Esophageal and Gastric

Esophageal Adenocarcinoma

Gastric Adenocarcinoma
Other Causes of UGIB

Vascular Ectasia  
Hemobilia  
Dieulafoy’s lesions
Vascular lesions

- Vascular ectasias
  - angiodysplasia, telangiectasia

- Gastric Antral Vascular Ectasia ("Watermelon stomach")

- Dieulafoy’s lesion

- Portal hypertensive gastropathy

- Cameron’s lesions/erosions
Duodenal Angioectasia

Acquired
- aging
- portosystemic shunts
- CREST
- radiation

Hereditary
- lips
- nose

Photograph Courtesy Brian Fennerty, MD
Gastric Antral Vascular Ectasia (GAVE)
Before, during, and after Endoscopic Therapy

Photographs Courtesy Brian Fennerty, MD
Dieulafoy’s Lesion

• Abnormally large submucosal artery
• Proximal stomach (duodenum, elsewhere)
• Intermittent, painless massive bleeding
• Often difficult to identify endoscopically
• Endoscopic therapy (epinephrine, polidocanol) ultimately effective for hemostasis in 96%
• Long-term hemostasis in 85-90%
• Late (post-discharge) bleeding after successful endoscopic hemostasis uncommon
  – 5% or less after 2 years follow-up

Baettig et al Gut 1993; 34:1418
Portal Hypertensive Gastropathy
Cameron’s Lesions

- Linear erosions in a hiatus hernia
- Usually sliding hernia
- Chronic or acute bleeding
- No abdominal pain, but may have reflux symptoms
- RX: Iron ± PPI

Photographs Courtesy Brian Fennerty, MD
Stress Ulcer Bleeding

- Patients admitted to an ICU demonstrate endoscopic evidence of GI damage within 24 hours
- Historically, GI bleeding occurred in approximately 15% of seriously ill ICU patients without prophylactic therapy
  - Much lower now with improved ICU care
  - Current incidence of clinically significantly bleeding is 1.5% or less
### Risk Factors for Clinically Important UGI Bleeding in ICU Patients

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Odds Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory failure</td>
<td>15.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>4.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypotension</td>
<td>3.7</td>
<td>0.08</td>
</tr>
<tr>
<td>Sepsis</td>
<td>2.0</td>
<td>0.17</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>1.6</td>
<td>0.27</td>
</tr>
<tr>
<td>Renal failure</td>
<td>1.6</td>
<td>0.26</td>
</tr>
<tr>
<td>Glucocorticoid administration</td>
<td>1.5</td>
<td>0.26</td>
</tr>
<tr>
<td>Organ transplantation</td>
<td>1.5</td>
<td>0.42</td>
</tr>
<tr>
<td>Anti-coagulant therapy</td>
<td>1.1</td>
<td>0.88</td>
</tr>
<tr>
<td>Enteral feeding</td>
<td>1.0</td>
<td>0.99</td>
</tr>
</tbody>
</table>

N=2252 patients

### Gastric pH and Clinical Effect

<table>
<thead>
<tr>
<th>Gastric pH</th>
<th>Clinical Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;4</td>
<td>Pepsin inactivated</td>
</tr>
<tr>
<td>&gt;6</td>
<td>Functional coagulation and platelet aggregation</td>
</tr>
<tr>
<td>&gt;7</td>
<td>Pepsin denatured</td>
</tr>
</tbody>
</table>

**Stress Ulcer Prophylaxis**

**Reduction of rebleeding after endoscopic intervention**

Stress Ulcer Prophylaxis: H₂RA vs PPI

359 mechanically-ventilated ICU patients with 1 additional risk factor.

UGI bleeding rate: 6.8% (cimetidine) vs. 4.5% (omeprazole) ⇒ noninferiority of PPI

*2 consecutive aspirates with pH ≤ 4
Adapted from: Conrad et al, Crit Care Med 2005; 33: 760
An 83-year-old woman presents with several episodes of hematemesis. Initial evaluation reveals a BP of 95/60 with orthostatic changes and maroon colored stools. There are no stigmata of chronic liver disease. Following resuscitation and admission to the ICU, she undergoes urgent upper endoscopy.

Which of the following endoscopic findings requires endoscopic intervention and intravenous PPI therapy?
Which of the following endoscopic findings is associated with the greatest risk of rebleeding after endoscopic therapy?
Answer 1

Non-bleeding visible vessel
Question 2

A 58 yr old male with coronary artery disease and a prior MI on ASA and a beta-blocker presented overnight to the ER with an upper GI bleed. Nasogastric aspiration revealed bright red blood. He was resuscitated with IV saline and an IV PPI drip was started. You are consulted for an urgent upper endoscopy the next morning. His Hgb is 12.2 mg/dl, platelet count is 150k, BUN is 20 mg/dl with a creatinine of 0.8 mg/dl and his INR is 1.1. EGD reveals a clean-based ulcer of the antrum.

Which one of the following statements regarding the pre-endoscopic administration of IV PPI therapy is correct:
Question 2 (continued)

Which one of the following statements regarding the pre-endoscopic administration of IV PPI therapy is correct:

a) It has been associated with a reduced likelihood of re-bleeding in patients with high risk stigmata at endoscopy
b) It reduces the need for endoscopic intervention at endoscopy
c) It improves visibility at endoscopy
d) It is only of benefit prior to endoscopy in patients with variceal bleeding
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a) It has been associated with a reduced likelihood of re-bleeding in patients with high risk stigmata at endoscopy
b) It reduces the need for endoscopic intervention at endoscopy
c) It improves visibility at endoscopy
d) It is only of benefit prior to endoscopy in patients with variceal bleeding
Question 3

A 76 year old man on 81 mg ASA for secondary prophylaxis after an MI 2 years ago (also taking a B-blocker and a lipid lowering agent) presents with a hemodynamically significant upper GI bleed. His ASA is held and he undergoes urgent EGD in the presence of an IV PPI continuous infusion to reveal an actively bleeding gastric ulcer. Hemostasis is achieved with epinephrine injection and placement of two clips.

Which of the following statements regarding his ASA therapy is correct?
Which of the following statements regarding his ASA therapy is correct?

a) His ASA therapy should not be restarted
b) His ASA should be restarted after repeat EGD documents healing of the ulcer in 6-8 weeks time
c) His ASA should be restarted before discharge
d) He should be switched to coumadin instead of ASA
Answer 3

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