Management of Acute Non-Variceal Upper GI Bleed

Christie J. Blanton, M.D.
Tulane Gastroenterology
Pre-Endoscopy

• Initial Assessment
• Prokinetics
• NG Aspirate and Lavage
• PPI Initiation
• Timing of Endoscopy
Initial Assessment

- Determine urgent vs. delayed intervention
- ACG Recommendations

**Initial assessment and risk stratification**

1. Hemodynamic status should be assessed immediately upon presentation and resuscitative measures begun as needed (Strong recommendation).

2. Blood transfusions should target hemoglobin $\geq 7$ g/dl, with higher hemoglobins targeted in patients with clinical evidence of intravascular volume depletion or comorbidities, such as coronary artery disease (Conditional recommendation).

3. Risk assessment should be performed to stratify patients into higher and lower risk categories and may assist in initial decisions such as timing of endoscopy, time of discharge, and level of care (Conditional recommendation).

4. Discharge from the emergency department without inpatient endoscopy may be considered in patients with urea nitrogen $< 18.2$ mg/dl; hemoglobin $\geq 13.0$ g/dl for men (12.0 g/dl for women), systolic blood pressure $\geq 110$ mmHg; pulse $< 100$ beats/min; and absence of melena, syncope, cardiac failure, and liver disease, as they have $< 1\%$ chance of requiring intervention (Conditional recommendation).
**Initial Assessment**

**Rockall 1996 Gut**
- Clinical
  - Age
  - Blood pressure (and heart rate)
  - Comorbidities
    - Cardiac, liver, cancer
- Post endoscopy
  - Diagnosis
  - Evidence of bleeding

<table>
<thead>
<tr>
<th></th>
<th>Rebleed</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2</td>
<td>&lt;5%</td>
<td>~ 0%</td>
</tr>
<tr>
<td>&gt;8</td>
<td>41%</td>
<td>41%</td>
</tr>
</tbody>
</table>

**Blatchford 2000 Lancet**
- BUN
- Hemoglobin
- Blood pressure
- Heart rate
- Presence of
  - Melena
  - Syncope
  - Liver disease
  - Cardiac disease
- Score of 0 is low risk, 1 or above is high risk for need for intervention
Initial Assessment

- Prospective, multicenter validation study
  - 123 patients with Blatchford score of 0
    - 84 not admitted
    - 23 with outpatient scope
      - No ulcers, malignancies, or varices
    - 61 no scope, but did not require admission or die during the 6 month follow up
Prokinetics

• Erythromycin 250 mg intravenous
• Metoclopramide 10 mg intravenous
• ASGE Guidelines:
  – Routine use not recommended
  – May have higher diagnostic yield in patients with high probability of having fresh blood or clot in stomach
• ACG Guidelines:
  – Consider erythromycin, but not consistent in clinical studies
Prokinetics: Quality of Endoscopy

- Frossard et al 2002
- Prospective, double-blind, monocentric, randomized
- Erythromycin vs. placebo
- Primary end points
  - Endoscopic yield
  - Duration of endoscopy

Carbonell et al. also showed improved visualization, quality of EGD, and decrease of gastric clots but was Erythromycin + NG lavage vs. Placebo vs. NG lavage

Reglan used in two small studies, appeared to have same effect but not powered to show a significant difference
Nasogastric Aspirate and Lavage

**ASGE**
- Controversial
- Consider placement
- Presence of bright red blood can be useful in identifying high risk lesions
- Not as useful in coffee ground or other findings
- Absence in 15% of patients with active bleeding
- Associated Risks

**ACG**
- Nasogastric or orogastric lavage is not required for diagnosis, prognosis, visualization, or therapeuetic effect (conditional recommendation)
NG Aspirate: Predicting Lesions

Gastrointest Endosc 2004

- Retrospective Canadian study with 1,880 patients
- NG aspirate taken immediately prior to endoscopy

<table>
<thead>
<tr>
<th></th>
<th>Clear/bile</th>
<th>Coffee grounds</th>
<th>Bloody</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRL</td>
<td>14.7%</td>
<td>23%</td>
<td>45.4%*</td>
</tr>
<tr>
<td>Clot</td>
<td>1.5%</td>
<td>10.3%</td>
<td>12.3%</td>
</tr>
<tr>
<td>Other</td>
<td>83%</td>
<td>66%</td>
<td>42%</td>
</tr>
</tbody>
</table>

**Performance in predicting HRL**
- Bloody NG aspirate: Sn 48% Sp 75% OR 4.8
- Bloody + Coffee grounds: Sn 80% Sp 31% OR 2.8
- Clear NG predictive value 85% for LRL
NG Aspirate: Interpreting

- *Arch Intern Med* 1990

62 patients with upper GI bleed

Aspirate evaluated by the fellow for:
- Presence of bile
- Whether believed patient was actively bleeding
NG Aspirate: Timing of Endoscopy

*J Clin Gastroentrol* 1996

- Randomized, prospective
- N=325
- Early vs. Delayed Endoscopy
  - Grouped by NG aspirate
    - Clear
    - Coffee grounds
    - Bloody
- Bloody NG
  - Decreased transfusions
  - Shorter hospital stay

<table>
<thead>
<tr>
<th>Results</th>
<th>Patients with EE (n=53)</th>
<th>Patients with DE (n=54)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number with rebleeding after endoscopic therapy</td>
<td>3/0</td>
<td>3/2</td>
</tr>
<tr>
<td>Number with endoscopic therapy injection HP</td>
<td>18/5</td>
<td>12/11</td>
</tr>
<tr>
<td>Number with endoscopic therapy injection MPEG</td>
<td>6/3</td>
<td>6/5</td>
</tr>
<tr>
<td>Number with emergency operation</td>
<td>4/1</td>
<td>5/3</td>
</tr>
<tr>
<td>Number with rebleeding after endoscopic therapy</td>
<td>8/1</td>
<td>1/3</td>
</tr>
<tr>
<td>Number with endoscopic therapy injection HP</td>
<td>2/1</td>
<td>0/4</td>
</tr>
<tr>
<td>Blood transfusion after entry (ml)</td>
<td>431 ± 494/450 ± 465</td>
<td>397 ± 488/666 ± 549$^\text{a}$</td>
</tr>
<tr>
<td>Number of deaths due to bleeding</td>
<td>1/0</td>
<td>0/1</td>
</tr>
<tr>
<td>Number of deaths due to underlying illness</td>
<td>1/0</td>
<td>0/0</td>
</tr>
<tr>
<td>Days in hospital</td>
<td>4.7 ± 4.4/4 ± 3.5</td>
<td>4.2 ± 6/14.5 ± 10.8$^\text{a}$</td>
</tr>
</tbody>
</table>

HP, heater probe; MPEG, multipolar electrocoagulation.

$^\text{a}$ No statistically significant differences were observed between the two groups.

$^\text{a}$ p < 0.001 between patients with bloody aspirate in both groups.
NG Lavage: Quality of Endoscopy

**J Clin Gastroenterol 2004**

- Randomized, controlled
- N=39
- Hematemesis, >250 cc bloody or coffee grounds NGA
- Large volume NG lavage+EGD vs. EGD alone
- Fundus visualization improved
- No improvement in clinical outcomes
NG Lavage vs. Erythromycin

**Ann Emerg Med 2011**

- Prospective, randomized, multicenter
- N=253 with melena or hematemesis
- Erythromycin, NG lavage, or both
- Quality of endoscopy measured using Frossard scoring system
- No difference in groups

### Table 2. Endoscopic features and treatment in each group.*

<table>
<thead>
<tr>
<th>Endoscopic Features and Treatment</th>
<th>No. (%) or Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endoscopic score</td>
<td>ER (N=84)</td>
</tr>
<tr>
<td>Interval between onset of bleeding and endoscopy, h</td>
<td>5.3 (3, 12.5)</td>
</tr>
<tr>
<td><strong>Endoscopic findings</strong></td>
<td></td>
</tr>
<tr>
<td>Esophageal varices</td>
<td>25 (30)</td>
</tr>
<tr>
<td>Ulcer</td>
<td>36 (22)</td>
</tr>
<tr>
<td>Gastritis</td>
<td>8 (10)</td>
</tr>
<tr>
<td>Mallory-Weiss syndrome</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Other</td>
<td>11 (13)</td>
</tr>
<tr>
<td>Empty stomach</td>
<td>69 (84)</td>
</tr>
<tr>
<td>Hemostatic treatment</td>
<td>31 (38)</td>
</tr>
<tr>
<td>Ability to identify the source of bleeding</td>
<td>64 (78)</td>
</tr>
<tr>
<td>Duration of endoscopy (min)</td>
<td>10 (7, 16)</td>
</tr>
<tr>
<td>Need for a second endoscopy</td>
<td>14 (20)</td>
</tr>
</tbody>
</table>

*IQR*, Interquartile range.
*There were no significant differences between groups for any variable.*
**NG Aspirate: Mortality**

National ASGE Survey on Upper GI Bleeding II

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**Table 19.**
Association of nasogastric aspirate color on presentation with outcome.

<table>
<thead>
<tr>
<th>NG aspirate color</th>
<th>No. of patients with aspirate color</th>
<th>% mortality</th>
<th>% incidence of complications</th>
<th>% requiring &gt;5 units blood</th>
<th>% requiring surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear</td>
<td>234</td>
<td>6.0</td>
<td>8.6</td>
<td>12.0</td>
<td>9.8</td>
</tr>
<tr>
<td>Coffee grounds</td>
<td>650</td>
<td>9.7</td>
<td>10.6</td>
<td>26.0</td>
<td>12.9</td>
</tr>
<tr>
<td>Red blood</td>
<td>734</td>
<td>17.9</td>
<td>18.9</td>
<td>41.1</td>
<td>22.9</td>
</tr>
</tbody>
</table>

Trend p <0.001

Deviations p NS

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**Table 20.**
Association of stool color and nasogastric aspirate color with mortality in 1565 patients.

<table>
<thead>
<tr>
<th>NG aspirate color</th>
<th>Stool color</th>
<th>No. of patients with color combination</th>
<th>% mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clear</td>
<td>Brown</td>
<td>38</td>
<td>7.9</td>
</tr>
<tr>
<td></td>
<td>Black</td>
<td>149</td>
<td>4.7</td>
</tr>
<tr>
<td></td>
<td>Red</td>
<td>41</td>
<td>7.3</td>
</tr>
<tr>
<td>Coffee grounds</td>
<td>Brown</td>
<td>128</td>
<td>7.8</td>
</tr>
<tr>
<td></td>
<td>Black</td>
<td>412</td>
<td>8.3</td>
</tr>
<tr>
<td></td>
<td>Red</td>
<td>84</td>
<td>19.1</td>
</tr>
<tr>
<td>Red blood</td>
<td>Brown</td>
<td>160</td>
<td>19.4</td>
</tr>
<tr>
<td></td>
<td>Black</td>
<td>382</td>
<td>12.3</td>
</tr>
<tr>
<td></td>
<td>Red</td>
<td>171</td>
<td>28.7</td>
</tr>
</tbody>
</table>
Proton Pump Inhibitors Prior to Endoscopy

**ASGE**
- PPI therapy recommended for patients suspected of having acute UGIB

**ACG**
- Pre-endoscopic IV PPI drip may be considered to:
  - Decrease higher risk stigmata
  - Decrease need for endoscopic therapy
- If endoscopy will be delayed or not performed, reduce further bleeding
PPI for Clot Stabilization

**PPI Mechanism of Action**
- Weak bases: activate and accumulate in acid environments
- Aggregate on luminal side of parietal cells
- Covalently binds to H+/K+ ATPase blocking acid secretion
- Acid recovery requires synthesis of new pumps and slow dissolution of PPI from pump (36-72 hours)

**PPI Role in Clot Formation**
- Clot formation over arteries is pH dependent
- A gastric pH above 6 is thought to be critical for platelet aggregation
- Labenz et al
  - Drip of omeprazole vs. ranitidine
  - Omeprazole achieved and maintained pH 6
PPI Drip


- Double-blind, placebo-controlled, randomized
- 638 patients with overt upper GIB
  - Melena
  - Hematemesis
- Primary endpoint: need for endoscopic therapy
PPI Prior to Endoscopy

Cochrane Meta-Analysis
6 RCTs of pre-endoscopic PPI

• Reduced the following at index endoscopy:
  – High risk stigmata
  – Need for endoscopic intervention

• No difference seen:
  – Mortality
  – Need for surgery
  – Rebleeding
Timing of Endoscopy

**ASGE**
- In appropriate settings, endoscopy can be used to assess the need for inpatient admission

**ACG**
- Patients with UGIB should generally undergo endoscopy within 24 hours of admission
- Hemodynamically stable patients without serious comorbidities should receive endoscopy as soon as possible in a non-emergent setting
- High risk patients within 12 hours
  - Tachycardic
  - Hypotensive
  - Bloody emesis
  - Bloody NG aspirate
## Timing of Endoscopy: Low Risk

<table>
<thead>
<tr>
<th>Gastrointest Endosc 1999</th>
<th>Gastrointest Endosc 2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early (2 h) vs. Delayed (48 h) endoscopy</td>
<td>Early (6 h) vs. Delayed (48 h) endoscopy</td>
</tr>
<tr>
<td>Hemodynamically stable, no serious comorbidities</td>
<td>Hemodynamically stable, no serious comorbidities</td>
</tr>
<tr>
<td>No improvements in bleeding, surgery, or mortality</td>
<td>No improvement in clinical outcomes or resource utilization</td>
</tr>
<tr>
<td>Decreased hospital stay, costs</td>
<td>Early discharge recommended in 40% of cases, advice followed by primary physician only 9% of time</td>
</tr>
<tr>
<td>46% could be immediately discharged</td>
<td></td>
</tr>
</tbody>
</table>
Timing of Endoscopy: High Risk

**J Clin Gastroenterol 1996**
- Early vs. Delayed cut-off of 12 h
- Benefit in patients with bloody aspirate
  - Decreased transfusions
  - Shorter hospital stay
- Sub-group analysis of bloody NG aspirate
  - SBP<100
  - Pulse >100

**Endoscopy 2011**
- Observational study
- Mortality in timing of endoscopy for both low and high risk UGIB
  - High risk defined as Blatchford>12
- 12 h cut-off
- 44% vs. 0% (P<0.001) mortality in high risk patients with delayed vs. early endoscopy
Risk of Urgent Endoscopy

• Emergency Department
  – Yen et al. in 1997
    • Non-sedated patients in ED
    • Desaturations more common in emergent (2 h) endoscopy in ED than in controls (24 h)

• Intensive Care Unit
  – Lipper et al. in 1991
    • Sedated patients in ICU
    • Increase in severe desaturations (<90%) and pulmonary aspiration
Post-Endoscopy

- PPI
- Repeat Endoscopy
- Diet
- Length of Hospitalization
- Prevention of Recurrence
PPI

High Risk Lesions

• ACG recommends PPI drip for 72 hours
  • 3 Meta-analysis

<table>
<thead>
<tr>
<th>Condition</th>
<th>PPI drip vs. placebo for 72 h</th>
<th>Intermittent PPI vs. Placebo</th>
<th>PPI drip vs. intermittent PPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rebleed</td>
<td>RR=0.4</td>
<td>Rebleed RR=0.53</td>
<td>ARR: 1% with intermittent PPI</td>
</tr>
<tr>
<td>Surgery</td>
<td>RR=0.43</td>
<td>Surgery N/D</td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>RR=0.41</td>
<td>Mortality N/D</td>
<td></td>
</tr>
</tbody>
</table>

Low Risk Lesions

• Rebleed rates low
  • Oral PPI q day recommended
Repeat Endoscopy

• ACG

  • Routine second-look endoscopy not recommended
  • Is recommended in setting of clinical evidence of recurrent bleed
  • If further bleeding after second endoscopic therapeutic session, surgery or IR is recommended
Repeat Endoscopy: Benefit?

- Meta-analysis in 2010 *J Gastroenterol Hepatol*
- 5 Randomized trials

<table>
<thead>
<tr>
<th></th>
<th>Second-look with thermal coagulation vs.</th>
<th>Second-look with epi injection vs. Single endoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Single endoscopy</td>
<td></td>
</tr>
<tr>
<td>rebleeding</td>
<td>4.2% vs. 15.7%*</td>
<td>17.6% vs. 20.8%</td>
</tr>
<tr>
<td>surgery</td>
<td>0.8% vs. 5.2%</td>
<td>4.3% vs. 6.2%</td>
</tr>
<tr>
<td>mortality</td>
<td>2.5% vs. 3.5%</td>
<td>4.3% vs. 5.1%</td>
</tr>
</tbody>
</table>

*Statistically significant

No statistical significance

Suggested high risk features for ulcer rebleeding after initial treatment per *Am J Gastroenterol* 2008
- Hemodynamic instability  OR=2.75
- Active bleeding at endoscopy  OR=1.93
- Large ulcer size (>1 cm)  OR=2.01
- Posterior duodenal or lesser curvature location
Diet per ACG

Low Risk Ulcers
- Clean based ulcers may immediately have regular diet assuming hemodynamic stability and no other comorbidities preventing such

High Risk Ulcers
- Ulcers at risk for rebleeding should receive clear liquids as anesthesia can be administered ~2h after
  - RCT in *Gastroenterology* 1995
    - regular diet vs. npo for 24 h in high risk ulcers
    - No difference in rebleeding
Length of Hospitalization per ACG

Low Risk Ulcers
• Can be discharged immediately assuming no comorbidities requiring hospitalization and satisfactory home/social support

High Risk Ulcers
• Observed for 72 h assuming no rebleeding
Prevention of Recurrence

ACG Guidelines

- **H. pylori**
  - **H. pylori therapy**
    - Document cure; stop PPI/H2RA

- **NSAID**
  - Stop NSAID; if NSAID required, use coxib+ PPI

- **Low-dose aspirin**
  - Primary CV prevention
    - Do not resume aspirin in most patients
  - Secondary CV prevention
    - Resume aspirin soon after hemostasis (e.g., 1–7 days) in most patients and start PPI

- **Idiopathic**
  - Maintenance PPI
References

- ACG guidelines
- ASCGE guidelines