Upper GI Bleeding

Tasos Manokas, MD
Assistant Professor of Gastroenterology

Introduction

• GI bleeding results in over 300,000 hospitalizations annually in U.S.
• Upper GI bleeding accounts for 75-80% of all acute GI bleeding cases
  ✓ More common in men and elderly
  ✓ Incidence: 50-100 per 100,000 patients/year
  ✓ 20,000 deaths annually in United States

Clinical presentation

• Hematemesis
  ✓ Reflects bleeding proximal to ligament of Treitz
• Melena
  ✓ Can be seen with 100 cc blood in UGI tract
• Hematochezia
  ✓ Usually lower GI source or very rapid UGI blood loss (1000 cc blood)
  ✓ If associated with bright red NG aspirate, high mortality

Prognosis

• Wide spectrum of severity
  ✓ Trivial bleeding to variceal bleeding
• Emphasis on early identification and intervention of significant bleeds
• 2 most important prognostic factors
  ✓ Cause of bleeding (variceal)
  ✓ Underlying comorbid conditions
• Mortality from acute UGI bleeding: 5-10%
  ✓ Unchanged over last 50 years despite development, refinement of endoscopic therapy
### Risk factors

- Risk factors associated with increased mortality
  - Age > 70
  - Significant comorbid conditions
    - Serious systemic disease
    - Leukocytosis, thrombocytopenia, coagulopathy
  - Large volume bleeding
    - Fresh hematemesis, bright red NG aspirate
    - Shock
    - Transfusion > 6 units PRBC

### Overview

<table>
<thead>
<tr>
<th>Non-variceal bleeding</th>
<th>Variceal bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etiology</td>
<td>Primary prophylaxis</td>
</tr>
<tr>
<td>Acute management</td>
<td>Acute management</td>
</tr>
<tr>
<td>Medical</td>
<td>Medical</td>
</tr>
<tr>
<td>Endoscopic</td>
<td>Endoscopic</td>
</tr>
<tr>
<td>Recurrent bleeding</td>
<td>Recurrent bleeding</td>
</tr>
<tr>
<td>Prevention</td>
<td>Secondary prophylaxis</td>
</tr>
</tbody>
</table>

### Etiology of UGI bleeding

- Peptic ulcers (40-50%)
- Varices (5-30%)
- Mallory-Weis tear (5-15%)
- Mucosal erosions (15-25%)
- Other causes

### Non-variceal bleeding
### Peptic ulcer disease

- Most common cause of UGI bleeding
- H.pylori and aspirin/NSAIDs
  - 2 most common causes of ulcer formation
- Duodenal ulcers 2x more likely to bleed than gastric ulcers
  - High risk locations for bleeding:
    - Lesser curve of stomach (L gastric a.)
    - Posterior duodenal bulb (gastroduodenal a.)

### Aspirin

- Increased risk of GI complications
  - Dose-dependent relationship
- Even low dose (75 mg/day) shown to increase risk for GI bleeding
- Enteric coated formulations no proven benefit to reducing risk of GI bleeding

### Risk Factors

- Risk factors for NSAID-induced ulcer formation/complication
  - Prior history of ulcer disease or complication
  - Advanced age
    - Risk increases linearly
  - High or multiple doses of NSAIDs
  - Concomitant anticoagulants
  - Concomitant glucocorticoids
    - Steroids alone not a risk factor
  - Comorbid conditions
    - Especially heart disease
  - Ethanol use

### Mallory-Weis tear

- Mucosal tears located at the G-E junction
- Stop spontaneously in 80-90% of cases
- Usually caused by retching
- Rarely a severe cause of bleeding
  - Managed with supportive care
  - Rarely require endoscopic/surgical intervention
Mucosal erosions

- Esophagitis, gastritis, duodenitis
  - Appear as erythema or superficial erosions endoscopically
  - Cameron’s lesions: linear erosions within a large hiatal hernia
- Rarely associated with significant UGI bleeding
- Related to NSAID use, alcohol, or stress gastritis
- Bleeding and stress gastritis: < 3% of pts in ICU
  - High risk: mechanical ventilation > 48 hours, coagulopathy, head injury, extensive burn injuries
  - Prophylaxis: H2-blockers > sucralfate
    - Limited data on PPI

Hemobilia

- Bleeding into biliary tree
  - Vascular communication with bile ducts
- Causes: trauma, liver biopsy most common
  - Also gallstones, vascular aneurysms, liver abscess, neoplasia
- Diagnosis difficult
  - Clinical history and endoscopic appearance of blood coming from papilla
  - Can be missed with standard-viewing endoscope
  - Diagnosis made angiographically

Aortoenteric Fistula

- Rare causes of life-threatening GI bleed
- Primary risk factor: Abdominal aortic graft reconstruction
  - Occur with 0.5% of aortoiliac surgery
  - Most commonly develop 3-5 years after surgery
  - More common with infected grafts
- Most communicate with 3rd portion of duodenum
- “Herald” bleed: self-limited bleed hours/days before severe bleeding

Hemosuccus Pancreaticus

- Bleeding into pancreatic duct
- Complication of chronic pancreatitis, pseudocysts
  - Aneurysm/pseudoaneurysm of peripancreatic, splenic arteries eroding into pancreatic duct
- Diagnosis difficult
  - Clinical history and endoscopic appearance of blood coming from papilla
  - Can be missed with standard-viewing endoscope
  - Diagnosis made angiographically
### Vascular Lesions

- Vascular ectasia, AVM's
  - Associated with connective tissue dz's (scleroderma, CREST), renal failure, radiation tx, cirrhosis, HHT
  - Watermelon stomach: diffuse, linear AVM's in gastric antrum; often found in elderly women
- Dieulafoy lesions
  - Large, submucosal artery usually located in gastric cardia
  - Moderate to severe bleeding

### Neoplasms

- Neoplasms
  - Primary adenocarcinoma, lymphoma, neuroendocrine
  - Stromal tumors (GIST): rare, often present in men > 50 with UGI bleeding
  - Bleeding rarely from metastatic lesions (melanoma, breast)

### GIST

- Initial management - Resuscitation
  - ABC’s
  - IV (preferably large-bore peripheral), O₂, monitor
  - Type and cross, volume expansion (crystalloid, PRBC’s, FFP if underlying coagulopathy)
  - NG tube and lavage
  - ?Intubation for airway protection?
### Laboratory Evaluation

- **Hematocrit**
  - Initial Hct may not reflect degree of blood loss accurately
  - Hct falls over 24-72 hours as extravascular fluid enters vascular space to restore volume
  - Hct may continue to trend down for days after bleeding stops
  - Not clinically relevant if no signs of active bleeding (hematemesis, melena, hematochezia)

### IV PPI

- **Peptic ulcer bleeding**
  - 2 large meta-analysis demonstrate significantly lower rebleeding rates and surgery in pt’s treated with IV PPI compared to placebo\(^1,2\)
    - 1 review also found significant benefit in mortality
  - All cause UGI bleeding
    - 1 large meta-analysis demonstrated no benefit in rebleeding rates, surgery or mortality when compared to placebo\(^3\)

### Medical Management

- **IV proton pump inhibitors (PPI)**
  - Promotes clot stabilization by maintaining intragastric pH > 6
  - Clot lysis by pepsin at pH < 5
    - Pepsin irreversibly inactivated at pH > 6
  - Platelet aggregation improved at pH > 6

### Medical Management

- **IV octreotide**
  - Somatostatin analogue
  - Physiologic effects:
    - Decreases gastroduodenal mucosal blood flow
    - Inhibits gastric acid and pepsin secretion
    - Stimulates mucus production
  - Causes splanchnic vasoconstriction and subsequent decrease in splanchnic blood flow
  - Theoretical benefit over PPI in patients with peptic ulcer bleeding
    - More diverse physiologic effect on upper GI tract
### IV Octreotide

- **Peptic ulcer bleeding**
  - 1 large meta-analysis showed significant reduction in continued/recurrent bleeding
  - Trend toward significance in all cause UGI bleeding
- **All cause UGI bleeding**
  - 2 RCT’s demonstrated no significant benefit compared to placebo or H₂ blocker
  - 1 RCT showed significant benefit in initial hemostasis, blood transfusions, need for surgery, length of hospital stay compared to H₂ blocker

### Erythromycin before endoscopy

- Shown in multiple studies to improve the quality of endoscopic exam
- Some studies also show decreased need for second look EGD
- Given as a single 250 mg IV dose
- Must check ECG before giving to assess QTc

### Role for urgent endoscopy

- Within 6 hours of presentation
- Indications
  - Recurrent/continued UGI bleeding
  - Ongoing hematemesis, active melena/hematochezia
  - Risk for variceal hemorrhage
  - High risk for recurrent bleeding

### Endoscopic Findings

- Clotted blood in stomach
**Endoscopic Findings**

- Active bleeding

**Endoscopic Findings**

- Adherent clot

**Endoscopic Findings**

- Visible vessel

**Endoscopic Therapy**

- High risk lesions treated with dual therapy
  - Injection with epinephrine (1:10,000)
  - Thermal therapy
    - Heater probe (monopolar)
    - Bipolar gold probe
    - Argon plasma coagulation (APC)
- Dual therapy superior in preventing rebleeding rates
### Risk of Rebleeding

- Rebleeding after endoscopic therapy occurs in 20-30%
- Most (95%) occur within 1st 72 hours
- Risk factors
  - Significant bleeding
    - Hemodynamic instability (HR>100; SBP<100)
    - Transfusion > 4 units PRBC
  - Anticoagulation
  - Endoscopic stigmata

### Repeat Endoscopy

- “2nd look” endoscopy often performed 24 hours after initial procedure
- In absence of rebleeding, not warranted for all patients
  - Only certain high risk groups shown to benefit
- In patients with rebleeding (rebleeding rate: 20-30%), repeat endoscopy warranted for further treatment

### Endoscopic Stigmata

- High risk for rebleeding
  - Active bleeding (70-90%)
  - Visible vessel (40-50%)
  - Adherent clot (10-35%)
  - Ulcers > 2 cm
  - Posterior duodenal bulb ulcers
- Low risk
  - Flat spot
  - Clean ulcer base

### Angiography

- Indicated in refractory bleeding
  - Not amenable to endoscopic therapy
  - Poor surgical candidates
- Requires fast bleeding rate (>0.5 ml/min)
- Can embolize left gastric a. or gastroduodenal a. empirically based on endoscopic localization of bleeding
Surgery

• Changing role of surgery
  ✓ No longer used to cure ulcer disease
    • PPI's, H.pylori eradication now cures most cases of PUD
  ✓ Now utilized to stop life-threatening bleeding

• Indications
  ✓ Bleeding where endoscopy and/or angiography has failed
  ✓ Large visible vessels (>2-3 mm) along lesser curve of stomach and in duodenal bulb

H. pylori treatment

• Documenting clearance
  ✓ Failure of therapy associated with ulcer recurrence
  ✓ Simple, cost-effective, non-invasive tests available (urea breath, stool antigen tests)
  ✓ Must wait 4 weeks after completion of therapy
    • Must hold PPI 1 week prior to test
  ✓ Once clearance confirmed, re-infection rare

Prevention of future bleeding

• Eliminating NSAID’s
• Eradication of H. pylori
  ✓ Triple therapy for 10-14 days first line therapy
  ✓ Bismuth + Metronidazole + Tetracycline
    • QID dosing can decrease compliance
  ✓ PPI + Amoxicillin + Clarithromycin
  ✓ Increasing resistance to metronidazole, clarithromycin
  ✓ Most commonly used regimens cure 80% of cases

Variceal Bleeding

Jim Hanje, MD
Assistant Professor of Gastroenterology
Ohio State University Medical Center
Cirrhosis

Normal

Cirrhosis

Irregular surface

Nodules

Portal Hypertension

- Progressive complication of cirrhosis
- Marks transition from early compensated cirrhosis to decompensated, end-stage liver disease

Portal Hypertensive Bleeding

- Esophagogastric varices, portal hypertensive gastropathy, gastric antral vascular ectasias
- Clinical Presentation
  ✓ Hematemesis
  ✓ Melena
  ✓ Shock
- Variceal hemorrhage most common manifestation, often life-threatening
Prevalence of Esophageal Varices in Cirrhosis

Diagnostic

- Screening EGD should be performed at time of diagnosis of cirrhosis to screen for varices
- Varices progress at a rate of 8% per year
- Repeat EGD every 2-3 years depending on size of varices to evaluate for progression

Prevalence and Size of Esophageal Varices in Patients with Newly-Diagnosed Cirrhosis

Varices Increase in Diameter Progressively

Pagliaro et al., In: Portal Hypertension: Pathophysiology and Management, 1994: 72

Merli et al., J Hepatol 2003;38:266
Large Varices Are More Likely To Rupture

% Patients without bleeding

2-year probability of first bleed:

- Small varices: 7%
- Large varices: 30%

* Merli et al., Hepatol 2003; 38:266
* Conn et al., Hepatology 1991; 13:902

Primary Prophylaxis: Non-Selective Beta-Blockers

<table>
<thead>
<tr>
<th>Bleeding rate (2 year)</th>
<th>Control</th>
<th>Beta-blocker</th>
<th>Absolute rate difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>All varices 25%</td>
<td>15%</td>
<td>-10%</td>
<td></td>
</tr>
<tr>
<td>(11 trials) (n=600)</td>
<td>(n=590)</td>
<td>(-16 to -5)</td>
<td></td>
</tr>
<tr>
<td>Large varices 30%</td>
<td>14%</td>
<td>-16%</td>
<td></td>
</tr>
<tr>
<td>(8 trials) (n=411)</td>
<td>(n=400)</td>
<td>(-24 to -8)</td>
<td></td>
</tr>
<tr>
<td>Small varices 7%</td>
<td>2%</td>
<td>-5%</td>
<td></td>
</tr>
<tr>
<td>(3 trials) (n=100)</td>
<td>(n=91)</td>
<td>(-11 to 2)</td>
<td></td>
</tr>
</tbody>
</table>

D’Amico et al., Sem Liver Dis 1999; 19:475

Primary Prophylaxis: Non-Selective Beta-Blockers

<table>
<thead>
<tr>
<th>Bleeding rate (2 year)</th>
<th>Control</th>
<th>Beta-blocker</th>
<th>Absolute rate difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>All varices 25%</td>
<td>15%</td>
<td>-10%</td>
<td></td>
</tr>
<tr>
<td>(11 trials) (n=600)</td>
<td>(n=590)</td>
<td>(-16 to -5)</td>
<td></td>
</tr>
<tr>
<td>Large varices 30%</td>
<td>14%</td>
<td>-16%</td>
<td></td>
</tr>
<tr>
<td>(8 trials) (n=411)</td>
<td>(n=400)</td>
<td>(-24 to -8)</td>
<td></td>
</tr>
<tr>
<td>Small varices 7%</td>
<td>2%</td>
<td>-5%</td>
<td></td>
</tr>
<tr>
<td>(3 trials) (n=100)</td>
<td>(n=91)</td>
<td>(-11 to 2)</td>
<td></td>
</tr>
</tbody>
</table>

D’Amico et al., Sem Liver Dis 1999; 19:475
Primary Prophylaxis: Nonselective Beta-Blockers

- Reduce portal pressure via:
  - Splanchnic vasoconstriction (β-2 effect)
  - Decreased cardiac output (β-1 effect)
- Nadolol, Propranolol
  - Titrated weekly to goal: ↓ HR by 25%

Primary Prophylaxis – Endoscopic Band Ligation (EBL)

- Prophylactic EBL every 4 weeks until variceal obliteration
- Esophageal ulcerations form following EBL
  - Can cause dysphagia, chest pain in most patients
  - PPI BID shown to decrease post-EBL bleeding
- Fewer side effects than β-blockers, but more severe
  - Bleeding due to esophageal ulcerations, variceal rupture

Primary Prophylaxis: EBL vs Beta-Blockers (BB)

- Limited utility in clinical practice:
  - Frequent side effect/contraindications (20%)
  - Limited reduction in portal pressures at doses tolerated
  - Need for long-term/lifelong therapy
  - Rebound bleeding with cessation of therapy

### Acute Variceal Bleeding

#### Evolution of Varices

<table>
<thead>
<tr>
<th>Cirrhosis with no varices</th>
<th>Small varices</th>
<th>Medium / large varices</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-primary prophylaxis</td>
<td>Repeat endoscopy in 1-2 years</td>
<td>Repeat endoscopy in 2-3 years</td>
</tr>
<tr>
<td></td>
<td>Small varices</td>
<td>Medium/Large varices</td>
</tr>
<tr>
<td></td>
<td>No specific therapy</td>
<td>Non-selective beta-blockers</td>
</tr>
</tbody>
</table>

#### Level of Intervention

- Pre-primary prophylaxis
- Primary prophylaxis

#### Management Recommendations

- Repeat endoscopy in 2-3 years
- No specific therapy

#### Predictors of hemorrhage:
- Variceal size
- Red signs
- Child B/C

**N Engl J Med** 1988; 319:983
Acute Variceal Bleeding

- Initial management - Resuscitation
  - ABC’s
  - IV (preferably large-bore peripheral), O₂, monitor
  - Type and cross, volume expansion
    - Goal Hgb 8 g/dl; over-resuscitation can ↑ portal pressure and ↑ risk of rebleeding and death
  - Correct coagulopathy
    - FFP, platelets, DDAVP, cryoprecipitate
    - Recombinant factor Vila
      - Multi-center RCT showed no overall benefit compared to standard therapy BUT…
      - CTP B/C patients ↓ bleeding rates

Probability of Remaining Free of Recurrent Variceal Hemorrhage

Prophylactic Antibiotics

- Higher incidence of bacterial infections in cirrhotic patients admitted with UGI bleed
  - Increased risk with increasing disease severity
- Fluoroquinolone orally BID
  - Selective eradication of gram – bacteria in gut
  - Can administer IV if NPO
- Ceftriaxone IV more effective than oral Norfloxacin in CTP B/C patients

Prophylactic Antibiotics

- IMPROVED OUTCOMES:
  - Decreased rate of bacterial infections and SBP
  - Decreased rate of rebleeding
  - Improved survival
Pharmacologic Therapy

- Octreotide
  - Synthetic analogue of somatostatin
  - 50μg bolus, followed by 50μg/h continuous infusion
  - Safe, minimal side-effects, can be used for 5 days
  - Causes splanchnic vasoconstriction
  - Acutely lowers portal pressures by decreasing splanchnic blood flow
  - Decreases bleeding, no mortality benefit
  - Minimal benefit when used alone without EBL
  - Not as potent as other agents, can get tachyphylaxis

Endoscopy

- Endoscopic band ligation (EBL)
  - Treatment of choice for bleeding esophageal varices
  - Successful in 70-90% of cases
  - Superior to sclerotherapy with decreased rebleeding rates, mortality rates and incidence of complications
- EBL + Octreotide
  - Superior to either modality alone
  - Shown to significantly reduce rebleeding rates
  - No mortality benefit over banding alone

Refractory Bleeding

- Occurs in 10-20% of patients
  - HVPG > 20 mm Hg predicts failure/rebleeding
  - Transjugular intrahepatic portosystemic shunt (TIPS)
  - Most common salvage therapy for refractory variceal bleeds

Combination Drug / Endoscopic Therapy More Effective Than Endoscopic Therapy Alone

<table>
<thead>
<tr>
<th>Therapy Type</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sclero + Octreotide</td>
<td>Besson, 1995</td>
</tr>
<tr>
<td>Ligation + Octreotide</td>
<td>Sung, 1995</td>
</tr>
<tr>
<td>Sclero + Octreotide / ST</td>
<td>Signorelli, 1996</td>
</tr>
<tr>
<td>Sclero + Octreotide</td>
<td>Ceriani, 1997</td>
</tr>
<tr>
<td>Sclero + Octreotide</td>
<td>Signorelli, 1997</td>
</tr>
<tr>
<td>Sclero + ST</td>
<td>Aggerinos, 1997</td>
</tr>
<tr>
<td>Sclero + Octreotide</td>
<td>Zuberi, 2000</td>
</tr>
<tr>
<td>Sclero / ligation + Vapreotide</td>
<td>Cales, 2001</td>
</tr>
</tbody>
</table>

Favors endoscopic therapy alone
Favors endoscopic plus drug therapy

Relative Risk

---

Bañares R et al., Hepatology 2002; 35:609
Polytetrafluoroethylene-covered TIPS stents

Covered Stents vs Uncovered Stents

Bureau et al. Gastroenterology 2004; 126:469

Evolution of Varices

Cirrhosis with no varices
- Repeat endoscopy in 2-3 years
- No specific therapy

Small varices
- Pre-primary prophylaxis
- Beta-blocker to prevent enlargement (CTP B/C pts)

Medium / large varices
- Non-selective beta-blockers
- EVL in those who are intolerant to drugs
- Endoscopic/pharmacologic therapy
- Antibiotics in all patients
- TIPS or shunt surgery as rescue therapy

Level of Intervention

Primary prophylaxis

Management Recommendations

Bureau et al. Gastroenterology 2004; 126:469
**Secondary Prophylaxis**

- Cirrhotics with prior variceal bleed have high risk of rebleeding and death
- If untreated, 60-70% will rebleed within 1-2 years with 30% mortality rate

- **Nonselective β-blockers**
  - Reduces rebleeding rates to 40%

- **EBL**
  - Reduces rebleeding rates to 30%
- **EBL + nonselective β-blocker**
  - Combination therapy superior to either modality alone
  - Rebleeding rates: 15-25%

---

**Evolution of Varices**

<table>
<thead>
<tr>
<th>Level of Intervention</th>
<th>Management Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-primary prophylaxis</td>
<td>+ Repeat endoscopy in 2-3 years</td>
</tr>
<tr>
<td>Primary prophylaxis</td>
<td>+ No specific therapy</td>
</tr>
<tr>
<td>TIPS/shunt surgery</td>
<td>+ Beta-blockers + EVL</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>+ Endoscopic/pharmacologic therapy</td>
</tr>
<tr>
<td>Beta-blocker to prevent enlargement</td>
<td>+ Antibiotics in all patients</td>
</tr>
</tbody>
</table>

**Cirrhosis with no varices**

- Small varices
  - No hemorrhage
  - Repeat endoscopy in 1-2 years
  - Beta-blocker to prevent enlargement (CTP B/C pts)

**Medium / large varices**

- No hemorrhage
  - Non-selective beta-blockers
  - EVL in those who are intolerant to drugs

**Variceal hemorrhage**

- Medium/Large varices
  - Endoscopic/pharmacologic therapy
  - Antibiotics in all patients
  - TIPS or shunt surgery as rescue therapy

**Secondary variceal hemorrhage**

- Repeat endoscopy in 2-3 years
- No specific therapy
Summary

• ALL CIRRHOTICS WITH AN EPISODE OF VARICEAL BLEEDING SHOULD BE REFERRED TO A TRANSPLANT CENTER
• EGD should be performed at time of diagnosis of cirrhosis to screen for varices
• Primary prophylaxis with B-blocker vs EBL in all patients with medium or large esophageal varices
• Prophylactic antibiotics in acute variceal bleeding improves outcomes