Overview of Gastrointestinal Bleeding

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Disclosures

- I have no financial disclosures.
- I have no conflict of interest to declare.

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Overview

- Epidemiology
- Definitions of gastrointestinal (GI) bleeding
- Differential diagnosis
- Clinical history and examination- key points
- Initial evaluation and management
- Diagnostic evaluation options

Epidemiology

- Upper GI bleed is approximately 67/100,000 people
- Lower GI bleed is approximately 36/100,000 people
- Morbidity and mortality with over $1 billion in direct medical costs annually
- Hospitalization rate of upper GI bleed in the USA decreased by 21% from 2002 to 2012
  - Increase use of treatments, improved hemostatic techniques.

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Definitions of GI Bleed

- Hematemesis
  - Vomiting of fresh blood

- Coffee ground emesis
  - Slowed or stopped
  - Within red blood cells, iron oxidizes following exposure to gastric acid

- Melena
  - Black tarry stool
  - NOT typically dark, formed stool
  - Only needs 50-100cc of blood to become melena

- Hematochezia
  - Passage of bright red blood per rectum (BRBPR), maroon colored, or clots

- Upper GI bleed vs lower GI bleed
  - ~5-10% can be from small bowel or proximal colon

Overt vs Occult

- Overt:
  - Visible blood
  - Bright red, altered blood (melena)

- Occult:
  - No visible blood identified
  - Presents as iron deficiency anemia, positive stool test for occult blood

- Obscure:
  - No bleeding source identified
  - May be overt or occult

Factors that increase the likelihood of upper GI bleed:

- Patient history of melena (LR 5.1-5.9)
- Melena on examination (LR 25)
- Nasogastric lavage with blood or coffee ground contents (LR 3.6)
- BUN/Cr >30 (LR 7.5)
Differential Diagnosis - Upper

- Gastric/duodenal ulcers*
- Esophagitis/gastritis
- Esophageal or gastric varices
- Portal hypertensive gastropathy
- Arteriovenous malformations (AVM)
- Mallory-Weiss tear
- Erosions
- Dieulafoy lesion
- Gastric antral vascular ectasia (GAVE)
- Mass lesions
- Hemobilia
- Hemosuccus pancreaticus
- Aortoenteric fistula
- Cameron lesions
- Iatrogenic

- Gastric ulcer
- Esophageal ulcer/esophagitis
- Duodenal ulcer
- Esophageal varices

- Portal hypertensive gastropathy
- Mallory-Weiss tear
- Gastric Antral Vascular Ectasia
- Cameron Lesions
Differential Diagnosis - Lower

- Diverticulosis
- Angiodysplasia
- Hemorrhoids
- Ischemic
- Post biopsy or polypectomy
- Anal fissures
- Radiation-induced telangiectasia
- Infectious
- Inflammatory bowel disease
- Ulcers
- Polyp
- Carcinomas

History

- Past medical history
  - Prior episodes of bleeding
  - Liver disease, cardiac disease (including aortic aneurysms), kidney disease, hematologic disorders
  - History of peptic ulcer disease (PUD) or H pylori
  - Malignancy
  - History of alcohol abuse
  - Recent procedures: colonoscopy, AAA repair, radiation
  - History of gastroenteric anastomosis
History
- Medications review
  - Non steroidal anti inflammatory drugs (NSAIDs)
  - Aspirin
  - Medications associated with pill esophagitis
  - Antiplatelet and anticoagulants
  - Other less obvious medications have been associated with GI bleeding
    - Psychiatric medications, blood pressures medications
    - Bismuth, iron can turn the stool black

Physical
- Evaluate for signs of hemodynamic instability
  - Vitals/orthostatic
  - Abdominal exam
  - Rectal exam- evaluate for fissures, hemorrhoids, mass, stool exam

Initial Evaluation and Management
- Assessment of hemodynamic status
- Placement of 2 large bore IV lines or central line
- Secure airway if needed
- Labs: Complete blood count, PT/INR, lactate, liver function tests, type and cross
- Transfuse for hemoglobin <7 (or <8 if cardiac), platelet >50
- Resuscitate!

Initial Evaluation and Management
- Risk Stratification Scores
  - Glasgow Blatchford Score
    - Stratifies upper GI bleeding patients who are "low risk" and candidates for outpatient treatment
    - Score 0 is low risk
    - Evaluates: hemoglobin, systolic blood pressure, pulse, BUN, "no melena or syncope", no past or present liver disease or heart failure
**Medication Management**

- Proton pump inhibitor
  - Inhibit gastric acid secretion
  - Heal ulcers, improve platelet aggregation and clot development by raising gastric pH
  - Has been shown to reduce risk of rebleeding (high risk stigmata) and the need for endoscopic intervention
  - High dose PPI- comparable outcomes in dosing (bolus + drip vs bolus + 40mg IV BID)
- If concerned for variceal bleeding:
  - IV somatostatin like octreotide
  - IV antibiotic to empirically cover for spontaneous bacterial peritonitis
- Consider holding patient’s home blood thinners (risk vs benefits)

**Diagnostic Evaluation**

- Nasogastric tube
  - Used less often
  - Negative (clear) nasogastric tube aspirate does not rule out an upper GI source
  - Bile can help confirm tube in duodenum however may see in stomach due to reflux
  - Can be helpful for gastric emptying however inferior to pro-motility agents

**Medication Management**

- Pro-motility agent
  - Helps to clear the stomach for improved visualization and decreases the need for repeat endoscopy
  - Erythromycin 250 mg IV over 20-30 minutes about 30-120 minutes before EGD
  - Metoclopramide 10mg over 1-2 minutes

**Diagnostic Evaluation**

- Stool guaiac/ hemoccult
  - Great tool for colon cancer screening
  - NOT a test for acute GI bleed
  - False positives:
    - Medications (ASA, NSAIDs)
    - Extra-intestinal blood loss (epistaxis, hemoptysis)
    - Trauma
    - Exogenous peroxidase activity: red meat, fruits, uncooked vegetables
Diagnostic Evaluation

- Endoscopy
  - EGD/ upper endoscopy
  - Evaluates up to duodenum
  - Push enteroscopy
  - Evaluates small bowel
  - Capsule endoscopy
  - Evaluates entire GI tract
  - Single balloon enteroscopy (upper and lower)
  - Evaluates small bowel- much further than push enteroscopy
  - Colonoscopy
  - Evaluates terminal ileum and colon
- Timing:
  - Within 24-48 hours after presentation

Therapeutic Management

- Some bleeds typically resolve on their own!
- Endoscopic therapy
  - Epinephrine injection
  - Coagulation
  - Hemoclip
  - Band ligation
  - Interventional Radiology
  - Surgery

Key Takeaway Points

- Although upper GI bleed typically refers to melaena and lower GI bleed to hematochezia, this is not absolute
- There is no utility in hemoccult in active signs of GI bleeding
- Placement of nasogastric tube for the evaluation of GI bleeding is less frequently used
- Resuscitate!
Management of Acute Gastro-esophageal Variceal Bleed

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Objective
- Introduction
- Various Classifications of EV
- Predictors of bleeding including HVPG
- Varices management
  - Pre-primary prophylaxis
  - Primary prophylaxis
  - Active variceal bleed
  - Secondary prophylaxis

Introduction
- At diagnosis of cirrhosis, varices are present in:
  - 20-40% of compensated patients.
  - 40-60% of patients with ascites. (Scheeps F, et al. Hepatology 2001)
- 5% develop new varices per year.
- Once developed, varices increase from small to large at 10 – 15% per year.
- Once developed, 25% of varices bleed at 2 years. (deFranchis R, Primigagni M, Clin Liv Dis 2001)
- Mortality due to variceal bleed ranges: 5-15%

Pathophysiology of portal hypertension haemodynamic factors

 Portal pressure = resistance x blood flow

- Increased resistance (dynamic / mechanic)
- Increased blood flow (splanchnic vasodilation)

Increased portal pressure
Vasodilator/vasoconstrictor imbalance in the pathogenesis of increased intrahepatic vascular resistance in cirrhosis

Vasoconstrictors:
- Endothelin
- Angiotensin
- Norepinephrine
- Vasopressin
- Leukotrienes
- Thromboxane
- Other?

Vasodilators:
- Nitric oxide (NO)
- Carbon monoxide (CO)
- Other?

Classification of varices

<table>
<thead>
<tr>
<th></th>
<th>Japanese</th>
<th>US</th>
<th>Baveno</th>
<th>Paquet</th>
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<tbody>
<tr>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Grade 1: small EV not disappearing with insufflation</td>
<td>Small &lt;5 mm</td>
<td>I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 2: median varices occupying &lt;1/3 of lumen</td>
<td>Medium &gt;5 mm</td>
<td>II</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 3: large EV occupying &gt;1/3 of lumen</td>
<td>Large &gt;5 mm</td>
<td>III</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Giant &gt;5 mm</td>
<td>IV</td>
<td></td>
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</table>

Upper GI Endoscopy

Presence?

Size?
- small <5cm
- large >5cm

Red Spots?

Predictors of Bleeding

1. Variceal size:
   - Small varix 10% at 2 years.
   - Large varix 30% at 2 years.
2. Presence of red signs.
3. Severity of underlying liver disease:
   - Child A - 17%.
   - Child B - 31%.
4. MELD score
5. Hepatic Venous Pressure Gradient (HVPG)
Hepatic Venous Pressure Gradient

- Most commonly used for measurement of portal pressure
- HVPG—gradient between the wedged and free hepatic venous pressure (normal gradient, <5 mm Hg).

free hepatic venous pressure

wedge hepatic venous pressure

Portal Pressure

HVPG
Measurement | Significance
---|---
1-5 mm Hg | Normal
6-10 mm Hg | Preclinical sinusoidal portal HTN
≥10 mm Hg | Clinically significant portal HTN (CSPH)
≥12 mm Hg | Increased risk for rupture of varices
≥16 mm Hg | Increased risk of mortality
≥20 mm Hg | Treatment failure and mortality in AVB

Case: Acute Variceal Bleed
- Actively drinking for >10 yrs. H/o IVDU in 1990s.
- Blood work: Hb: 6.5; Plat: 65; LFTs: bili: 3.5, AP: 151; INR: 1.8.
- US shows features of cirrhosis, ++ ascites, no HCC.
- EGD: large >5 mm EV with red wale signs and cherry red spots.
Management of Acute Variceal Hemorrhage

- Prompt resuscitation, hemodynamic support, and correction of hemostatic dysfunction.
- Empirical vasoactive pharmaco-therapy is indicated in variceal hemorrhage.
- Subsequently, EGD facilitates an accurate diagnosis and endoscopic therapy.

Pharmacologic Therapy

- An attractive first-line approach in patients with probable variceal hemorrhage.
- Terlipressin:
  - Synthetic vasopressin analogue.
  - Longer half-life has led to its successful use for variceal bleeding.
  - Terlipressin appears to be as effective as vasopressin or somatostatin.

Somatostatin

- Naturally occurring peptide, and its synthetic products — octreotide and vapreotide.
- Stops variceal hemorrhage in up to 80% of patients.
- Octreotide works:
  - by preventing postprandial hyperemia or
  - by reducing portal pressure through effects on vasoactive peptides.
- Excellent safety profile.
- The addition of octreotide to EST or EVBL resulted in improved control of bleeding and reduced transfusion requirements.


  - Consecutive cirrhotic patients with EV bleed were randomized to Terlipressin (Group A, 163) or Octreotide (Group B, 161).
  - Outcomes: Efficacy, safety, overall survival and length of hospital stay.
  - Control of variceal bleed: 151 (92.63 % ) in TERLI and 154 (95.6 % ) patients in OCTREO (CI: 9.22 – 1.5).
  - Death : overall 16 deaths (3 failure to control bleed and 13 from other causes).
  - LOS: TERLI (108.40 ± 34.81) has shorter LOS as compared to OCT (126.39 ± 47.45 h), ( P ≤ 0.001).
  - CONCLUSION: The efficacy of TERLI was not inferior to OCTREO as an adjuvant therapy for the control of EV bleed and in-hospital survival.
  - The length of hospital stay in the TERLI was significantly shorter.
Endoscopic Therapy

- **Endoscopic Sclerotherapy:**
  - It stops bleeding in 80 to 90% of acute variceal hemorrhage.

- **The advantages of EST:**
  - Ability to establish definitive control of bleeding under direct vision.

- **Drawbacks:**
  - Risk of local complications, including perforation, ulceration, thrombosis and stricture.

Endoscopic band ligation

- RCTs of acute variceal bleeding have shown that EBL is equivalent to sclerotherapy in achieving initial hemostasis.

- The complications associated with EBL are fewer and include superficial ulcerations and, rarely, the formation of strictures.

**References:**

Secondary Prophylaxis

- **Secondary prophylaxis** should be instituted after initial episode due to high risk of recurrent bleed.
- Variceal hemorrhage recurs in approximately 2/3 of patients.
- **Endoscopic predictors of early recurrence:**
  - active bleeding at the time of the initial endoscopy,
  - stigmata of recent bleeding and
  - large varices.

NSBB Therapy

- Reducing the portal pressure by > 20% from the base-line value results in a reduction in the cumulative probability of recurrent bleeding from 28% @ 1 yr, 39% @ 2 yr, and 66% @ 3 yrs to 4%, 9%, and 9%, respectively.

- Several RCTs, including a meta-analysis, have demonstrated that non-selective BB (Nadolol, Carvedilol) decrease the risk of recurrent bleeding and prolong survival.

Endoscopic Band Ligation

- EVBL is highly effective in obliterating varices.
- Ligation is associated with a lower risk of recurrent bleeding and fewer complications,
- EVBL is performed 2-4 weekly until varices are eradicated, which typically requires 3-4 sessions.
- Approaches that combine methods, usually including an endoscopic treatment and a pharmacologic treatment are effective.


- **Study selection:** RCTs comparing endoscopic plus BB therapy with either therapy alone.
- **Data synthesis:** 23 trials (1860 patients) included.
- **Results:** Combination therapy reduced overall rebleeding more than endoscopic therapy alone (RR: 0.68; CI: 0.52 to 0.89) or beta-blocker therapy alone (RR: 0.71; CI: 0.59 to 0.86).
- Combination therapy also reduced variceal rebleeding and variceal recurrence.
- Reduction in mortality from combination therapy did not statistically significantly differ from that from endoscopic (OR: 0.78; CI: 0.58 to 1.07) or drug therapy (OR: 0.70; 0.46 to 1.06).
- **Conclusion:** A combination of endoscopic and drug therapy reduces overall and variceal rebleeding in cirrhosis more than either therapy alone.
Relative Effectiveness of Available Therapies for the Prevention of Recurrent Variceal Bleeding

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Approx. Risk of Recurrence (%)</th>
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<tbody>
<tr>
<td>No Treatment</td>
<td>100</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>80</td>
</tr>
<tr>
<td>Beta-Nitrate</td>
<td>60</td>
</tr>
<tr>
<td>Sclerotherapy</td>
<td>40</td>
</tr>
<tr>
<td>EVBL</td>
<td>20</td>
</tr>
<tr>
<td>TIPS</td>
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</table>

**Conclusion**

- Bleeding from esophageal varices is dependent on severity of liver cirrhosis.
- Resuscitation is integral in management of EVB
- Vasopressors are helpful in initial stability of EVB
- Endoscopic band ligation is effective in securing initial active EV bleeding.
- Combination of repeated EBL and NSBB is effective for secondary prophylaxis.
- TIPS is needed in selective patients who don’t respond to endoscopic intervention.