Overview of Gastrointestinal Bleeding

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Disclosures

- I have no financial disclosures.
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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.
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

Definitions of GI Bleed

- Melena
  - Black tarry stool
    - NOT typically dark, formed stool
  - Only needs 50-100cc of blood to become melena
  - Upper GI bleed vs lower GI bleed
    - ~5-10% can be from small bowel or proximal colon

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

- 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

Upper vs lower GI Bleed

- 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

Duodenal ulcer

Esophageal ulcer/esophagitis

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

![Diverticulosis](Author: MAC 06 (CC BY 4.0))

![Angiodysplasia](Author: Samir (CC BY-SA 3.0))
- Hemorrhoids
- Ulcerative colitis

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)

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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

- **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

- **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

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Diagnostic Evaluation

- **Imaging**
  - CT angiography
    - Diagnostic and therapeutic
    - Bleeding rate at least 0.3-0.5 to 1.0cc/min
  - Tagged RBC scan
    - Not therapeutic
    - Bleeding rate at least 0.1-0.5cc/min
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 melena 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. (Schepis 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

\[ \Delta \text{Portal pressure} = \text{resistance} \times \text{blood flow} \]

- 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?

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**Classification of varices**
Japanese, US, Baveno, Paquets

<table>
<thead>
<tr>
<th>Japanese</th>
<th>US</th>
<th>Baveno</th>
<th>Paquet</th>
</tr>
</thead>
<tbody>
<tr>
<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</td>
<td>&lt;5 mm</td>
<td>I</td>
</tr>
<tr>
<td>Grade 2: median varices occupying &lt;1/3rd of lumen</td>
<td>Medium</td>
<td>&gt;5 mm</td>
<td>II</td>
</tr>
<tr>
<td>Grade 3: large EV occupying &gt;1/3rd of lumen</td>
<td>Large</td>
<td>&gt;5 mm</td>
<td>III</td>
</tr>
<tr>
<td></td>
<td>Giant</td>
<td>&gt;5 mm</td>
<td>IV</td>
</tr>
</tbody>
</table>
Upper GI Endoscopy

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).
wedge hepatic venous pressure

HVPG

Portal Pressure

?
Prognostic value of HVPG in patients with chronic liver disease

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-5 mm Hg</td>
<td>Normal</td>
</tr>
<tr>
<td>6-10 mm Hg</td>
<td>Preclinical sinusoidal portal HTN</td>
</tr>
<tr>
<td>≥10 mm Hg</td>
<td>Clinically significant portal HTN (CSPH)</td>
</tr>
<tr>
<td>≥12 mm Hg</td>
<td>Increased risk for rupture of varices</td>
</tr>
<tr>
<td>≥16 mm Hg</td>
<td>Increased risk of mortality</td>
</tr>
<tr>
<td>≥20 mm Hg</td>
<td>Treatment failure and mortality in AVB</td>
</tr>
</tbody>
</table>

Lin et al. J Hepatol 1989
Natural history of oesophageal varices

- Increased portal pressure (HVPG > 10 mmHg)
- Formation of varices
- Dilatation of varices
- Rupture of varices (HVPG > 12 mmHg)

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: 0.22 – 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.


Suggested Algorithm of Acute Variceal Hemorrhage

- Esophageal Variceal Bleed
  - Vasopressors
  - Urgent Endoscopic therapy
  - Continue Vasopressors for 2-3 days
    - No Further bleeding
      - Institute prevention program
    - Early recurrence
      - Repeat EGD
      - Recurrent or continuous bleeding
        - Balloon Tamponade
        - Consider TIPS
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

- No Treatment
- Beta-blockers
- BB+Nitrate
- Sclerotherapy
- EVBL
- TIPS

Approx risk of recurrence of bleed (%)

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.