Overview of Gastrointestinal Bleeding

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

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

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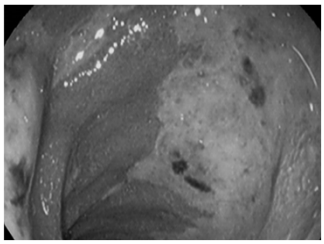
- Duodenal ulcer



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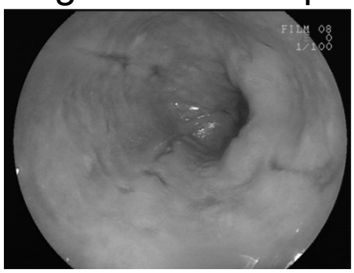
- Esophageal ulcer/esophagitis



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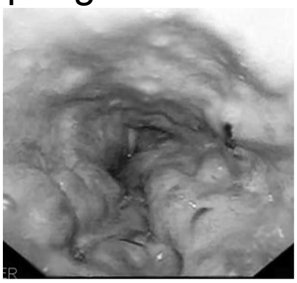
- Esophageal varices



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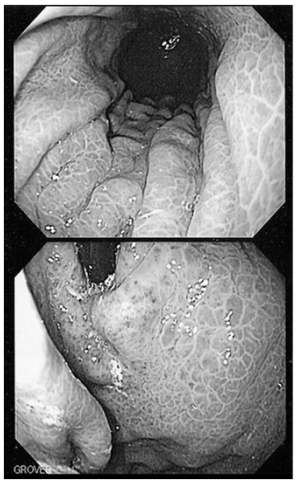
- Portal hypertensive gastropathy



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- Mallory Weiss tear

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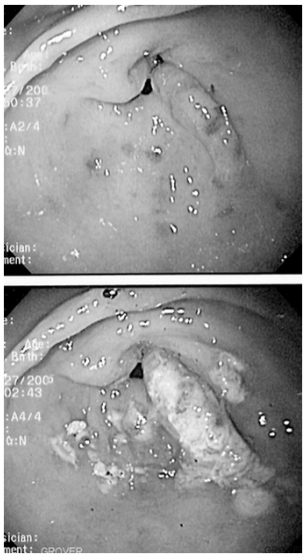
- Gastric Antral Vascular Ectasia



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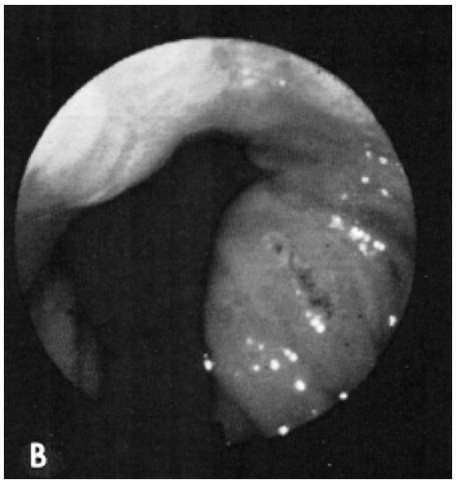
- Cameron Lesions



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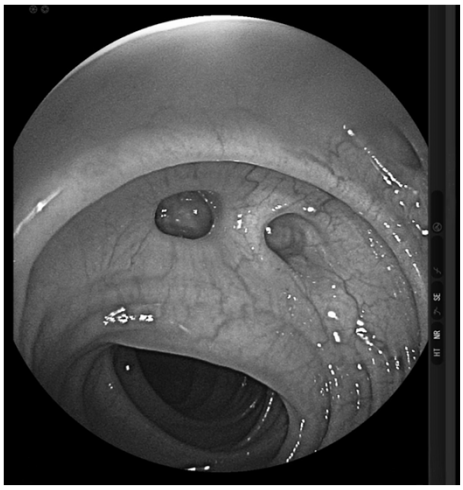
Differential Diagnosis- Lower

- **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

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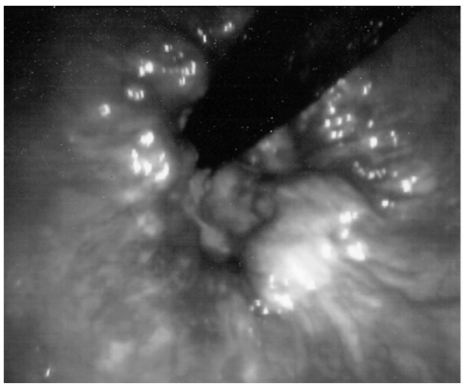
- Hemorrhoids



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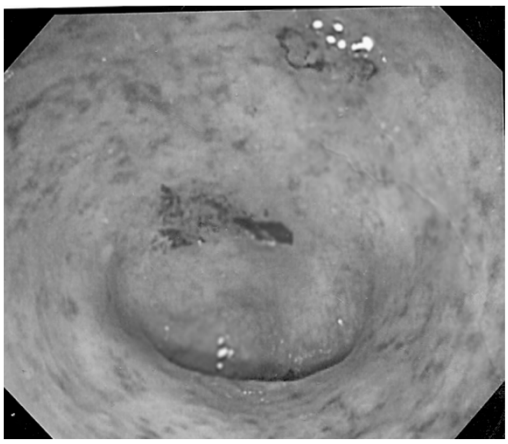
- Ulcerative colitis



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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

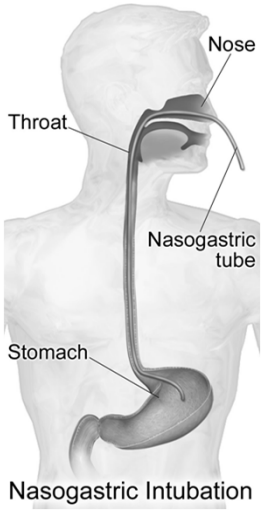
- Proton pump inhibitor
  - Inhibit gastric acid secretion
  - Heal ulcers, improve platelet aggregation and clot development by raising gastric pH
  - Has been shown to reduce risk of rebleeding (high risk stigmata) and the need for endoscopic intervention
  - High dose PPI- comparable outcomes in dosing (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)

Medication Management

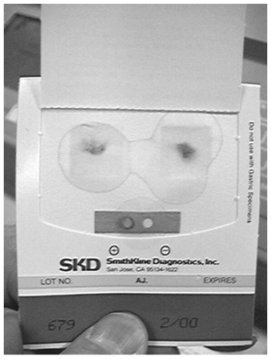
- Pro-motility agent
  - Helps to clear the stomach for improved visualization and decreases the need for repeat endoscopy
  - Erythromycin 250 mg IV over 20-30 minutes about 30-120 minutes before EGD
  - Metoclopramide 10mg over 1-2 minutes

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



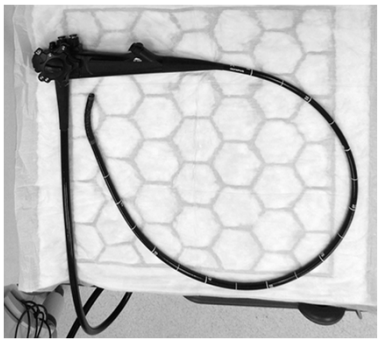
Diagnostic Evaluation



- 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



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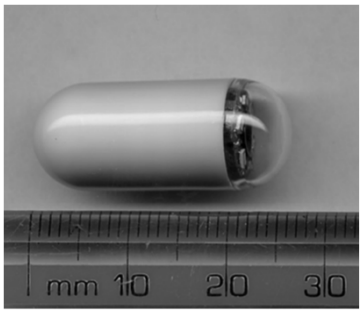


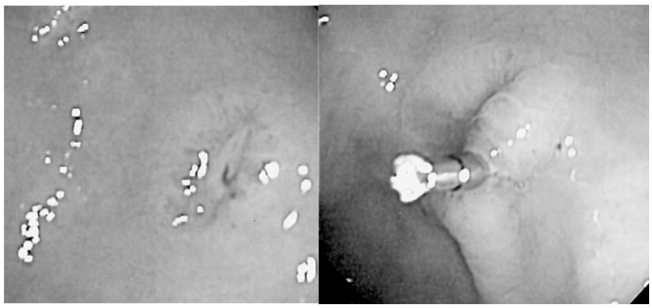
Diagnostic Evaluation

- 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



Author: Samir - (CC BY-SA 3.0) Author: Kogando

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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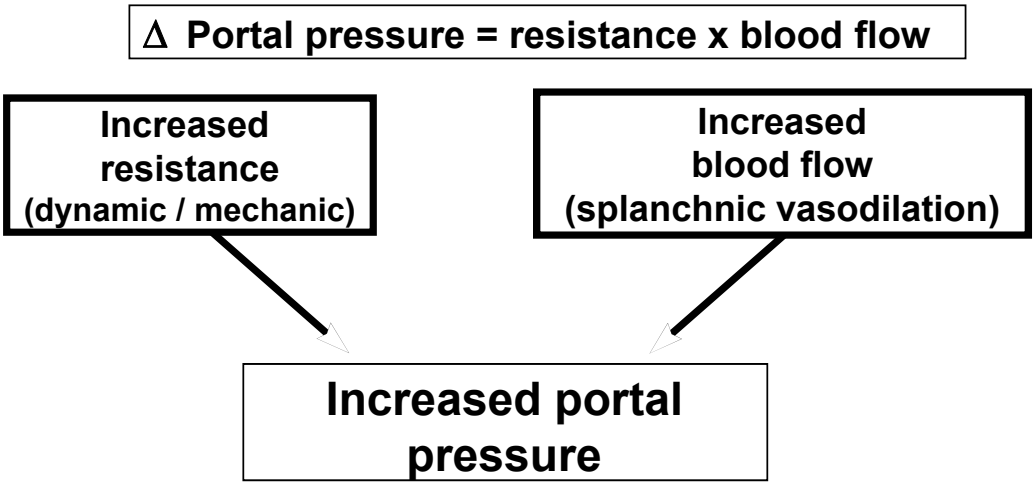
Objective

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

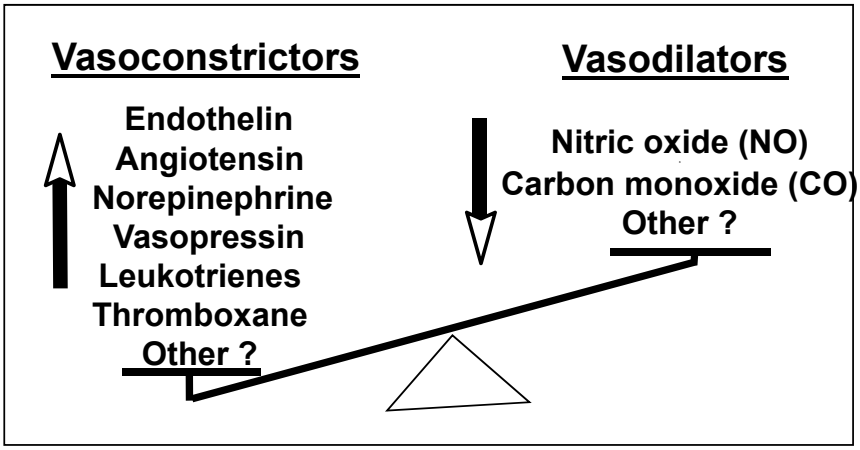
Introduction

- 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



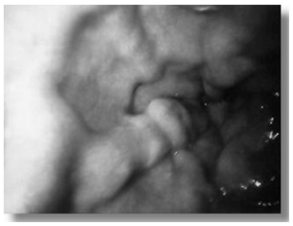
Vasodilator/vasoconstrictor imbalance in the pathogenesis of increased intrahepatic vascular resistance in cirrhosis



Classification of varices Japanese, US, Baveno, Paquets

Japanese	US	Baveno	Paquet
Absent	Absent	Absent	Absent
Grade 1: small EV not disappearing with insufflation	Small	<5 mm	I
Grade 2: median varices occupying <1/3rd of lumen	Medium	>5 mm	II
Grade 3: large EV occupying >1/3rd of lumen	Large	>5 mm	III
	Giant	>5 mm	IV

Upper GI Endoscopy



Presence ?

Size ?

small <5cm

large >5cm

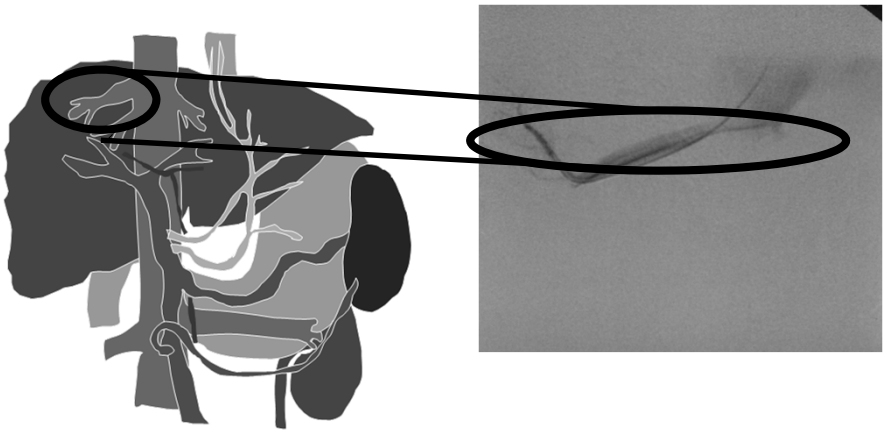
Red Spots ?

Predictors of Bleeding

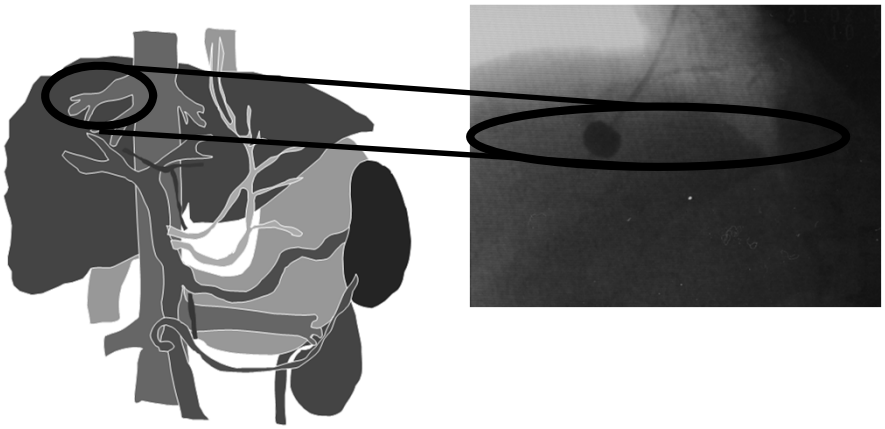
1. Variceal size:
   - Small varix 10% at 2 years.
   - Large varix 30% at 2 years.
2. Presence of red signs.
3. Severity of underlying liver disease:
   - Child A - 17%.
   - Child B - 31%.
   - Child C - 39%. (NIEC New Engl J Med 1988)
4. MELD score
5. Hepatic Venous Pressure Gradient (HVPG)

Hepatic Venous Pressure Gradient

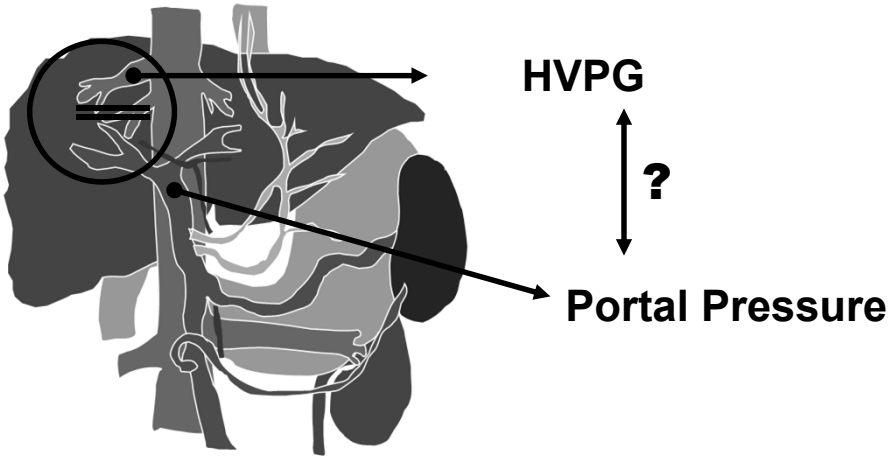
- Most commonly used for measurement of portal pressure
- **HVPG—**gradient between the wedged and free hepatic venous pressure (normal gradient, <5 mm Hg).
  - Polio J, et al. Hemodynamic factors involved in the development and rupture of esophageal varices. Semin Liver Dis 1986;6:318-331

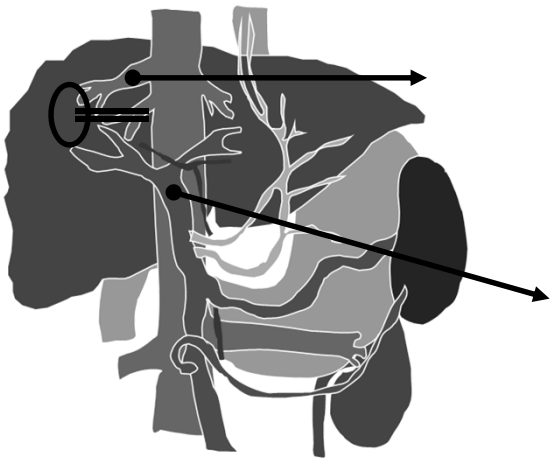


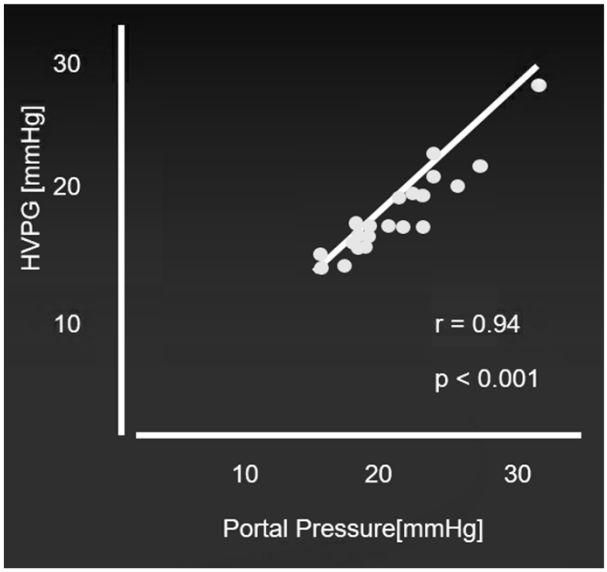
free hepatic venous pressure



wedge hepatic venous pressure





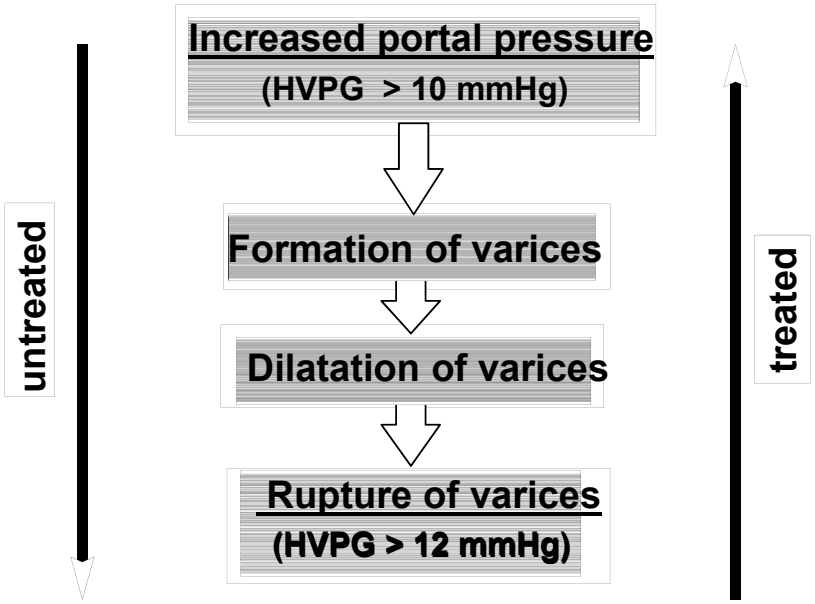


Lin et al. J Hepatol 1989

Prognostic value of HVPG in patients with chronic liver disease

Measurement	Significance
1-5 mm Hg	Normal
6-10 mm Hg	Preclincal 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 morality
≥ 20mm Hg	Treatment failure and mortality in AVB

Natural history of oesophageal varices



Case : Acute Variceal Bleed

- 55 M with HCV and ETOH cirrhosis with moderate ascites. Presenting with UGI bleed. BP: 95/55; HR:110.
- 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.**

Levacher S, et al. Early administration of terlipressin plus glyceryl trinitrate to control active UGI bleeding in cirrhotic patients. Lancet 1995;346:865-868.
Calès P, et al. Early administration of vapreotide for variceal bleeding in patients with cirrhosis. N Engl J Med 2001;344:23-28

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.

Feu F, et al. Double-blind RCT comparing terlipressin and somatostatin for acute variceal hemorrhage. Gastroenterology 1996;111:1291-1299

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.

- Besson I, et al. Sclerotherapy with or without octreotide for acute **variceal bleed**ing. N Engl J Med 1995;333:555-560.
- Hasnain A. Shah, **Khalid Mumtaz**, et al.. Sclerotherapy Plus Octreotide Versus Sclerotherapy alone in the management of GOV Hemorrhage. *J Ayub Med Coll Abbotabad* 2005:17(1).

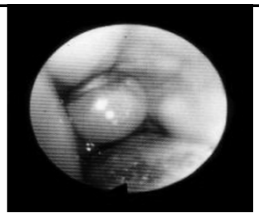
Abid S, Mumtaz K, et al. Efficacy And Safety Of Terlipressin Vs Octreotide As Adjuvant Therapy In Bleeding Esophageal Varices. *Am J Gastroenterol* 2009; 104:617–623;

- 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), ($P \leq 0.001$).**
- **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

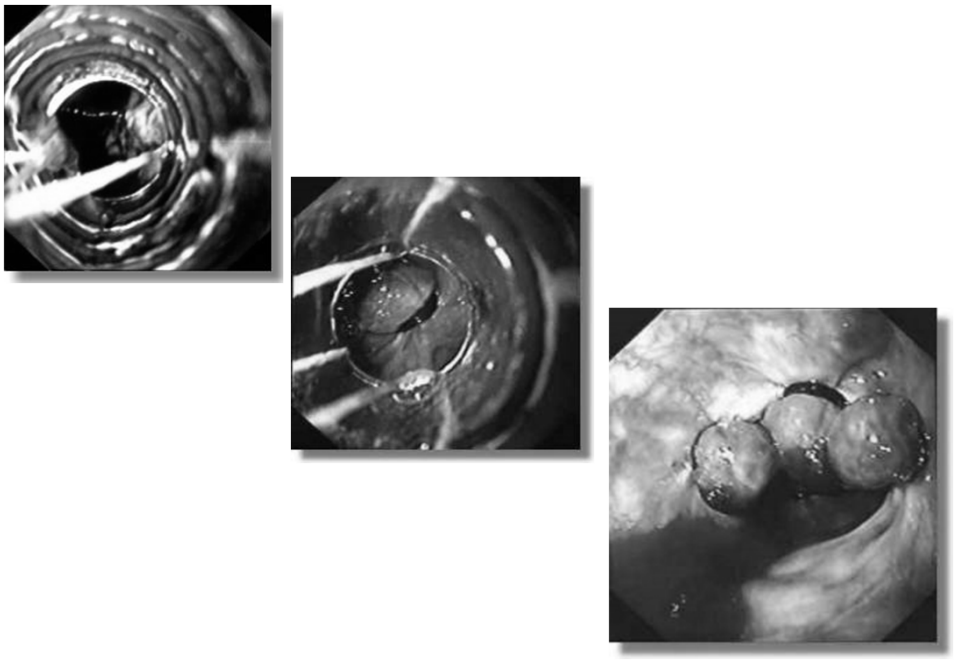
- **Endoscopic Sclerotherapy:**
  - It stops bleeding in 80 to 90% of acute variceal hemorrhage.
- **The advantages of EST:**
  - ability to establish definitive control of bleeding under direct vision.
- **Drawbacks:**
  - risk of local complications, including perforation, ulceration, thrombosis and stricture.

Endoscopic band ligation

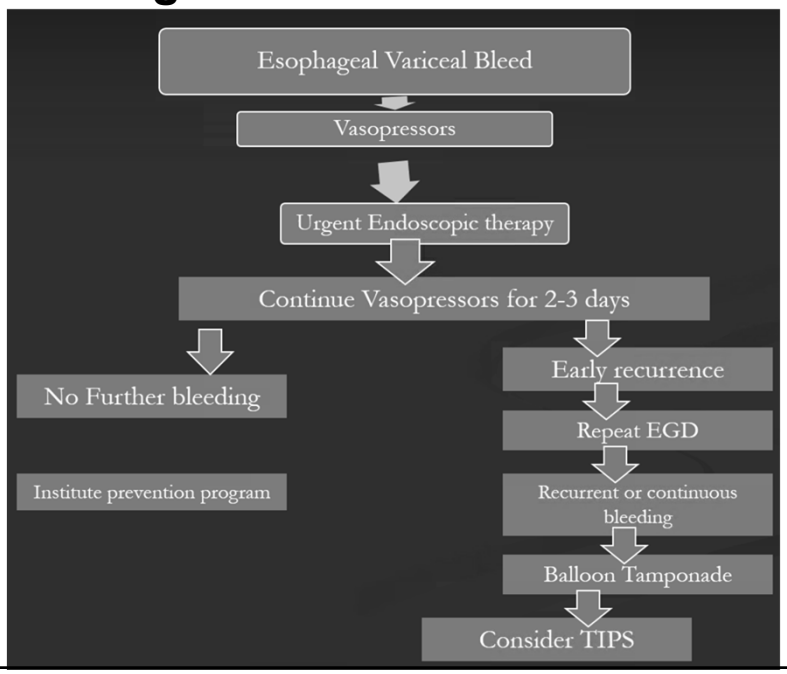


- RCTs of acute **variceal bleed**ing have shown that **EBL is equivalent to sclerotherapy** in achieving initial hemostasis.
- The **complications associated with EBL are fewer** and include superficial ulcerations and, rarely, the formation of strictures.

- **Khalid Mumtaz**, Hasnain Shah, et al. Comparison of EBL with EST in bleeding esophageal varices. Gastroenterology suppl. (Abstract) No. M1263 Apr. 2004; 126(4): A728.
- Lo GH, et al. Emergency banding ligation versus sclerotherapy for the control of active bleeding from esophageal varices. Hepatology 1997;25:1101-1104.



Suggested Algorithm of Acute Variceal Hemorrhage



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.
  - Feu F, et al. Relation between portal pressure response to pharmacotherapy and risk of recurrent variceal haemorrhage. Lancet 1995;346:1056-1059
- Several RCTs, including a meta-analysis, have demonstrated that **non-selective BB** (Nadolol, Carvedilol) decrease the risk of recurrent bleeding and prolong survival.
  - **Bernard B, et al. . B-adrenergic antagonists in prevention of GI rebleeding in patients with cirrhosis: a meta-analysis. Hepatology 1997;**

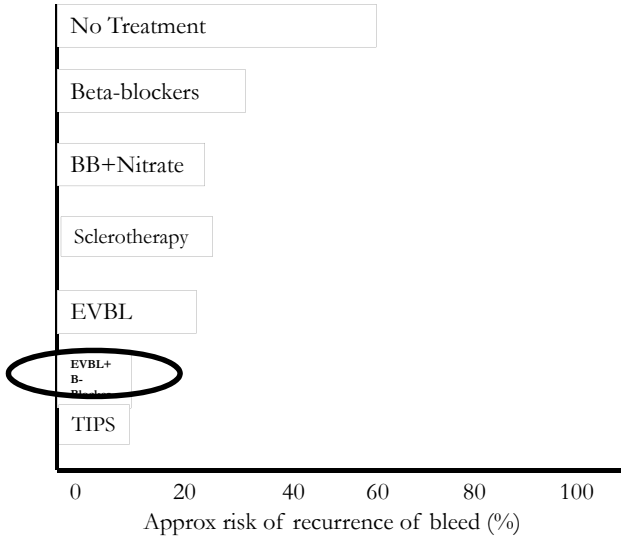
Endoscopic Band Ligation

- **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.
  - **Rosario Gonzalez, et al. Meta-analysis: Combination Endoscopic and Drug Therapy to Prevent Variceal Rebleeding in Cirrhosis. *Ann Intern Med.* 2008**

Rosario Gonzalez, et al. Meta-analysis: Combination Endoscopic and BB Therapy to Prevent Variceal Re-bleeding in Cirrhosis. *Ann Intern Med.*

- **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



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.