Esophageal Variceal Hemorrhage

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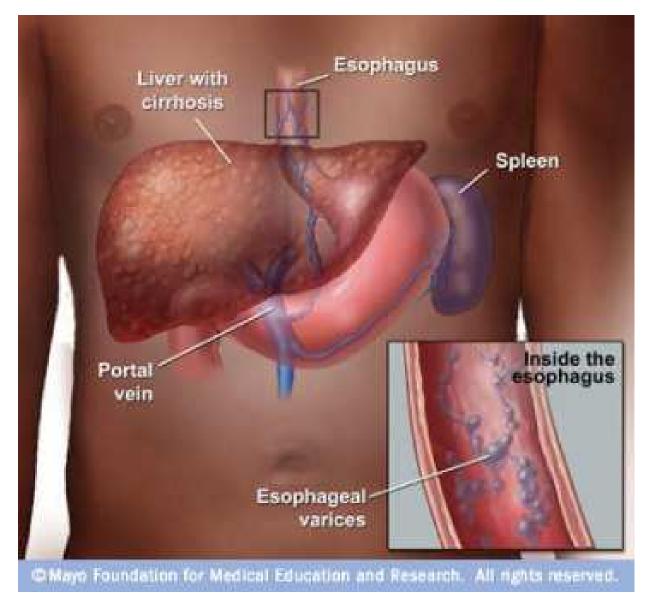
Objectives

- 1. Describe the pathophysiology of esophageal varices and variceal hemorrhage
- Recommend a plan for emergent pharmacological treatment of esophageal variceal hemorrhage
- 3. Identify non-pharmacologic treatment options for esophageal variceal hemorrhage

Esophageal Varices

- Porto-systemic collaterals resulting from portal hypertension
 - Cirrhosis of the liver
 - Portal/systemic circulation
- Elevated hepatic venous pressure gradient (HVPG)
 - Normal: 3-5 mmHg
 - ->10 mmHg strong predictor of varices development

Esophageal Varices

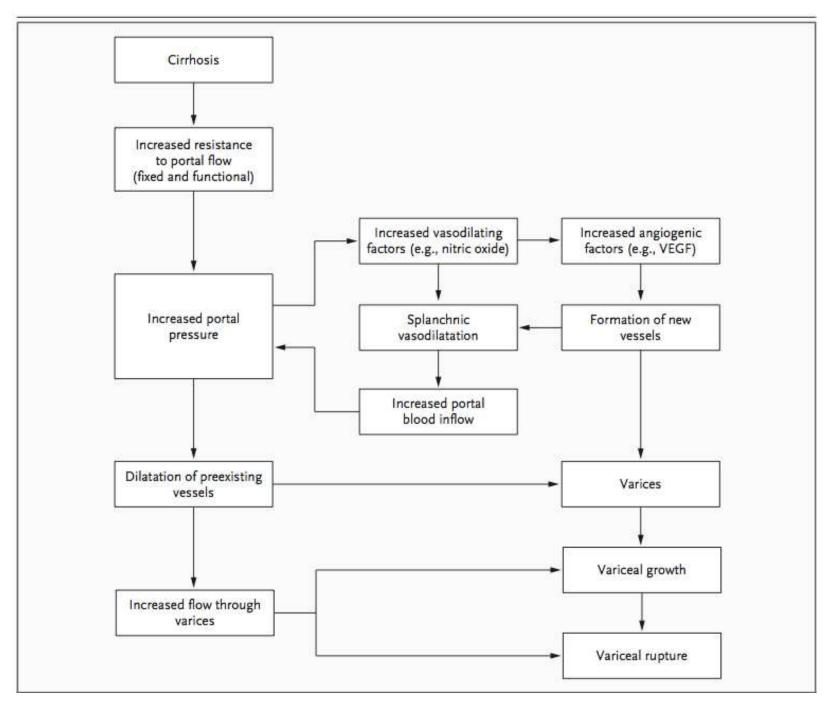


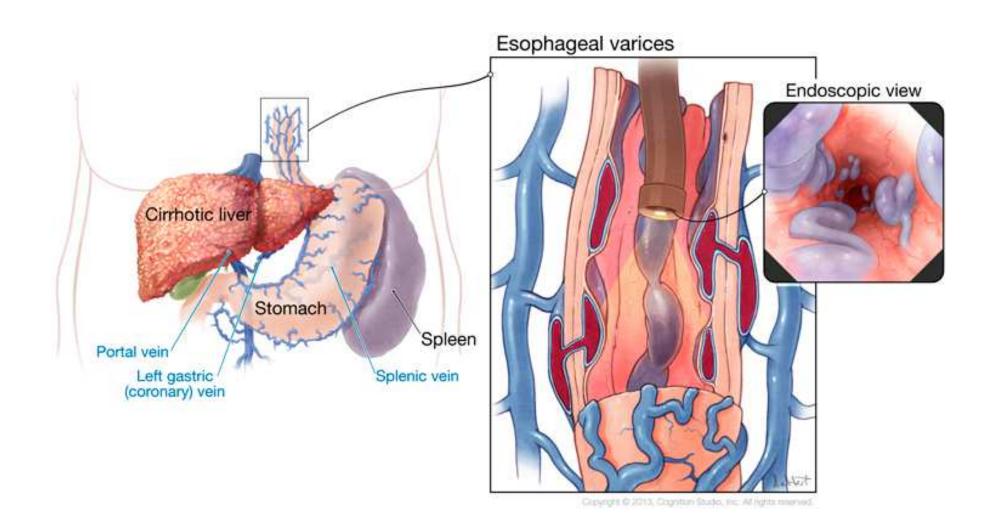
Portal Hypertension

- Increased resistance to blood flow in liver
 - Structural: cirrhotic liver (fibrous tissue, nodules)
- Intrahepatic vasoconstriction
 - Dynamic: decreased nitric oxide production
- Varix development does not affect portal hypertension
 - Increased resistance to portal flow
 - Increased portal inflow

Variceal Hemorrhage

- Gastroesophageal varices present in 50% of patients with cirrhosis
 - Highest rate Child Class B & C liver disease
- 2007 variceal hemorrhage rate 5-15%
- Six week mortality rate 20%
- Variceal wall tension
 - Primary predictor of rupture
 - Larger diameter varix > smaller varix
 - Same HVPG
- Lethal complication





- 70 yo male presented to the ED with gross hematemesis beginning that evening
- Stated complaint: "Upper GI bleed"
- PMH

– Cirrhosis
CAD s/p CABG

Esophageal varices Hypertension

– GI bleedHyperlipidemia

SplenomegalyNeuropathy

PancytopeniaCOPD

- Social History
 - No alcohol for 7+ years (extensive history)
 - Dips snuff
- Home Medications

Metoprolol 12.5 mg daily

Lasix 60 mg

Prinvil 10 mg BID

Zocor 20 mg daily

Folic acid 1 mg daily

Neurontin 300 mg BID

Prilosec 20 mg daily

MVT daily

- Vital Signs
 - HR 71
 - -BP79/33
- Laboratory Data
 - Hemoglobin 8.5
 - Hematocrit 25.1
 - Platelets 125

- Emergency Department management
 - Protonix 80 mg IV bolus, followed by Protonix drip
 - Sandostatin (octreotide) 50 mcg bolus, followed by 50 mcg/hr drip
 - Rocephin 1 gram IV x 1 dose
 - Erythromycin 250 mg IV x 1 dose
 - FFP & PRBC transfusions x 3
 - -1LNS
 - GI consult

Emergency Management of Esophageal Variceal Hemorrhage

- Splanchnic vasoconstrictor, prompt initiation
 - Somatostatin analog IV
 - Sandostatin (octreotide) in U.S.
- Prophylactic antibiotic, short-term
 - Norfloxacin/ciprofloxacin
 - Rocephin
- Endoscopic treatment < 12 hours after admission
 - Diagnosis and treatment

Emergency Management of Esophageal Variceal Hemorrhage

- Intravascular volume support
- Blood transfusions
 - Maintain hemoglobin ~8 g/dL

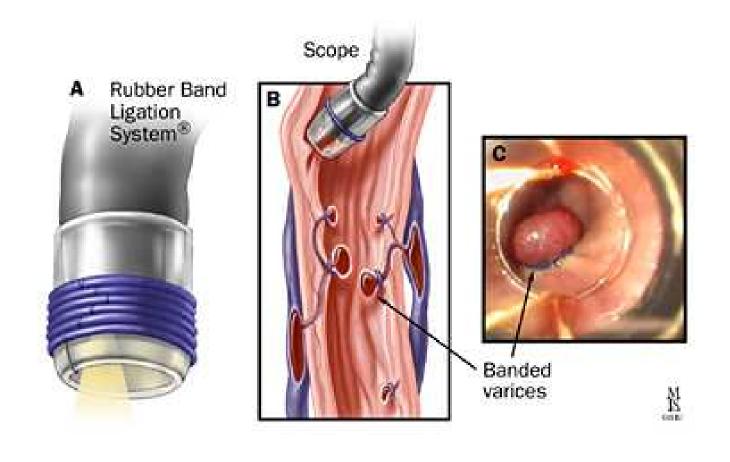
Sandostatin (octreotide)

- Somatostatin analog, synthetic octapeptide
 - Somatostatin is a naturally occurring hormone
 - Octreotide prolonged half life
 - IV or SQ administration
 - MOA: Splanchnic vasoconstriction to reduce portal venous inflow
 - Does not act systemically, acts locally

Sandostatin (octreotide)

- 50 mcg IV bolus, followed by 50 mcg/hr continuous IV infusion
 - 3-5 days per guidelines
- Can be administered > 24 hours
 - vs vasopressin
- No FDA indication for variceal bleeding

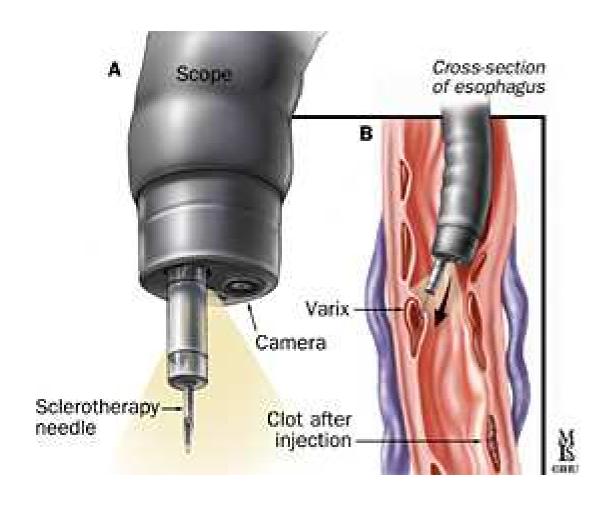
Endoscopic Variceal Ligation



Endoscopic Variceal Ligation



Sclerotherapy



Patient Case: ICU

- GI consult A/P
 - Upper GI bleed (rule out varices)
 - Plan for panendoscopy
- Esophagogastroduodenoscopy (EGD)
 - < 1 hour after transfer to ICU</p>
 - 16 hours from ED triage
 - Large varices found; 4 bands placed
- Antibiotic
 - IV Levaquin

Secondary Prophylaxis

Regimen	Dose	Goal	Duration	Follow-up
Beta-blocker				
Propranolol	Start at 20 mg orally twice a day	Increase to maximally tolerated dose or until heart rate is approximately 55 beats/min	Indefinite	Ensure heart-rate goals are met at eac clinic visit; no need for follow-up endoscopy
Nadolol	Start at 40 mg orally once a day	Increase to maximally tolerated dose or until heart rate is approximately 55 beats/min	Indefinite	Ensure heart-rate goals are met at each clinic visit; no need for follow-up endoscopy
Endoscopic variceal ligation	Ligate every 2–4 wk	Obliterate varices	Until variceal obliteration achieved (usually 2–4 sessions)	First surveillance endoscopy 1–3 mo after obliteration, then every 6–12 m indefinitely
Isosorbide mononitrate in association with a beta- blocker (either propranolol or nadolol)†	10 mg given orally every night, with stepwise increase to a maximum of 20 mg twice a day	Increase to maximally tolerated dose with maintenance of blood pressure at >95 mm Hg	Indefinite	Ensure compliance with medication regimen at each visit; no need for follow-up endoscopy

^{*} Only one beta-blocker plus ligation should be used. Therapies that should not be used for first-line prevention of recurrent variceal hemorrhage are nonselective beta-blockers alone, endoscopic variceal sclerotherapy, endoscopic variceal ligation alone, and endoscopic variceal ligation plus endoscopic variceal sclerotherapy.
† This therapy is being studied. 55,56 It is recommended for patients who are not candidates for ligation.

- ICU admission complicated by respiratory failure and opioid withdrawal
- Transferred to floor 3 days after ICU admission
 - Protonix drip discontinued
- Discharged home next day
 - Discharge diagnosis: Upper GI bleed from esophageal varices, acute anemia blood loss, hemorrhagic shock
 - Discharge medications:
 - Iron 324 mg as directed
 - Levaquin 750 mg PO x 4 days
 - Same as admission

	Hemoglobin (g/dL)	Hematocrit (%)
11/13	8.5	25.1
11/14	6.6	19.3
11/14	7.8	23.3
11/14	8.2	24.6
11/14	7.8	22.9
11/15	9.6	28.9
11/15	8.9	26.9
11/15	8.3	25.1
11/15	8.6	25.9
11/16	10.2	31.3
11/16	10.6	31.7
11/16	10.5	31.4
11/17	10.4	31.5
11/17	8.4	24.4
11/18	10.0	30.1

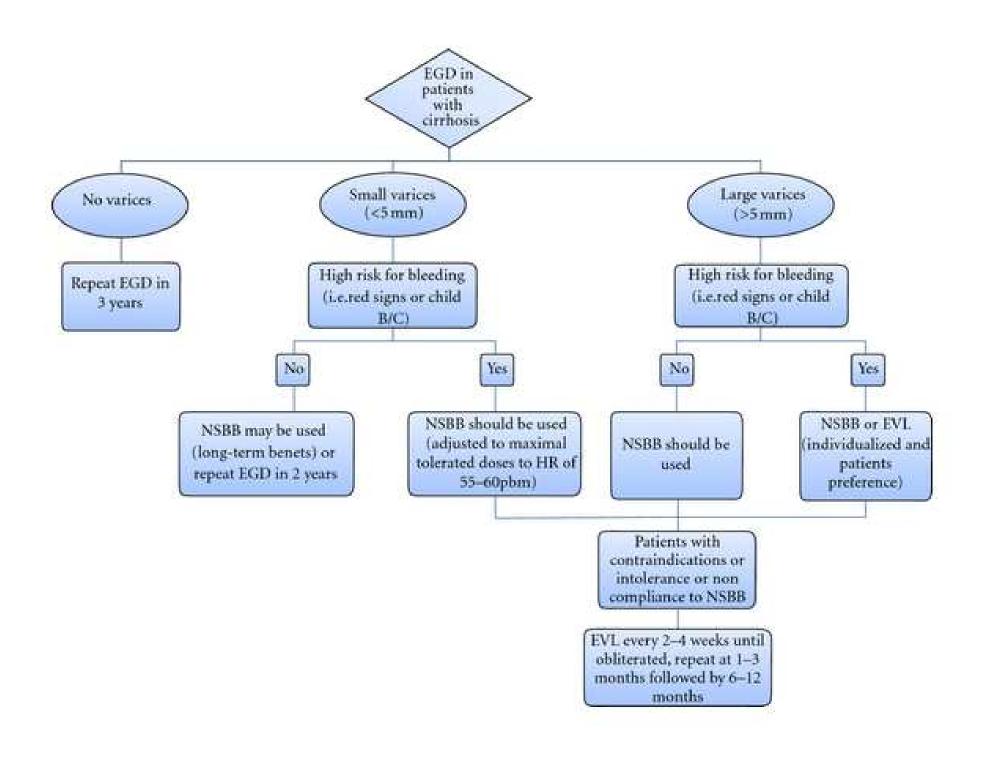
- Actual Treatment vs AASLD Guideline Recommendation
 - Octreotide initiated and continued until discharge
 - Levaquin continued 4 days post discharge
 - Protonix drip not addressed by guideline
 - EVL ideal per guideline
 - Blood transfusions per guideline
 - Not discharged on non-selective beta-blocker
 - CAD s/p CABG, Coreg?

Primary Prophylaxis

Regimen†	Dose	Goal	Duration	Follow-up
Propranolol	Starting dose of 20 mg given orally twice a day	Increase to maximally tolerated dose or until heart rate is approximately 55 beats/min	Indefinite	Ensure heart-rate goals met at each clinic visit; no need for follow-up endoscopy
Nadolol	Starting dose of 40 mg given orally once a day	Increase to maximally tolerated dose or until heart rate is approximately 55 beats/min	Indefinite	Ensure heart-rate goals met at each clinic visit; no need for follow-up endoscopy
Endoscopic variceal ligation	Every 2–4 weeks	Obliterate varices	Until variceal obliteration achieved (usually 2-4 sessions)	Perform first surveillance endoscopy 1–3 mo after obliteration, then every 6–12 mo indefinitely

^{*} Therapies that should not be used as prophylaxis include nitrates alone, endoscopic variceal sclerotherapy, shunt therapy (either transjugular intrahepatic portosystemic shunt or surgical shunt), nonselective beta-blockers plus endoscopic variceal ligation, and nonselective beta-blockers plus nitrates.

[†] Only one of the three regimens should be used.



Salvage/Rescue Therapy

- Hemorrhage uncontrollable OR re-bleeding despite pharmacologic and EVL therapy
 - Reverses portal hypertension
- TIPS (transjugular intrahepatic portosystemic shunt)
 - Percutaneous
- Shunt surgery
- Balloon tamponade

References

- Garcia-Tsao G, Sanyal AJ, Grace ND, et al. Prevention and management of gastroesophageal variceal hemorrhage in cirrhosis. AASLD practice guidelines. Hepatology; 2007; 46(3);922-938.
- Garcia-Tsao G, Bosch J. Management of varices and variceal hemorrhage in cirrhosis. N Engl J Med. 2010;362:823-32.
- Yan BM, Lee SS. Emergency management of bleeding esophageal varices: drugs, bands or sleep? Can J Gastroenterol 2006;20(3):165-170.
- Corley DA, Cello JP, Adkisson W, et al. Octreotide for acute esophageal variceal bleeding: a meta-analysis. Gastroenterology. 2001;120:946–954.

Questions?

