

Upper GI Bleeding

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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

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

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

- Non-variceal bleeding
 - ✓ Etiology
 - ✓ Acute management
 - Medical
 - Endoscopic
 - ✓ Recurrent bleeding
 - ✓ Prevention

- Variceal bleeding
 - ✓ Primary prophylaxis
 - ✓ Acute management
 - Medical
 - Endoscopic
 - ✓ Recurrent bleeding
 - ✓ Secondary prophylaxis

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

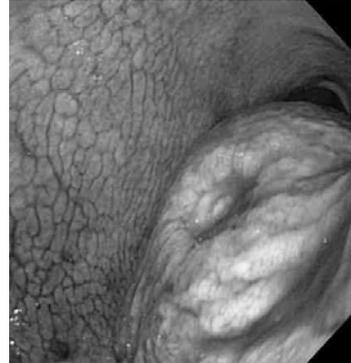
Hemosuccus Pancreaticus

- 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

GIST



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)

Management

- **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 placebo³

¹Bardou M, et al. Aliment Pharmacol Ther 2005.
²Leontiadis G, et al. Cochrane Database Syst Rev 2006.
³Conway S, et al. Cochrane Database Syst Rev 2005.

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 bleeding⁴
 - Trend toward significance in all cause UGI bleeding
- **All cause UGI bleeding**
 - ✓ 2 RCT's demonstrated no significant benefit compared to placebo⁵ or H₂ blocker⁶
 - ✓ 1 RCT showed significant benefit in initial hemostasis, blood transfusions, need for surgery, length of hospital stay compared to H₂ blocker⁷

⁴Imperiale T, et al. Ann Intern Med 1997.
⁵Christiansen J, et al. Gastroenterology 1988.
⁶Lin H, et al. J Clin Gastroenterol 1996.
⁷Lin H, et al. Hepatogastroenterology 1995.

Erythromycin before endoscopy

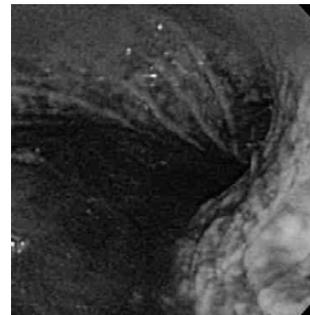
- Shown in multiple studies to improve the quality of endoscopic exam
 - ✓ Some studies also show decreased need for second look EGD
- Given as a single 250 mg IV dose
- Must check ECG before giving to assess QTc

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

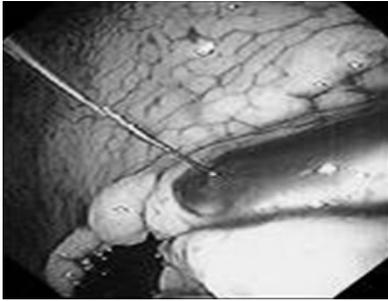
Endoscopic Findings

- Clotted blood in stomach



Endoscopic Findings

- Active bleeding



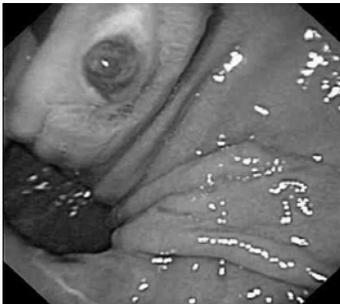
Endoscopic Findings

- Adherent clot



Endoscopic Findings

- Visible vessel



Endoscopic Therapy

- High risk lesions treated with dual therapy
 - ✓ Injection with epinephrine (1:10,000)
 - AND
 - ✓ 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

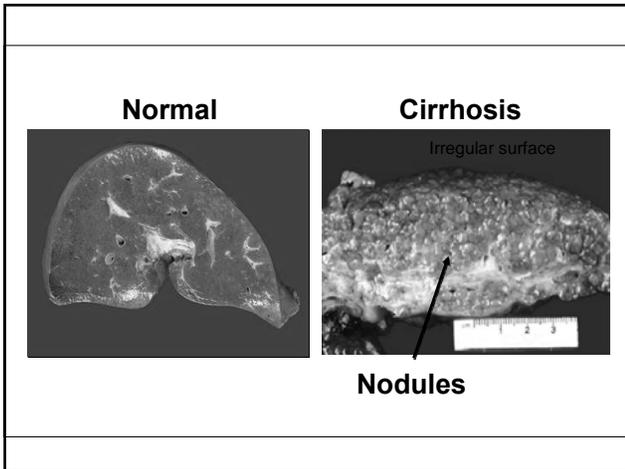
- **Eliminating NSAID's**
- **Eradication of H. pylori**
 - ✓ Triple therapy for 10-14 days first line therapy
 - ✓ Bismuth + Metronidazole + Tetracycline
 - QID dosing can decrease compliance
 - ✓ PPI + Amoxicillin + Clarithromycin
 - ✓ Increasing resistance to metronidazole, clarithromycin
 - ✓ Most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

Variceal Bleeding

Jim Hanje, MD

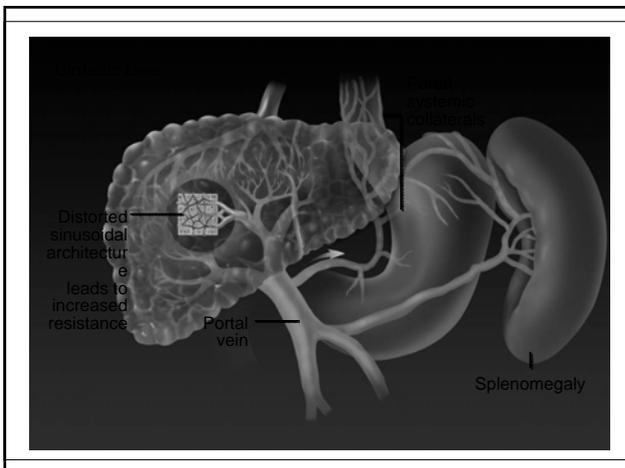
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Portal Hypertension

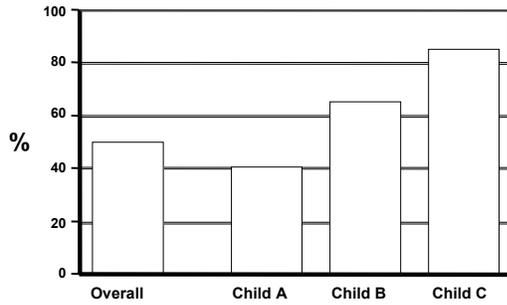
- Progressive complication of cirrhosis
- Marks transition from early compensated cirrhosis to decompensated, end-stage liver disease



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

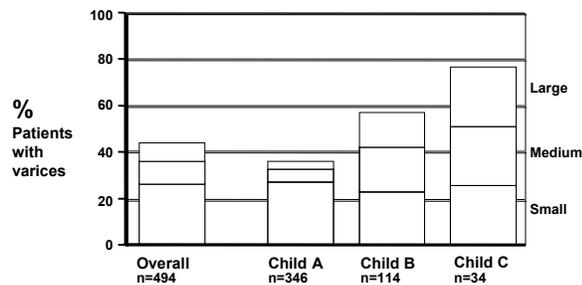


Pagliari et al., In: Portal Hypertension: Pathophysiology and Management, 1994: 72

Diagnosis

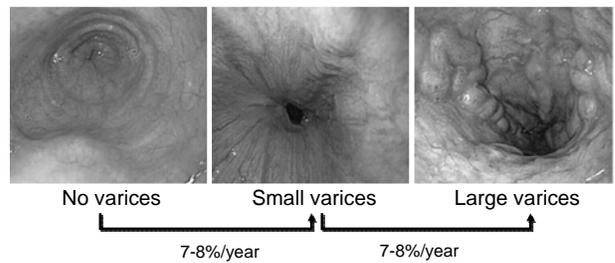
- Screening EGD should be performed at time of diagnosis of cirrhosis to screen for varices
- Varices progress at a rate of 8% per year
- Repeat EGD every 2-3 years depending on size of varices to evaluate for progression

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



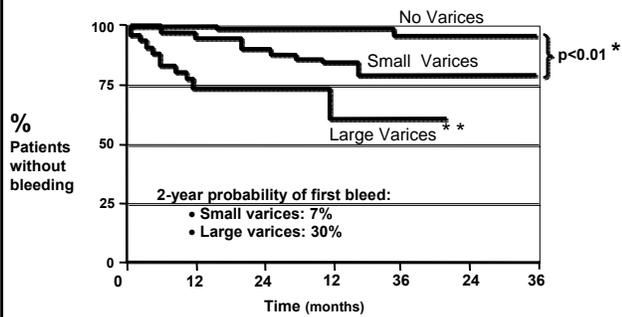
Pagliari et al., In: Portal Hypertension: Pathophysiology and Management, 1994: 72

Varices Increase in Diameter Progressively



Merli et al. J Hepatol 2003;38:266

Large Varices Are More Likely To Rupture



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

Primary Prophylaxis: Non-Selective Beta-Blockers

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

D'Amico et al., *Sem Liv Dis* 1999; 19:475

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Primary Prophylaxis: Nonselective Beta-Blockers

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

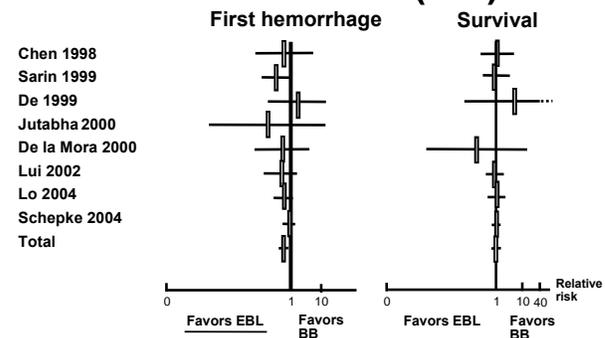
Primary Prophylaxis – Endoscopic Band Ligation (EBL)

- 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 B-blockers, but more severe
 - ✓ Bleeding due to esophageal ulcerations, variceal rupture

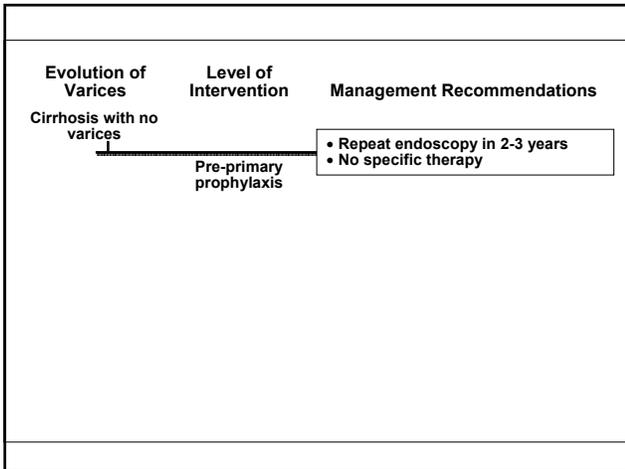
Primary Prophylaxis: Nonselective Beta-Blockers

- 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

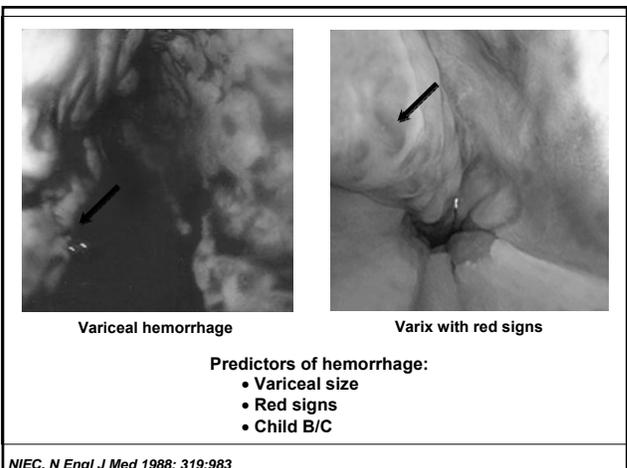
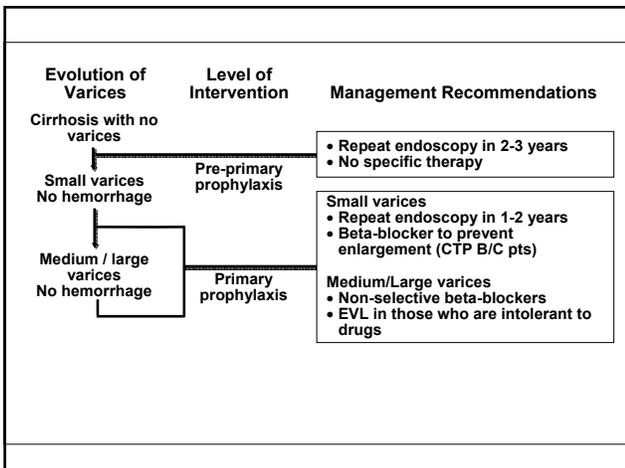
Primary Prophylaxis: EBL vs Beta-Blockers (BB)



Khuroo, et al., *Aliment Pharmacol Ther* 2005; 21:347



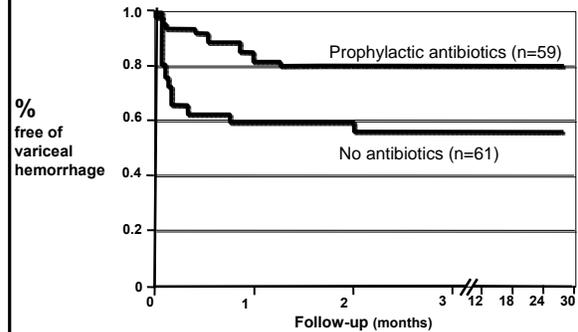
Acute Variceal Bleeding



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 VIIa
 - 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



Hou M-C et al., Hepatology 2004; 39:746

Prophylactic Antibiotics

- Higher incidence of bacterial infections in cirrhotic patients admitted with UGI bleed
 - Increased risk with increasing disease severity
- Flouoroquinolone 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

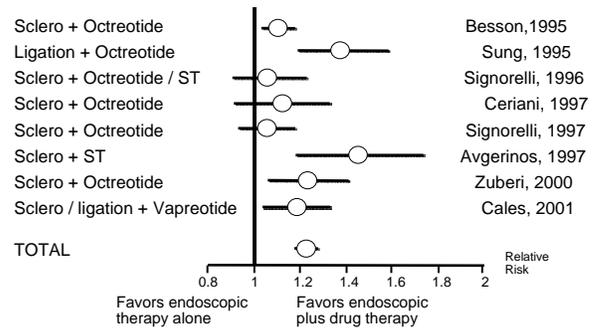
Prophylactic Antibiotics

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

Pharmacologic Therapy

- **Octreotide**
 - ✓ Synthetic analogue of somatostatin
 - 50ug bolus, followed by 50ug/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

Combination Drug / Endoscopic Therapy More Effective Than Endoscopic Therapy Alone



Bañares R et al., *Hepatology* 2002; 35:609

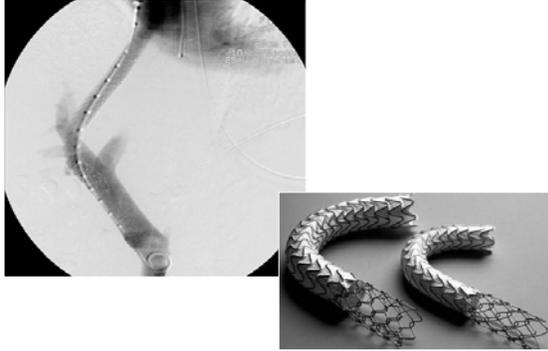
Endoscopy

- **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

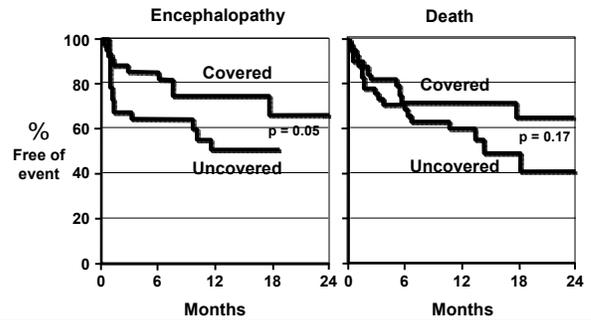
Refractory Bleeding

- 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

Polytetrafluoroethylene-covered TIPS stents

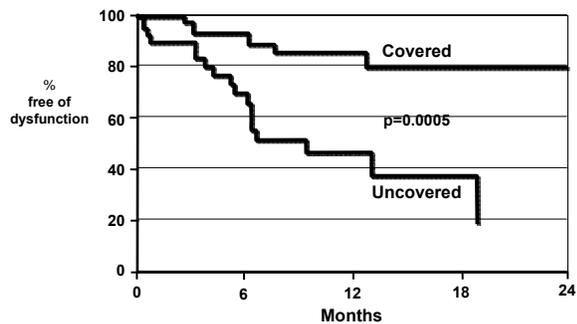


Covered Stents vs Uncovered Stents

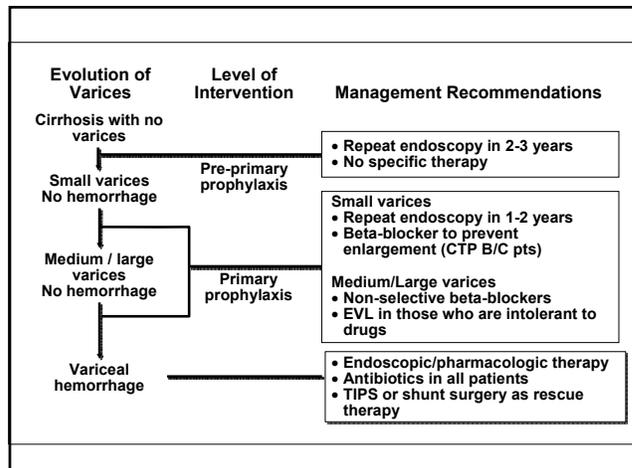


Bureau et al. Gastroenterology 2004; 126:469

Covered Stents vs Uncovered Stents



Bureau et al. Gastroenterology 2004; 126:469



Secondary Prophylaxis

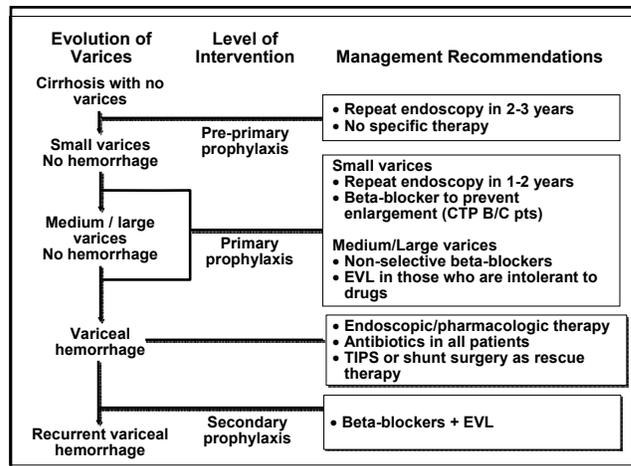
- Cirrhotics with prior variceal bleed have high risk of rebleeding and death
- If untreated, 60-70% will rebleed within 1-2 years with 30% mortality rate

Secondary Prophylaxis

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

Secondary Prophylaxis

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



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**