

# 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: H<sub>2</sub>-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 3<sup>rd</sup> portion of duodenum
- "Herald" bleed: self-limited bleed hours/days before severe bleeding

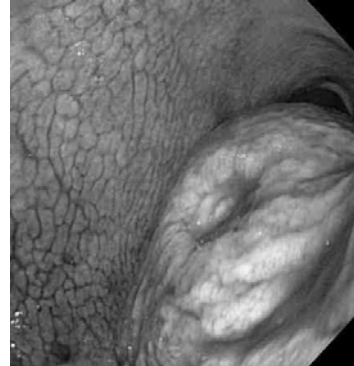
## Hemosuccus Pancreaticus

- 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), O<sub>2</sub>, 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<sup>1,2</sup>
    - 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 placebo<sup>3</sup>

<sup>1</sup>Bardou M, et al. Aliment Pharmacol Ther 2005.  
<sup>2</sup>Leontiadis G, et al. Cochrane Database Syst Rev 2006.  
<sup>3</sup>Conway 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 bleeding<sup>4</sup>
    - Trend toward significance in all cause UGI bleeding
- **All cause UGI bleeding**
  - ✓ 2 RCT's demonstrated no significant benefit compared to placebo<sup>5</sup> or H<sub>2</sub> blocker<sup>6</sup>
  - ✓ 1 RCT showed significant benefit in initial hemostasis, blood transfusions, need for surgery, length of hospital stay compared to H<sub>2</sub> blocker<sup>7</sup>

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

## Erythromycin before endoscopy

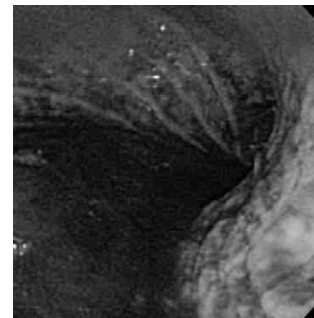
- Shown in multiple studies to improve the quality of endoscopic exam
  - ✓ Some studies also show decreased need for second look EGD
- Given as a single 250 mg IV dose
- Must check ECG before giving to assess QTc

## 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

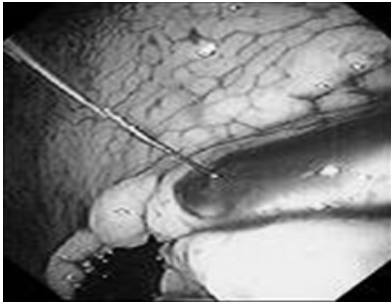
## Endoscopic Findings

- Clotted blood in stomach



## Endoscopic Findings

- Active bleeding



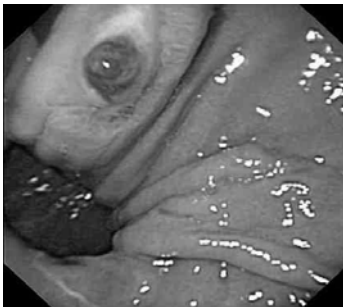
## Endoscopic Findings

- 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 1<sup>st</sup> 72 hours
- Risk factors
  - ✓ Significant bleeding
    - Hemodynamic instability (HR>100; SBP<100)
    - Transfusion > 4 units PRBC
  - ✓ Anticoagulation
  - ✓ Endoscopic stigmata

## Repeat Endoscopy

- “2<sup>nd</sup> 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

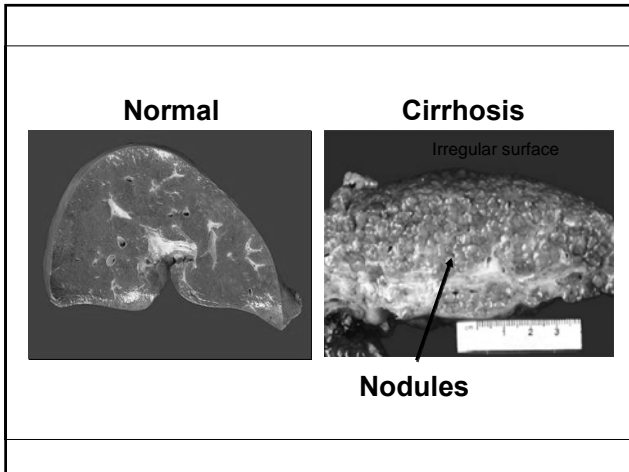
- **Eliminating NSAID's**
- **Eradication of H. pylori**
  - ✓ Triple therapy for 10-14 days first line therapy
  - ✓ Bismuth + Metronidazole + Tetracycline
    - QID dosing can decrease compliance
  - ✓ PPI + Amoxicillin + Clarithromycin
  - ✓ Increasing resistance to metronidazole, clarithromycin
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

## Variceal Bleeding

**Jim Hanje, MD**

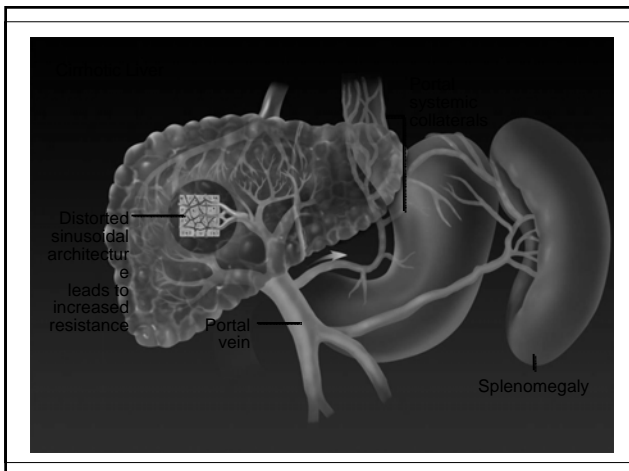
Assistant Professor of Gastroenterology

Ohio State University Medical Center



## Portal Hypertension

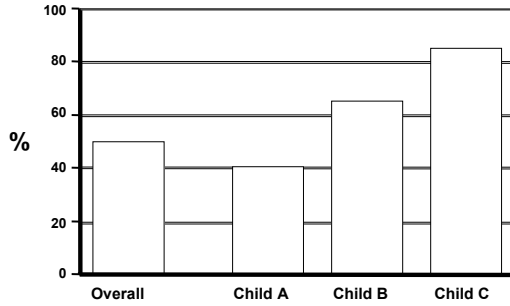
- Progressive complication of cirrhosis
- Marks transition from early compensated cirrhosis to decompensated, end-stage liver disease



## 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

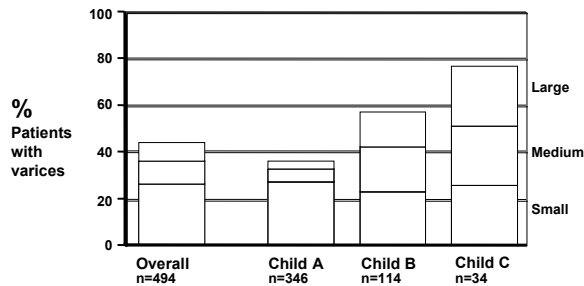


Pagliari et al., In: Portal Hypertension: Pathophysiology and Management, 1994: 72

## Diagnosis

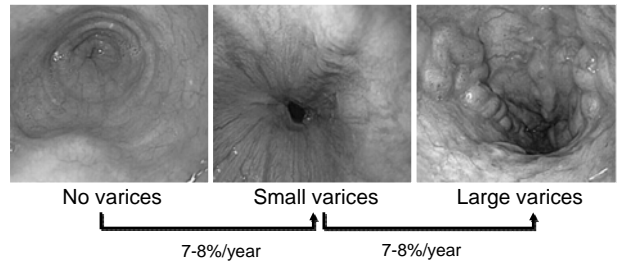
- Screening EGD should be performed at time of diagnosis of cirrhosis to screen for varices
- Varices progress at a rate of 8% per year
- Repeat EGD every 2-3 years depending on size of varices to evaluate for progression

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



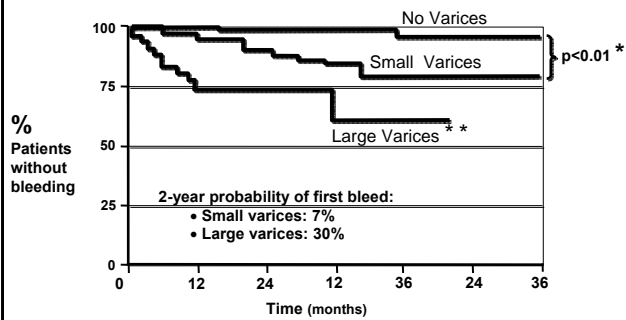
Pagliari et al., In: Portal Hypertension: Pathophysiology and Management, 1994: 72

### 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 ( $\beta$ -2 effect)  
PRIMARY
  - ✓ Decreased cardiac output ( $\beta$ -1 effect)
- Nadolol, Propranolol
  - ✓ Titrated weekly to goal:  $\downarrow$  HR by 25%

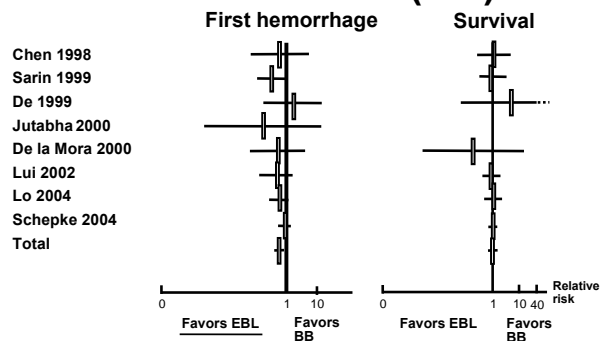
## Primary Prophylaxis – Endoscopic Band Ligation (EBL)

- 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

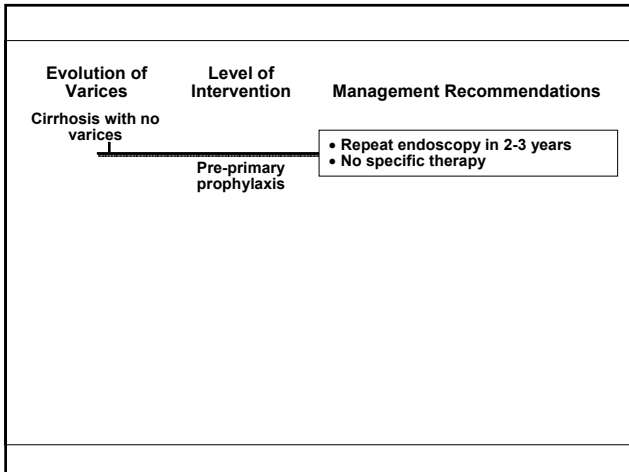
## Primary Prophylaxis: Nonselective Beta-Blockers

- 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

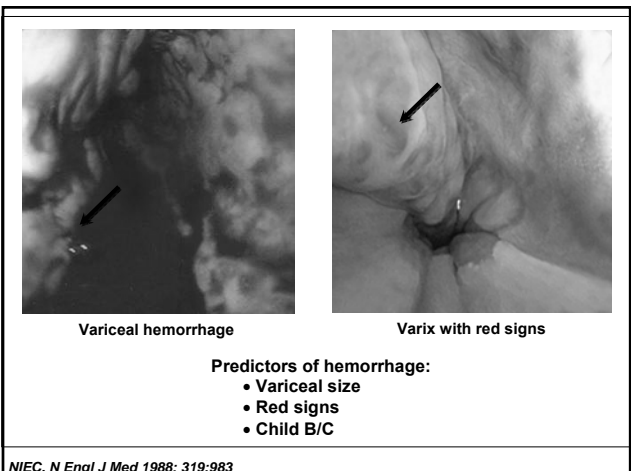
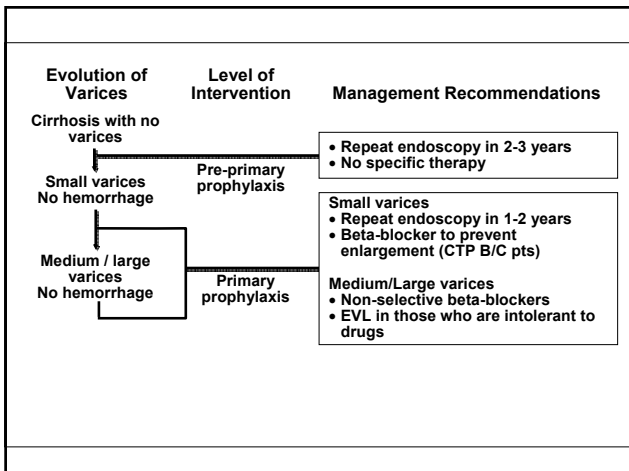
## Primary Prophylaxis: EBL vs Beta-Blockers (BB)



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



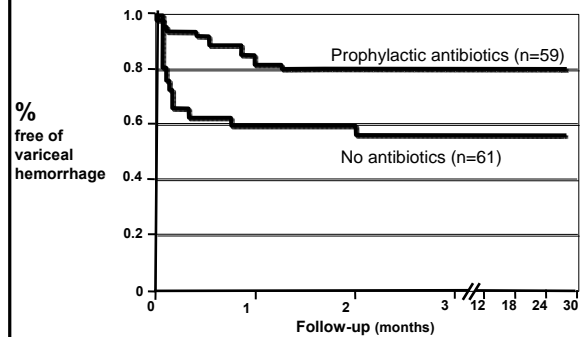
# Acute Variceal Bleeding



## Acute Variceal Bleeding

- Initial management - Resuscitation
  - ✓ ABC's
  - ✓ IV (preferably large-bore peripheral), O<sub>2</sub>, 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

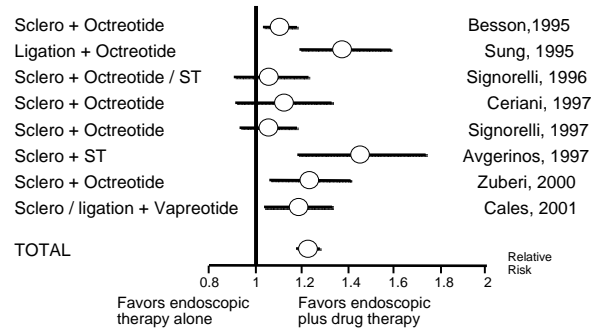
- **IMPROVED OUTCOMES:**
- Decreased rate of bacterial infections and SBP
- Decreased rate of rebleeding
- Improved survival



## 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

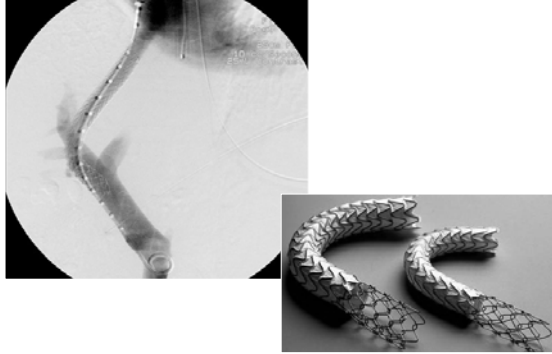
## Endoscopy

- **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

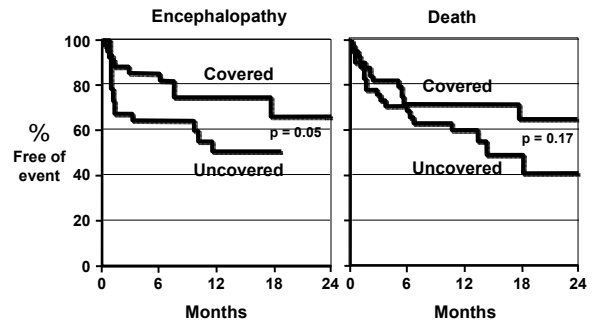
## Refractory Bleeding

- 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

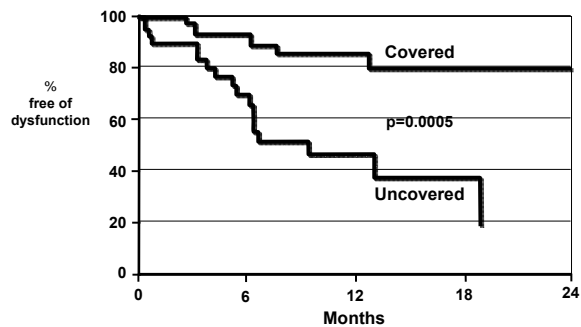


## Covered Stents vs Uncovered Stents

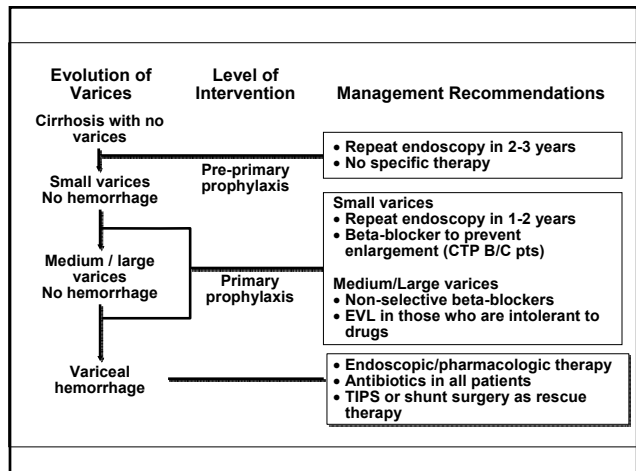


Bureau et al. Gastroenterology 2004; 126:469

## Covered Stents vs Uncovered Stents



Bureau et al. Gastroenterology 2004; 126:469



## Secondary Prophylaxis

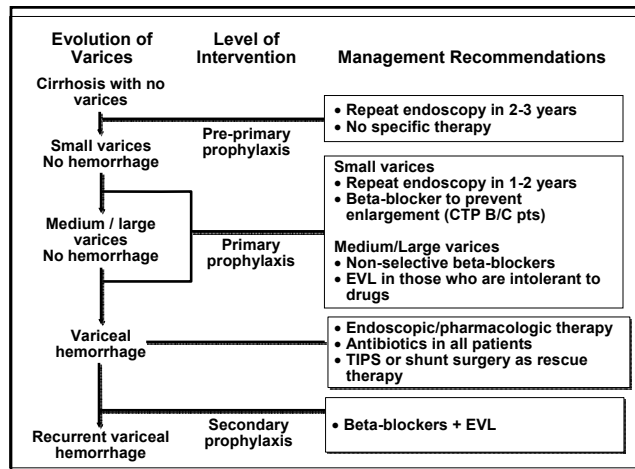
- Cirrhotics with prior variceal bleed have high risk of rebleeding and death
- If untreated, 60-70% will rebleed within 1-2 years with 30% mortality rate

## Secondary Prophylaxis

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

## Secondary Prophylaxis

- **Nonselective  $\beta$ -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**