

Upper Gastrointestinal Hemorrhage

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Acute Upper Non-Variceal Bleed

Magnitude of the Problem

- Incidence: 36-100 per 170,000 persons
- 40% > 60 years old
- Self limited in 80%
- EGD in < 24 hours done in 90%
- Endoscopic hemostasis done in 25%

Acute Upper Non-Variceal Bleed Mortality

- **Mortality:** 10,000 to 20,000 per year
 - Overall: 14 % (10-36%)
 - ***Admission*** for GI bleed: **11 %** mortality
 - GI bleed in ***the hospitalized***: **33 %** mortality

Acute Upper Non-Variceal Bleed Effect of EGD Timing

- **Timing of EGD** (“< 6 h”, VS. “within 48 h”) (Gastrointestinal Endoscopy 2004; 60:1-8) :
 - No effect in transfusion needs nor LOS
 - No effect on need for surgery
 - **No effect on mortality**
 - More “high risk” lesions found on early EGD
 - good for training &
 - may decrease re-bleeding rate.

Signs of GI Bleed

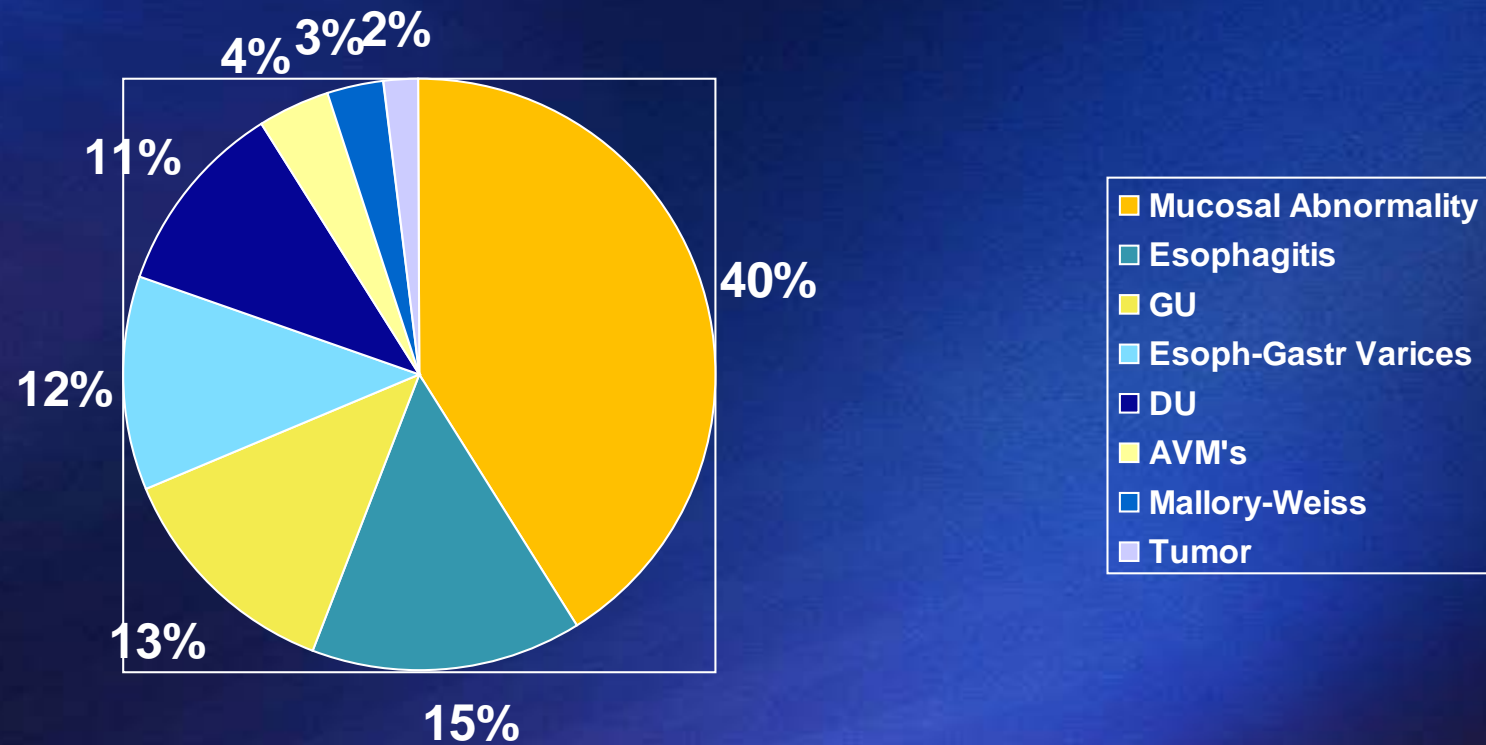
- **Hematemesis:** bleed above ligament of Treitz.
 - Red blood emesis, or
 - Coffee ground emesis
- **Melena:** may be upper or lower source
 - > 200 mL blood in stomach, or
 - Up to 150 mL blood in cecum)
- **Hematochezia:** - usually lower source;
 - Upper {
 - 11% from upper source.
 - Needs > 1000 mL blood from upper source
 - orthostatic @ 3 min: BPs drop \geq 10 mmHg and/or HR increase > 20 bpm.
 - > 150 mL blood in Right colon, or
 - > 100 mL blood in Left colon.

Utility of NGT Aspiration

- 50% of bleedings from duodenal lesion have (-) NGT aspirate
(Gastrointest Endosc 1981;27:94-103)
- Compared with endoscopy, NGT aspirate detects UGI bleeding with (Arch Intern Med 1990;150:1381-4) :
 - 79% Sensitivity &
 - 55% Specificity.
- Clear or bilious aspirate:
 - 14% have high-risk lesions (Gastrointest Endosc 2004;59:172-8).
- Aspirate of blood:
 - 42% have “clean base” or “pigmented spot”.
- **To do NGT aspiration has limited prognostic value and does not change management.**

Causes of UGI Bleeding

Boonpongmanee S et al. Gastrointest Endosc 2004;59:788



Severity Assessment

- Agitation
- Hypotension
- Pallor or Hemoglobin < 8 g/dL
- Tachycardia or Bradycardia (vagal)
- Orthostatic @ 3 minutes: 20% volume loss
 - Systolic drop \geq 10 mmHg, or
 - HR rise > 20/min

Initial Management

- Oxygen supplementation
- Central line or two large bore needles
- Resuscitate first with “0.9% NaCl” or “Lactate Ringer” solution
- Start blood transfusion if needed: **goal Hb & Hct** is
 - 7-8 g/dL & 21-24% in Variceal bleed & Non-Variceal bleed;
 - Exception: Consider transfusion when Hb < 8 g/dL in:
 - Acute coronary syndrome,
 - Exsanguination: Hypotension/tachycardia that indicates intravascular depletion with artificially high Hb.

Initial Management

- **Start PPI therapy** (Cochrane Database Syst Rev. 2010 Jul 7;(7):CD005415)
 - Reduces rates of high-risk EGD stigmata (OR 0.67) and
 - Reduces need for endoscopic therapy (OR 0.68).
 - Esomeprazole or Pantoprazole 80 mg bolus, then 40-80 mg BID
- **Plan & Prepare for Endoscopy**
 - Most patient need EGD within initial 24-48 hours.
 - Some patients need EGD within 12 hours if:
 - EGD will Change Management, or Patient has High Re-Bleeding Risk
 - Few patients (16%) do not need urgent EGD:
 - Glasgow-Blatchford Bleeding Score of 0.
- **Surgery consult**
- **If cirrhosis is known or suspected:**
 - Antibiotics: Ceftriaxone or Ciprofloxacin x 7 days.
 - **Octreotide** (or Somatostatin) drip

Early Disposition Tools

- **Glasgow-Blatchford score**

- score of 0 predicts low risk of re-bleeding; **consider early discharge from ED.**
- <http://www.mdcalc.com/glasgow-blatchford-bleeding-score-gbs>

- **Rockall score**

- score Before Endoscopy of 0, **or**
- score After Endoscopy of 0 to 2
 - predicts no mortality in present episode or in case of re-bleed;
 - **consider early discharge from ED.**
- <http://www.gastrotraining.com/calculators/rockall-score>

Glasgow–Blatchford Score

Laine L. N Engl J Med 2016;374:2367-2376

Table 1. Glasgow–Blatchford Score.*

Values at Admission	Points
Blood urea nitrogen — mg/dl	
<18.2	0
18.2 to <22.4	2
22.4 to <28.0	3
28.0 to <70.0	4
≥70.0	6
Hemoglobin — g/dl	
≥13.0 (men); ≥12.0 (women)	0
12.0 to <13.0 (men); 10.0 to <12.0 (women)	1
10.0 to <12.0 (men)	3
<10.0 (men and women)	6
Systolic blood pressure — mm Hg	
≥110	0
100–109	1
90–99	2
<90	3
Heart rate — beats/min	
<100	0
≥100	1
Other variables	
Melena	1
Syncope	2
Hepatic disease according to history or clinical and laboratory evidence	2
Cardiac failure according to history or clinical and echocardiographic evidence	2

* Glasgow–Blatchford scores range from 0 to 23, with higher scores indicating higher risk. Positive predictive values were calculated in a study by Laursen et al.¹⁰ Among 2305 patients presenting to a hospital with upper gastrointestinal bleeding, 313 (14%) had a score of 0 (positive predictive value, 99.0%), 562 (24%) had a score of 0 or 1 (positive predictive value, 98.8%), and 588 (26%) had a score of 0 to 2 and were younger than 70 years of age (positive predictive value, 99.0%). To convert the values for blood urea nitrogen to millimoles per liter, multiply by 0.357.



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Who can be D/C home from the ED without EGD? (Glasgow-Blatchford Bleeding Score of 0)

- Frequency: 5-20% (mean 16%) of UGI bleeders.
- Risk of needing intervention: < 1%
- FULLFILLS ALL THE CRITERIA:
 - Males with Hb \geq 13 g/dL, or Females with Hb \geq 12 g/dL, AND
 - BUN < 18.2 mg/dL, AND
 - Systolic BP \geq 110 mm Hg, AND
 - Pulse < 100 bpm, AND
 - Absence of: Melena, syncope, heart failure, and liver disease.
- Disposition: Discharge home from ED after EGD or with plans for outpatient EGD in the next few days.

Evaluating Prognosis: Rockall Score (1996)

Re-bleeding & Mortality Risk

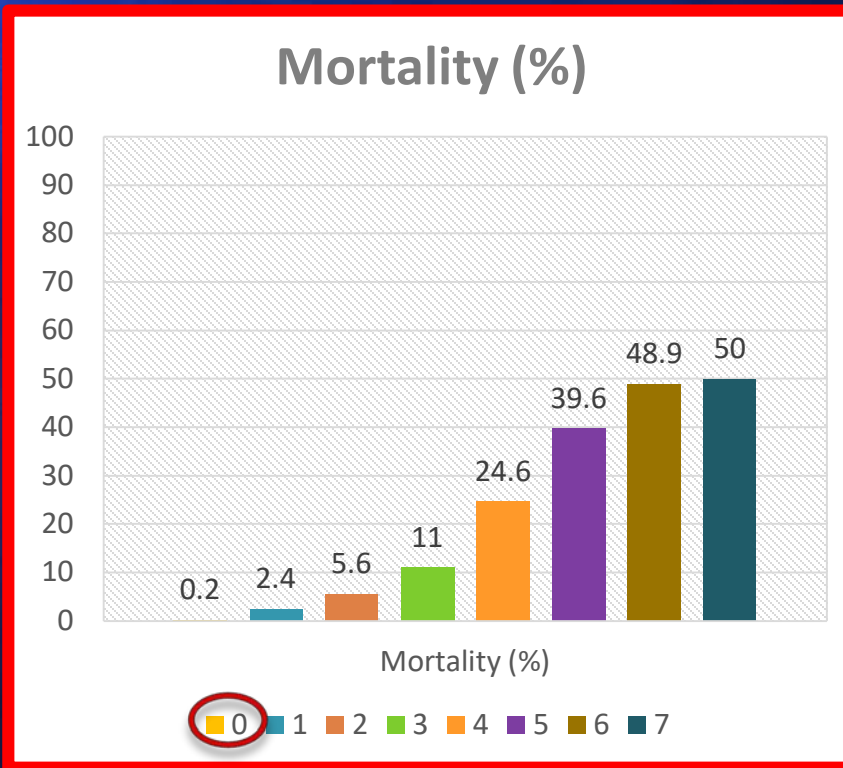
Points	0	1	2	3
Age	<60	60-79	>80	
Vitals	SBP>100 P<100	SBP>100 P>100	SBP<100	
Co-morbidity	None		CHF CAD	Renal failure Liver failure Cancer w/mets
EGD Diagnosis	MW tear	All other Dx	UGI cancer	
EGD Stigmata of bleed	Clean base Flat spot	Visible vessel Adherent clot Spurting vessel		
*Risk of re-bleeding and mortality increases with score: Low (0-2), Intermediate (3-4), High (5-10)				

Score before EGD of 0, or after EGD of ≤ 2 , predicts NO Mortality (even in re-bleed)
Consider discharge from ED

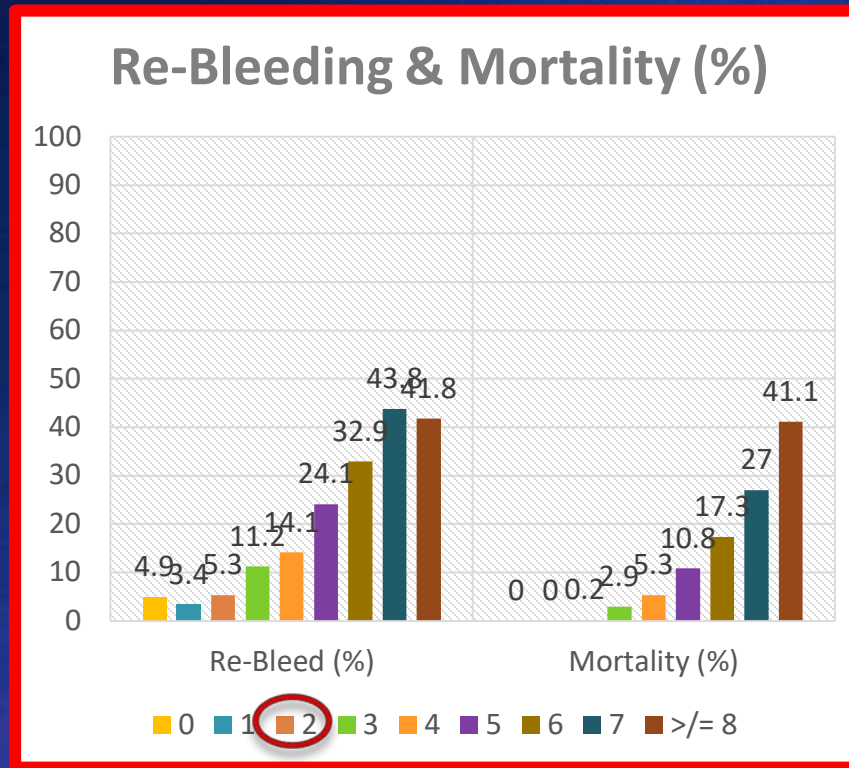
Pre-EGD and Post-EGD Rockall Score

Rockall TA et al. Gut 1996

Pre-EGD Rockall Score Effect



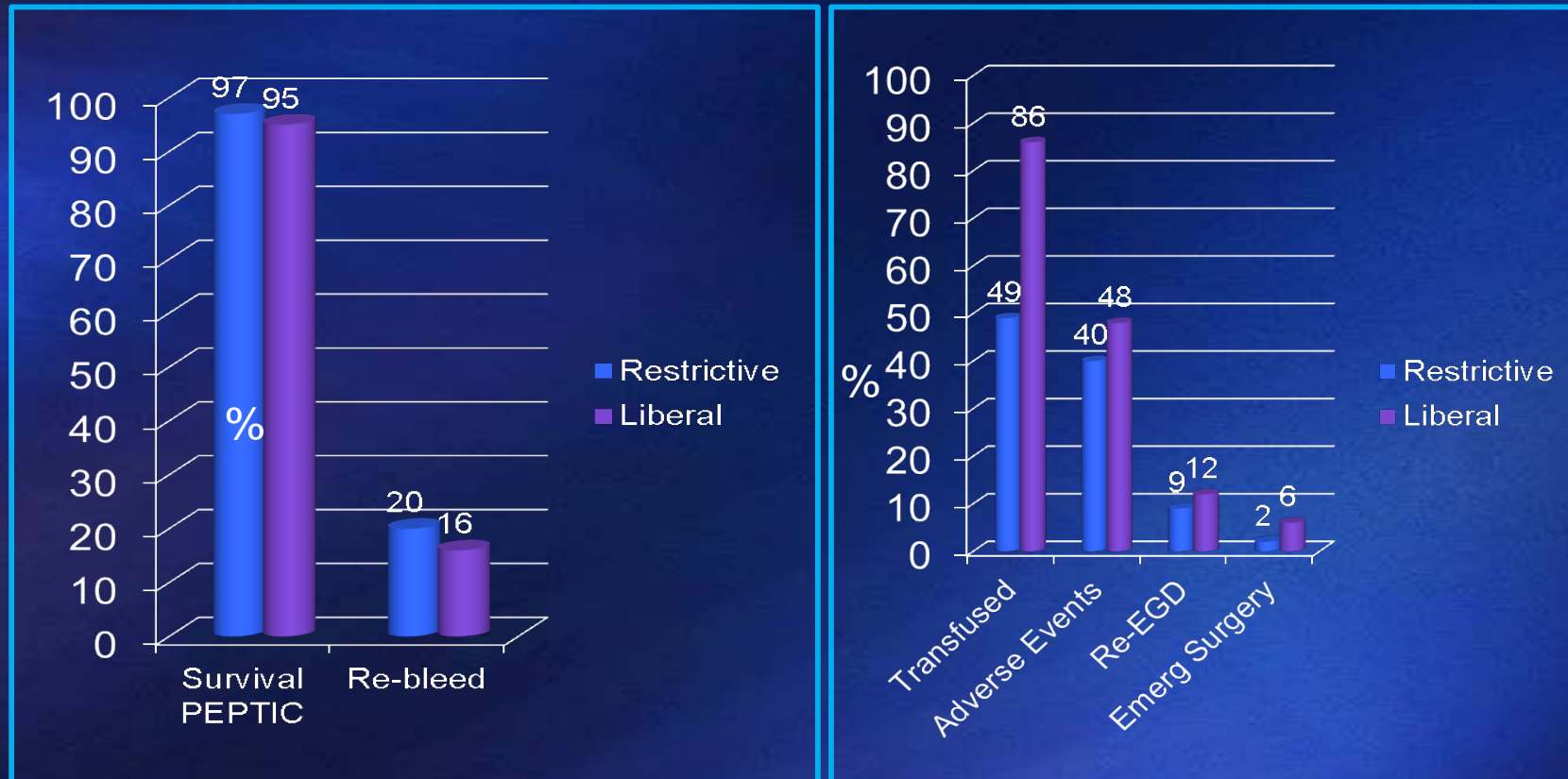
Post EGD Rockall Score Effect



Non-Variceal UGI Bleed

Restrictive (goal Hb 7-8) vs Liberal (goal Hb 10) Transfusion in GI Bleed

Villanueva C, N Engl J Med 2013; 368:11-21



Excluded: Exsanguinating bleed, Acute coronary syndrome, TIA, Stroke and Symptomatic peripheral vascular disease

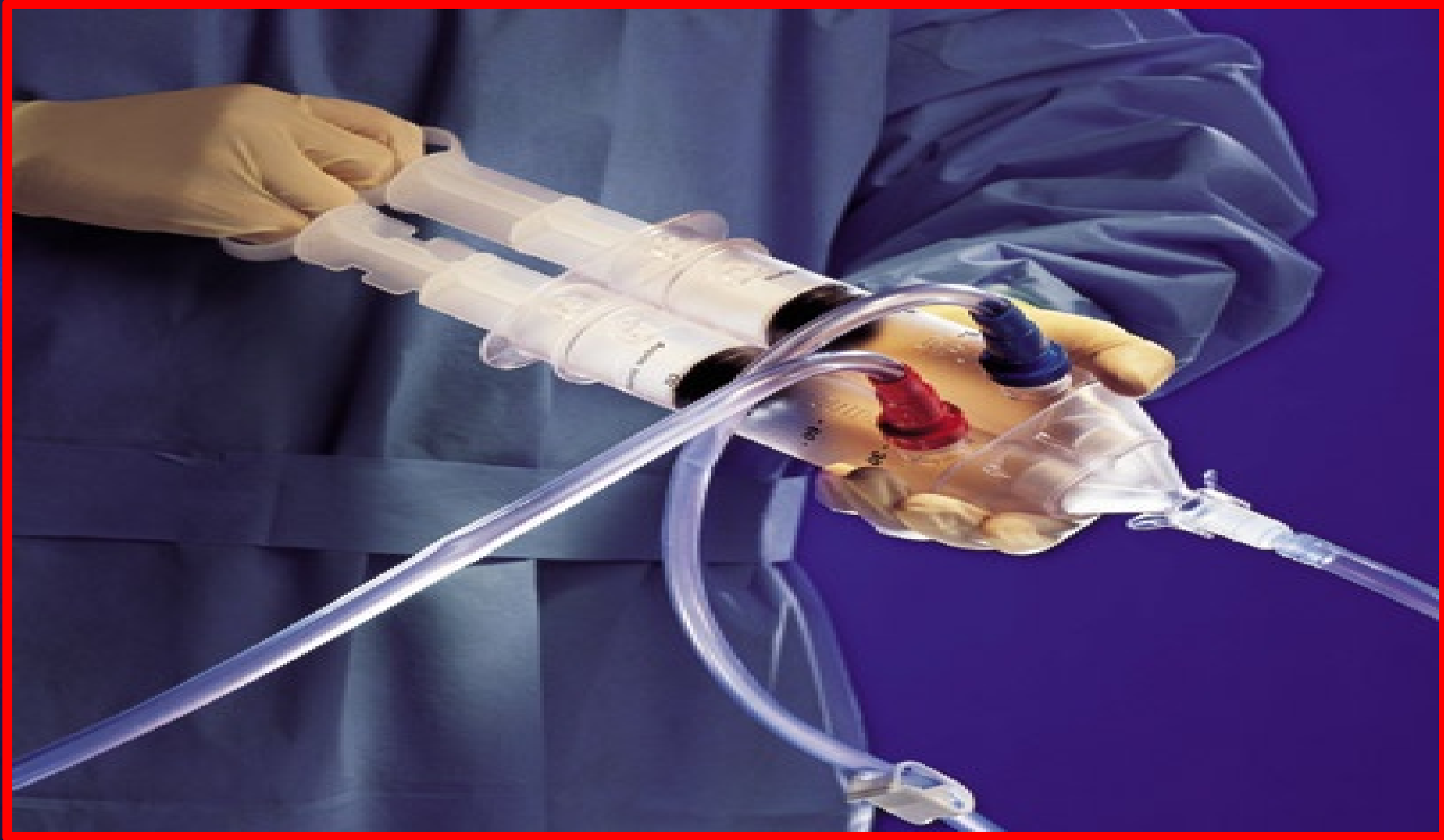
Initial Management & Preparation for Urgent Endoscopy

- Assess Risk/ Benefit of: correcting therapeutic anti-coagulation or giving anti-platelet therapy.
 - Correct excessive coagulopathy:
 - If INR > 2.5 or if Fibrinogen < 1 g/L: FFP 15 mL/kg, or Vit K 1-2 mg IV slowly to INR of ≤ 2.5
 - Not recommended in High INR of cirrhosis.
 - Correct thrombocytopenia if platelets < 50K or antiplatelet agent.
 - Platelets: 1 single donor unit, or 1 random pooled unit/ 10 kg;
 - Unclear utility in cirrhosis.
- Erythromycin 250 mg IV, 30-120 minutes before EGD
 - clears stomach 82% vs. 33% with placebo;
 - decreases need for re-EGD (OR 0.55).

Initial Management & Preparation for Urgent Endoscopy

- Consider Oro-gastric lavage (34 Fr Code-Blue Easy-Lav tube) to facilitate endoscopic visualization.
- Consider airway protection (?)
 - no demonstrated benefit for prophylactic intubation in: aspiration pneumonia, cardio-respiratory complications or mortality. ([Gastrointest Endosc.](#) 2003 Jan;57(1):58-61. *Gastrointest Endosc.* 2009 June ; 69(7): e55–e59.)
- Consider anesthesia consult.

Ballard Medical Easy-Lav Closed Gastric Lavage Tube



Evaluating Prognosis: AIMS 65 Score

ER Prediction of Mortality, LOS, & Cost

Saltzman JR et al. Gastrointest Endosc 2011;74:1215-24

FACTOR at ER ARRIVAL	1 point for each	Alternative Description
A lbumin	< 3 g/dL	
I NR	> 1.5	
M ental status	Glasgow score < 14	disorientation, lethargy, stupor, or coma
S ystolic Pressure	</= 90 mm Hg	
A ge	> 65	

Points	Mortality (%)	Length of Stay (days)
0 - 1	0.3 - 1	3 - 4
2	3	5.5
3	10	6.5
4	15	7.5
5	24	9

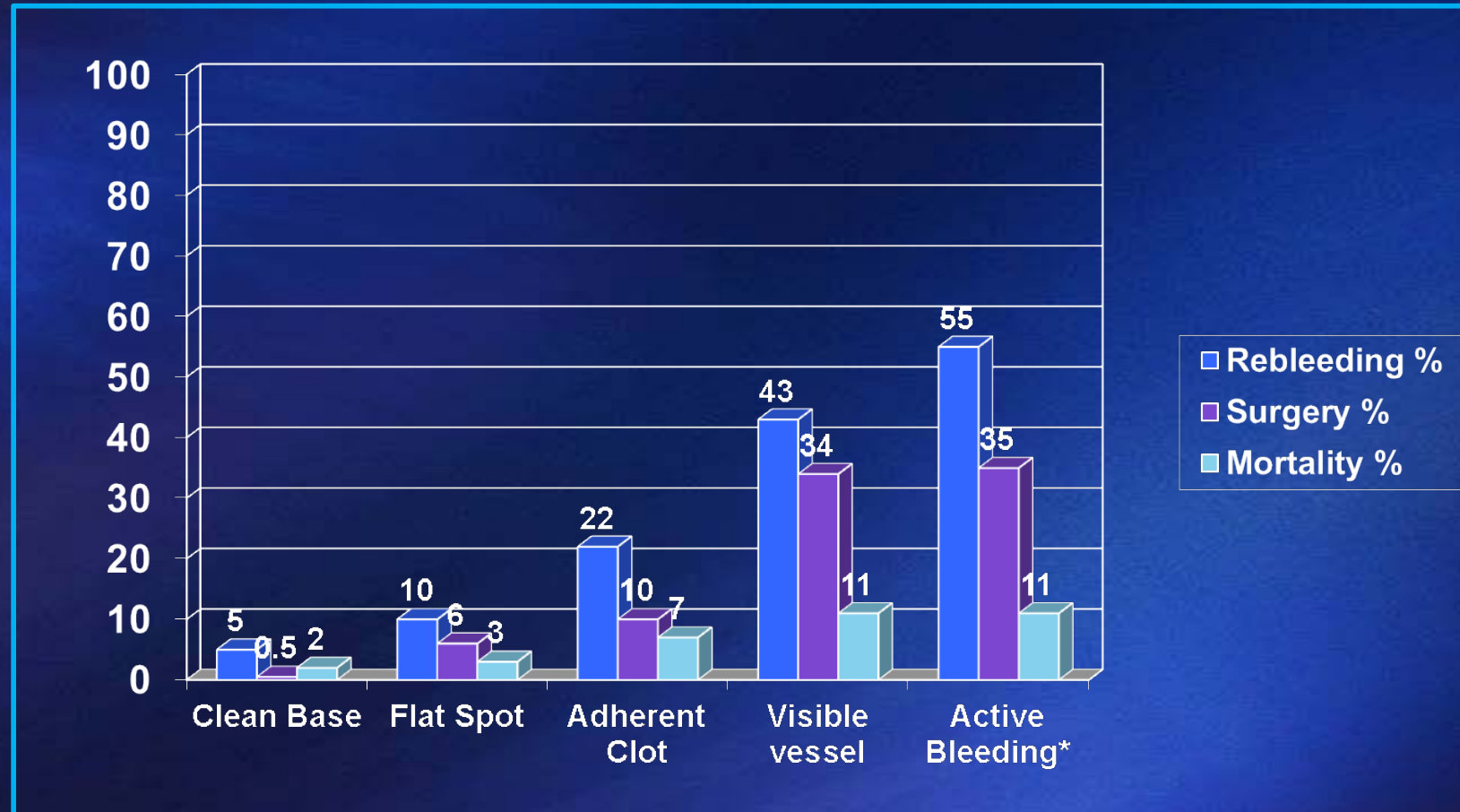
13.5% of patients

13.5% of patients have score ≥ 3 , with mortality of 10% or higher

Classification of Bleeding Ulcers

- **Forrest I:** Active hemorrhage Frequency
 - Forrest I a: Spurting hemorrhage 12%
 - Forrest I b: Oozing hemorrhage
- **Forrest II:** Signs of recent hemorrhage
 - Forrest II a: Visible vessel 8%
 - Forrest II b: Adherent clot 8%
 - Forrest II c: Hematin on ulcer base 16%
- **Forrest III:** Lesions without active nor recent bleeding 55%

Prognosis by Endoscopic Stigmata of Recent Hemorrhage



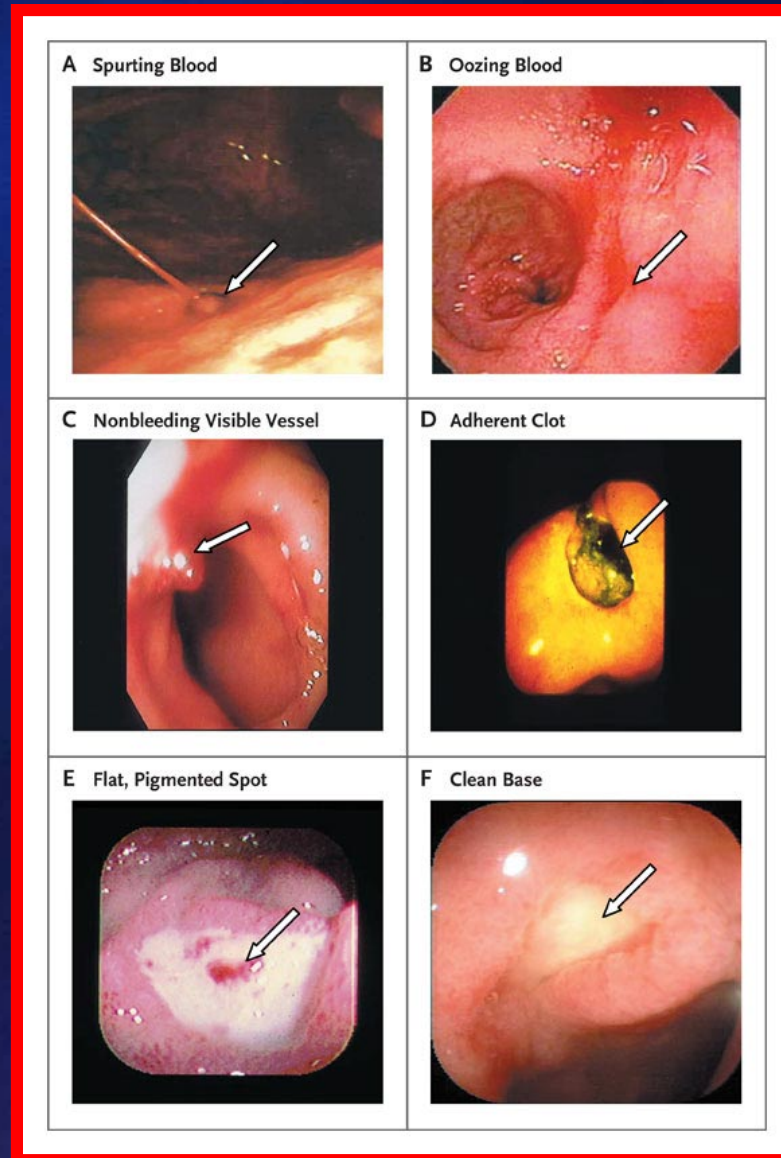
***Arterial bleeding:** 90% re-bleeding rate (15-30% after endoscopic therapy; same as in visible vessel). Needs IV PPI therapy.

***Oozing without adherent clot nor visible vessel:** 10% re-bleeding risk (0-5% after endoscopic therapy).

Its re-bleeding rate is not affected by high-dose IV PPI. OK to give PO PPI.

Endoscopic Stigmata of Bleeding Peptic Ulcer, Classified as High Risk or Low Risk

Gralnek I et al. N Engl J Med 2008;359:928-937



Endoscopy in Acute MI

- Patients with GI bleed leading to acute MI:
 - more likely to require endoscopic therapy than patients who develop GIB after treatment for acute MI (odds ratio 3.9; 95% CI, 1.8-8.5).
- In GI bleed in the setting of acute MI or Acute Coronary Syndrome:
 - upper endoscopy before cardiac catheterization is beneficial,
 - EGD reduces overall deaths from 600 to 97 per 10,000 patients,
- Endoscopy is NOT beneficial in patients who present with OCCULT GIB and acute MI.

Indications for Very early EGD

(Less than 12 h from onset)

- If likely to lead to Change in Management
- If patient has clinical features predictive of High Rebleeding Risk.

Indications for Very early EGD (< 12 h)

Change in Management

- Portal hypertension
- Cirrhosis
- History of aortic graft or aortic aneurism
- Possible hemobilia, or hemosuccus pancreaticus.

Indications for Very early EGD (< 12 h) *High Re-bleeding Risk*

- Presentation with shock
- Already hospitalized at time of bleed
- Age > 60
- Hemoglobin < 8 g/dL
- Hematemesis, hematochezia (or BRB in NGT)
- Severe co-morbidity
- Clinical Rockall score ≥ 3 (Intermediate or High)
- Glasgow-Blatchford score ≥ 12
- Continuous bleeding (RBC transfusion > 6 units)

Non-Variceal Upper GI Bleed

Initial Treatment & Hemostasis

- Techniques equivalent in initial hemostasis
 - 0.9% NaCl 1/10000 epinephrine injection
 - Hypertonic saline + 1/10000 epinephrine injection
 - Thermocoagulation (Heater Probe),
 - BICAP electrocoagulation,
 - Hemoclipping,
 - Argon Plasma Coagulation, and
 - Laser thermocoagulation.
- Initial hemostasis: 95-97 %

Non-Variceal Upper GI Bleed

Initial Treatment & Re-bleeding Rate

- Re-bleeding rate: 15-20 % for visible vessel or active bleed (other than oozing without adherent clot nor visible vessel).
- Techniques equivalent in Re-bleeding Rate:
 - Hemocclipping
 - Hypertonic saline (3.6 – 5%) + 1/10000 epinephrine injection
 - BICAP or Heater Probe alone ?
 - 0.9% NaCl 1/10000 epinephrine injection +
 - BICAP, or
 - Heater Probe, or
 - APC
- **RECOMMENDATION:** If 0.9% NaCl 1/10000 epinephrine is used for hemostasis of active bleed or visible vessel, a second technique should be added to decrease re-bleeding rate.

Predictors of High Risk of:

Re-bleeding After Endoscopic Hemostasis
Endoscopic Therapy Failure if Re-bleeding

Predictive Factor	% Re-bleeding Risk
Posterior-wall Duodenal ulcer (gastroduodenal artery)	43-57
Hemodynamic Instability *	19-47
Active Bleeding	12-49
Lesser-curve Gastric Ulcer	23-35
Higher Lesser Curvature GU (Lt gastric artery)	20-36
Ulcer size > 2 cm *	15-36

***Predictor of failure for endoscopic therapy in re-bleeding:**
hypotension and/or ulcer > 2 cm are independent predictors
Do therapeutic angiography or surgery.

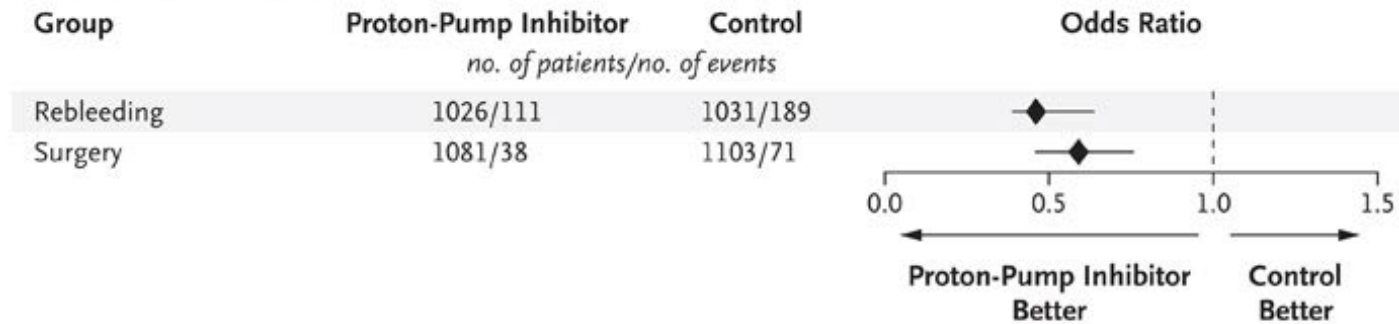
Medical Therapy

- **Ulcer requiring Endoscopic therapy:** PPI 80 mg IV bolus followed by high-dose continuous intravenous infusion 8 mg/hour or 80 mg BID for 3 days, decreases re-bleeding in patients with ulcers that require endoscopic intervention (6.7% vs 22.5% with placebo).
 - In a Cochrane Systematic Review (2006), only “High-dose PPI” after endoscopic hemostasis reduces the need for surgery with odds ratio of 0.61 (vs low-dose).
 - In active oozing, without adherent clot nor visible vessel, IV PPI does not decrease re-bleeding risk, which is only 5%; oral PPI once a day is OK.
 - In ulcers with “flat pigmented spot” or “clean base”: oral PPI once a day.
- **Cirrhotic patients with GI bleed of any source** have less infections and lower re-bleeding rate with antibiotic therapy:
 - Ceftriaxone 1 gm/d x 7 days, or
 - Norfloxacin 400mg p.o. BID or Ciprofloxacin 500 mg BID x 7 days

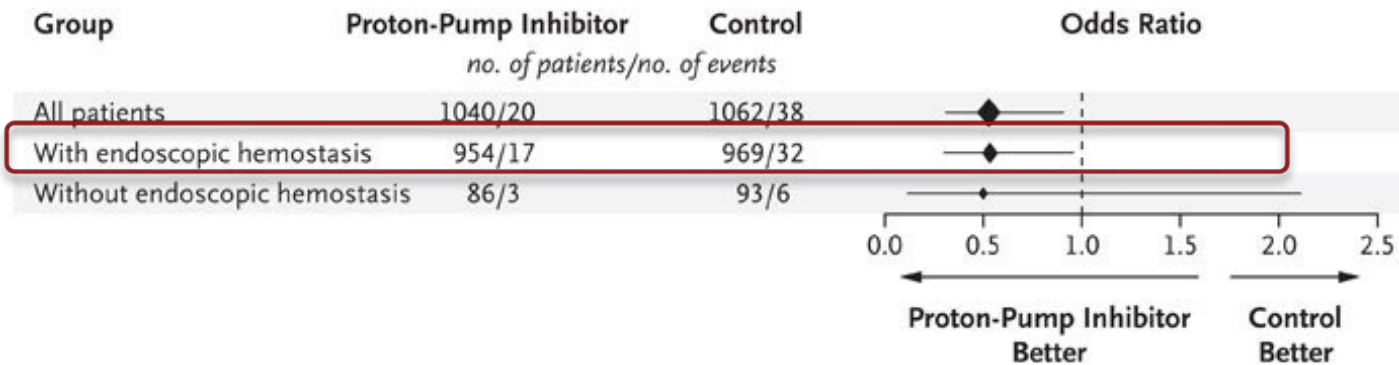
Effect of Proton-Pump Inhibition in Peptic-Ulcer Bleeding

Gralnek I et al. N Engl J Med 2008;359:928-937

A Rebleeding and Surgery



B Death



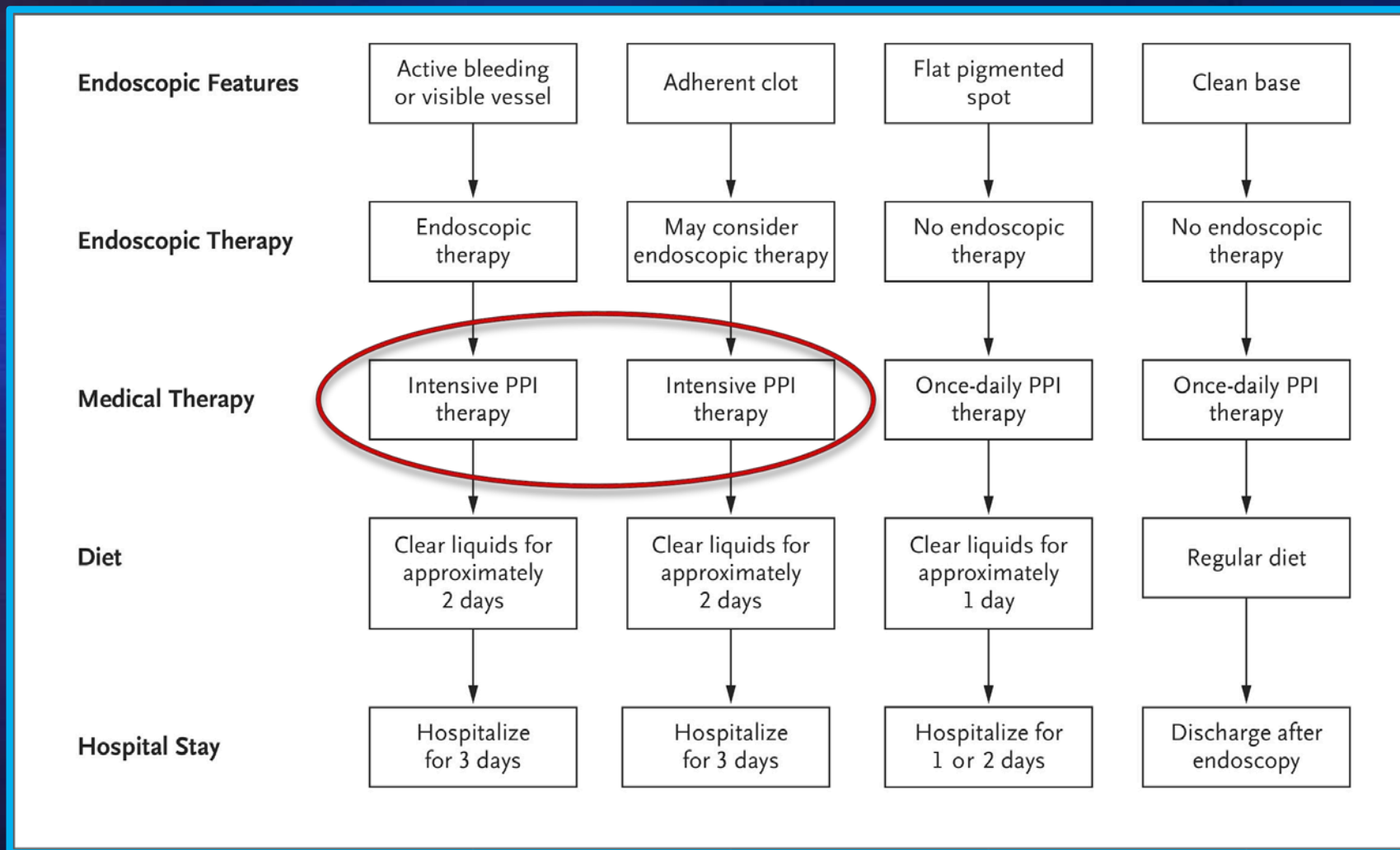
Intensive PPI therapy (IV bolus + infusion x 3 days) decreases mortality in patients who required endoscopic hemostasis

Medical Therapy

- In idiopathic PUD (non-H. pylori, non-NSAID),
 - give long term PPI or H₂ blocker.
- In cirrhosis with PUD,
 - propranolol decreases recurrence of PUD bleed by 22%(Hsu et al. Hepatology 2012;56:698-705)
- In H. Pylori (+) Peptic Ulcer: eradication decreases ulcer recurrence:
 - DU: from 67% to 6%, and
 - GU: from 59% to 4%.

Initial Treatment of Patients with Ulcer Bleeding, According to the Endoscopic Features .

Laine L. N Engl J Med 2016;374:2367-2376



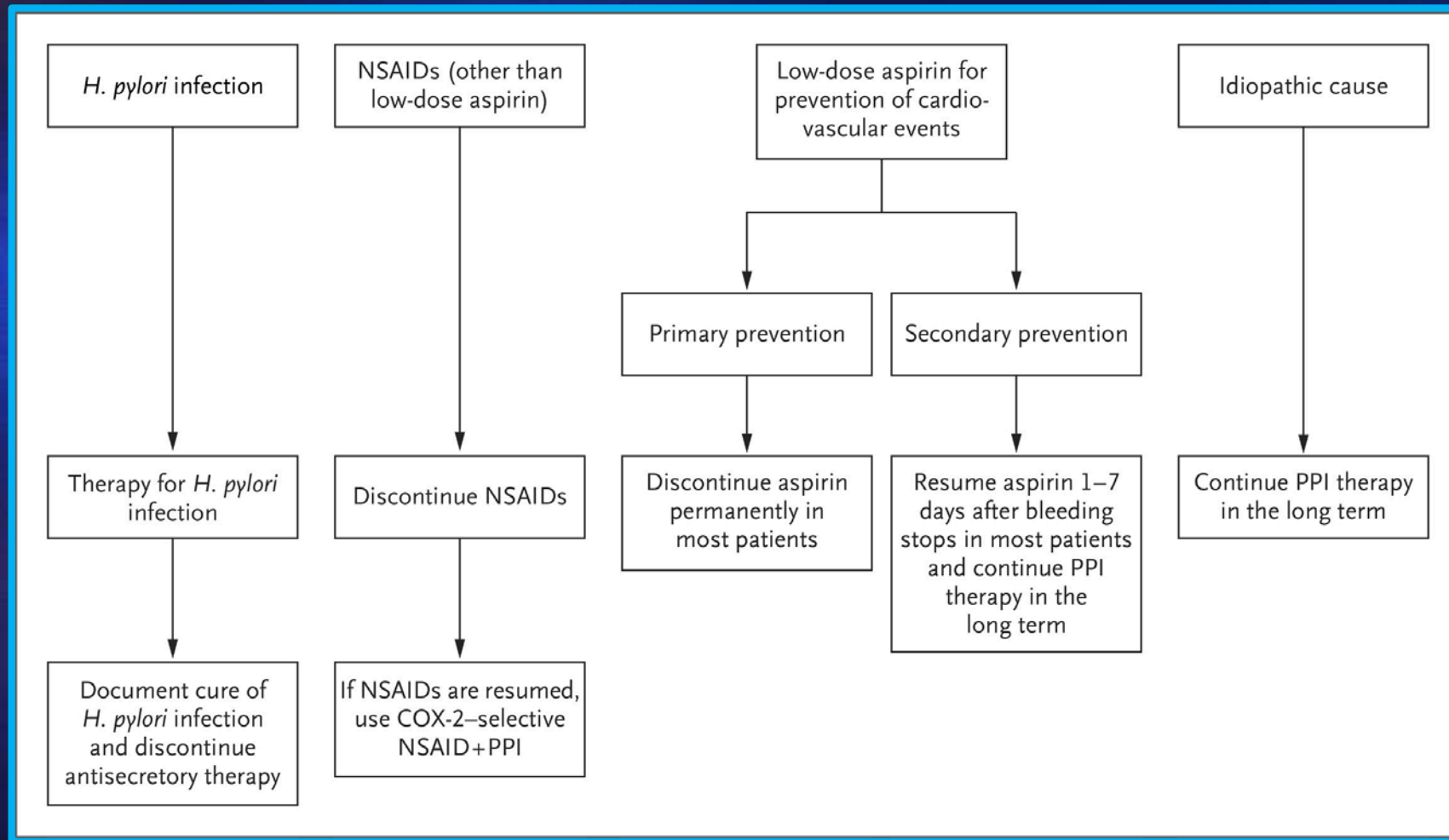
Intensive PPI = 80 mg IV bolus + 8 mg/h IV infusion x 3 days, or 80 mg IV bolus + 40 mg IV BID, change to PO after 72 h if no rebleed, or 80 mg PO BID x 3 days + 40 mg PO BID x 11 days; then daily x 14 days



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Long-Term Treatment of Patients with Bleeding Ulcers, According to the Cause of the Ulcer.

Laine L. N Engl J Med 2016;374:2367-2376



Regimen	Drugs (doses)	Dosing frequency	Duration (days)	FDA approval
Clarithromycin triple	<i>PPI (standard or double dose)</i>	<i>BID</i>	<i>14</i>	<i>Yes^a</i>
	<i>Clarithromycin (500 mg)</i>	<i>BID</i>		
	<i>Amoxicillin (1 grm BID) or Metronidazole (500 mg TID)</i>			
Bismuth quadruple	PPI (standard dose)	BID	10–14 (14 if salvage therapy)	No ^b
	Bismuth subcitrate (120–300 mg) or subsalicylate (300 mg)	QID		
	Tetracycline (500 mg)	QID		
	Metronidazole (250–500 mg)	QID (250)		
		TID to QID (500)		
Concomitant	<i>PPI (standard dose)</i>	<i>BID</i>	<i>10–14 (same as salvage therapy)</i>	<i>No</i>
	<i>Clarithromycin (500 mg)</i>	<i>BID</i>		
	<i>Amoxicillin (1 grm)</i>	<i>BID</i>		
	<i>Nitroimidazole (500 mg)^c</i>	<i>BID</i>		
Sequential	PPI (standard dose)+Amoxicillin (1 grm)	BID	5–7	No
	PPI, Clarithromycin (500 mg)+Nitroimidazole (500 mg) ^c	BID	5–7	
Hybrid	<i>PPI (standard dose)+Amox (1 grm)</i>	<i>BID</i>	<i>7</i>	<i>No</i>
	<i>PPI, Amoxicillin, Clarithromycin (500 mg), Nitroimidazole (500 mg)^c</i>	<i>BID</i>	<i>7</i>	
Levofloxacin triple	PPI (standard dose)	BID	10–14 (14 if salvage therapy)	No
	Levofloxacin (500 mg)	QD		
	Amoxicillin (1 grm)	BID		
Levofloxacin sequential	<i>PPI (standard or double dose)+Amox (1 grm)</i>	<i>BID</i>	<i>5–7</i>	<i>No</i>
	<i>PPI, Amox, Levofloxacin (500 mg QD), Nitroimidazole (500 mg)^c</i>	<i>BID</i>	<i>5–7</i>	
LOAD	Levofloxacin (250 mg)	QD	7–10	No
	PPI (double dose) (Omeprazole)	QD		
	Nitazoxanide (500 mg) (Alinia)	BID		
	Doxycycline (100 mg)	QD		

Indications for Surgery (or Angiographic Therapy)

- First re-bleeding after endoscopic hemostasis, with:
 - ulcer > 2 cm, or
 - hypotension/shock.
- Active bleeding not controlled after 2 endoscopic interventions(Lau J et al. N Engl J Med 1999; 340:751).
 - *First two endoscopic treatments have similar mortality but less complications (15% in endoscopy therapy vs. 36% with surgery).*
- Recurrent hemorrhage after stabilization and 2 endoscopic therapies.
- Hemodynamic instability despite vigorous resuscitation and 3 units of PRBC.
- Continuous slow bleed of > 3 units PRBC/day.

Embolic Agents for UGI Bleed

Temporary	Permanent
Vasopressin (less effective in duodenum)	Coils (20-30% larger than vessel); (need second agent in coagulopathy).
Autologous blood clot	
Gelfoam (high early re-bleeding; add second agent)	Large Vessel Occluders (Amplazter plug, MVP, Azur CX)
Microfibrillar bovine collagen (Avitene)	Particles (Polyvinyl alcohol, Microspheres)
Thrombin	Liquid Agents (N-Butyl Cyanoacrylate, Ethylene Vinyl); (rapid hemostasis even in coagulopathy)
Biodegradable Starch Microspheres (EmboCept)	

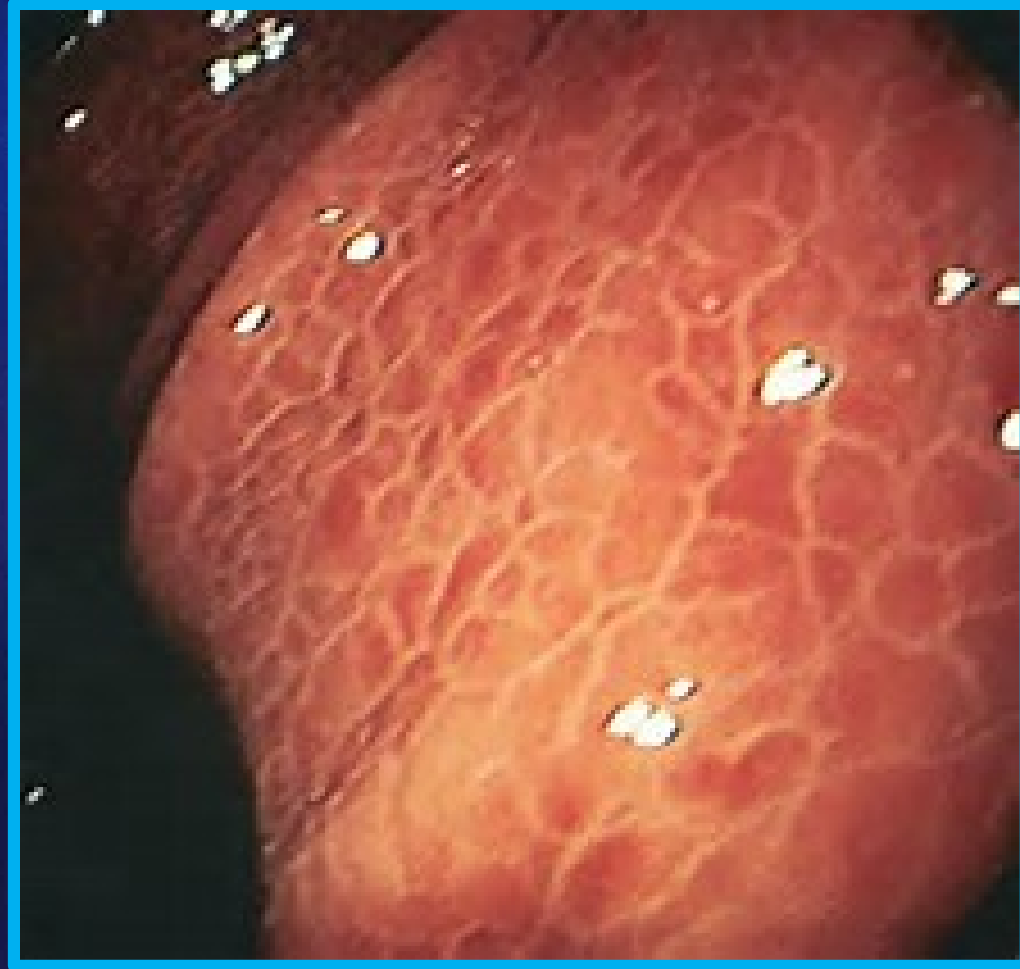
50% need re-embolization due to recurrent bleed

Selected Causes of Non-Variceal UGI Bleeding

Portal Hypertensive Gastropathy

- **Cause:** Increased gastric mucosal blood flow.
- **Pathogenesis:** related to both congestion and hyperemia in the stomach .
 - Mucosal ischemia and increased nitric oxide synthase activity.
 - No relationship with *Helicobacter pylori* infection.
- **Aggravating factors:**
 - Endoscopic sclerotherapy or ligation of esophageal varices increase hyperdynamic congestion.
 - Others: etiology of portal hypertension, and coexistence of gastric varices;
 - It is not directly correlated with intravariceal pressure.
- **Diagnosis:**
 - Fine white reticular pattern separating areas of pinkish mucosa on endoscopy, with "snakeskin" appearance.
 - Most evident in the fundus and body.
 - In severe cases: oozing, bleeding, subepithelial hemorrhages, and increased vascularity similar to angiomas, involving the fundus as well as body and antrum.

Portal Hypertensive Gastropathy



Portal Hypertensive Gastropathy

- **Pathology:** extensive edema. In severe cases has capillary and venous dilatation in the submucosa extending into the mucosa.
- **Natural history:** Over 3 years:
 - 29 % remain stable,
 - 23 % worsen,
 - 23% improved, and
 - 25% fluctuated.
 - Acute bleeding occurs in 2.5 %; death is rare.
 - Chronic bleeding occurs in 11% patients.
- **Treatment:** decrease portal pressure.
 - Porta-cava shunt surgery, TIPS, propranolol, and liver transplantation.
 - Non-selective beta blockers and TIPS decrease transfusion needs.
 - Vasopressin, somatostatin, or octreotide may also decrease bleeding from portal hypertensive gastropathy.
 - Endoscopic thermal coagulation may be effective for focally bleeding angiomata associated with cirrhosis

Gastric Antral Vascular Ectasia (GAVE) Watermelon Stomach

- **Significance:**

- Causes 0.5% of non-variceal upper gastrointestinal bleeding;
- 31% of patients with GAVE have portal hypertension.

- **Endoscopy:**

- Longitudinal rows of flat, reddish stripes radiating from the pylorus into the antrum, that resemble the stripes on a watermelon.
- The red stripes represent ectatic and sacculated mucosal vessels.
- In cirrhosis: A punctate form is more common.

- **Associations:**

- Most cases are idiopathic.
- 31% have associated portal hypertension.
- Has been associated with cirrhosis and systemic sclerosis.

- **Clinical picture:**

- Elderly (mean age 74) female (80%) with iron deficiency anemia, slow GI blood loss (FOBT+), and no history of cirrhosis.
- Presentation with portal HTN is similar.

Endoscopic Types of GAVE

Ito M et al. *Gastrointest Endosc* 2001;53:764-70

Classic GAVE
(cirrhosis & non-cirrhosis)



Punctate GAVE
(cirrhosis)



Gastric Antral Vascular Ectasia (GAVE) Watermelon Stomach

- **Diagnosis:**

- Endoscopic appearance.
- It may be confirmed with endoscopic biopsy.

- **Histopathology:**

- vascular ectasia, spindle cell proliferation, and fibrohyalinosis.

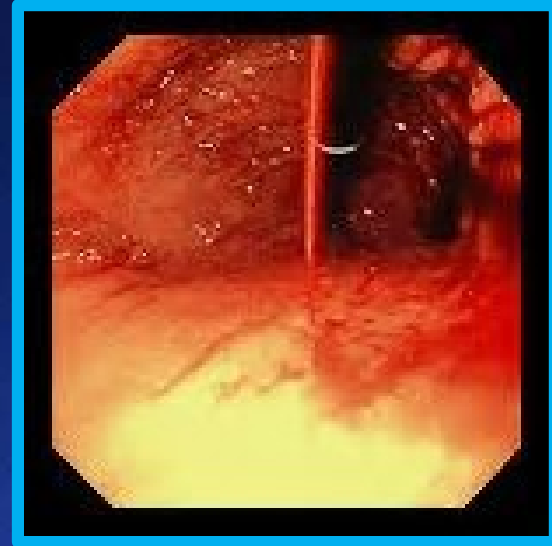
- **Treatment:**

- Episodic transfusions are required in some chronic cases, but the bleeding is rarely acute and massive.
- Endoscopic coagulation with a heater probe, Gold probe, Argon plasma coagulator, BarrX radiofrequency, or laser therapy obliterates the vascular ectasia and decreases the degree of bleeding.
- Antrectomy prevents recurrent bleeding, but is usually reserved for patients who fail endoscopic therapies.
- TIPS does **not** reduce bleeding.

Dieulafoy

- **Definition:** Aberrant submucosal artery, without ramification in gastric wall, which erodes the overlying epithelium in the absence of a primary ulcer.
 - Causes less than 1 percent of cases of severe UGI hemorrhage.
 - Caliber of the artery is 1 to 3 mm (10-times the caliber of mucosal capillaries).
 - Usually located in the upper stomach along the lesser curvature near the gastro-esophageal junction (fundus, within 6 cm of EGJ).
 - May be found in all areas of the gastrointestinal tract, including the esophagus, duodenum, Small bowel, and colon..
 - Bleeding is often self-limited, although it is usually recurrent and can be profuse
- **Etiology:** is unknown, likely congenital.
- **Causes of bleeding:** not well-understood.
 - Associations: cardiovascular disease, hypertension, chronic kidney disease, diabetes, or alcohol abuse.
 - Use of NSAIDs is common; NSAIDS may incite bleeding by causing mucosal atrophy and ischemic injury.

Dieulafoy lesion



Aorto-Enteric Fistula

- Rare cause of acute UGI bleeding, but associated with high mortality if undiagnosed and untreated.
- **Location:** The third or fourth portion of the duodenum is the most common site for aorto-enteric fistulas, followed by the jejunum and ileum .
- **Presentation:**
 - Repetitive “herald bleed” with moderate hematemesis and/or hematochezia; this may be followed by massive bleeding and exsanguination.
 - Intermittent bleeding can be seen if clot temporarily seals the fistula.
 - Other signs and symptoms may include abdominal or back pain, fever, and sepsis.
 - Infrequently, an abdominal mass is palpable or an abdominal bruit is heard.
- **Pathophysiology:** Aorto-enteric fistulas arise from direct communication between the aorta and the gastrointestinal tract.

Aorto-Enteric Fistula

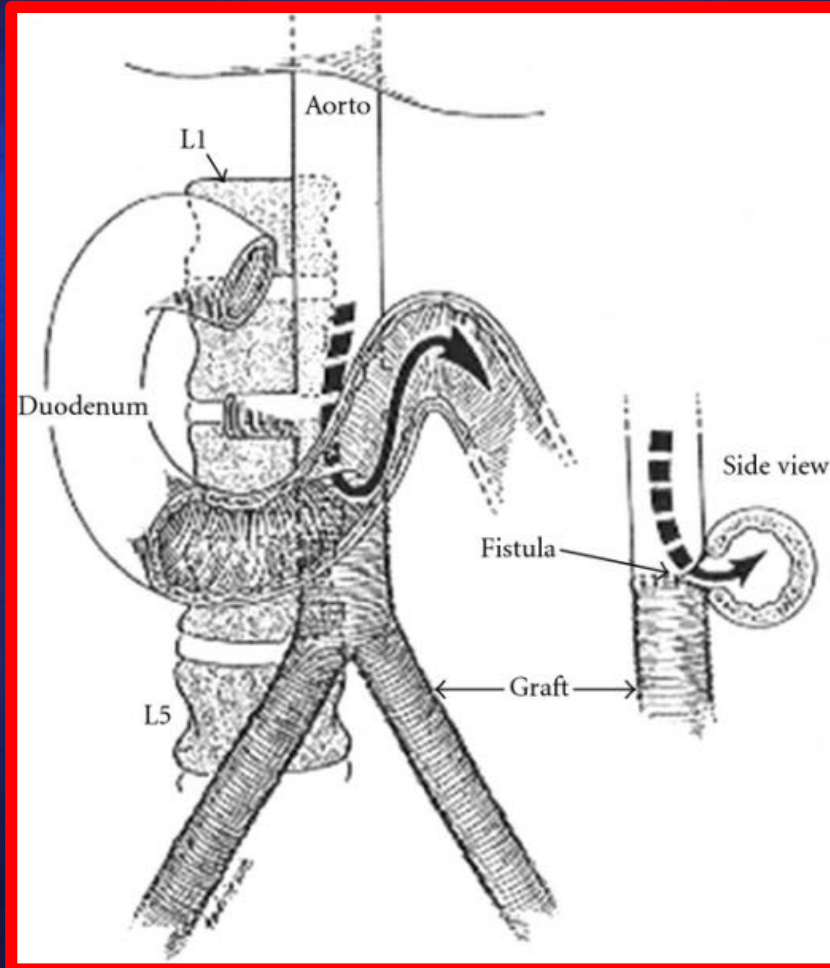
• Causes:

- Primary A-E fistula in USA are due to atherosclerotic aortic aneurysm.
 - In other parts of the world are infectious aortitis due to syphilis or tuberculosis.
- Secondary A-E fistula most commonly due to prosthetic abdominal aortic vascular graft. May have pressure necrosis or graft infection causing the fistula.
 - Other secondary causes include penetrating ulcers, tumor invasion, trauma, radiation therapy, and foreign body perforation.

• Diagnosis:

- A high index of suspicion.
- Should be considered in all patients with massive or repetitive UGI bleeding and a history of a thoracic or abdominal aortic aneurysm, or prosthetic vascular graft.
- Endoscopy is the procedure of choice for diagnosis and exclusion of other causes of acute UGI bleeding.
- Endoscopy with an enteroscope or side-viewing endoscope may reveal a graft, an ulcer or erosion at the adherent clot, or an extrinsic pulsatile mass in the distal duodenum or esophagus.
- Abdominal CT scan and aortography can be useful in confirming the diagnosis, but may be unreliable.

Aorto-Enteric Fistula



Aorto-Enteric Fistula

- **Treatment:**

- Exploratory laparotomy is indicated for patients with suspected aorto-enteric fistula and severe ongoing bleeding.
- The mortality rate of an untreated aorto-enteric fistula that presents with UGI hemorrhage is nearly 100 percent.
- Surgical repair of the aortic aneurysm and fistula is the standard treatment regardless of the cause.
- Therapy of an aorto-enteric fistula due to an infected graft consists of intravenous antibiotics and emergency surgery with removal of the infected graft and extra-anatomic bypass. Infected graft removal with in-situ graft replacement has been proposed as an alternative treatment.

Atrial-Esophageal Fistula

- Adverse event from cardiac catheter ablation for atrial fibrillation with thermal injury to atrium and esophagus.
- Occurs in 0.1-0.25% of procedures.
- Bleed 1-6 weeks after ablation.
- Forms 1-way valve from esophagus to atrium;
 - Embolic strokes in > 50%.
- Positive esophageal pressure in endoscopy can cause embolic stroke.
 - Avoid endoscopy.
- Diagnosis: CT Scan
- Treatment: Surgery

Hemobilia

- **Definition:** Bleeding from the hepato-biliary tract;
 - rare cause of acute UGI bleeding.
- **Causes:** Should be considered in a patient with acute UGI bleeding and a recent history of:
 - hepatic parenchymal or biliary tract injury,
 - percutaneous and transjugular liver biopsy,
 - percutaneous transhepatic cholangiogram,
 - cholecystectomy,
 - endoscopic biliary biopsies or stenting,
 - TIPS,
 - Angio-embolization (eg: TACE), or
 - blunt abdominal trauma .
 - Other causes include gallstones, cholecystitis, hepatic or bile duct tumors, intrahepatic stents, hepatic artery aneurysms, and hepatic abscesses.

Hemobilia

- **Signs & Symptoms:**

- Classic triad is biliary colic, obstructive jaundice, and occult or acute GI bleeding.
- Hemobilia can result in obstructive jaundice with or without biliary sepsis.

- **Diagnosis:**

- Often overlooked in the absence of active bleeding.
- A side-viewing duodenoscope is helpful for visualizing the ampulla or for performing diagnostic endoscopic retrograde cholangiography (ERCP).
- Technetium-tagged red blood cell scan or
- Selective hepatic artery angiography to reveal the source of hemobilia and for treatment.

- **Treatment:** directed at the primary cause of bleeding;

- embolization or surgical resection of a hepatic tumor, or
- arterial embolization following liver biopsy or PTC,
- laparoscopic cholecystectomy

Hemobilia

(blood flowing from Vater's papillae)



Hemosuccus Pancreaticus

- **Definition:** Bleeding from the pancreatic duct; rare cause of UGI bleeding.
- **Causes:** chronic pancreatitis, pancreatic pseudocysts, and pancreatic tumors.
- **Pathogenesis:**
 - Pseudocyst or tumor erodes into a vessel, forming a direct communication between the pancreatic duct and a blood vessel.
 - May be seen after therapeutic endoscopy of the pancreas or pancreatic duct, including pancreatic stone removal, pancreatic duct sphincterotomy, pseudocyst drainage, or pancreatic duct stenting.
- **Diagnosis:** confirmed by abdominal CT scan, ERCP, angiography, or intraoperative exploration.
 - CT scan is performed first (least invasive).
- **Treatment:**
 - Mesenteric arteriography with coil embolization can control acute bleeding.
 - If bleeding persists or is massive: pancreatico-duodenectomy or pseudocyst resection and ligation of the bleeding vessel.

Cameron Lesions

- **Definition:** erosions or ulcers occurring in the sac of a hiatal hernia.
- **Frequency:** up to 5 percent of patients with a hiatal hernia + EGD.
- **Significance:**
 - usually an incidental finding
 - rarely causes acute or chronic upper gastrointestinal bleeding and iron deficiency anemia.
- **Pathogenesis:** incompletely understood; trauma of diaphragm causing ischemia (?).
 - Contributing factors include reflux esophagitis and mechanical trauma.
- **Management:** depends upon the clinical setting and should thus be individualized.
 - Acute bleeding can be treated endoscopically.
 - Chronic bleeding with iron deficiency can be treated with a PPI after iron repletion, which may help prevent recurrence of anemia.
 - Surgery to repair the hiatal hernia can be considered in patients with recurrent bleeding despite the above measures.

Cameron's lesion



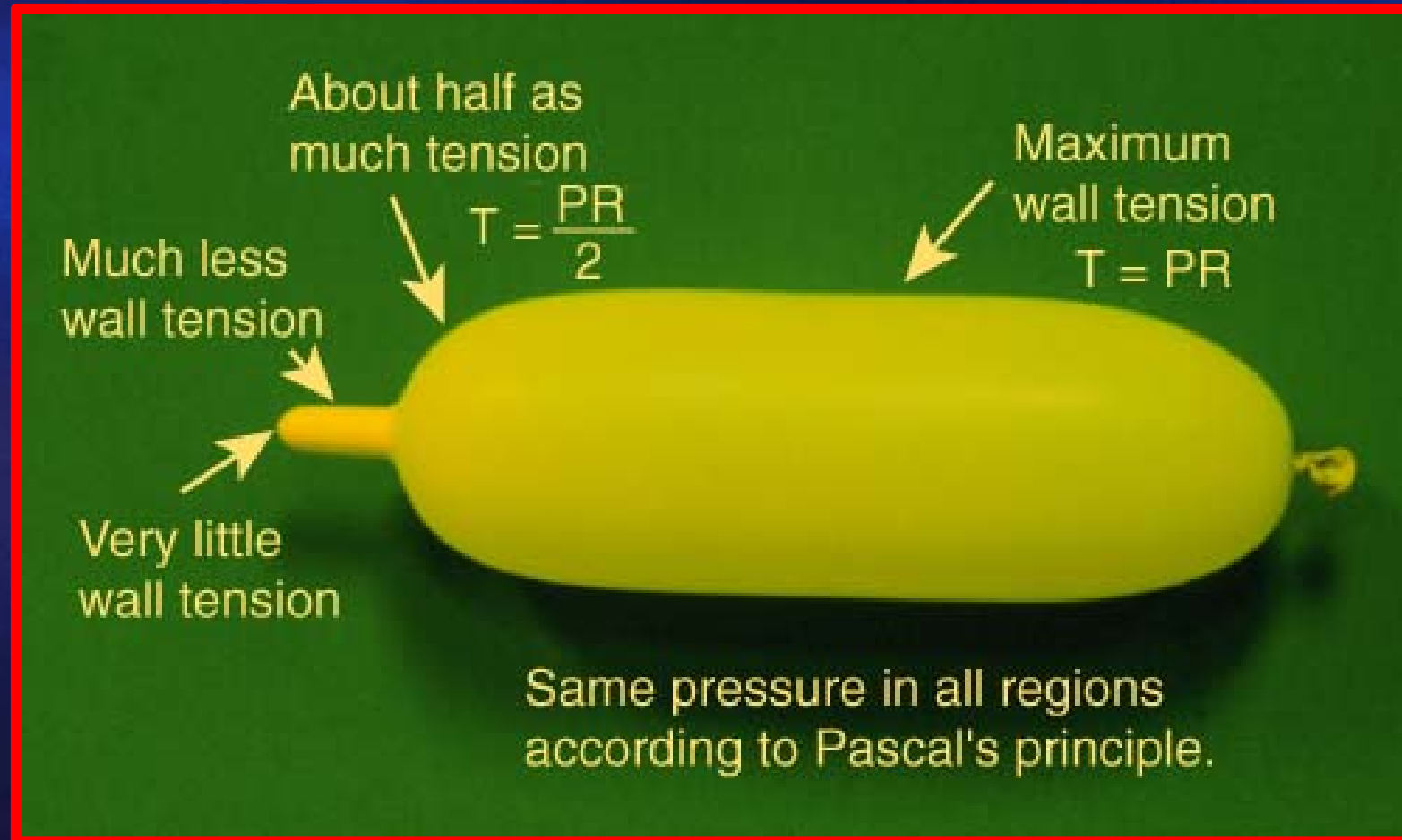
Upper Variceal Hemorrhage

VARICEAL HEMORRHAGE

- Gastro-esophageal varices = 50% cirrhotics
 - Child A = 40%
 - Child C = 85%
- Varices form at rate of 5-15%/year
 - in 30% (25-40%) they will bleed at some time;
 - mean bleed 2.9 units.
- Bleeding only if Portal Pressure >12mm Hg;
 - “clinically significant portal HTN” is ≥ 10 mm Hg
- Risk of bleeding:
 - a) small varices ≤ 5 mm (F1) < 10% /y
 - b) medium/large (F2/F3) = 30% /year
- Mortality from variceal bleed = 15-30% (mean 20%)/ episode
- If untreated, 70% will die within a year.

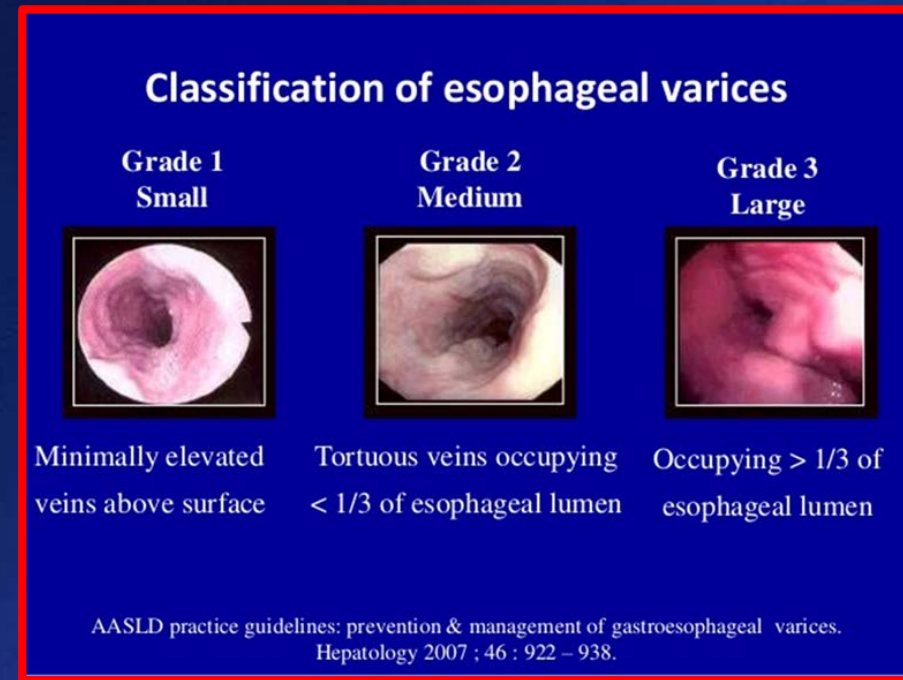
Determinants of Variceal Bleeding

Laplace's Law



Morphologic Classification of Esophageal Varices

- **Grade F0:** no EV detected;
- **Grade F1:** small (≤ 5 mm) straight EV;
- **Grade F2:** slightly enlarged (6 mm or more) tortuous EV occupying less than one-third of the esophageal lumen; and
- **Grade F3:** large coil-shaped EV that occupied more than one-third of the esophageal lumen



Indications for Primary Prophylaxis of Esophageal Variceal Hemorrhage (VH)

- Annual rate of first hemorrhage: 12%
- **Medium or Large Varices (\geq F2; 6 mm or more):** Recommended therapy
 - Beta-Blockers: Traditional NSBBs (propranolol, nadolol), or carvedilol, or
 - Endoscopic Variceal Ligation.
 - Weight loss in obese patients.
- **Small Varices with high-risk:**
 - High-Risk defined as in CTP-C or with red wale marks;
 - Recommended therapy: NSBB or carvedilol (EVL difficult).
 - Weight loss in obese patients.

Indications for Primary Prophylaxis of Esophageal Variceal Hemorrhage (VH)

- **Choice of therapy and Follow-up:**

- Choice of treatment should be based on patient preference and characteristics.
- Patients on NSBBs or carvedilol for primary prophylaxis do not require monitoring with serial EGD.
- In EVL, follow with EGD q 6-months after initial eradication.

- **Not Recommended:**

- Combination therapy NSBB plus EVL.
- TIPS placement is not recommended in the prevention of first VH.

Management of Patients With Moderate/Large Varices That Have Not Bled

Therapy	Recommended Dose	Therapy Goals	Maintenance/Follow-up
Propranolol	<ul style="list-style-type: none"> •20-40 mg orally <i>twice</i> a day •Adjust every 2-3 days until treatment goal is achieved •Maximal daily dose: <ul style="list-style-type: none"> • 320 mg/day in patients without ascites • 160 mg/day in patients with ascites 	<ul style="list-style-type: none"> •Resting heart rate of 55-60 beats per minute •Systolic blood pressure should not decrease <90 mm Hg 	<ul style="list-style-type: none"> •At every outpatient visit make sure that heart rate is on target •Continue indefinitely •No need for follow-up EGD
Nadolol	<ul style="list-style-type: none"> •20-40 mg orally <i>once</i> a day •Adjust every 2-3 days until treatment goal is achieved •Maximal daily dose: <ul style="list-style-type: none"> • 160 mg/day in patients without ascites • 80 mg/day in patients with ascites 	<ul style="list-style-type: none"> •Resting heart rate of 55-60 beats per minute •Systolic blood pressure should not decrease <90 mm Hg 	<ul style="list-style-type: none"> •At every outpatient visit make sure that heart rate is on target •Continue indefinitely •No need for follow-up EGD
Carvedilol	<ul style="list-style-type: none"> •Start with 6.25 mg <i>once</i> a day •After 3 days increase to 6.25 mg twice-daily •Maximal dose: 12.5 mg/day (except in patients with persistent arterial hypertension) •Not recommended in Secondary prophylaxis. 	<ul style="list-style-type: none"> •Systolic arterial blood pressure should not decrease <90 mm Hg 	<ul style="list-style-type: none"> •Continue indefinitely •No need for follow-up EGD
EVL	<ul style="list-style-type: none"> •Every 2-8 weeks until the eradication of varices 	<ul style="list-style-type: none"> •Variceal eradication (no further ligation possible) 	<ul style="list-style-type: none"> •First EGD performed 3-6 months after eradication and every 6-12 months thereafter

Algorithm for Primary Prophylaxis (Baveno VI)

(de Franchis R.; J Hepatology 2015; DOI: <http://dx.doi.org/10.1016/j.jhep.2015.05.022>)

FINDING	RESPONSE
Diagnosis of Cirrhosis	EGD to R/O Varices
No Varices	-Compensated cirrhosis + no active injury: re-scope in 3 years -Compensated cirrhosis + active injury: re-scope in 2 years -Decompensated cirrhosis: re-scope in 1 year
F1 without red wale and Child-Pugh A	-Compensated cirrhosis + no active injury: re-scope in 2 years -Compensated cirrhosis + active injury: re-scope in 1 year -Decompensated cirrhosis: re-scope in 1 year
F1 and Red wale or Child-Pugh B or C	-Beta Blocker
F2 without Red wale and Child-Pugh A	-Beta Blocker
F2 and Red wale or Child-Pugh B or C	-Beta Blocker, or -EVL
F3	-Beta Blocker, or -EVL

No Need for EGD if liver stiffness < 20 kPa and platelet count > 150,000
(Baveno VI: Repeat both tests yearly)

Acute Esophageal Variceal Hemorrhage

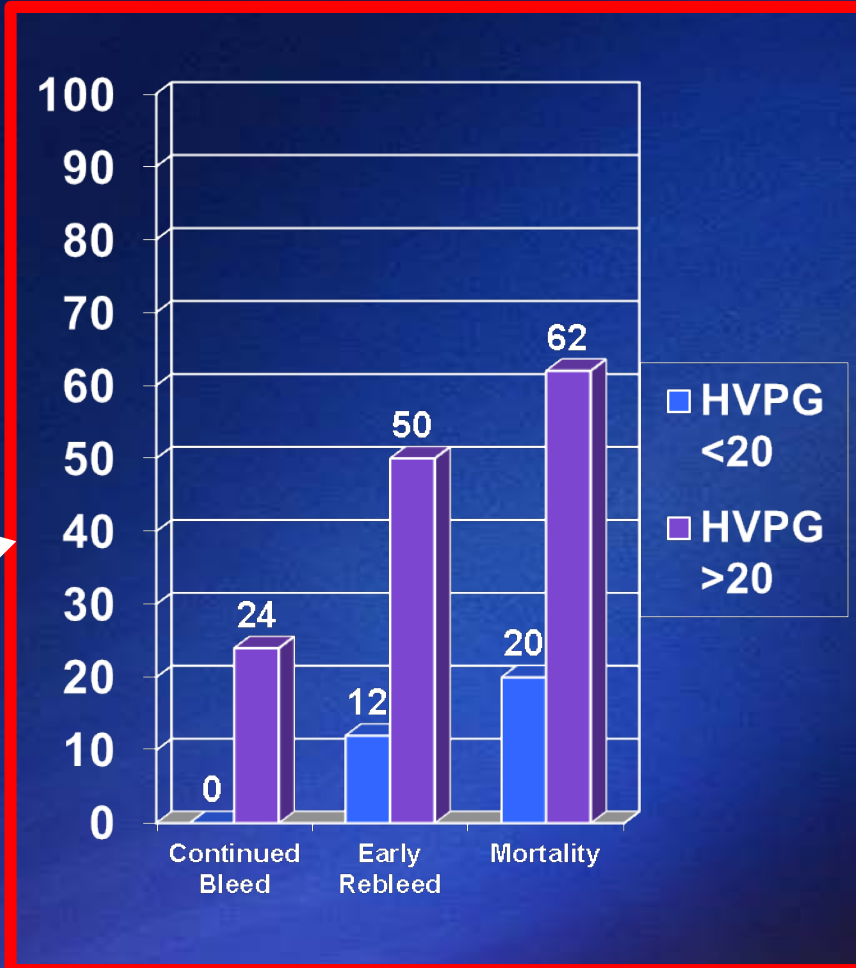
Natural History of Esophageal Variceal Hemorrhage

- **Spontaneous hemostasis: 50%**
 - **Therapeutic failure:** continuous bleeding or re-bleed within the initial 120 h (5 days), with:
 - hematemesis > 100 mL > 2 hours after treatment (EVL or drug), hypovolemic shock, or Hb drop ≥ 3 gm in 24 h period
 - **Early re-bleed:** after day 5 but within 6 weeks
 - **Late re-bleed:** after 6 weeks
- **Re-bleeding risk: 30% in 1st 6 weeks; 70% at 1 year.**
 - A) Maximum: first 48 hours,
 - B) High: within 3-4 initial days (> 50%),
 - C) Medium: 10 days to 6 weeks,
 - D) Average: after initial 6 weeks (risk identical to that who has never bleed).
- **In-hospital mortality: 40 %** (due to continuous bleed, re-bleed, advanced disease, infection, HRS)
- **Mortality after 2 week survival: 52 % at 1 year**

Risk Factors

Failure to Control Acute Hemorrhage (initial 5 days)

- Spurting varix
- Child-Pugh C
- Portal vein thrombosis
- Infection
- HVPG > 20 mm Hg (present in 80% of CTP-C)



Gastroenterology 1999;117(3):626-31

Risk Factors

Early Re-bleeding: day 6 and up to 6 weeks

- Age > 60
- Ascites
- Infection
- Renal Failure
- Severe Initial Bleed (Hb < 8 g/dL)
- HVPG > 20 mm Hg (present in 80% of CTP-C)
- Active bleeding at Endoscopy
- Red-color signs
- Platelet plug on varix
- Thrombocytopenia
- Hepatic Encephalopathy
- Alcoholic cirrhosis
- Bleeding from gastric varix
- Over transfusion to Hb >= 9; (Hct goal 24%)

Treatment of Esophageal Variceal Bleed

- Antibiotic Prophylaxis
- Intravenous Terlipressin, Octreotide or Somatostatin
- Urgent Endoscopic Variceal Ligation (within 12 hours).
- Restrictive Blood Transfusion
- Selective use of Early TIPS
- Evaluate for Portal Vein Thrombosis and HCC.
- Correction of Coagulation Disorder:
 - No recommendations can be given regarding (but reasonable):
 - Platelet transfusion if $< 50,000$; 1 single donor unit increases plat by 5 -10K
 - Cryoprecipitate if Fibrinogen < 120 mg/dL; 1 unit per 10 kg weight will increase it 50 mg/dL.
 - NOT RECOMMENDED:
 - Correction of INR with FFP or factor VIIa.
 - The INR is not a reliable indicator of coagulation status in cirrhosis.

Risk of Infection

Cirrhotic with Gastrointestinal Hemorrhage

- Risk of Infection: 60%
- Acquisition time:
 - A) 1/3 before or at time of admission,
 - B) 2/3 after hospital admission.
- Types of Infection:
 - UTI (20-25%), - SBP (15-20%),
 - Respiratory (8%), - Bacteremia (8%).
- **In Child-Pugh A the risk of infection is very low (5%) and mortality is low:**
consider no antibiotics to decrease antibiotic-resistant infections (Tandon P et al. AASLD 2013) (Pauwels A et al. Hepatology 1996;24:802-806)

Effect of Antibiotics

Cirrhotic with Gastrointestinal Hemorrhage

- **Prophylactic antibiotics vs Placebo** (several meta-analysis; Soares-Weiser K et al. Scan J Gastroenterol 2003;38:193 and Chavez-Tapia NC et al. Aliment Pharmacol Ther 2011;34:509-5018):
 - Decreases mortality by 21% (**RR 0.79**),
 - Reduces infection risk by 65% (**RR 0.35**)
 - Reduces mortality from infection by 57% (**RR 0.43**)
 - Decrease re-bleeding rate by 47% (**RR 0.53**)
 - Decreases Transfusion needs (**2.7 vs 0.7 units**)
- **Regimens: 7 to 10 days of**
 - A) Ofloxacin 200 mg BID,
 - B) Norfloxacin 400 mg BID,
 - C) Ciprofloxacin 500 mg BID
 - **D) Ceftriaxone 1 g/d** (preferred in malnutrition, encephalopathy, ascites, jaundice or high quinolone-resistance prevalence) (de Franchis R. J Hepatol 2010;53:762-768)

Vasoactive Agents Used in the Management of Acute Variceal Hemorrhage

Drug	Recommended Dose	Duration
Octreotide (SMT analogue)	Initial IV bolus of 50 micrograms (can be repeated in first hour if ongoing bleeding) Continuous IV infusion of 50 µg/hr	2-5 days
Vasopressin	Continuous IV infusion: 0.2-0.4 U/min; can be increased to 0.8 U/min It should always be accompanied by IV nitroglycerin at a starting dose of 40 µg/min, which can be increased to a maximum of 400 µg/min, adjusted to maintain a systolic blood pressure 90 mm Hg.	24 hours
SMT	Initial IV bolus 250 µg (can be repeated in the first hour if ongoing bleeding) Continuous IV infusion of 250-500 µg/h	2-5 days
Terlipressin (VP analogue)	Initial 48 hours: 2 mg IV every 4 hours until control of bleeding Maintenance: 1 mg IV every 4 hours to prevent re-bleeding	2-5 days

Endoscopic Band Variceal Ligation (EVL)

Uses

- Treatment of acute hemorrhage
- Eradication after Index Bleed
- Primary prevention



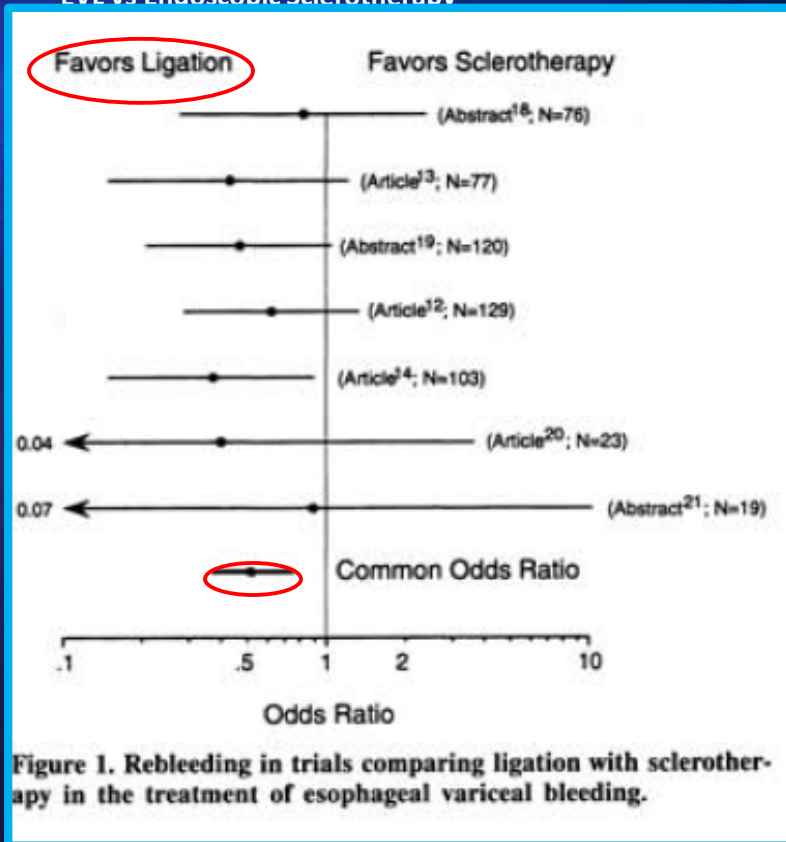
Give 250 mg of IV Erythromycin 30-120 minutes before EGD

Meta-Analysis of Endoscopic Variceal Ligation (EVL) vs Endoscopic Sclerotherapy (ES)

Laine L et al. Ann Intern Med 1995;123:280-287

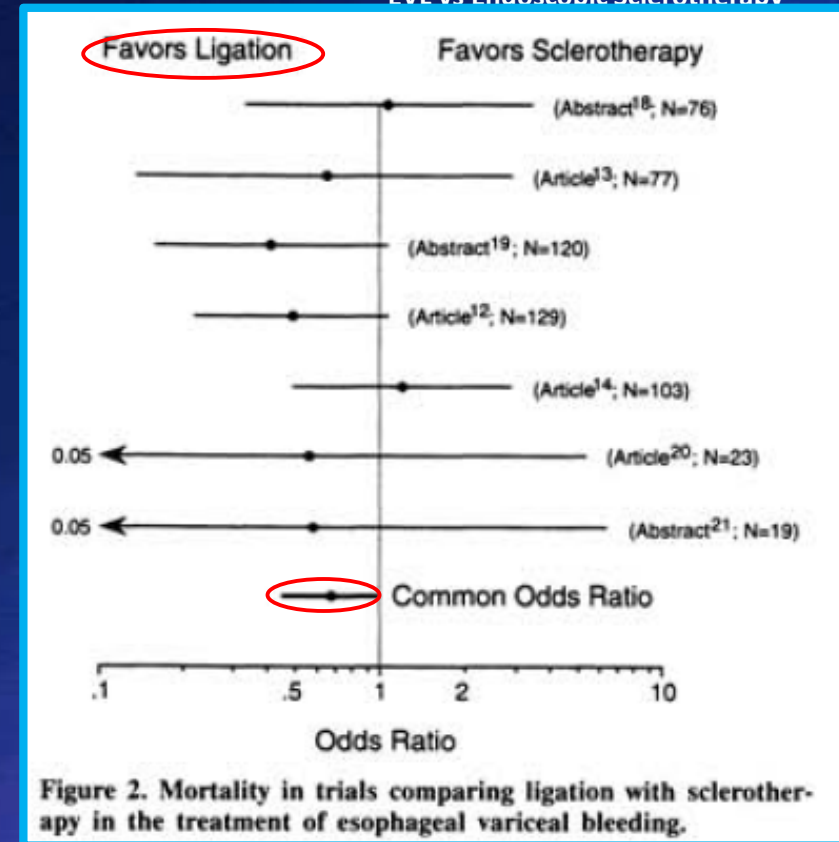
Esophageal varix Re-Bleed

EVL vs Endoscopic Sclerotherapy



Mortality

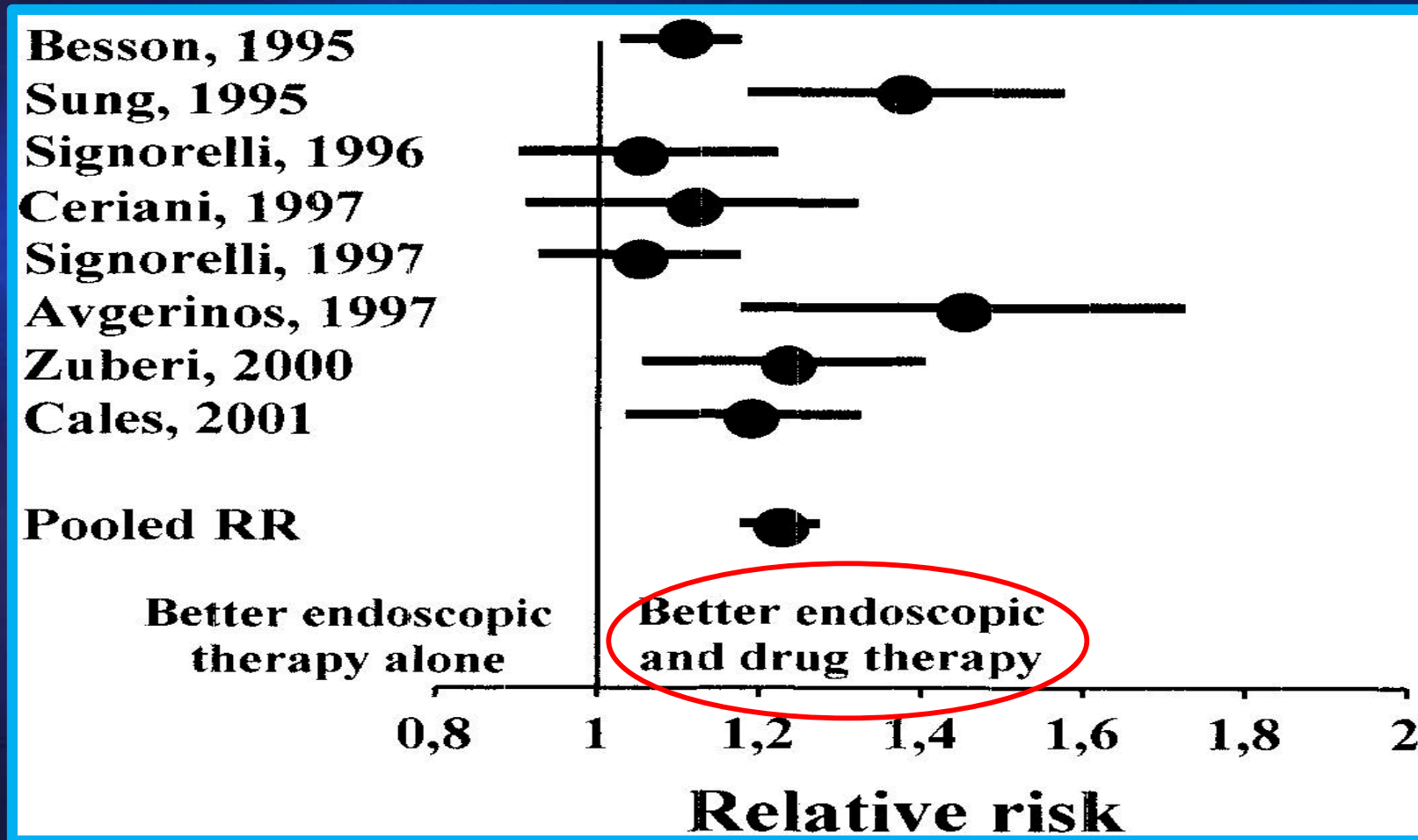
EVL vs Endoscopic Sclerotherapy



Endoscopy vs Endoscopy + Octreotide/Somatostatin

5-days Hemostasis in Acute Esophageal Variceal Hemorrhage

Banares R et al. *HEPATOLOGY* 2002;35:609-615

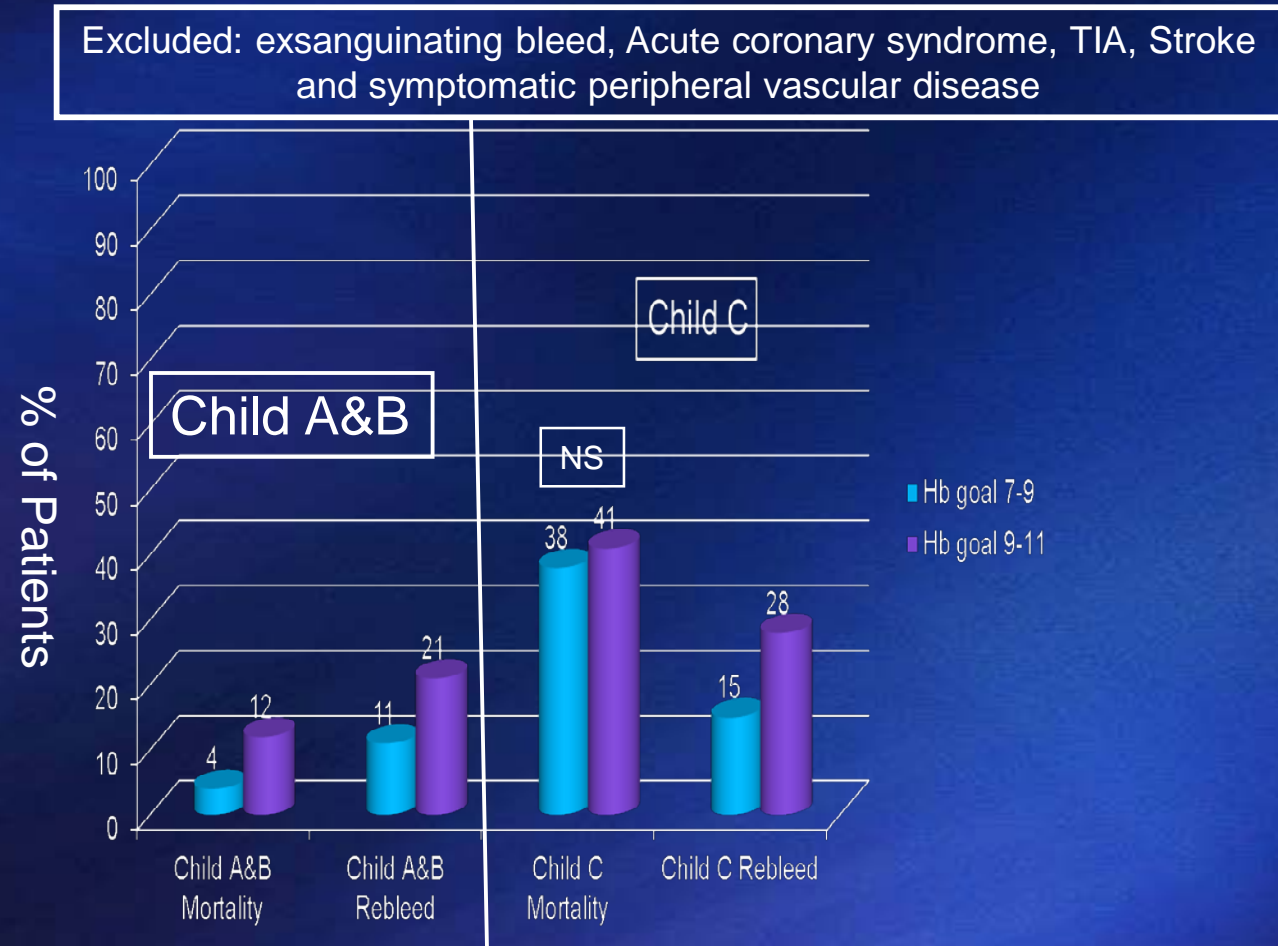


**DECREASES RE-BLEEDING RATE
NO EFFECT ON SURVIVAL**

Blood Transfusion in Acute GI Bleed in Cirrhosis

Restrictive (Hb goal 7-8) vs Liberal (Hb goal 10) Transfusion in GI Bleed

Villanueva C; N Engl J Med 2013; 368:11-21



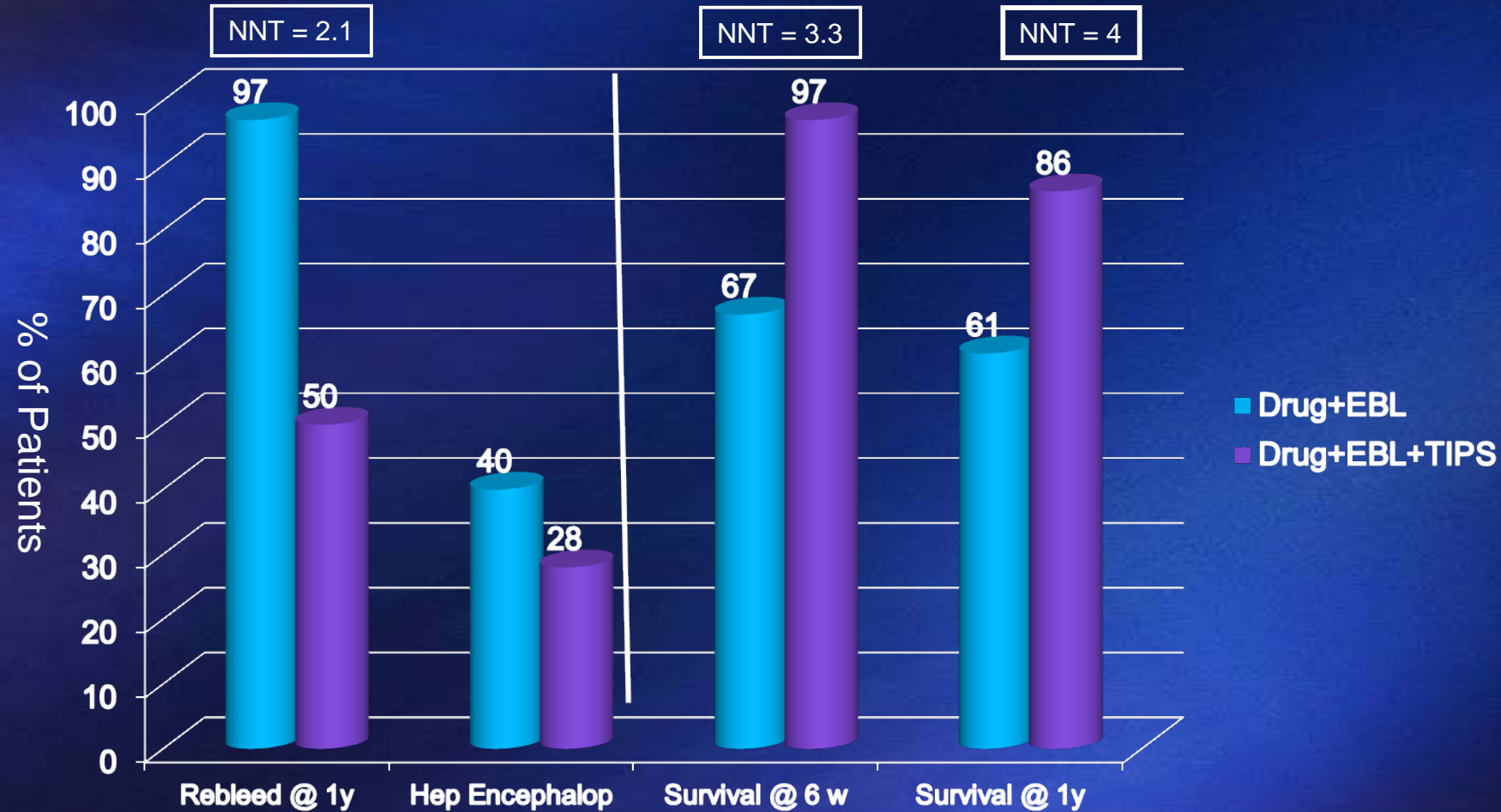
Restrictive transfusion (Hb goal 7-8) decreases re-bleeding rate in all patients and decreases mortality in Child-Pugh A and B patients

Acute GI Bleed in Cirrhosis

Variceal Bleed: **Actively bleeding Child B, or any Child C (10-13)**

Garcia-Pagan JC; N Engl J Med 2010; 362:2370-2379

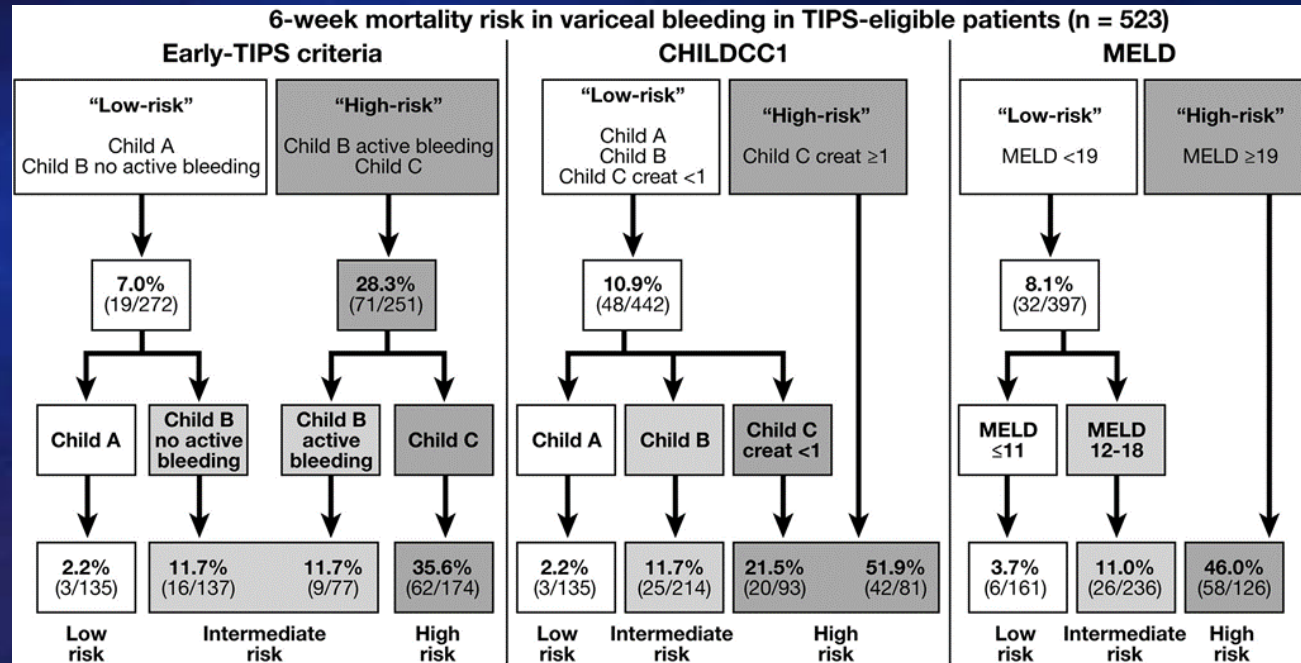
Early TIPS with PTFE stent in



Conclusion: TIPS with PTFE covered stent is superior to EBL+BB in the treatment of first esophageal variceal bleed in:
Child B actively bleeding at time of EGD, and in
Child C with score 10-13.

Mortality (6-weeks) in Acute Variceal Bleeding without Early TIPS

Clinical Gastroenterology and Hepatology 2018;16:132–139



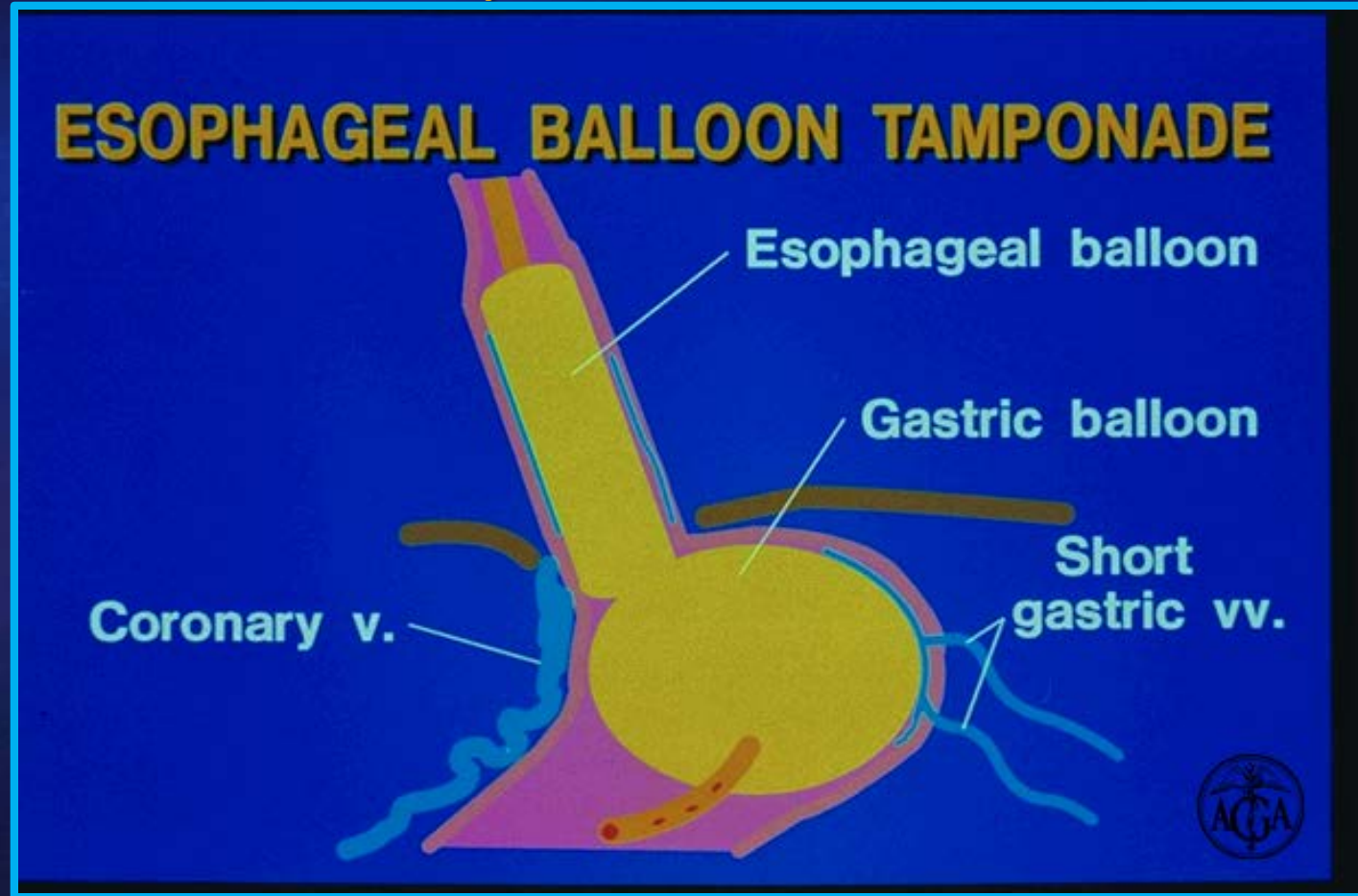
Eligible criteria for early TIPS included the following: age younger than 75 years, creatinine level less than 3 mg/dL, Child-Pugh score lower than 14, hepatocellular carcinoma within Milano criteria or Barcelona Clínic Liver Cancer staging system stages C or D, and no portal thrombosis.

6-week mortality with early TIPS is 3%;

Child-Pugh B with or without active bleeding at Endoscopy and MELD ≥ 12 , Child-Pugh C up to 13 points with or without bleeding at Endoscopy (6% and 19% 1-y mortality with early-TIPS, respectively), and patients with MELD 12-18 benefit from early-TIPS

Acute Variceal Bleeding

Direct Pressure Technique – Minnesota Tube

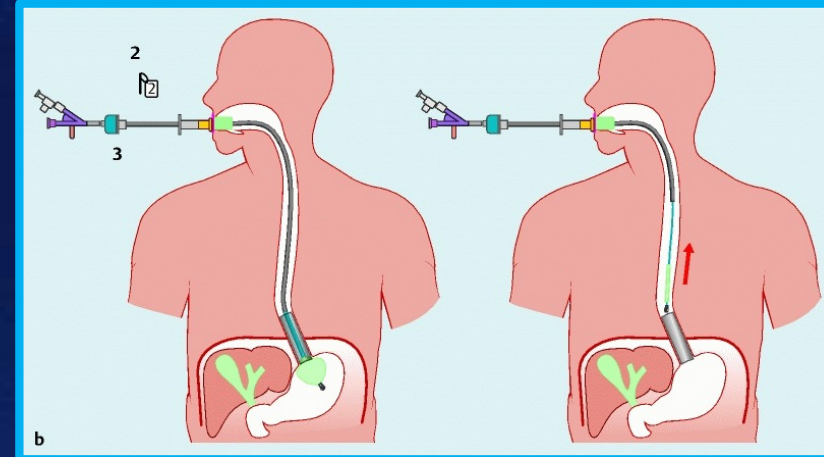


Patient intubated and Minnesota tube with 0.5-1 Kg traction
Bleeding Control 80%, complication rate 14%, mortality 20%
BRIDGE TO OTHER THERAPY FOR \leq 24 HOURS

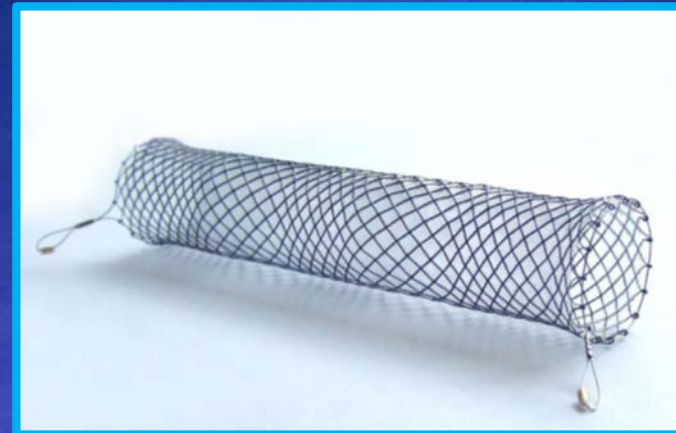
Direct Pressure Technique

Self-Expandable Stents in Esophageal Variceal Hemorrhage

- Approximately 60 case series: 100% bleed control.
- Used mostly as “bridge therapy” to TIPS; removed after 9-11 days. (Hubmann R et al. Endoscopy 2006;38:896-901)
- There is an ongoing prospective study comparing with balloon tamponade.
- Supported by BavenoVI (potentially as efficacious and safer than balloon tamponade) (de Franchis R.; J of Hepatol 2015;DOI:<http://dx.doi.org/10.1016/j.jhep.2015.05.022>)
- Has been used as “definitive treatment” in a few (up to 214 days) (Holster IL et al. Endoscopy 2013;45:485-488)



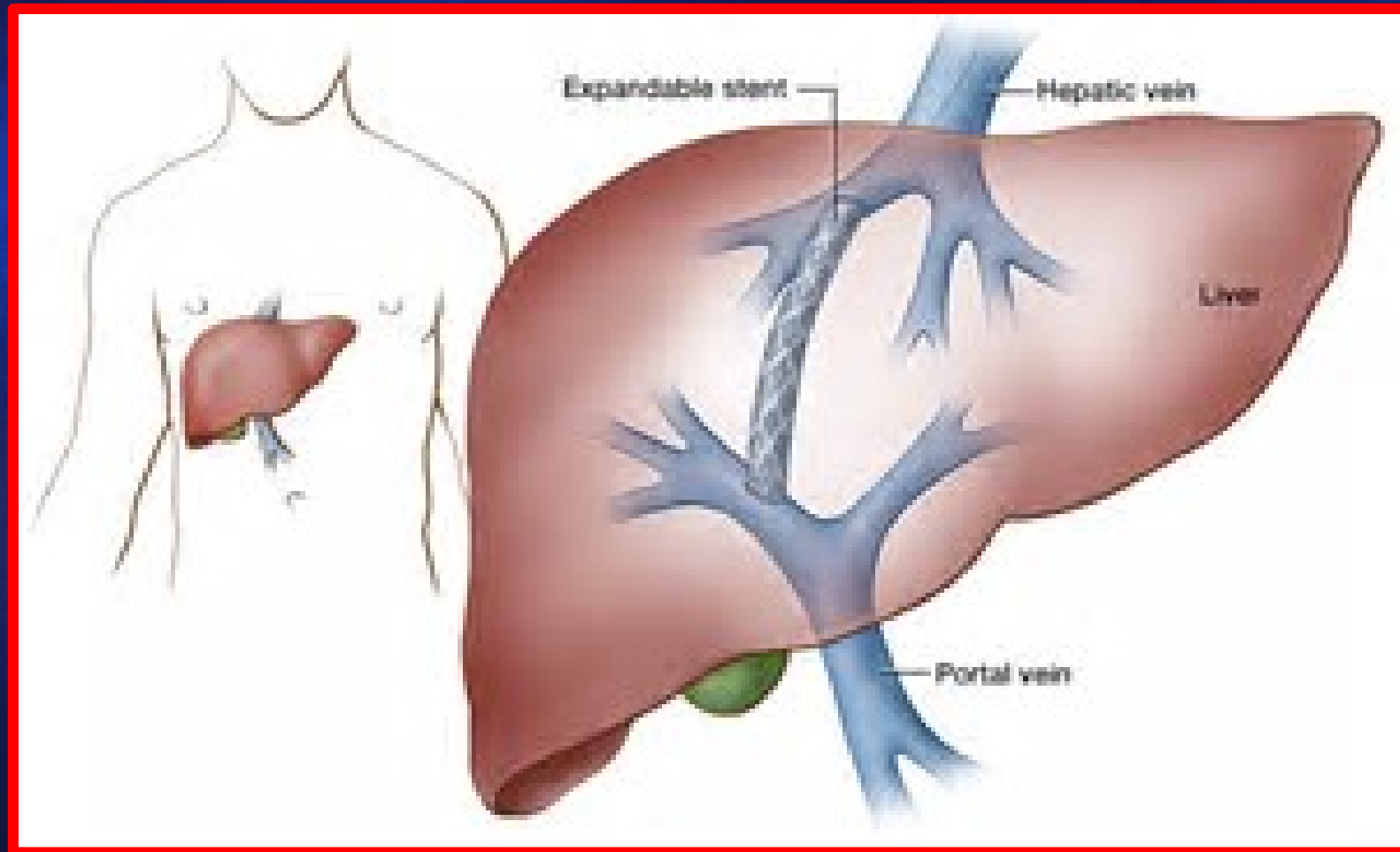
SX-Ella Stent Danis 135 mm x 25 mm
Nitinol cubierto con lamina de poliuretano



TIPS as Rescue Treatment

- Bleeding Control: 90%
- Re-bleeding Rate: 16-30%
- Mortality: 20-30%
- 30-day survival is 67% when rescuing endoscopic + medical therapy failure.
- Predictors of poor post-TIPS survival:
 - Age > 60
 - Emergency TIPS
 - ALT > 100 U/L
 - Bilirubin > 4 mg/dL increases mortality
 - Pre-TIPSS encephalopathy not related to bleed
 - Pre-TIPSS MELD Score (> 15-18 has high mortality; done only if there are no other options)

TIPS



Contraindications for TIPSS

ABSOLUTE

- Severe CHF
- Severe Pulmonary HTN (45 mm Hg)
- Polycystic liver disease
- Severe hepatic failure
- Portal V thrombosis with cavernoma
- Severe tricuspid regurgitation

RELATIVE

- Active infection
- Poorly controlled PSE
- Hypervascular liver tumor
- Portal V thrombosis without cavernoma
- Biliary obstruction

Management of Acute Esophageal Varices Hemorrhage

- Vasoactive drugs (SMT or its analogue, octreotide; VP or its analogue, terlipressin) should be initiated as soon as VH is suspected.
- PRBC transfusion should be done conservatively, starting to transfuse when the hemoglobin reaches a threshold of around 7 g/dL with the goal of maintaining it between 7 and 9 g/dL.
- Short-term (maximum 7 days) antibiotic prophylaxis should be instituted in any patient with cirrhosis and GI hemorrhage.
- Intravenous ceftriaxone 1 g/24 h is the antibiotic of choice and should be used for a maximum of 7 days.
 - consider discontinuing when hemorrhage has resolved and vasoactive drugs discontinued.

Management of Acute Esophageal Varices Hemorrhage

- EGD should be performed within 12 hours of admission and once the patient is hemodynamically stable.
- If a variceal source is confirmed/suspected, EVL should be performed.
- In patients at high risk of failure or re-bleeding (CTP class C cirrhosis or CTP class B with active bleeding on endoscopy) who have no contraindications for TIPS, an “early” (preemptive) TIPS within 72 hours from EGD/EVL may benefit selected patients.
- For patients in whom an early TIPS is not performed, intravenous vasoactive drugs should be continued for 2-5 days and NSBBs initiated once vasoactive drugs are discontinued.
 - Rescue TIPS is indicated in these patients if hemorrhage cannot be controlled or if bleeding recurs despite vasoactive drugs + EVL.
- In patients in whom TIPS is performed successfully, intravenous vasoactive drugs can be discontinued.

Bleeding After Endoscopic Therapy

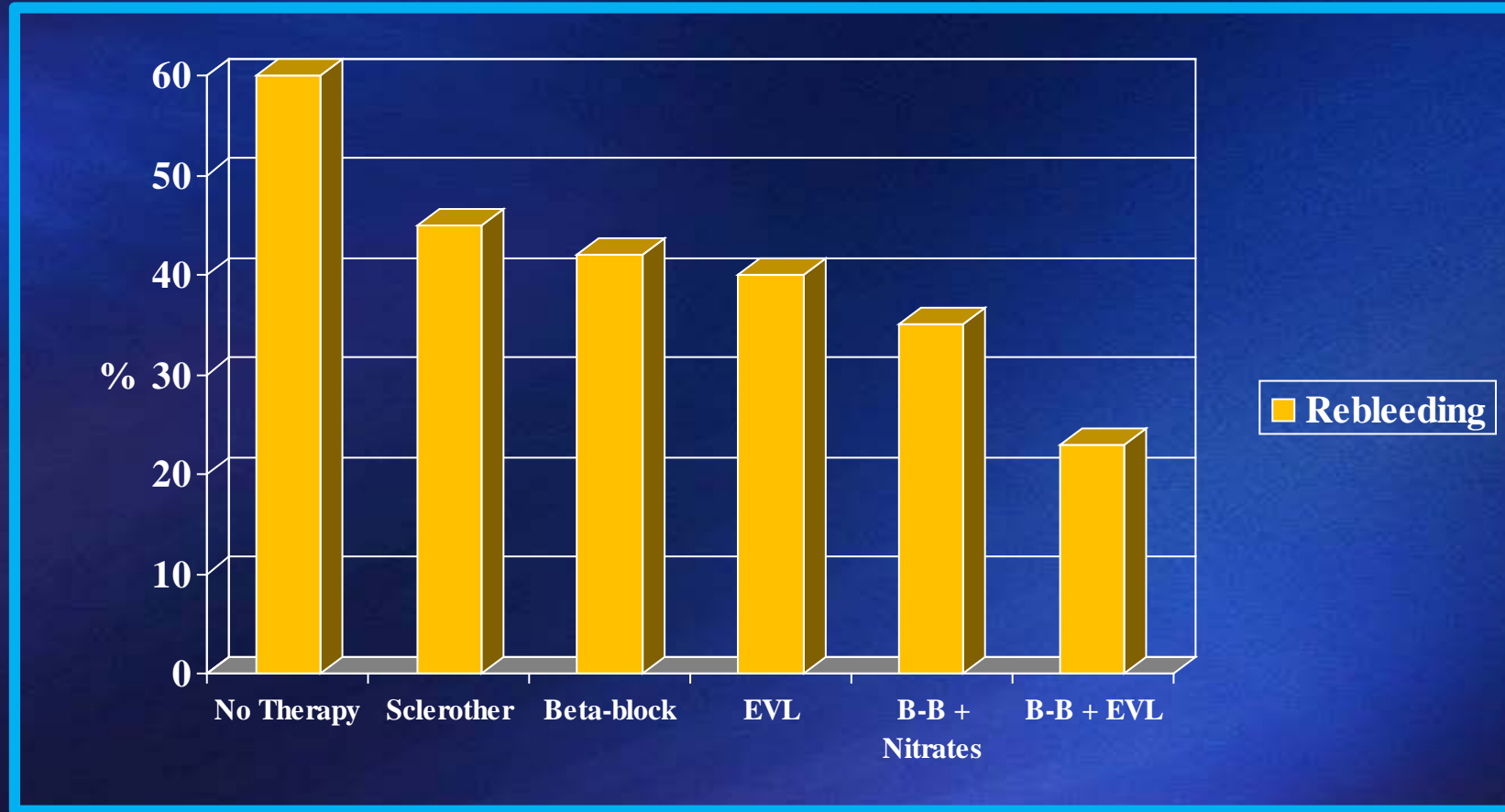
- Repeat EGD to see if re-therapy is needed.
- Give Platelets if $< 50,000$
 - 1 single donor unit increases plat by 5-10K
- Give Cryoprecipitate if Fibrinogen < 120 mg/dL.
 - 1 unit per 10 kg weight will increase it 50 mg/dL.
- In bleeding after procedure consider **Antifibrinolytic agents**:
 - Aminocaproic acid 3 grams oral QID, or Intravenous 5 grams in 250 mL NS over 1 hour + 1 gm in 50 mL NS per hour until bleeding stops
 - Tranexamic acid 1 gm IV every 6 hours, until bleeding stops.

Variceal Re-bleed

LONG TERM PROPHYLAXIS

LONG TERM Rebleeding Risk

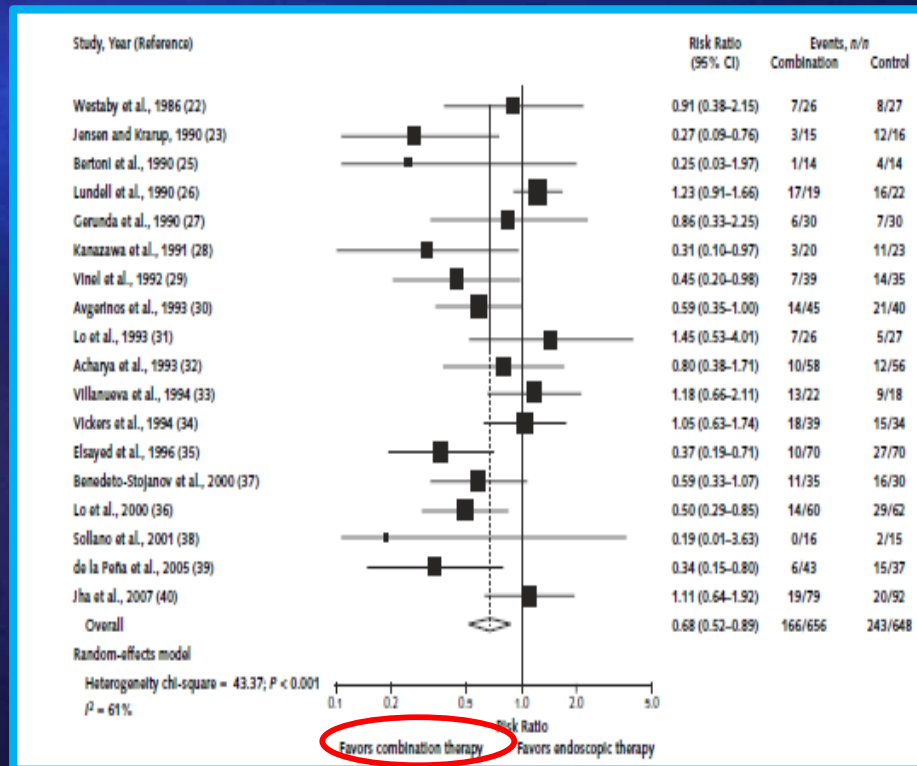
Different Prophylaxis



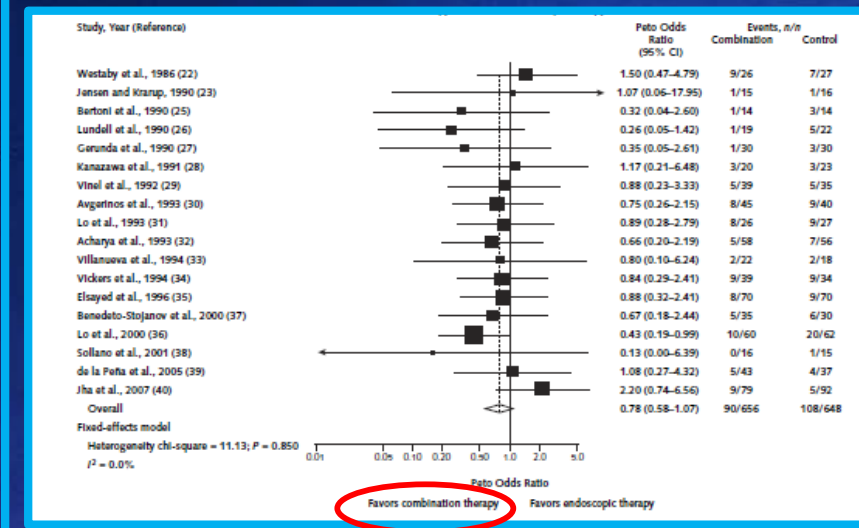
Meta-Analysis of [Endoscopy + Drug therapy] vs Drug-Therapy to Prevent Variceal Re-bleeding

Gonzalez R et al. Ann Intern Med 2008;149:109-122

Re-Bleeding Rate



Mortality



The combination of Beta-blocker + Endoscopy is superior to endoscopy alone in decreasing re-bleeding rate and mortality.

Secondary Prophylaxis for Esophageal Variceal Hemorrhage

EVL + NSBB

Therapy	Recommended Dose	Therapy Goals	Maintenance/Follow-up
Propranolol	<ul style="list-style-type: none"> •With EVL. •20-40 mg orally <i>twice</i> a day •Adjust every 2-3 days until treatment goal is achieved •Maximal daily dose: <ul style="list-style-type: none"> • 320 mg/day in patients without ascites • 160 mg/day in patients with ascites 	<ul style="list-style-type: none"> •Resting heart rate of 55-60 beats per minute •Systolic blood pressure should not decrease <90 mm Hg 	<ul style="list-style-type: none"> •At every outpatient visit make sure that heart rate is on target •Continue indefinitely
Nadolol	<ul style="list-style-type: none"> •With EVL. •20-40 mg orally <i>once</i> a day •Adjust every 2-3 days until treatment goal is achieved •Maximal daily dose: <ul style="list-style-type: none"> • 160 mg/day in patients without ascites • 80 mg/day in patients with ascites 	<ul style="list-style-type: none"> •Resting heart rate of 55-60 beats per minute •Systolic blood pressure should not decrease <90 mm Hg 	<ul style="list-style-type: none"> •At every outpatient visit make sure that heart rate is on target •Continue indefinitely
EVL	<ul style="list-style-type: none"> •With NSBB. •Every 1-4 weeks until the eradication of varices 	<ul style="list-style-type: none"> •Variceal eradication (no further ligation possible) 	<ul style="list-style-type: none"> •First EGD performed 3-6 months after eradication and every 6-12 months thereafter

NSBB is the main component of the therapy. If intolerant to NSBB, consider TIPS
Carvedilol has not been study well for secondary prophylaxis.

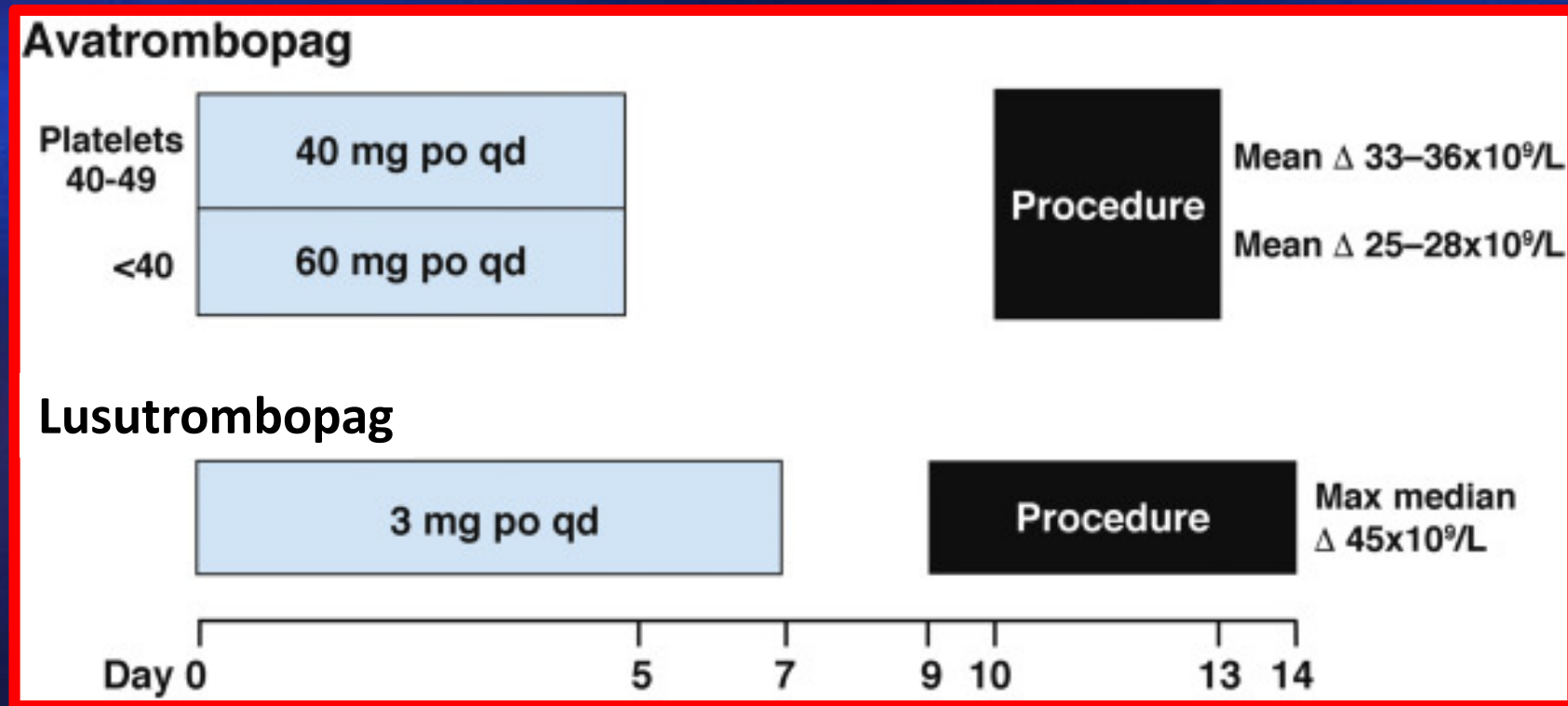
Discontinuation of Beta-blockers as Secondary Prophylaxis (Baveno VI)

- Until randomized trials are available NSBB should be reduced/discontinued if a patient with refractory ascites develops any of the following events:
 - Systolic blood pressure <90 mmHg
 - Hypo-Natremia < 130
 - Acute Kidney Injury
- If there was a clear precipitant for these events (e.g. spontaneous bacterial peritonitis, hemorrhage), re-initiation of NSBB should be considered after these abnormal parameters return to baseline values after resolution of the precipitant
 - If reinitiating NSBBs, dose should be re-titrated, starting at the lowest dose
 - If the patient continues to be intolerant to NSBB and is an appropriate TIPS candidate, covered TIPS placement may be considered

Correction of Coagulation Parameters Before Elective EGD with Banding

- No need to correct Platelet count nor INR before EGD with Banding (nor paracentesis or thoracentesis).
- INR has no value to predict bleeding in cirrhosis.
 - FFP infusions increase portal pressure and risk of bleeding.
- In high risk procedures, correction of **Platelet count < 50,000** is reasonable
 - Low platelets due to sequestration and low TPO. In elective procedures can be corrected with oral Avatrombopag 40-60 mg/days x 5d, or Lusotrombopag 3 mg a day x 7 days
 - Platelet dysfunction is offset by increased endothelial derived vWF.
 - One unit single donor platelets increases plat count by 5-10,000
- In high risk procedures, correction of **Fibrinogen < 120 mg/dL** is reasonable.
 - One unit of cryoprecipitate per 10 kg of weight, increase fibrinogen by 50 mg/dL
- In bleeding after procedure consider **Antifibrinolytic agents**:
 - Aminocaproic acid 3 grams oral QID, or Intravenous 5 grams in 250 mL NS over 1 hour + 1 gm in 50 mL NS per hour until bleeding stops
 - Tranexamic acid 1 gm IV every 6 hours, until bleeding stops.

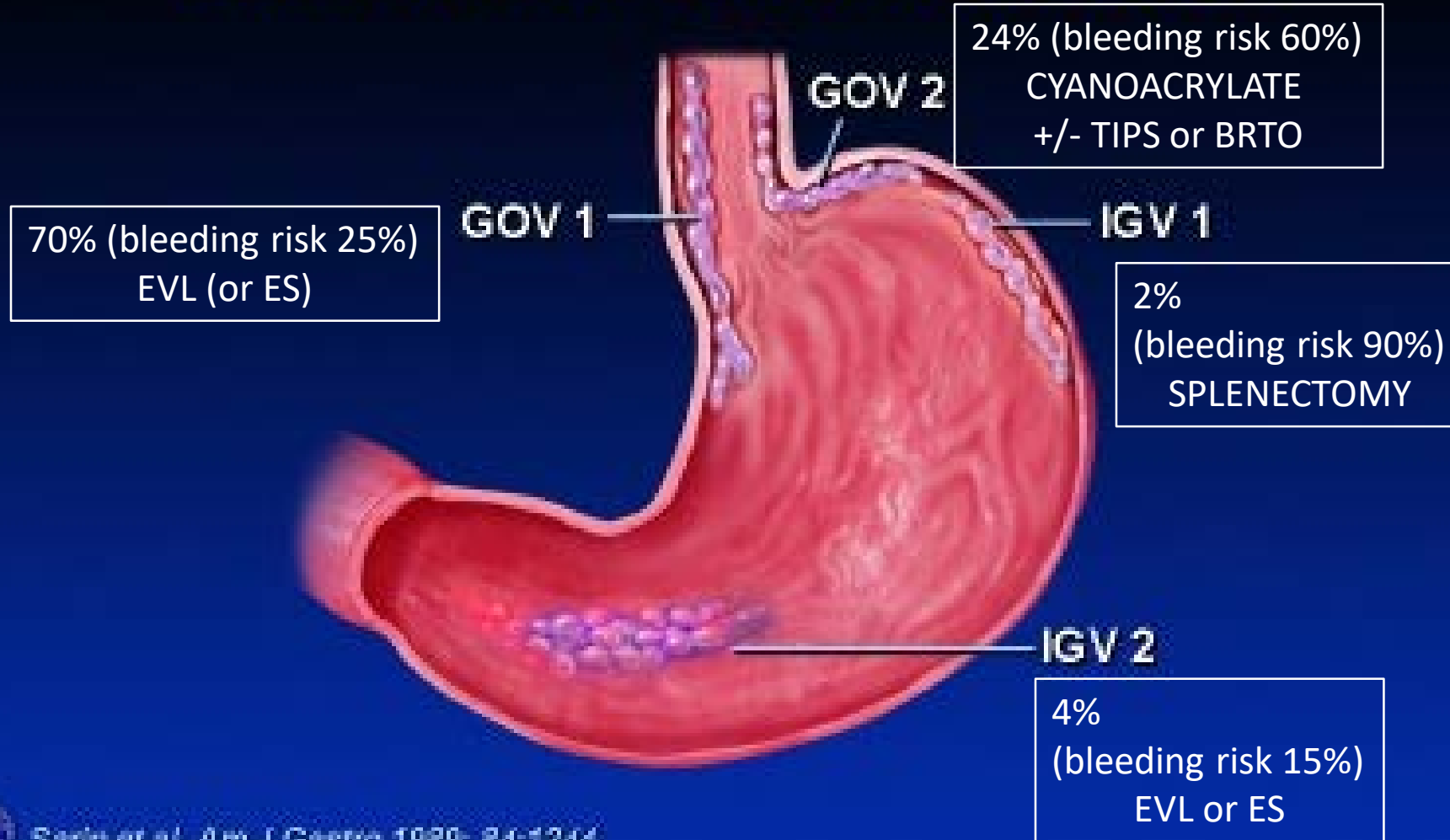
Oral Agent to Treat Thrombocytopenia



65 to 69% of patient reach platelet count \geq 50,000

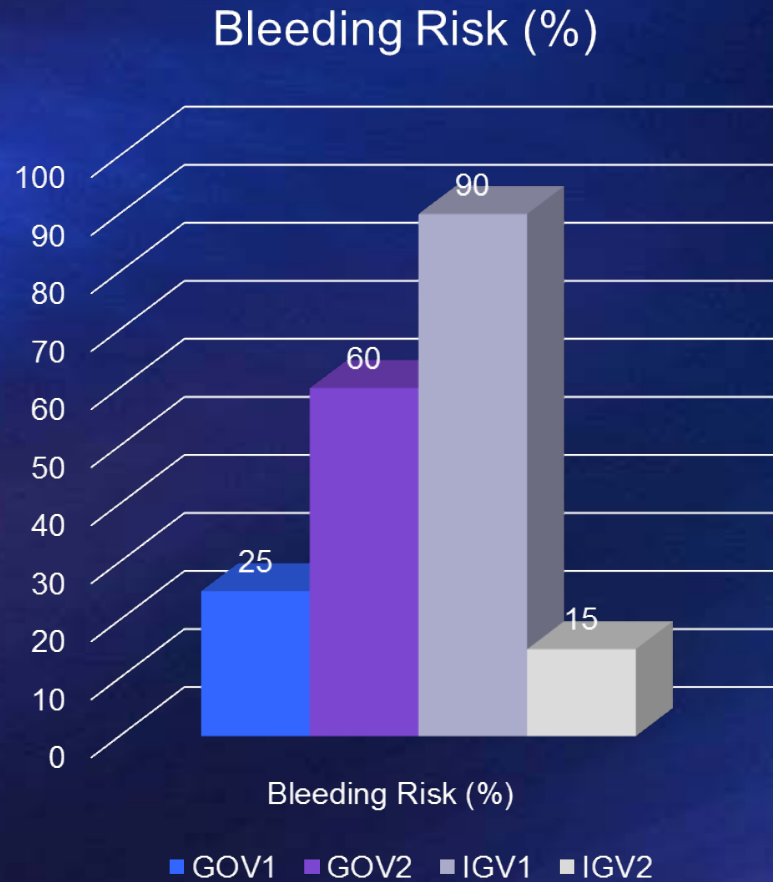
Gastric Variceal Bleed

Classification of Gastric Varices



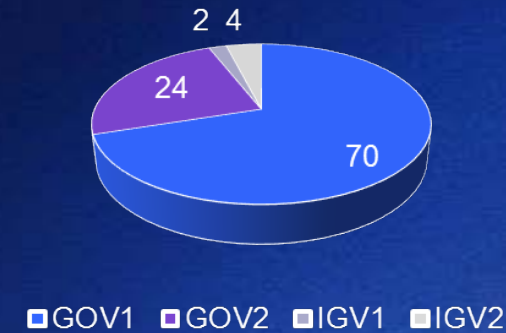
Gastric Variceal Bleed

Risk, Frequency & Origen

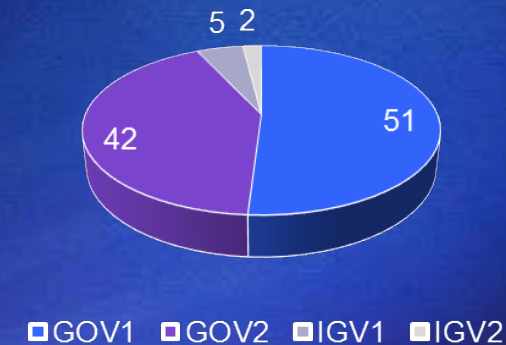


Lifetime Risk of Bleeding

Type of Gastric Varices (%)



Origen of Gastric Variceal bleed (%)

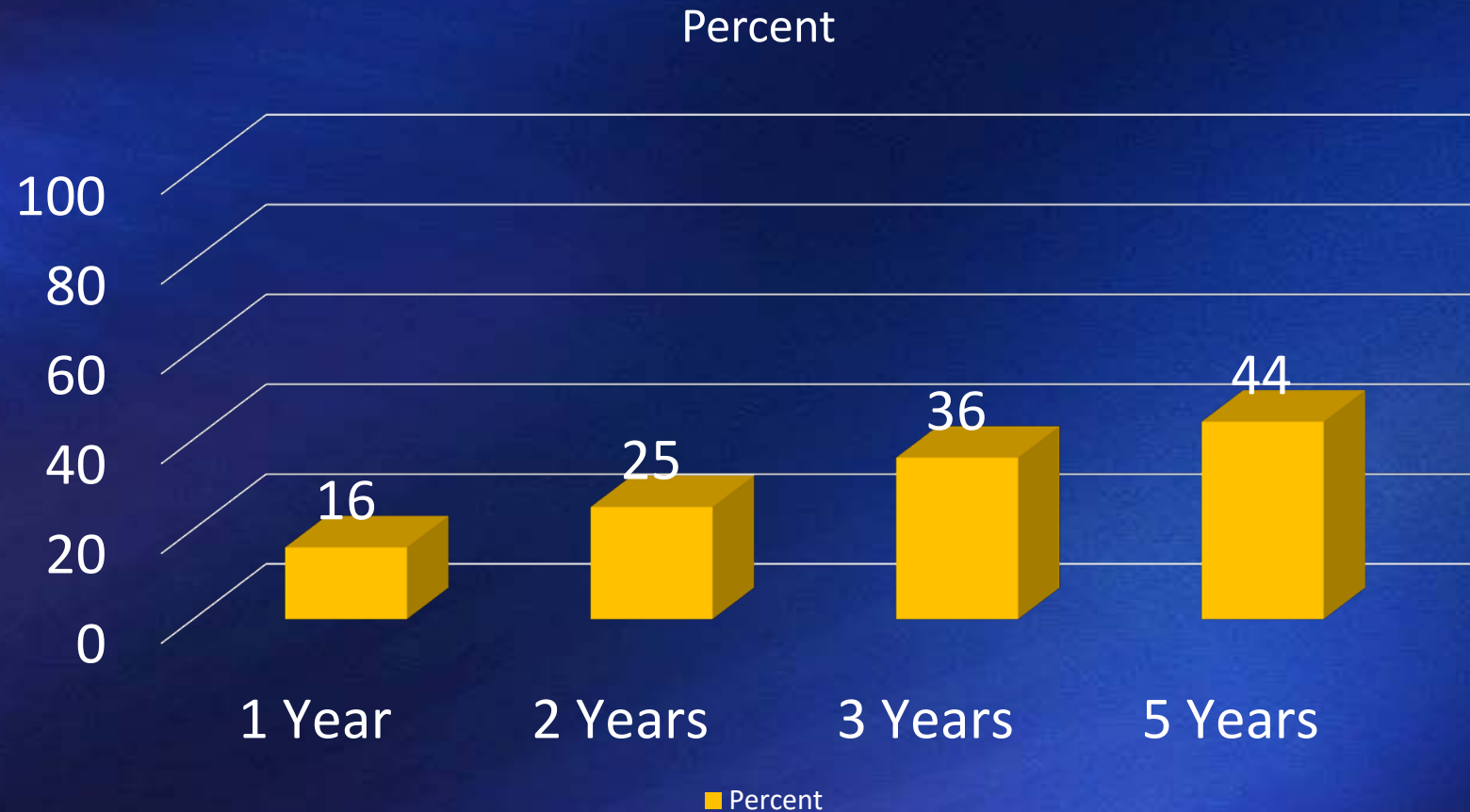


Gastric Variceal Bleed (GOV2)

- 10-15% of all variceal (esophageal + gastric) bleeds.
- Bleeding Risk:
 - Lifetime risk is 60%.
 - Mean bleed 4.8 units of blood.
 - Increases by size (> 10 mm, vs 5-10 mm, vs < 5 mm) and
 - Increases by Child Class (C>B>A);
 - Annual bleeding rate is 65% in Child C with large varix + red signs;
 - Annual bleeding rate is 4% in Child A with small varix without red markings.
- Mortality: 30-52%
- Re-bleeding Rate: 30%
- Gastric varix (GV) is usually a single large vessel; difficult to band or loop ligate.
- TIPS does not decrease diameter nor thickness of varix wall, and GV bleed at lower portal pressures.

Cumulative Bleeding Risk of GOV2 varices by time

Kim T et al. Hepatology 1997;25:307-12.



Primary Prophylaxis for Gastric Variceal Hemorrhage

- Prevention of First Hemorrhage:
 - **GOV1 Varices:** May follow the recommendations for EV.
 - **GOV2 or IGV1:** NSBBs can be used, although the data are not as strong as for EV.
 - Neither TIPS nor Balloon-Occluded Retrograde Transvenous Obliteration (BRTO) are recommended to prevent first hemorrhage in patients with fundal varices that have not bled.

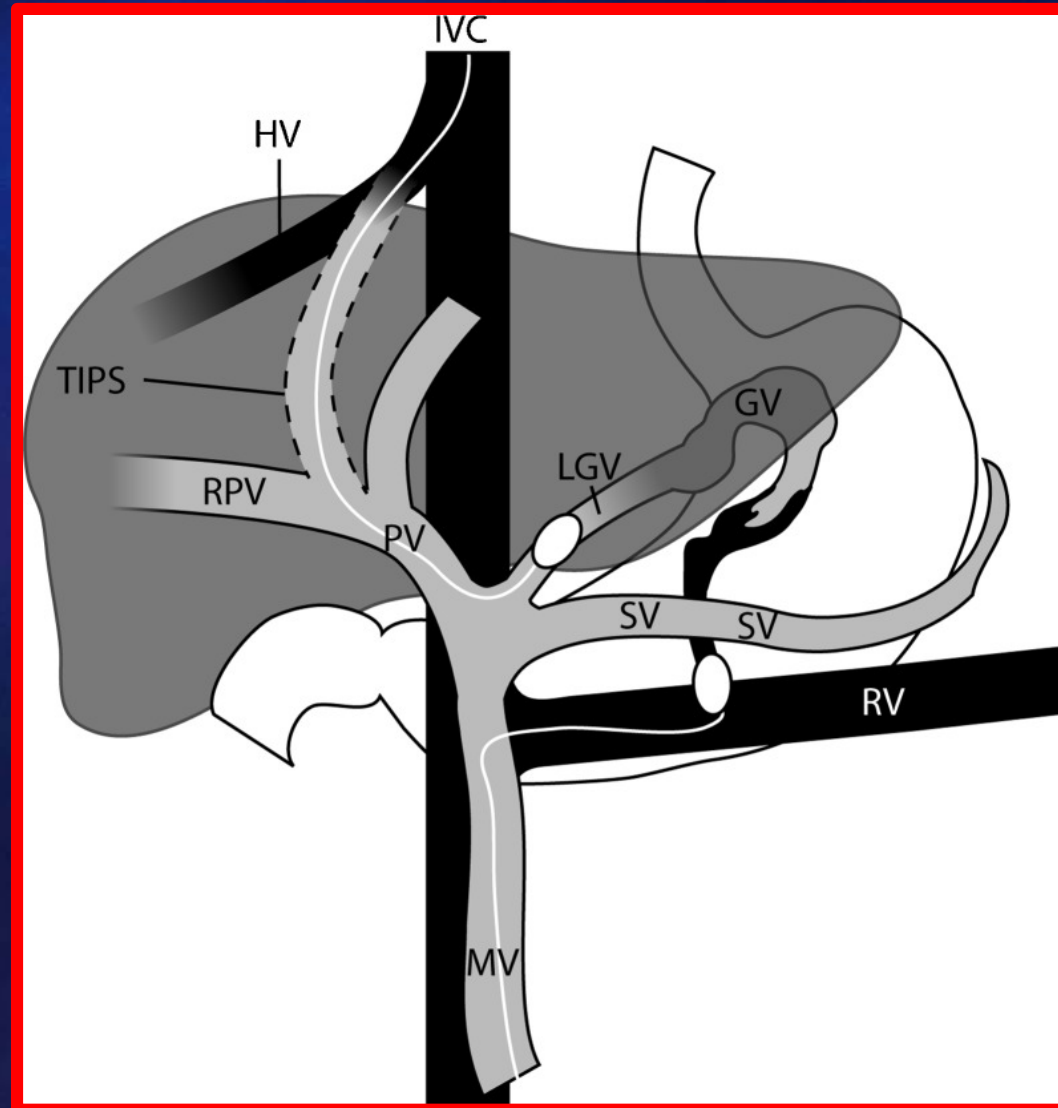
Treatment of Acute Gastric Variceal Bleed

- Intravariceal Cyanoacrylate injection (**Hystoacryl**, Dermabond) q 3-4 weeks until obliteration:
 - hemostasis in 90%;
 - embolization 0.7%;
 - re-bleeding at 3 d, 3 month and 1 year: 6.9%, 10.6%, and 10.0%.
- TIPS:
 - controls 90% of bleeds (goal HVPg pressure \leq 8 mmHg);
 - re-bleeding at 3 d, 3 month and 1 year: 9.5%, 20.7%, and 25% (Procaccini NJ et al. Gastrointestinal Endoscopy 2009;70:881-7)
- Vasoactive drugs + antibiotics (used but not studied).
- BRTO (Balloon-Occluded Retrograde Transvenous Obliteration)
- BRTO + TIPS: less ascites, hydrothorax, esophageal varices and re-bleeding.
- Balloon (Linton-Nacklas or modified Minnesota) as bridge to TIPS or BRTO

Balloon-Occluded Retrograde Transvenous Obliteration (BRTO)

- BRTO needs a Gastro-Renal Shunt (present in 85% of GV patients).
- Technique: instillation of sclerosant or foam into the GV via a balloon-occluding catheter placed through the Gastro-Renal Shunt.
- Indication: GVB who have failed endoscopic therapy and are poor candidates for TIPS.
 - In Japan: prevention of initial bleed and secondary prophylaxis of GVB.
- Initial control of bleeding > 90%,
- Re-bleeding rates 0%-9%,
- Variceal eradication rates 75%-100%,
- Adverse effects: fever, ascites, pleural effusions, and development of Esophageal Varices in up to two-thirds of patients.
- Partial splenic embolization preceding BRTO reduces incidence of Esophageal Varices compared with BRTO alone (9% versus 45%) by reducing blood inflow into the portal vein.

Balloon-Occluded Retrograde Transvenous Obliteration (BRTO)



Treatment of Gastric Variceal Hemorrhage

- Patients with acute bleeding from GV should be initially managed in a similar fashion to those bleeding from EV
 - using a restrictive transfusion policy, vasoactive drug infusion, and antibiotic prophylaxis.
- In patients bleeding from GOV1 varices, either EVL (if technically feasible) or cyanoacrylate glue injection, if available, are the recommended endoscopic treatments.
- TIPS is the treatment of choice in the control of bleeding from cardiofundal varices (GOV2 or IGV1).
- Cyanoacrylate glue injection is an option for cases in which TIPS is not technically feasible, but it is not approved for treatment of GV in the United States and should be performed only in centers where the expertise is available.

Secondary Prophylaxis of Gastric Variceal Hemorrhage

- In patients who have recovered from a GOV1 hemorrhage:
 - the combination of NSBBs and endoscopic variceal therapy (EVL or cyanoacrylate injection) is the first-line therapy.
- In patients who have recovered from GOV2 or IGV1 hemorrhage:
 - TIPS and/or BRTO are first-line treatments.
 - Cyanoacrylate glue injection is an option for cases in which TIPS or BRTO are not technically feasible,
 - It is not approved for the treatment of GV in the United States, and
 - Should be performed only in centers where the expertise is available.

Thank you for your attention