UGI Bleeding & Hemostasis

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Topics

- Acute Upper GI Non-Variceal Bleed
- Acute Upper GI Variceal Bleed
- Selected Causes of Non-Variceal UGI Bleed

Acute Upper Non-Variceal Bleed

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")
  (Gastrointest Endosc 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 rebleeding rate.

Signs of GI Bleed

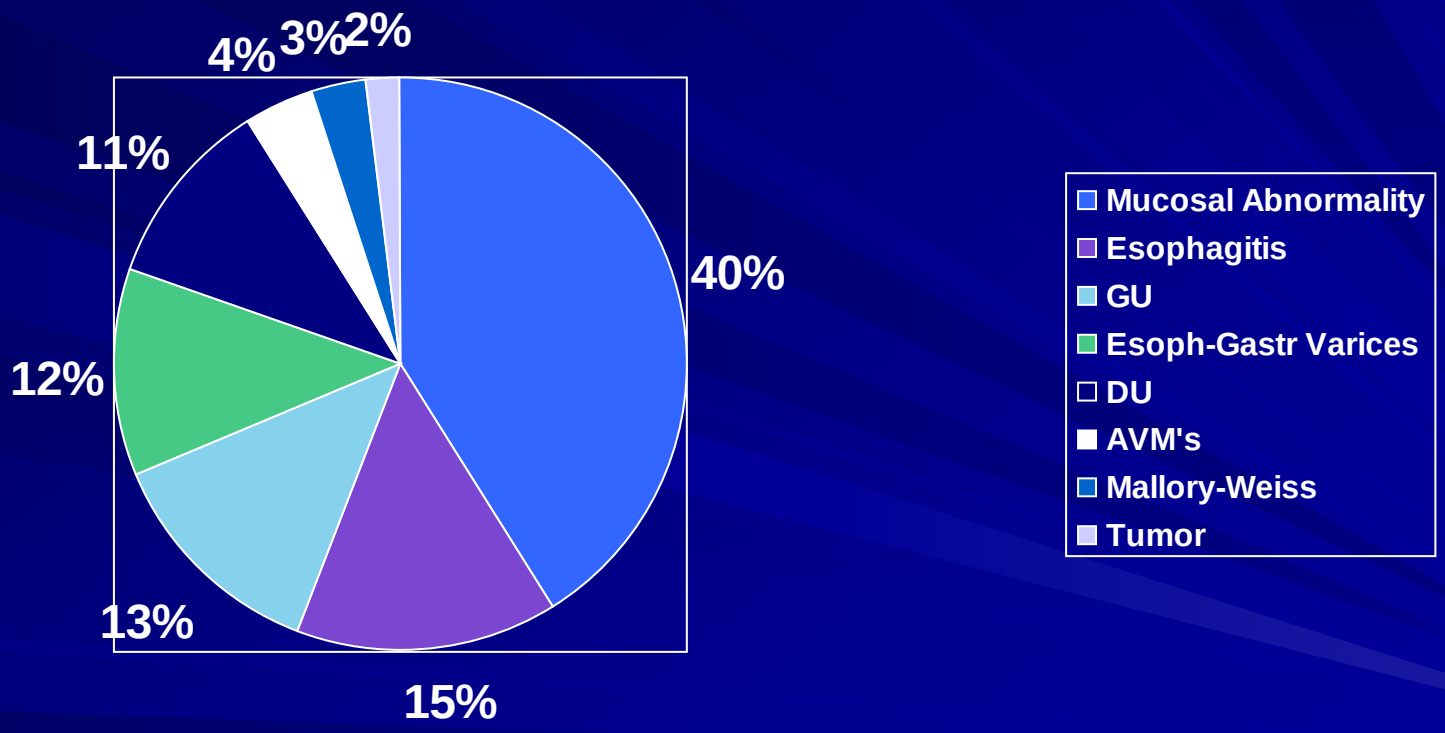
- Hematemesis (above ligament of Treitz)
- Coffee ground emesis (above lig. Treitz)
- Melena: may be upper or lower source
  - > 200 mL blood in stomach, or
  - Up to 150 mL blood in cecum)
- Hematochezia: - usually lower source;
  - 11% from upper source.
  - > 1000 mL upper bleed
    - (orthostatic @ 3 min: BPs drop =/> 10 mmHg and/or HR increase > 20 bpm).
  - > 150 mL blood in Right colon, or
  - > 100 mL blood in Lefyt 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
  - Sytolic drop =/> 10 mmHg, or
  - HR rise > 20/min

AIMS 65 Score

ER Prediction of Mortality, LOS, & Cost

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

FACTOR	1 point for each	Alternative Description
Albumin	< 3 g/dL	
INR	> 1.5	
Mental status	Glasgow score < 14	disorientation, lethargy, stupor, or coma
Systolic Pressure	</= 90 mm Hg	
Age	> ***65***	

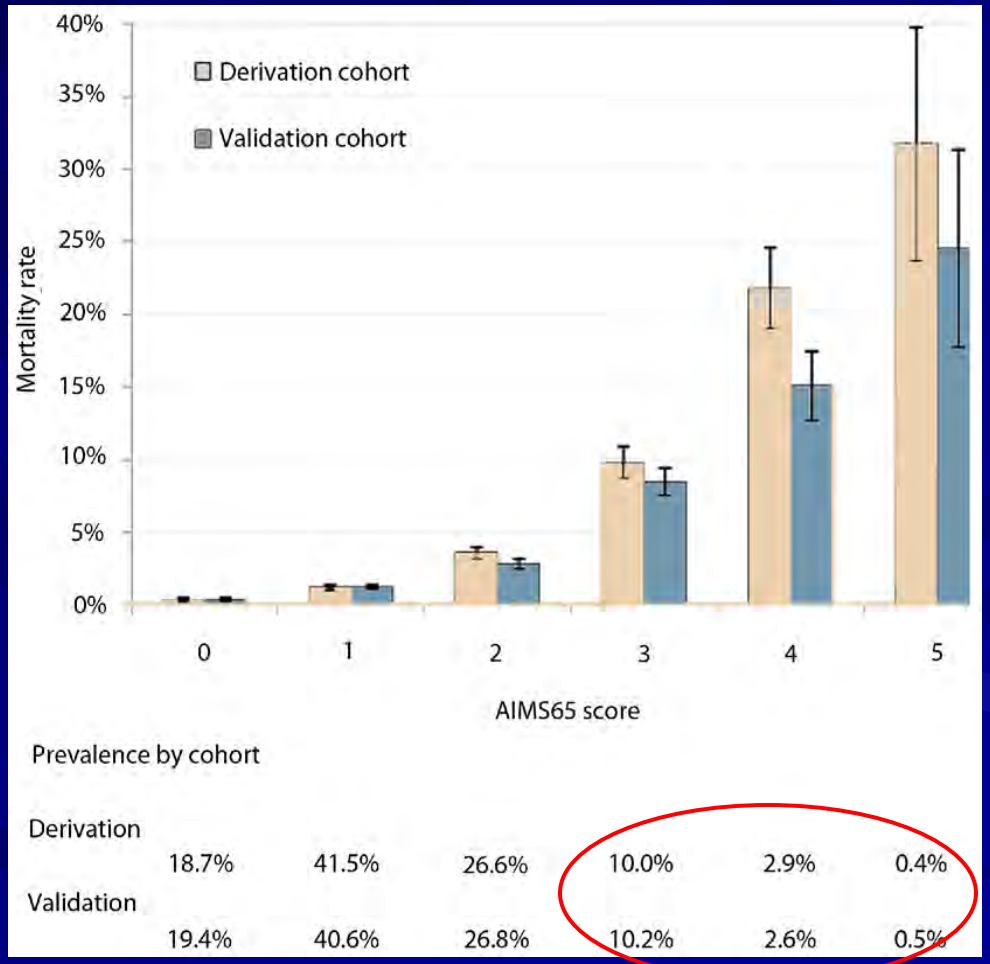
All factors are the ones present at time of arrival to ER

Mortality/LOS: 2 pts = 3%/5.5 d; 3 pts = 10%/6.5 d; 4 pts = 15%/7.5 d; 5 pts = 24%/9 d

13.5% of patients have score =/> 3, with mortality of 10% or higher

Mortality by AIMS-65 Score

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



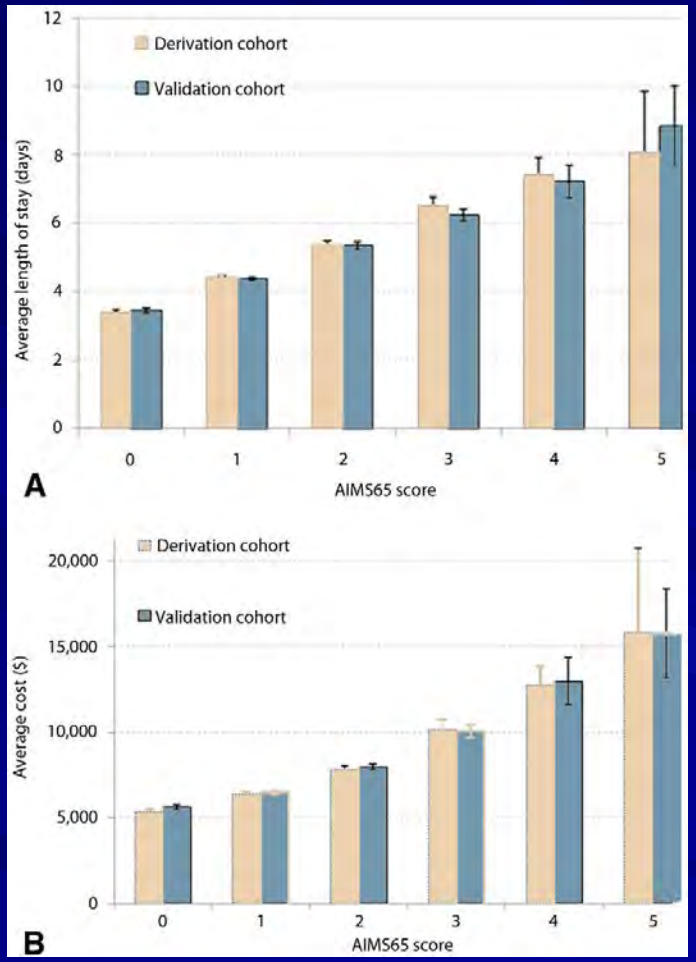
Prevalence by cohort

Derivation	18.7%	41.5%	26.6%	10.0%	2.9%	0.4%
Validation	19.4%	40.6%	26.8%	10.2%	2.6%	0.5%

13.5% with High Mortality

LOS & Cost by AIMS-65 Score

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



L.O.S

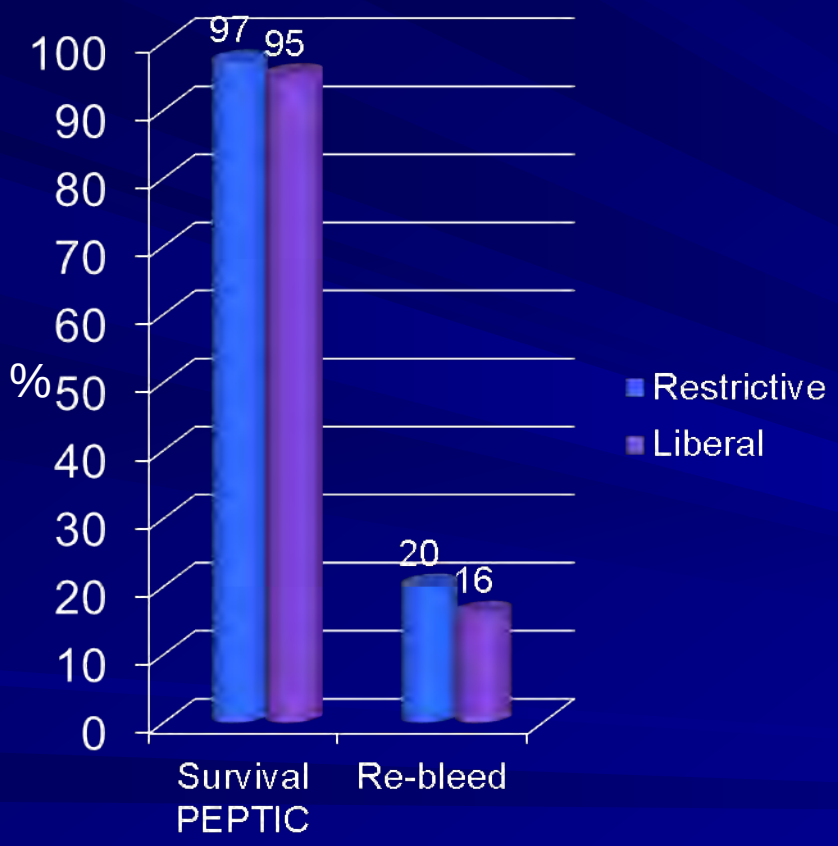
COST

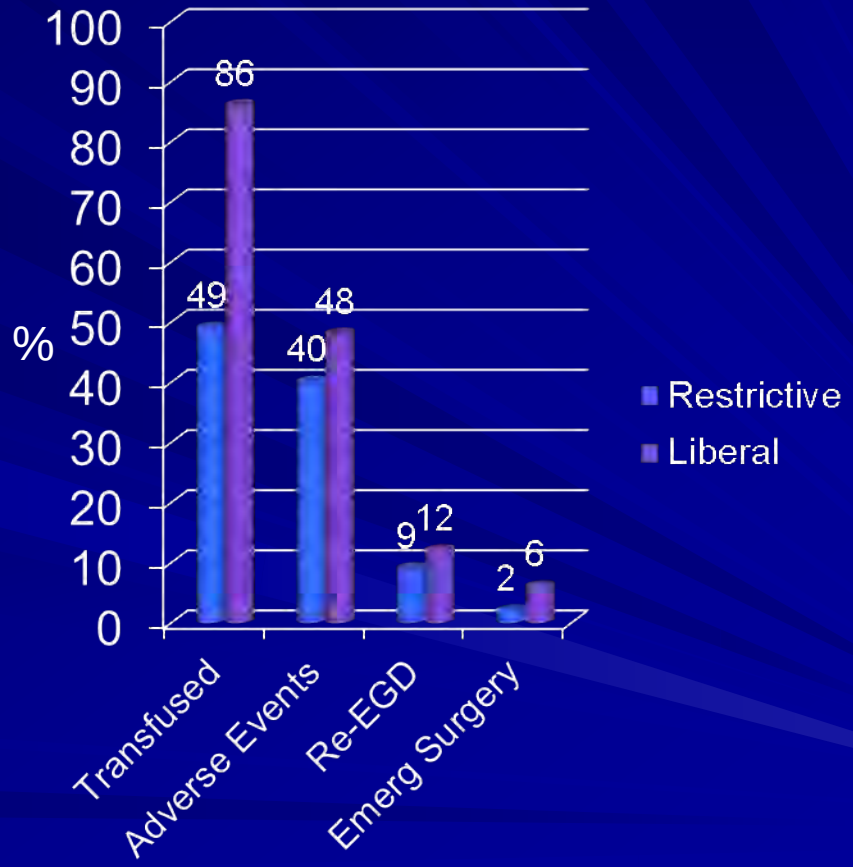
Initial Management

- 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 < 9 g/dL in:
    - Acute coronary syndrome,
    - Exsanguination: Hypotension/tachycardia that indicates intravascular depletion with artificially high Hb.
- Surgery consult
- If cirrhosis is known or suspected:
  - Antibiotics: **Ceftriaxone** or Norfloxacine x 7 days.
  - **Octreotide** (or Somatostatine) drip

Non-Variceal UGI Bleed
Restrictive vs Liberal Transfusion in GI Bleed

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





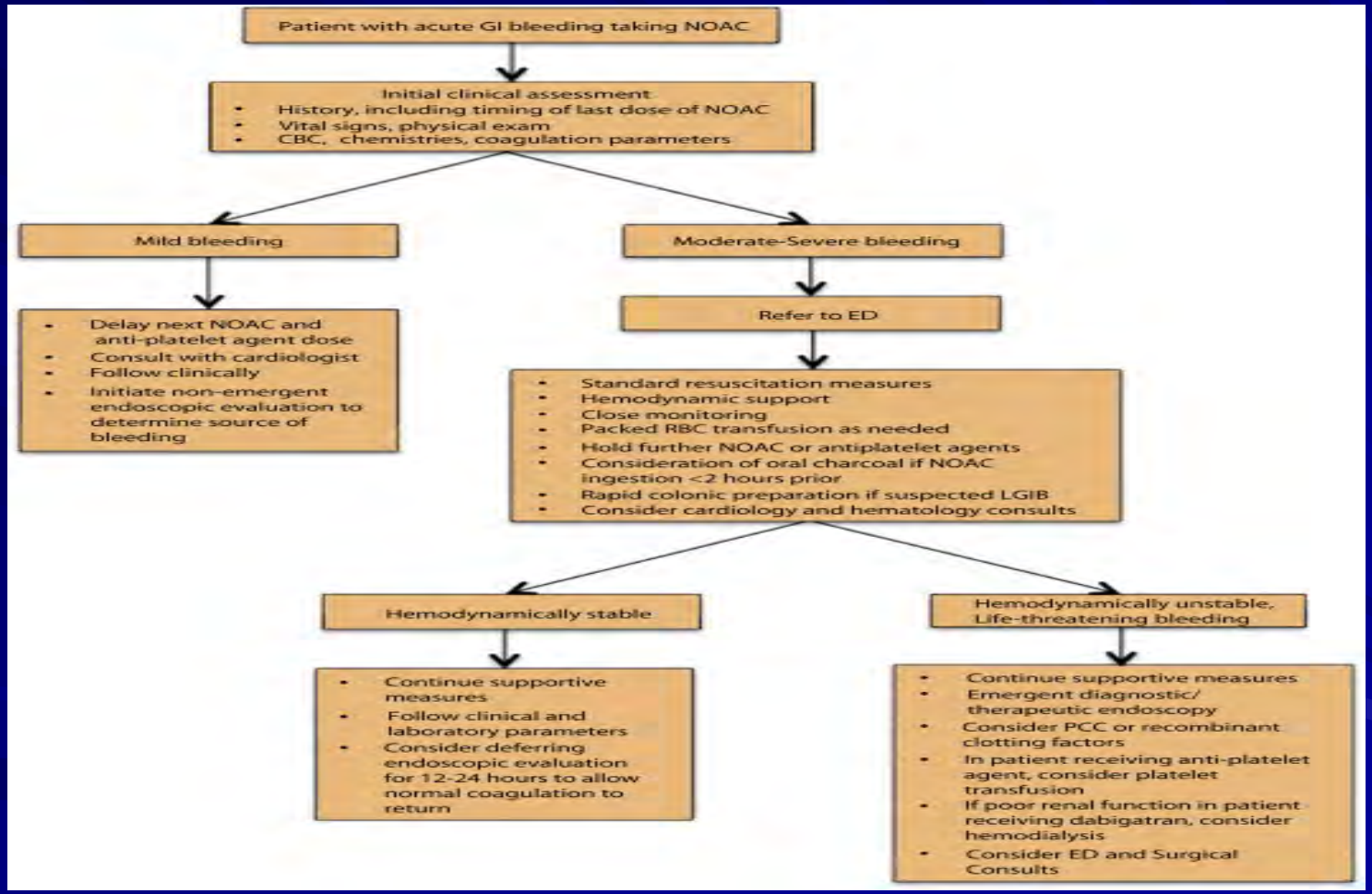
Excluded: Exsanguinating bleed, Acute coronary syndrome, TIA, Stroke and Symptomatic peripheral vascular disease

Initial Management & Preparation for Urgent Endoscopy

- Asses Risk/ Benefit or correcting therapeutic anti-coagulation or anti-platelet therapy.
  - Correct coagulopathy (FFP 15 mL/kg, or Vit K 1-2 mg IV slowly)
  - Correct thrombocytopenia if platelets < 50K or antiplatelet agent. (Platelets: 1 single donor unit, or 1 random pooled unit/ 10 kg)
- Erythromycin 250 mg IV, 30-120 minutes before EGD
  - clears stomach 82% vs. 33% with placebo.
- 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.

Suggested algorithm for GI bleeding management in the patient receiving novel oral anticoagulant therapy

Desai J et al. Gastrointestinal Endoscopy, 2013-08-01, Volume 78, Issue 2, Pages 227-239



NOAC, novel oral anticoagulant; *CBC,* complete blood count; *ED,* emergency department; *LGIB,* lower GI bleeding; *PCC,* prothrombin complex concentrate

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 Rebleeding Risk

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

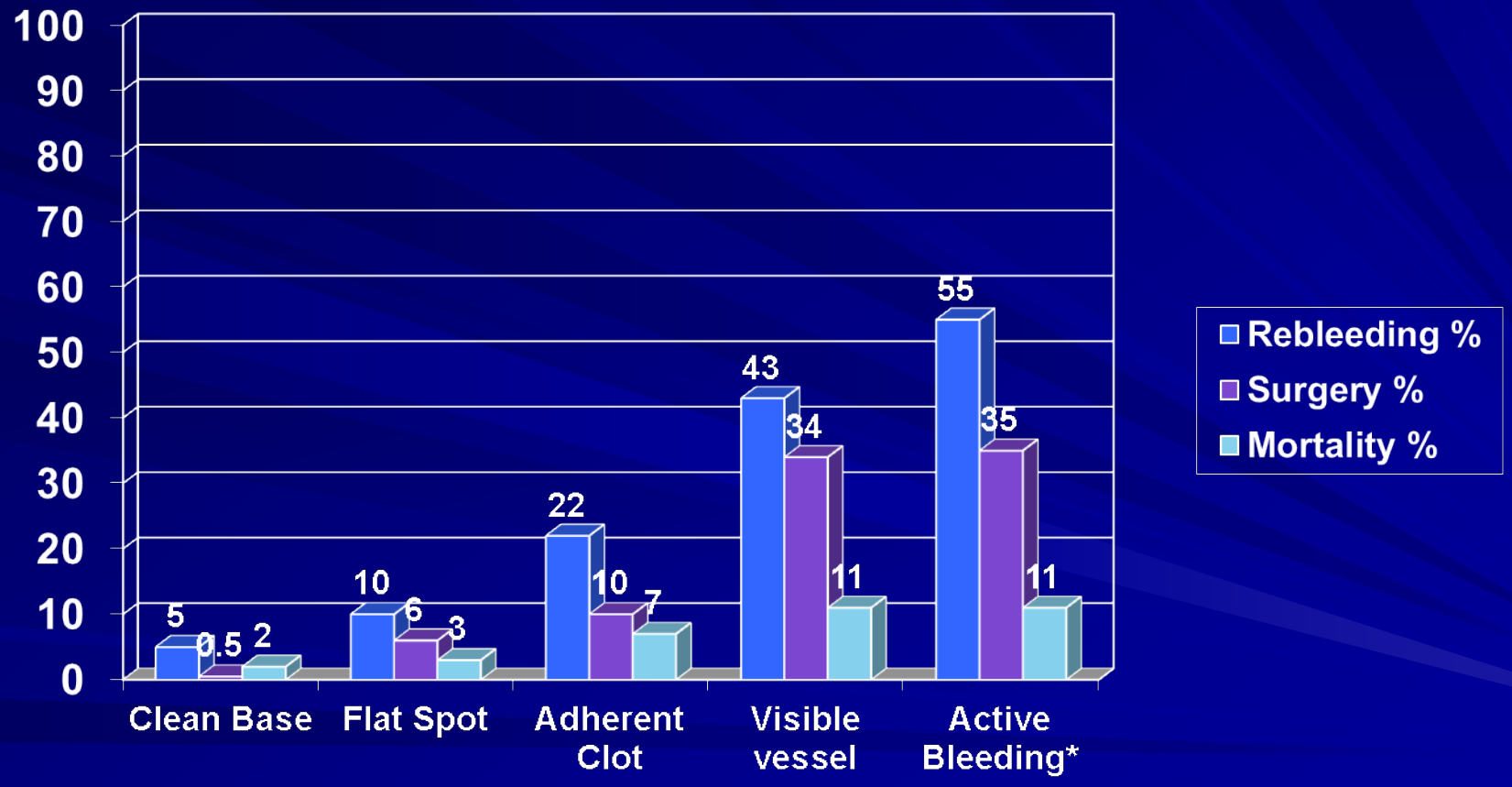
UGI Bleed Score – Rockall 1996

Rebleeding & Mortality Risk

*	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	Clean base Flat spot	Visible vessel Adherent clot Spurting vessel		

*Risk of rebleeding and mortality increases with score: Low (0-2), Intermediate (3-4), High (5-10)

Prognosis by Endoscopic Stigmata of Recent Hemorrhage



*Oozing, without adherent clot nor visible vessel, has low risk of re-bleeding after endoscopic therapy, and its re-bleeding rate is not affected by high-dose IV PPI. OK to give PO PPI.

Early Disposition Tools

- **Glasgow-Blatchford score**
  - score of 0 predicts low risk of rebleeding; 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 rebleed;
    - consider early discharge from ED.
  - http://www.gastrotraining.com/calculators/rockall-score

Who can be D/C home from the ED?
(Blatchford Score of 0)

- Frequency: 5-20% of UGI bleeders.
- Risk of needing intervention: < 1%
- CRITERIA:
  - Males with Hb >/= 13 g/dL, or Females with Hb >/= 12 g/dL, AND
  - BUN < 18.2 mg/dL, AND
  - Systolic BP >/= 110 mm Hg, AND
  - Pulse < 100 bpm, AND
  - Absence of: Melena, syncope, heart failure, and liver disease.
- Disposition: Discharge home from ED

Classification of Bleeding Ulcers

- **Acute hemorrhage**
  - Forrest I a (Spurting hemorrhage)
  - Forrest I b (Oozing hemorrhage)
- **Signs of recent hemorrhage**
  - Forrest II a (Visible vessel)
  - Forrest II b (Adherent clot)
  - Forrest II c (Hematin on ulcer base)
- **Lesions without active nor recent bleeding**
  - Forrest III (Lesions without signs of recent hemorrhage; clean base)[1]

Management of Adherent Clot

- Retrospective study of [clot removal + endoscopy therapy] vs [medical therapy] (Gastrointest Endosc 2003;58:707-14)
  - Decrease in rebleeding rate (27.4% vs 8.7%)
  - Less transfusion needs, LOS, need for re-EGD
- Prospective RCT [epi inject + clot removal + BICAP when indicated] vs [medical therapy] (Gastroenterol 2002;123:407-13) :
  - Decrease in rebleeding rate (35.3% vs 0%)
- **Meta-analysis (Gastroenterol 2005;129:855-62)**
  - **Decrease in rebleeding rate from 24.7% to 8.2%**

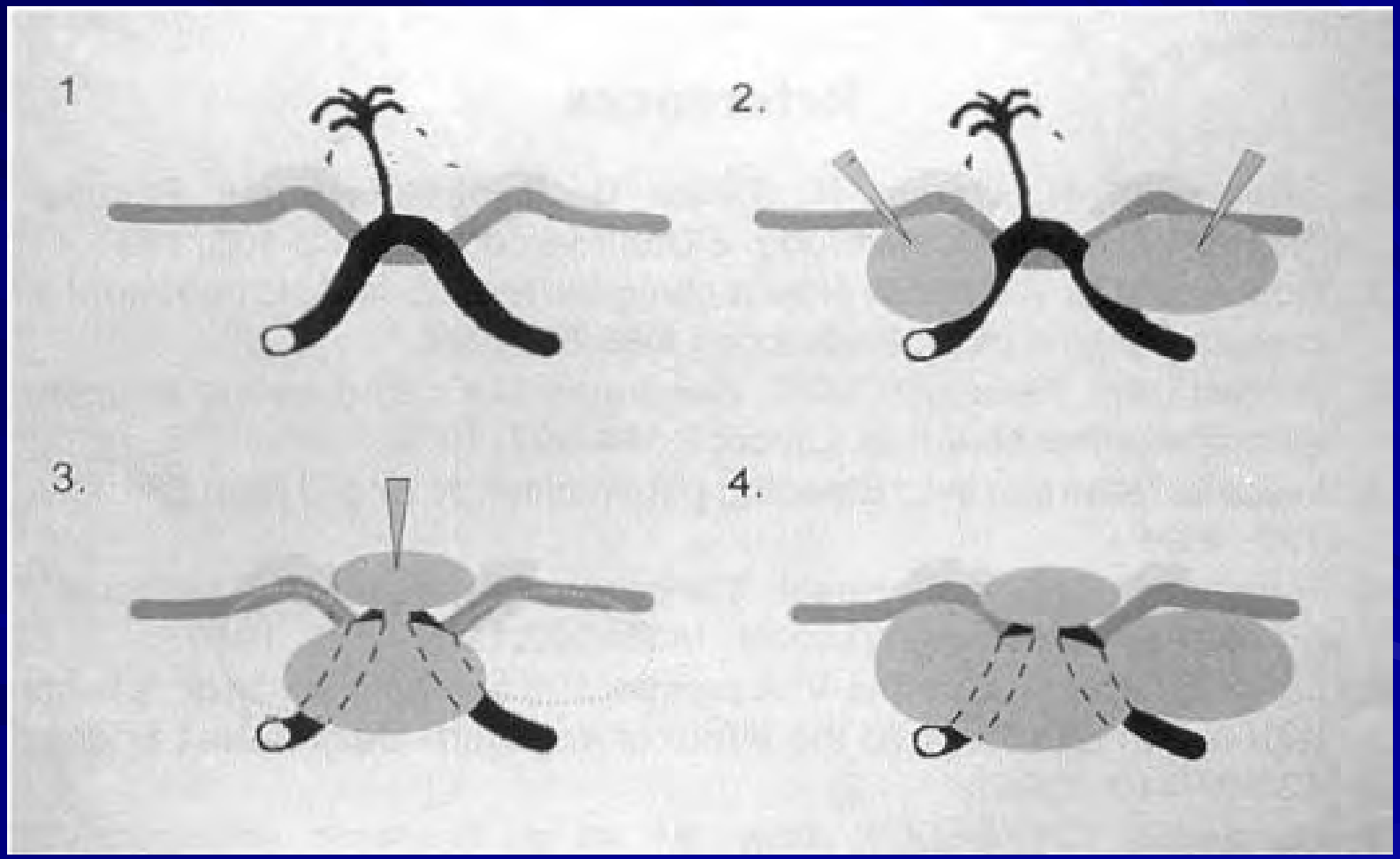
Non-Variceal Upper GI Bleed
Initial Treatment & Hemostasis

- 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 & Rebleeding Rate

- Rebleeding rate: 15-20 % for visible vessel or active bleed (other than oozing without adherent clot nor visible vessel).
- Techniques equivalent in Rebleeding Rate:
  - Hemoclipping
  - 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 rebleeding rate.**

Injection Technique



Indications for Combination Therapy
Injection + Heater Probe or BICAP

- In patients with ulcer actively bleeding or with visible vessel (Lin HJ et al. Gut 1999;44:715-9)
  - Decreases rebleeding & transfusion needs
  - No change in emergency surgery or mortality
- Mainly beneficial for patients with ***arterial spurting*** (Chung S et al. BMJ 1997;314:1307-11)
  - Shortens length of stay (4 d vs. 6 d)
  - Decreases emergency surgery (6.5 vs 29.6%)

TTS Hemoclips

	QuickClip2 **Olympus**	**QuickClipPro** **Olympus**	**Resolution** **Boston Scientific**	**Instinct** **Cook Medical**
Jaw span (mm)	7-11	11	11	16
Rotation	Yes	Yes	Limited (sheath off)	yes
Reopens	No	Yes	Yes	Yes
Retention length	2 weeks	Not stated	4 weeks	Not stated

Endoscopic Band Ligation

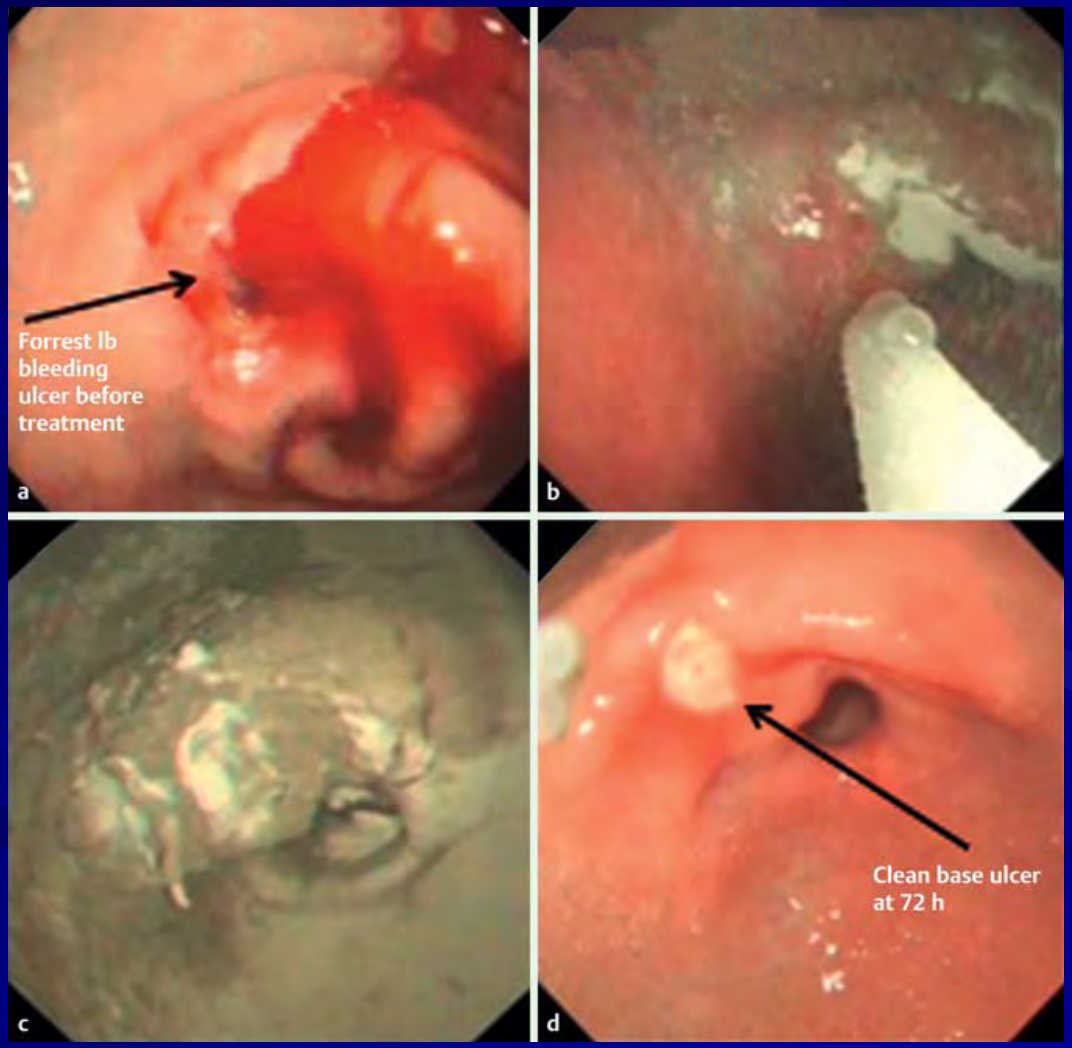
- Extremely effective in esophageal varices; has less complications than sclerotherapy.
- Other uses:
  - Dieulafoy's lesions
  - Mallory-Weiss tears
  - Gastric angiodysplasia
  - Gastric post-polypectomy ulcer bleed
  - Colonic diverticular bleed (inversion + band)

Hemospray

Endoscopy 2011;43:291-295

- Hemospray catheter gun: 21 g powder syringe + CO_2 propeller canister
  - Fire from 1-2 cm distance
  - Observe 5 min; re-spray if needed.
  - Maximun 150 g (7 canisters)
- Patients (20): Forrest 1a (1) (spurting) + Forrest 1b (19) (oozing)
  - mean age 60 (37-85);
  - melena 20, hematemesis 7;
  - GU in 6, DU in 14
- Hemospray
  - applications: 1 in 5%; 2 in 15%;
  - syringes: 1 in 65%, 2 in 25%, > 2 in 10%
- Hemostasis:
  - At 24h = 95%; (Initial failure in Forrest 1a)
  - At 72h = 85%;

Hemospray Effect



Predictors of High-Risk of Re-bleeding After Endoscopic Hemostasis

Predictive Factor	% Re-bleeding Risk
Posterior-wall Duodenal ulcer	43-57
Hemodynamic Instability *	19-47
Active Bleeding	12-49
Lesser-curve Gastric Ulcer	23-35
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

- PPI, high-dose continuous intravenous infusion 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 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 rebleeding rate with “selective intestinal decontamination” with:
  - Ceftriaxone 1 gm/d x 7 days, or
  - Norfloxacin 400mg p.o. BID x 7 days

Medical Therapy

- In idiopathic PUD (non-H. pylori, non-NSAID),
  - give long term PPI or H_2 blocker.
- In cirrhosis,
  - 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%.

H. Pylori Therapy

- **First line:**
  - Esomeprazole 40 BID + Amoxi 1g BID + Levoflox 500 BID + Tinidazole 500 BID x 5 d + Lactobacillus GG x 13 d (during + 7 days after antibiotics)
  - PPI QD + Tetra 500 QID + Pepto 2 QID + Metro 500 QID x 14d + Lactob GG
  - [PPI BID + Amoxi 1g BID x 5d], then [PPI BID + Clari 500 BID + Tinidazole 500 BID x 5d] + Lactobacillus GG
  - PPI BID + Clari 500 BID + Amoxi 1g BID x 10-14d + Lactobacillus GG (?)
  - PPI BID + Clari 500 BID + Metro 500 BID x 10-14d + Lactobacillus GG (?)
- **Salvage Therapy:**
  - PPI QD + Tetra 500 QID + Pepto 2 QID + Metro 500 QID x 14d
  - PPI BID + Amoxi 1 g BID + Levoflox 500 QD x 10-14d
  - PPI BID + Levo 500 QD + Nitazoxanide 500 BID+ Doxycycline 100 mg QD x 10d

H. Pylori Therapy

- Patients who have received Macrolides should not use Clarithromycin regimen.
- If exposed to Metronidazole in past, give 500 mg (no 250 mg).
- Lactobacillus GG or Bifidobacteria **during therapy and for 1 week after therapy** improves tolerability and response to therapy.
- Post therapy testing:
  - Monoclonal Fecal Ag > 4 wk after, or UBT 4 wk after.

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 endoscopies therapies.
- Hemodynamic instability despite vigorous resuscitation and 3 units of PRBC.
- Continuous slow bleed of > 3 units PRBC/day.

Variceal Bleed

VARICEAL HEMORRHAGE

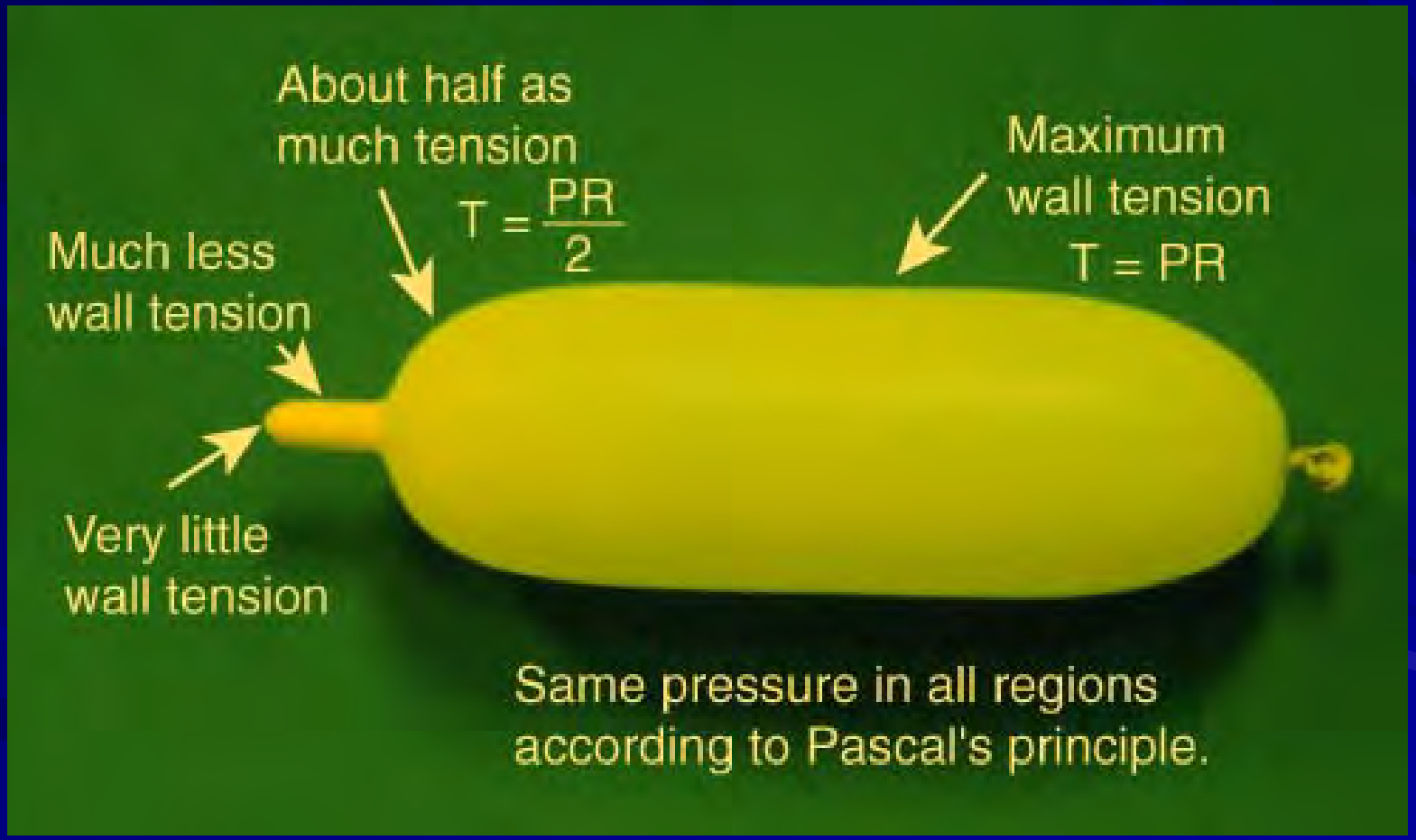
- **Gastro-esophageal varices = 50% cirrhotics**
  - **Child A = 40%**
  - **Child C = 85%**
- **Varices form at rate of 5-15%/year; in 30%** (25-40%) **they will bleed at some time; mean bleed 2.9 units.**
- **Bleeding only if Portal Pressure >12mm Hg;**
  - **“clinically significant portal HTN” is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

Morphologic Classification of Esophageal Varices

- Grade F0: no EV detected;
- Grade F1: small (</= 5 mm) straight EV;
- Grade F2: slightly enlarged 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

Determinants of Variceal Bleeding

Laplace's Law



Primary Prophylaxis

Primary Prophylaxis for Esophageal Variceal Hemorrhage

- Annual rate of first hemorrhage: 12%
  - Mortality per episode 15-20%
- Recommended Therapies:
  - Prophylaxis with non-selective beta blocker (nadolol or propranolol) without nitrates or
  - Endoscopic Variceal Ligation (EVL) reduces risk of first variceal hemorrhage.
  - Weight loss in obese patients
- Use of Beta-Blockers
  - Decreases 1st bleed rate (12 vs 23% with placebo) and death rate from bleeding; trend to improved survival.
  - NNT to prevent one bleed = 11
  - Reduces progression from small to large varices.
  - Titrate to resting pulse of 55-60 bpm, or
  - Titrate to HVPG < 12 mmHg or 20% drop (>/= 10% drop with IV propranolol)
  - Caution in refractory ascites and low MAP < 84 mmHg; Also in SBP?

One-year Risk of Bleeding (%) of Esophageal Varices

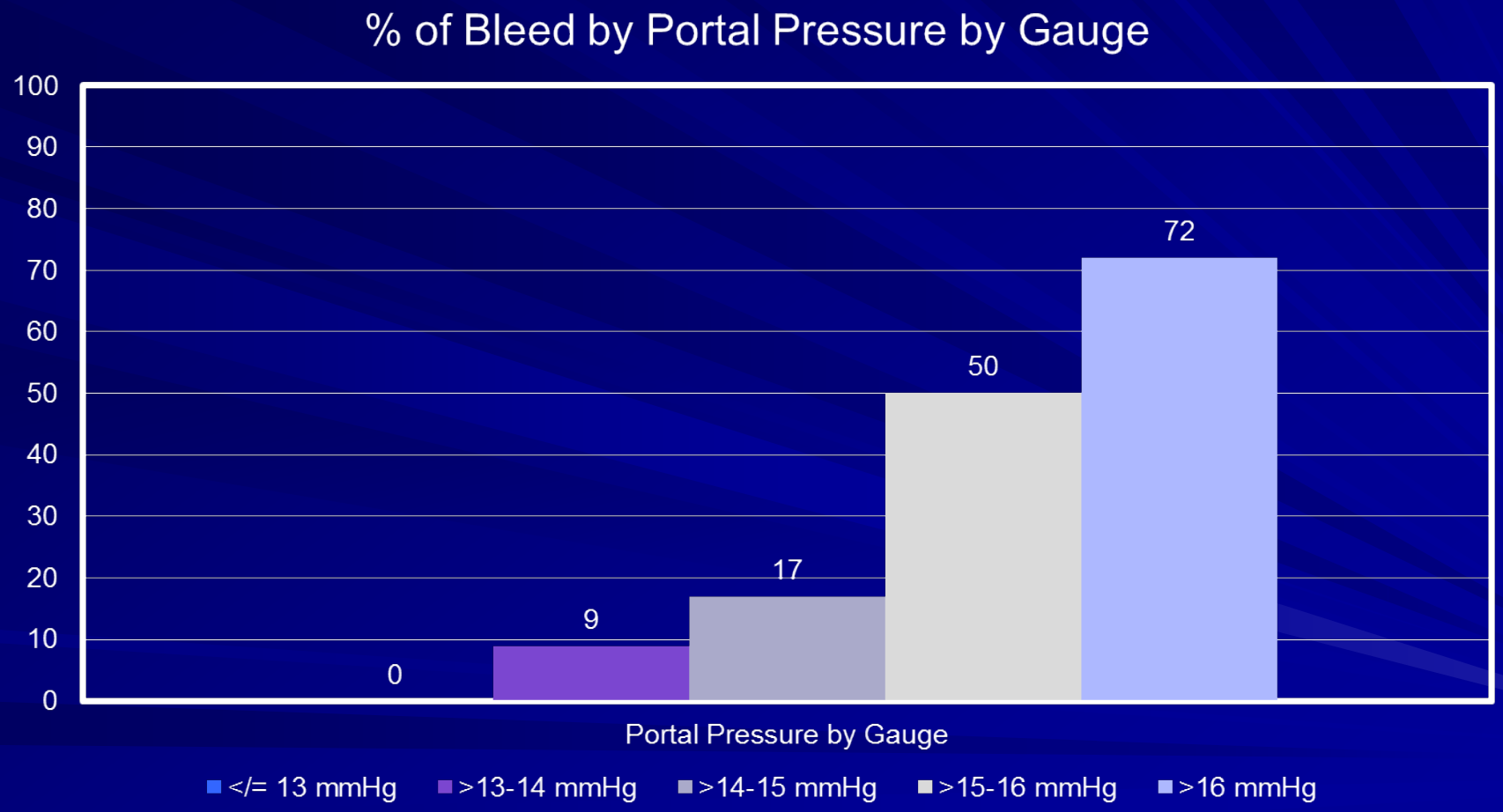
Red wale markings and Child-Pugh Score

de Franchis R et al. N Engl J Med 1988;319:983

Red Wale Markings	Child-Pugh A			Child-Pugh B			Child-Pugh C		
	F1	F2	F3	F1	F2	F3	F1	F2	F3
-	6	10	15	10	16	26	20	30	42
+	8	12	19	15	23	33	28	38	54
++	12	16	24	20	30	42	36	48	64
+++	16	23	34	28	40	52	44	60	76

Incidence of Variceal Bleeding According to Variceal Pressure (by gauge)

Nevens F et al. Hepatology 1998; 27:15



Primary Prophylaxis for Esophageal Variceal Hemorrhage
Controversial & Not-Indicated Therapies

- Carvedilol is non-selective beta-blocker with mild anti-alpha-1 effect hence also decreases hepatic vascular resistance (now supported in Baveno VI).
  - More potent than propranolol but also drops MAP more.
  - More effective than EVL in preventing first bleed.
  - Dose: * Child A: 12.5 mg BID; * Child B or C: 6.25 BID
- Addition of Nitrates to beta-blocker:
  - NNT 10 to prevent one additional hemorrhage over Beta Blocker.
  - No clear survival benefit but had a trend (Merkel C et al. Lancet 1996;348:1677)
- Simvastatin (Zocor): increase hepatic nitric oxide; decrease HVPG by up to 8% (Abraldes JG et al. Gastroenterol 2009;136:1651)
  - 20 mg/day x 2 weeks, then 40 mg/day
- **NOT INDICATED:**
  - Variceal Sclerotherapy: not effective
  - Surgical Shunt: higher mortality and PSE.
  - TIPS: Lack of Evidence.
  - Cyanoacrylate injection in gastric varices: effective but high complication risk (Mishra SR et al. J Hepatol 2011;54:1161)

Algorithm for Primary Prophylaxis
(Baveno VI)

FINDING	RESPONSE
Diagnosis of Cirrhosis	EGD to R/O Varices
No Varices	-Compensated cirrhosis + no injury: re-scope in 3 years -Compensated cirrhosis + injury: re-scope in 2 years -Decompensated cirrhosis: re-scope in 1 year
F1 without red wale and Child-Pugh A	-Compensated cirrhosis + no injury: re-scope in 2 years -Compensated cirrhosis + 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 with a platelet count > 150,000
(Baveno VI: Repeat both tests yearly)

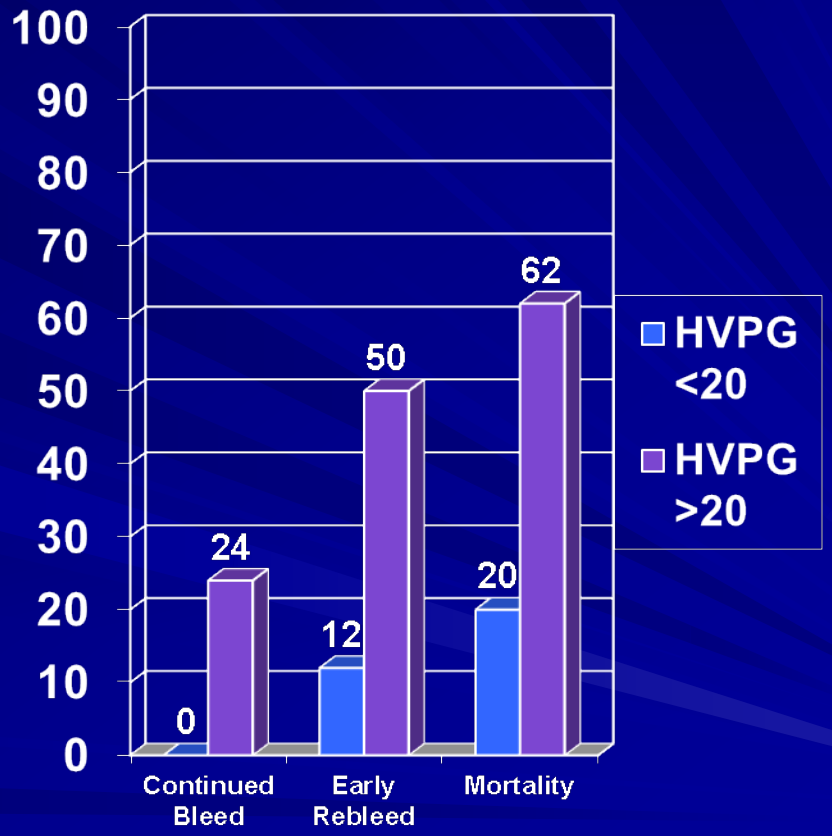
Acute Variceal Hemorrhage

Natural History of Esophageal Variceal Hemorrhage

- **Spontaneous hemostasis**: 50%
  - Re-bleed: bleed after 24 h without bleeding but within initial 48 h.
  - Early re-bleed: within 6 weeks
  - Late re-bleed: after 6 weeks
- **Rebleeding 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, rebleed, advanced disease, infection, HRS)
- **Mortality after 2 week survival**: 52 % at 1 year

Risk Factors
Failure to Control Acute Hemorrhage

- Spurting varix
- Child-Pugh C
- Portal vein thrombosis
- Infection
- HVPG > 20 mm Hg



Gastroenterology 1999;117(3):626-31

Risk Factors

Rebleeding in < 6 weeks

- Age > 60
- Ascites
- Infection
- Renal Failure
- Severe Initial Bleed (Hb < 8 g/dL)
- HVPG > 20 mm Hg
- 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%)

Risk Factors
Rebleeding in > 6 weeks

- Severity of Liver Failure
- Ascites
- Hepatoma
- Red-color signs
- Active Alcohol abuse

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)

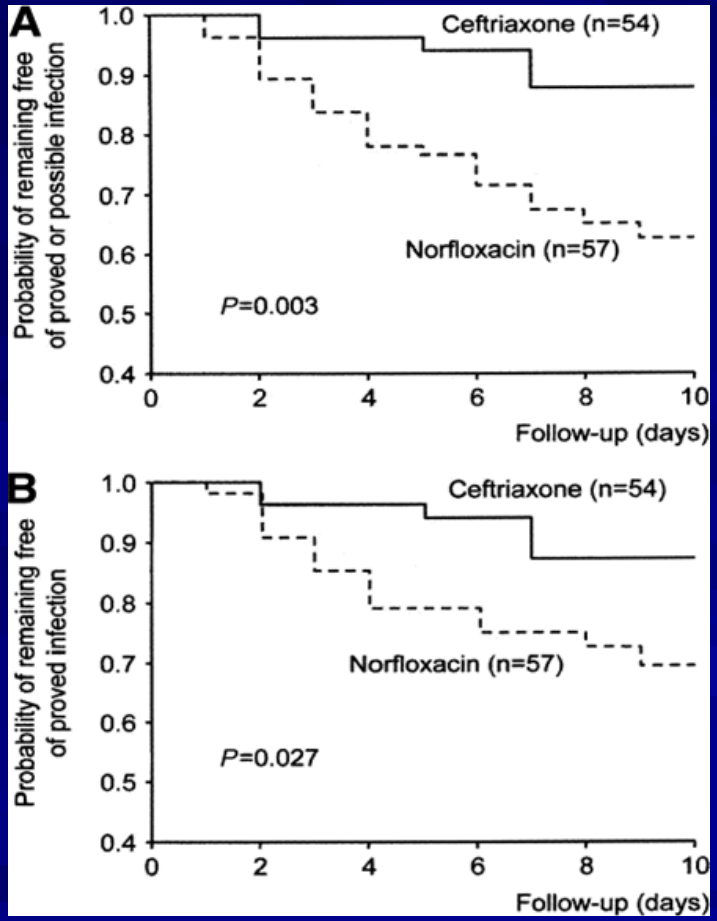
Effect of Antibiotics

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)

Ceftriaxone 1 g/d x 7 d is superior to Norfloxacin 400 BID x 7d in preventing infections in cirrhosis with GI bleed

Fernandez J; Gastroenterology 2006;131:1049–1056



Free of Possible or Proved Infection

Free of Proved Infection

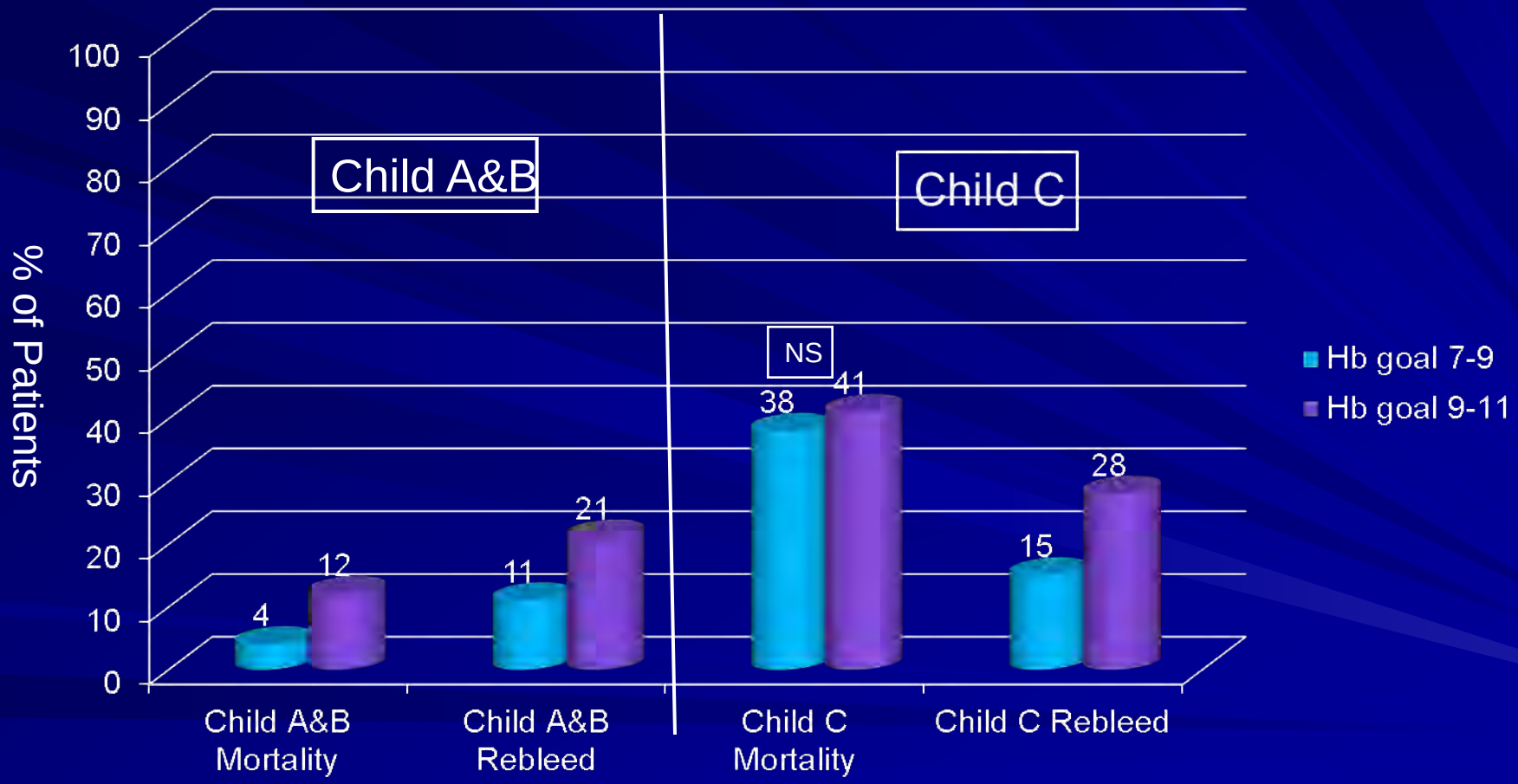
In cirrhosis with GI bleed, Ceftriaxone:

- decreases hospital infections & SBP,
- has no effect in hospital mortality.

Acute GI Bleed in Cirrhosis

Restrictive vs Liberal 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

Acute Variceal Bleed Treatment

GOAL

- *Control Hemorrhage*:
  -Local control
  -Decrease Portal Pressure
- *Prevent Infection*
- *Prevent Rebleeding*
- *Decrease mortality*

INTERVENTIONS

- ***Banding***
- ***Terlipressin x 5 days***
- ***Octreotide x 5 days***
- ***Ceftriaxone 1 gm/d x 7 days.***
- ***Transfuse to Hct 24***
- Sclerotherapy (+/-)
- TIPSS (rescue)
- Shunt surgery (+/- ; for rescue)

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

Endoscopic Band Variceal Ligation (EVL)

- Almost all bleeds from esophageal varices are from the distal 5 cm of the esophagus.
- Multiple bands are deployed, starting at E-G junction, to “saturate” the distal 5 cm
- EVL decrease:
  - re-bleeding to 31% (47% with endoscopic sclerotherapy - ES)
  - mortality to 24% (32% with ES).
- Banding is repeated at **2** week intervals, until complete “obliteration”; then every 6-12 months.
  - PPI therapy accelerates healing of “post-banding” ulcers.

Banding (EVL) vs. Sclerotherapy (ES) in Acute Variceal Bleed

- **Hemostasis**: 86%-90% with both.
- **Complications**: **2% in banding vs. sclerotherapy 22%**
- **Effectiveness**:

  (***Relative Risk***: Banding vs. Sclerotherapy)
  - **A) Re-Bleed: 0.52,**
  - **B) Mortality from bleeding: 0.49,**
  - **C) Total Mortality: 0.67**
- **<u>Conclusion</u>: Banding is the endoscopic therapy of choice for esophageal varices.**

Meta-Analysis of EVL vs ES

Laine L et al. Ann Intern Med1995;123:280-287

Esophageal varix Re-Bleed
EVL vs Endoscopic Sclerotherapy

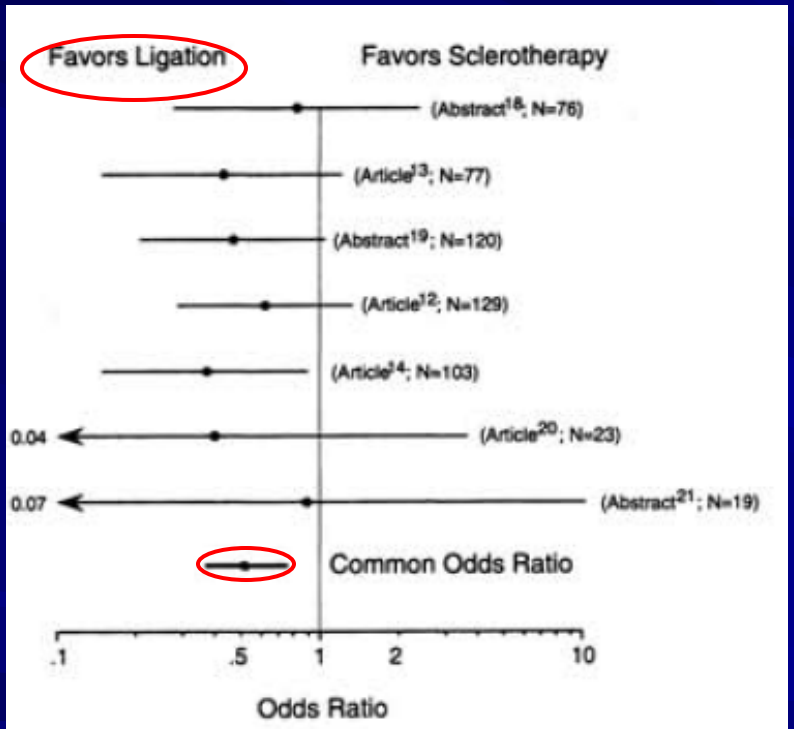


Figure 1. Rebleeding in trials comparing ligation with sclerotherapy in the treatment of esophageal variceal bleeding.

Mortality
EVL vs Endoscopic Sclerotherapy

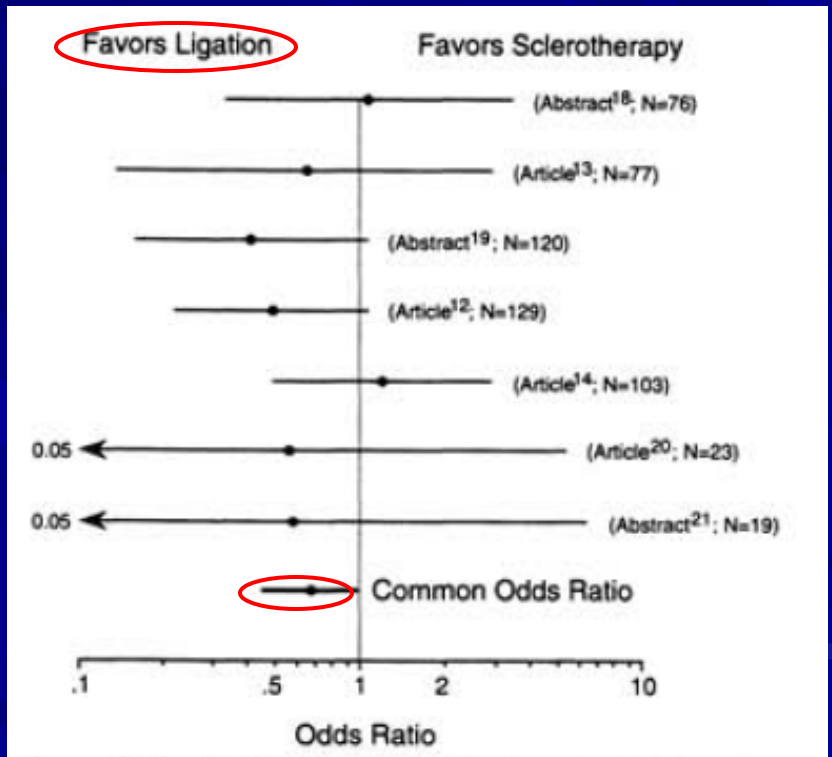


Figure 2. Mortality in trials comparing ligation with sclerotherapy in the treatment of esophageal variceal bleeding.

Complications of ES

Local & Regional

- Ulcer
- Bleeding
- Stricture
- Pain
- Odynophagia
- Esophageal dysmotility
- Laceration
- Perforation
- Mediastinitis
- Pleural Effusion
- Acute gastric dilation

Systemic

- Sepsis
- Aspiration pneumonia
- SBP
- Candidemia
- Ventilation-perfusion mismatch (hypoxia)
- ARDS
- Portal V Thrombosis

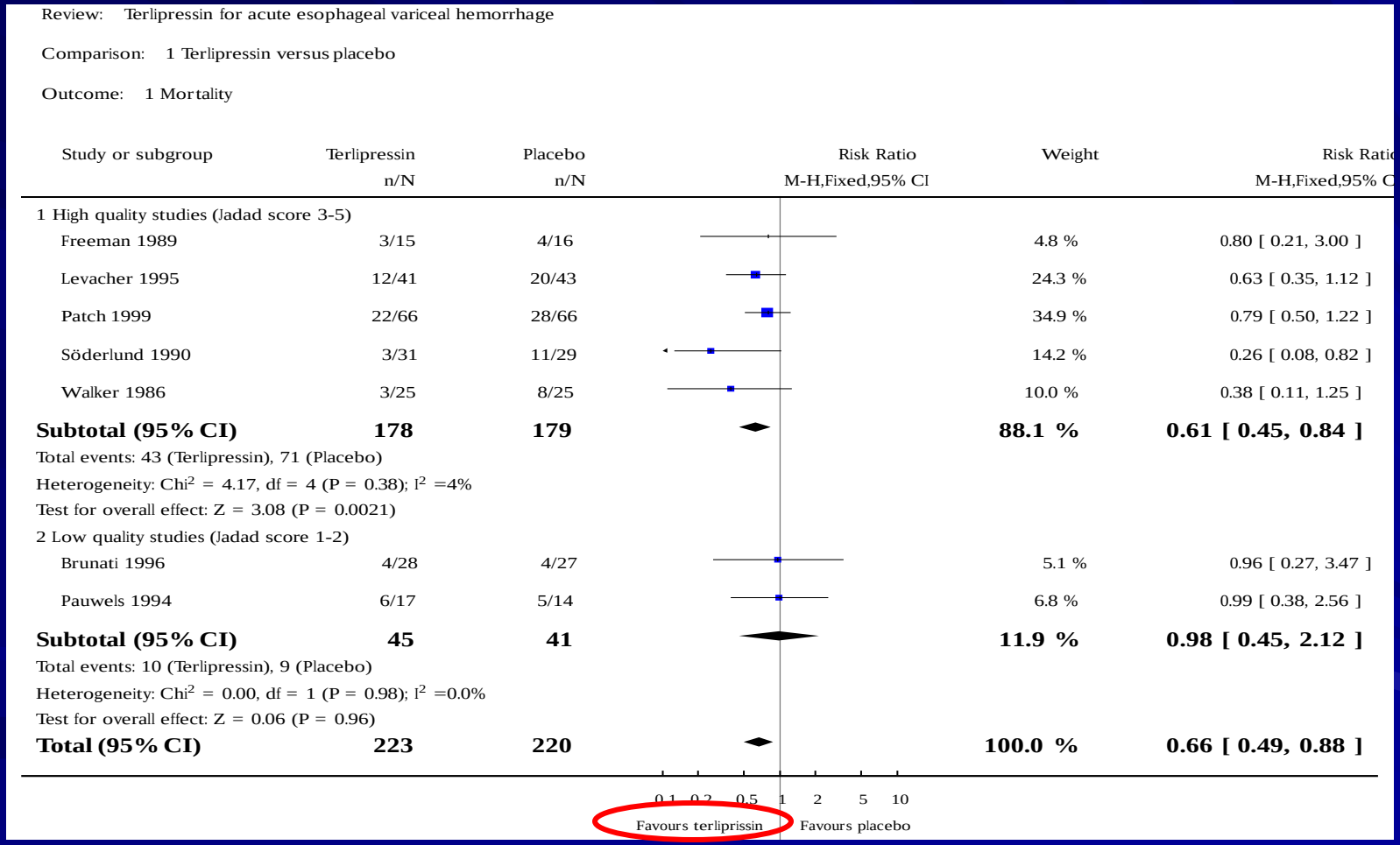
Terlipressin in Variceal Bleeding

- Dose: 2 mg IV q 4 hours; decrease to 1 mg q 4 hours after bleeding has bleed is controlled.
- Duration: 5 days
- Decreases all cause mortality (RR 0.66) (Cochrane Database Syst Rev 2003; CD002147)
- Bleeding control equal to Octreotide or Somatostatin
- Has sustained hemodynamic effect decreasing portal pressure and blood flow (Somatostatin and Octreotide have transitory hemodynamic effect).
- Risk of Hyponatremia: monitor closely.
- When combined with EVL, re-bleeding and mortality was similar to Somatostatin or Octreotide combined with EVL (Seo YS et al. Hepatology 2014;60:954-963)

Terlipressin vs Placebo

Acute Esophageal Variceal Hemorrhage Mortality

Ioannou G et al. Cochrane Database Syst Rev 2003 (CD 002147)



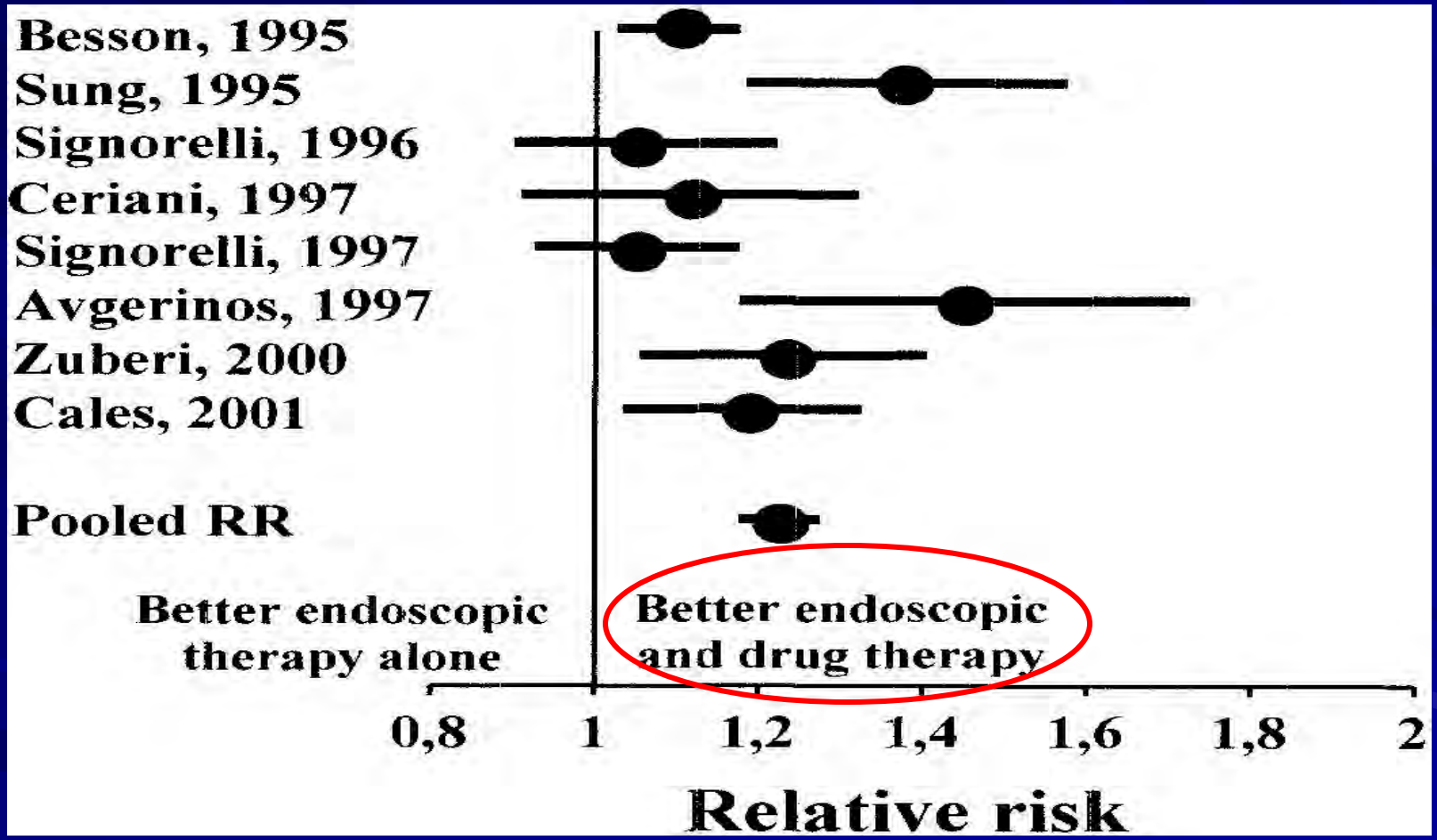
Octreotide or Somatostatin in Variceal Hemorrhage

- ***Octreotide Dose: 50 mcg bolus followed by 50 mcg/h infusion x 5 days.***
- ***Somatostatin dose: 250 mcg bolus + 250 mcg/h infusion x 5 days***
- ***In combination with endoscopic therapy decrease re-bleeding rate and major complications.***
- ***Octreotide and Somatostatin have no survival benefit.***
- ***When endoscopic hemostasis is not available, IV Octreotide or Somatostatin is:***
  - ***safer and more effective than vasopressin, and***
  - ***as effective as endoscopic therapy***

Endoscopy vs Endoscopy + Octreotide/Somatostatin

5-days Hemostasis in Acute Esophageal Variceal Hemorrhage

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

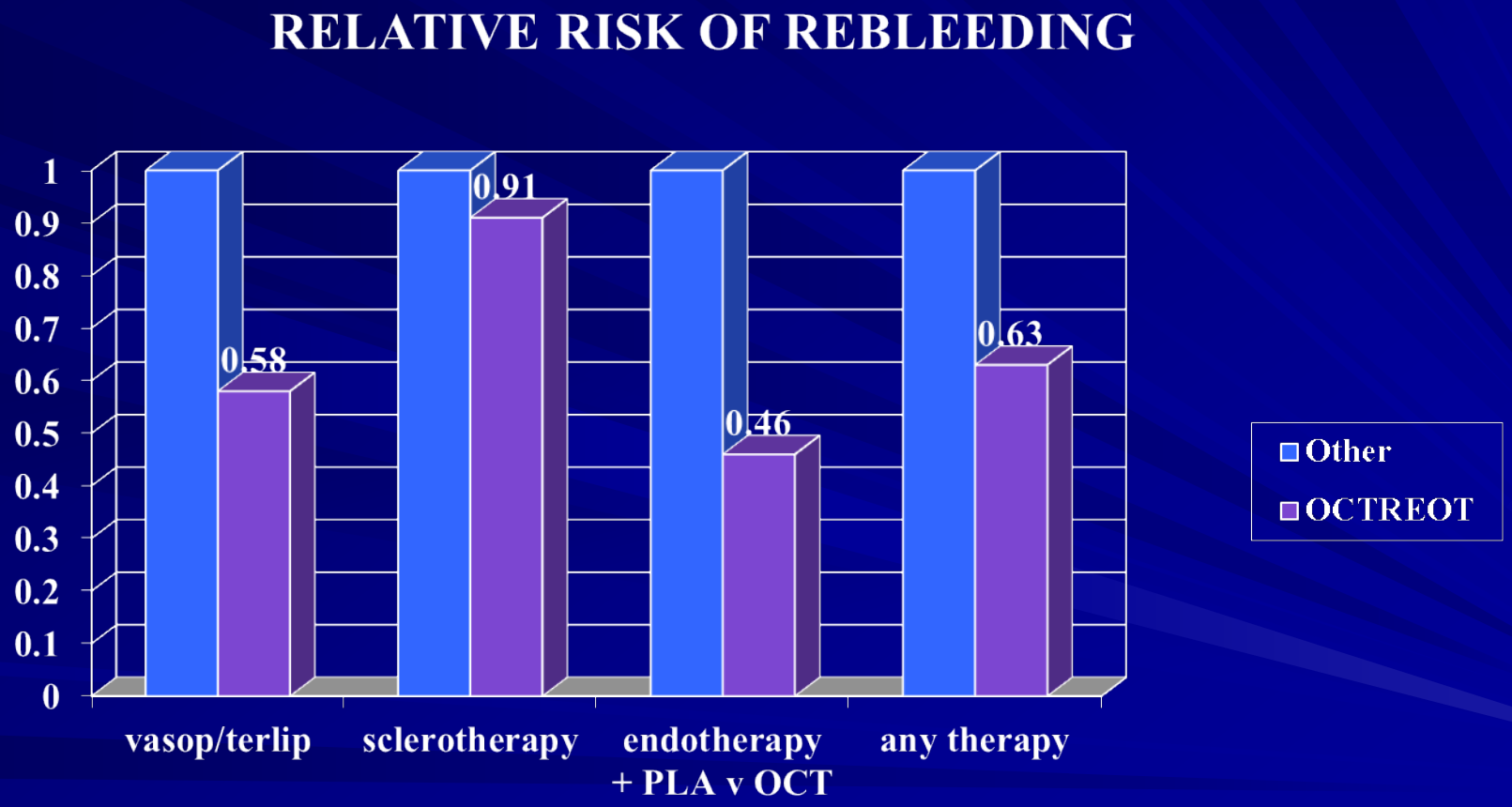


NO EFFECT ON SURVIVAL

Rebleed from Acute Variceal-bleed

Octreotide Meta-Analysis

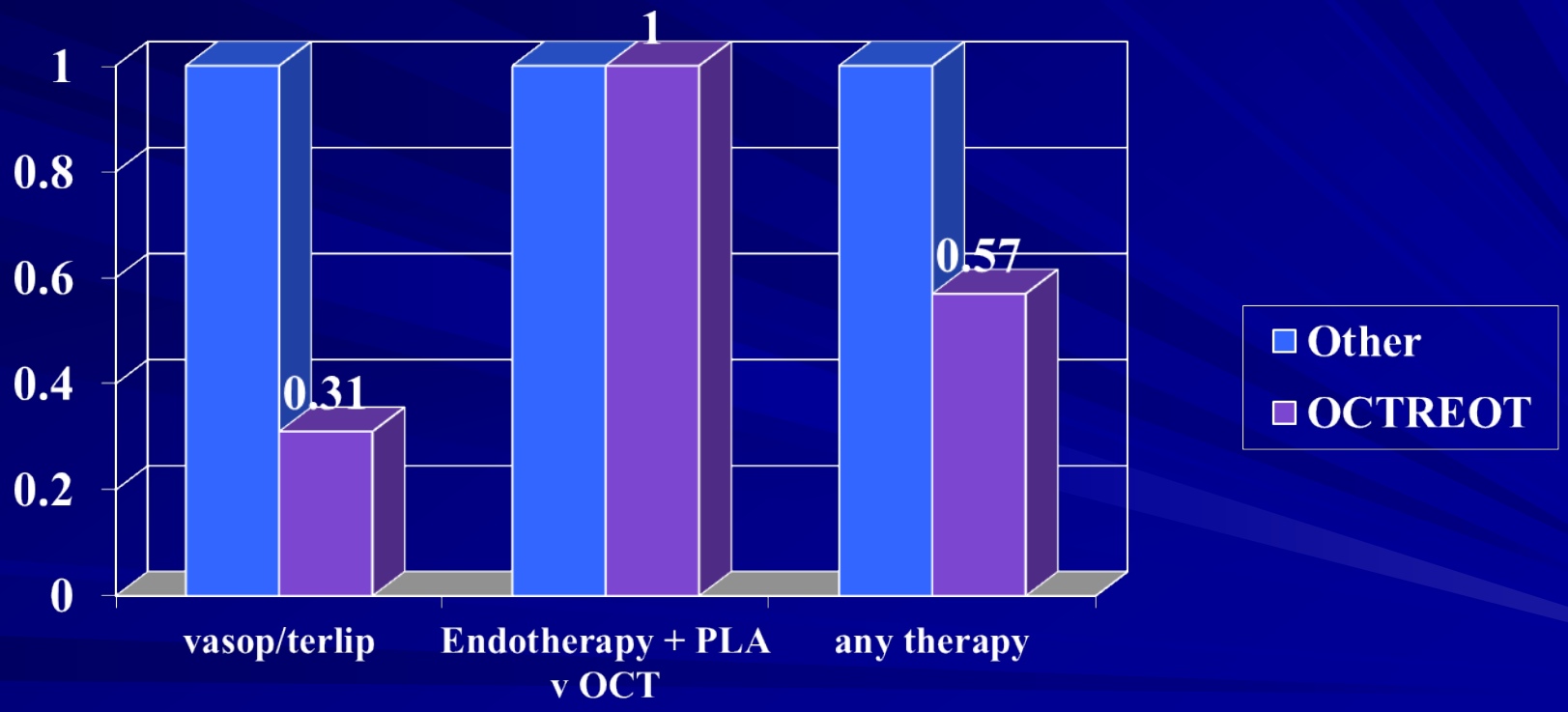
Gastroenterol 2001;120:946-954



Major Complications

Octreotide Meta-Analysis

Gastroenterol 2001;120:946-954



Esophageal Variceal Rebleed
Very Early TIPS vs EBL+BB

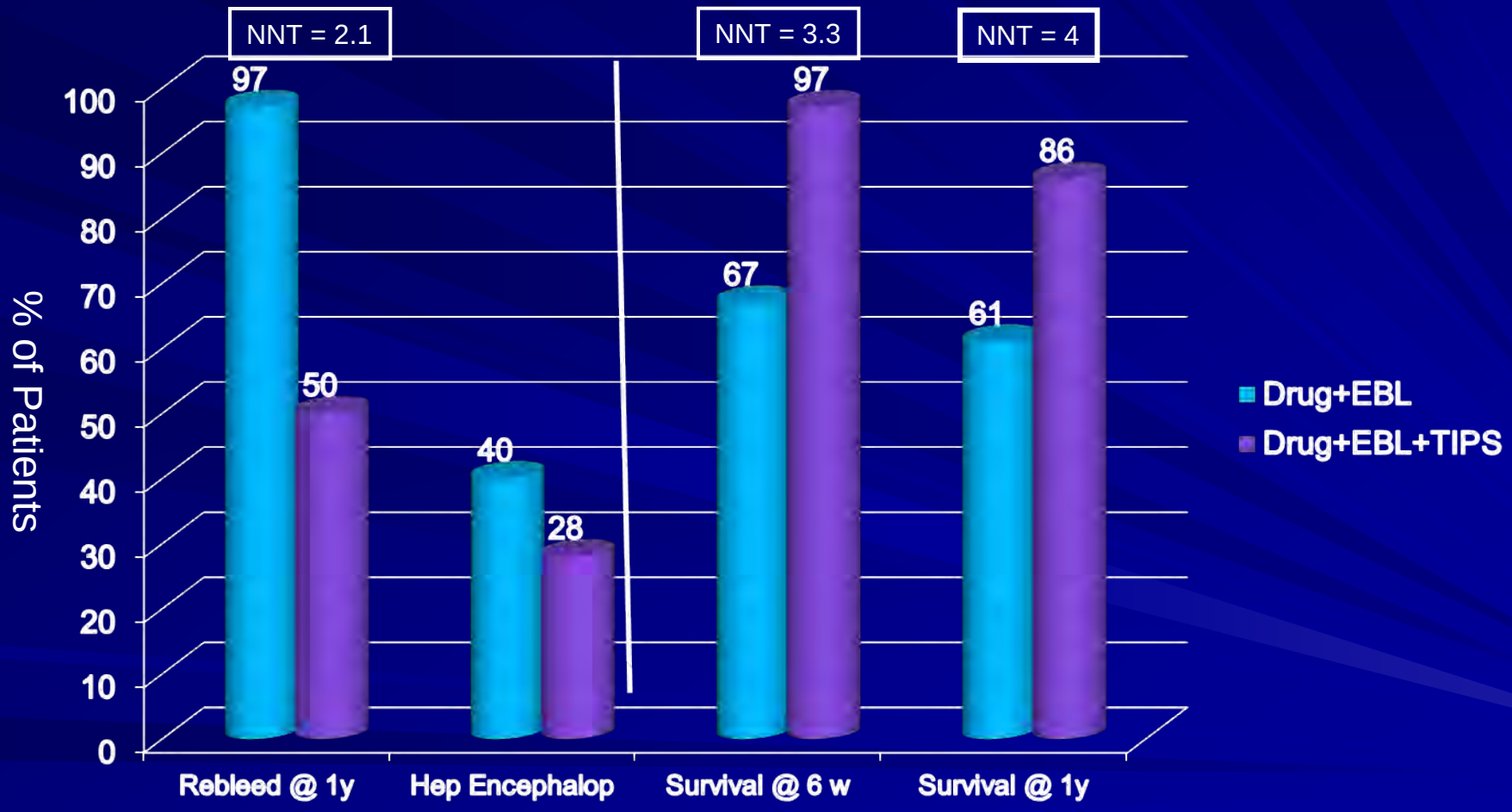
Garcia-Pagan JC; N Engl J Med 2010; 362:2370-2379

- Prospective, randomized study.
- Patients:
  - Cirrhotic Child B (score 7-9) with active bleeding, or C (only scores 10-13, with score 14 and 15 excluded due to expected high TIPS mortality) with/without active bleeding, who had esophageal variceal bleed, and no previous endoscopic therapy nor beta-blockers.
  - All patients received antibiotics, early banding (< 12h) and octreotide, somatostatin, or terlipressin
- Treatment arms:
  - a) TIPS within 24-72h with **Polytetrafluoroethylene (**PTFE)-covered stent (N=32);
  - b) EBL q 10-14d + B-blocker + PPI +/- ISMO (N=31)

Acute GI Bleed in Cirrhosis

Early TIPS in Variceal Bleed: Actively bleeding Child B, or any Child C

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



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.

Cyanoacrylate in Gastric Variceal Bleed

- Acute hemostasis: 90-95%
- Re-bleeding: 15%
- Follow-up: Repeat at 4 weeks to confirm effect or re-treat; then q 6 months.
- Is superior to Banding and to Endoscopic sclerotherapy.
- Addition of beta-blockers does not help
- More cost-effective than TIPS.
- TIPS compared with cyanoacrylate for prevention of recurrent bleeding
  - re-bleeding 11% in TIPS versus 38% in Cyanoacrylate;
  - survival is similar and
  - encephalopathy 26% in TIPS versus 3% in cyanoacrylate.

Technique of Gastric Variceal Obliteration - Cyanoacrylate

- Immerse tip of scope and Inject channel with silicon oil or lipiodol.
- Use 21-22 G x 8 mm sclerotherapy needle.
- Patient and Staff should have eye protection.
- Avoid suctioning.
- Give antibiotic prophylaxis
- DERMABOND (0.5 mL/amp): prime with 1 mL 0.9% NaCl and inject until no resistance; then inject undiluted Dermabond using 2 mL Luer-lock syringe @ 1 mL/20 sec for 2-5 mL until resistance is met; then flush with 1 mL saline while removing catheter by pulling the scope. Repeat in other site if needed. Maximum 5 mL per session.

Technique of Gastric Variceal Obliteration - Cyanoacrylate

- INDERMIL or HISTOACRYL (0.5 mL/amp): Diluted 1:1 with Lipiodol; prime with 1 mL of lipiodol and inject until no resistance; then inject 0.5-**1**-2 mL of diluted mixture with 2 mL Luer-lock syringe, followed by 1 mL of sterile water while removing the catheter by pulling the scope. Repeat in other site if needed. Maximum 10 mL per session
- DO NOT WITHDRAW CATHETER PULLING THROUGH SCOPE CHANNEL. Leave out hanging several centimeters and remove scope. Then cut catheter close to entrance port and pull it out from the scope tip.
- Before procedure consider Dynamic CT looking for large spleno-renal or gastro-renal shunt that increase risk of embolization (0.7% have significant glue embolization)
- Because 85% have gastro-renal or spleno-renal shunt, combined procedure with IR balloon occlusion of shunt + Endoscopic cyanoacrylate injection is promising.

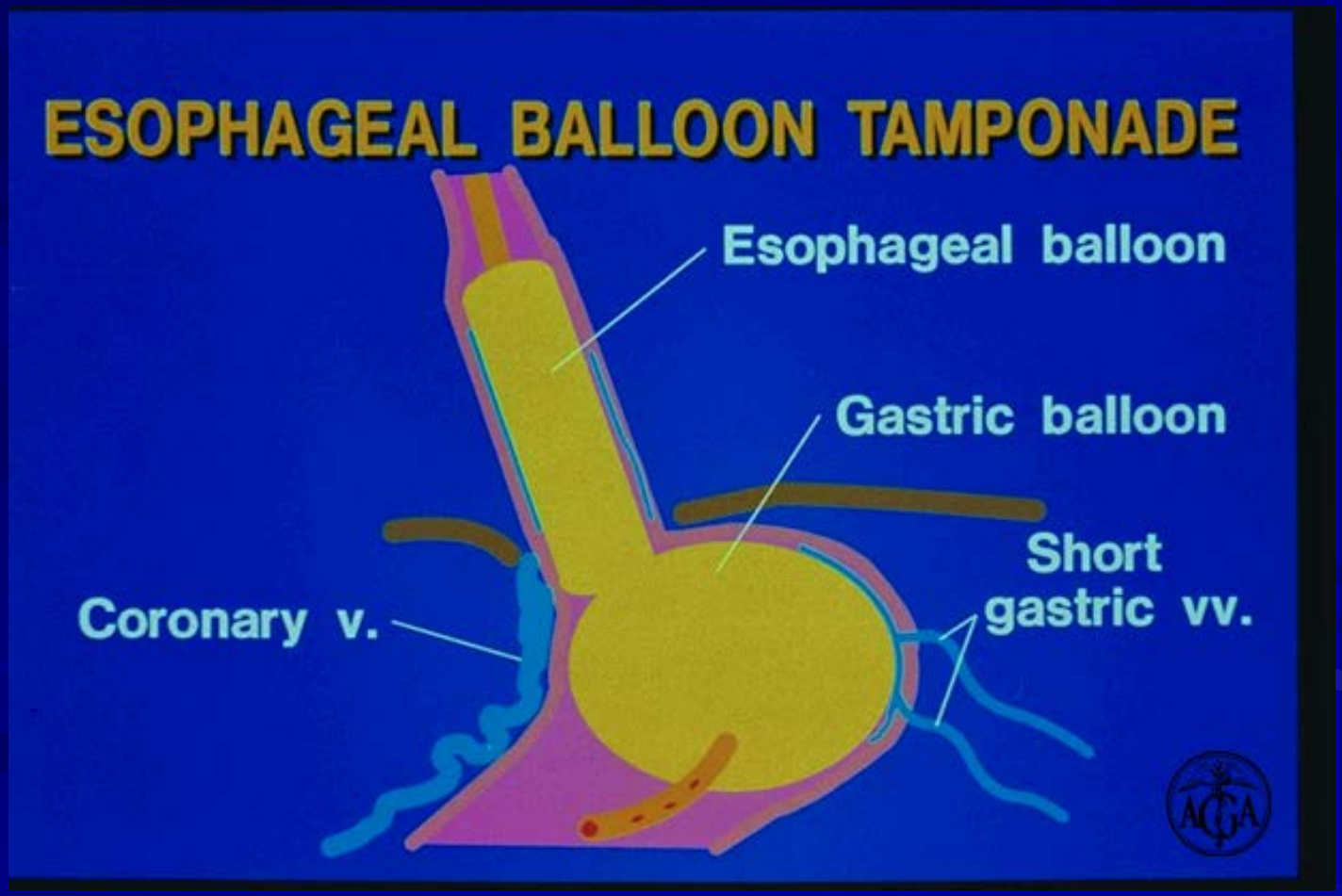
Balloon-Occluded Retrograde Transvenous Obliteration (BRTO)

- 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 GRS.
- 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 EV in up to two-thirds of patients.
- Partial splenic embolization preceding BRTO reduces incidence of EV compared with BRTO alone (9% versus 45%) by reducing blood inflow into the portal vein.

Minnesota Tube

- Has:
  - a) *Volume* “gastric balloon” (500 ml);
    - deflate q 12 h to check for re-bleed.
  - b) *Pressure* “esophageal balloon” (goal 40 mm Hg);
    - once bleeding is controlled, decrease by 5 mm Hg every 1-2 h with goal of 25; increase by 5 mm Hg if re-bleed,
  - c) Gastric suction/lavage port,
  - d) Esophageal suction/lavage port
- Bleeding control: 80% (Bridge to other therapy for </= 24 hours)
- Patient should be intubated (airway protection in case of tube migration)
- Ideally placed under fluoroscopy.
  - May use “pressure guidance” technique.
- Traction to 0.5-1 kg weight
- Major complications in 14%; Mortality up to 20%

Acute Variceal Bleeding
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.
- Has been used as “definitive treatment” in a few (up to 214 days) (Holster IL et al.Endoscopy 2013;45:485-488)

TIPSS as Salvage 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)

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

Practical Approach
Suspected or Proven Variceal Bleed

- Start empirical Terlipressin 2 mg q 4h IV or Octreotide 50 mcg bolus + 50 mcg/hour, at arrival, x 5 days.
- Antibiotic prophylaxis with ceftriaxone x 7 days; start at arrival.
- Esophageal variceal bleed: Banding at arrival, then
  - Banding q 2 weeks until obliteration if Child A, Child B without active bleeding at EGD, or MELD score 19 or higher.
  - Early TIPS (</= 72 hours) with PTFE stent, if MELD score </= 18 **and** Child B actively bleeding at EGD, or Child C.
  - Consider early TIPS if HPVG > 20 mm Hg (within 24 hours from bleed).
- Gastric variceal bleed: Cyanoacrylate (or acute sclerotherapy or banding), followed by urgent TIPSS or shunt
  - splenectomy in splenic vein thrombosis with isolated gastric varices
- Add Nadolol or Propranolol or Carvedilol long term.
- Liver Transplant evaluation.

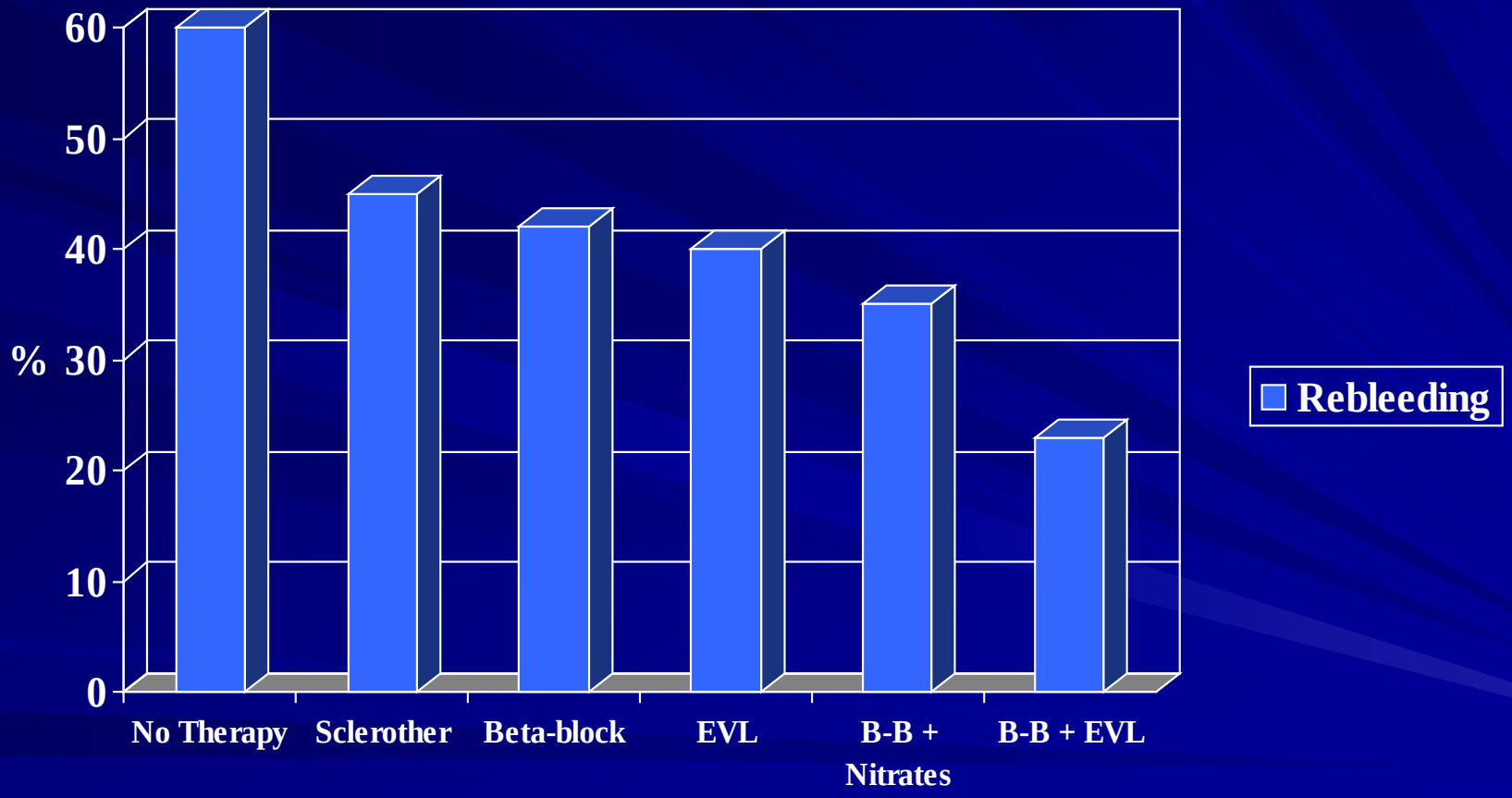
Beta Blockade +/- ISMO Protocol

- Nadolol is given orally at an initial dose of 40 mg/day.
- Then increased dose by 20 mg daily for a period of 5-7 days until:
  - intolerance appears, or
  - the heart rate decreases to 55 beats per minute, or
  - a maximal dose of 160 mg/day is reached, or
  - MAP is = 84 mm Hg if patient has ascites (MAP </= 83 is associated with high mortality; band instead of using beta blockers)
- Oral isosorbide mononitrate is started after beta blockade is reached, at 20 mg once at bedtime,
  - then followed by 20 mg twice a day for 1 day, and
  - finally increased to 40 mg BID if tolerated.
- Betablockers increase mortality in refractory ascites, especially if MAP is =/< 82;
  - D/C betablockers and band varices if needed.

Variceal Rebleed

LONG TERM PROPHYLAXIS

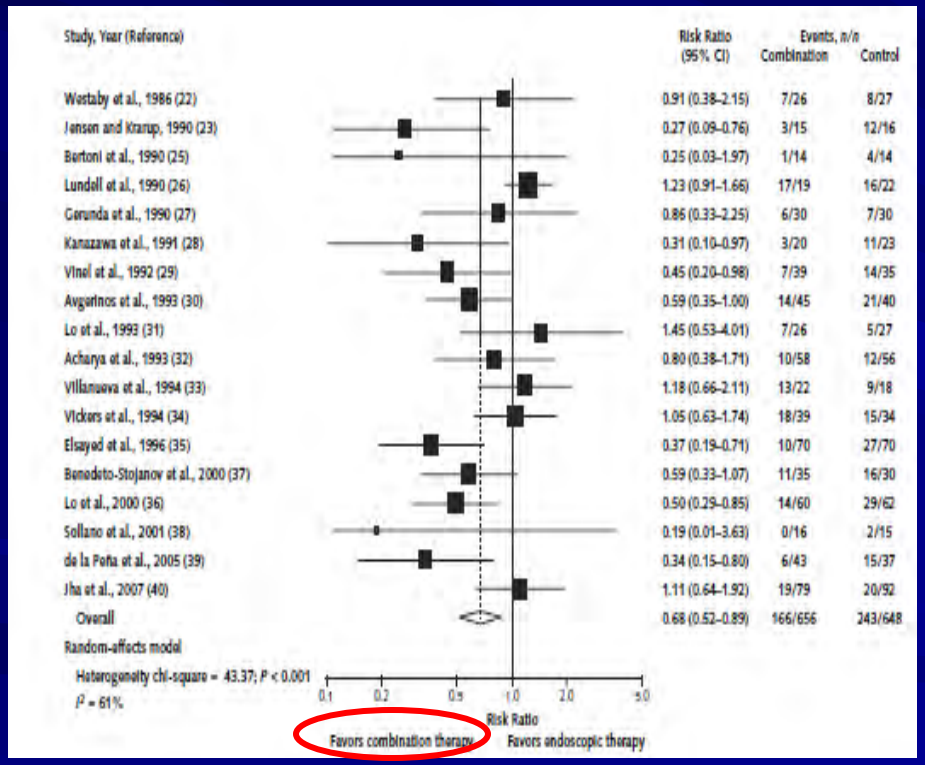
LONG TERM Rebleeding Risk
Different Prophylaxis



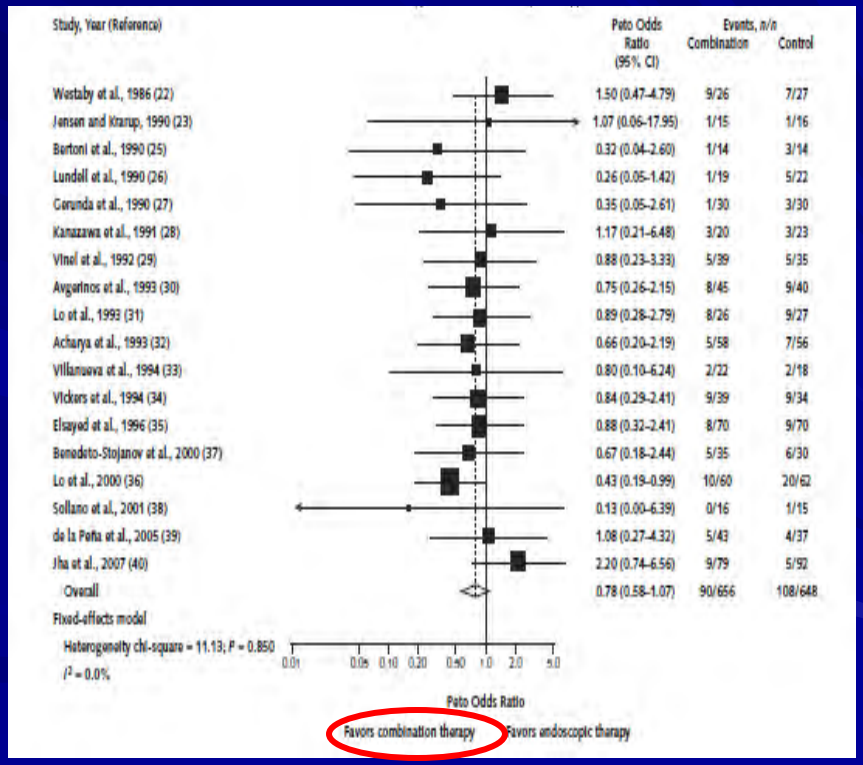
Meta-Analysis of [Endoscopy + Drug therapy] vs Drug-Therapy to Prevent Variceal Re-bleeding

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

Re-Bleeding Rate



Mortality



TIPSS VS. Endoscopic Treatment

(Papatheodoridis et al. Hepatology 1999; 30:612)

- Meta-Analysis:
  - 811 patients in 11 controlled studies.
- RESULTS:
  - Lower re-bleeding with TIPSS
  - Equal mortality.
  - More PSE and clinical deterioration with TIPSS (mostly bare-stents).
  - More costly: TIPSS
- **TIPSS should be used only when medical treatment fails*.**
- **Limitations:** most TIPSS were with “bare-stents”; current “covered stents” have better outcomes.
- ***NOTE**:
  - Child C (score 10-13), and Child B with active bleeding at EGD, get benefit from early PTFE TIPS.
  - If HVPG >/= 20 mm Hg, early TIPS decreases treatment failure and in-hospital and 1 year mortality (Monescillo A et al. Hepatology 2004;40:793-801)

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 (5;D):
  - 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

Practical Approach to Prevent Variceal Bleed

PREVENT 1st BLEED

- Cirrhotic: EGD to R/O varices
- No varices: re-scope
  - q 1 y (decompensated) or
  - q 3 y (compensated)
- F-1 and Child A without red-wale: re-scope q 1-3 y as above.
- F-1 (</= 5 mm) + Child B/C or red-wale = B-blocker
- F-2 varices Child A, no red-wale: Beta-blocker
- F-2 + Child B/C or red-wale: Beta-blocker and/or banding
- F-3 varices : Beta-blocker and/or banding

PREVENT RE-BLEED

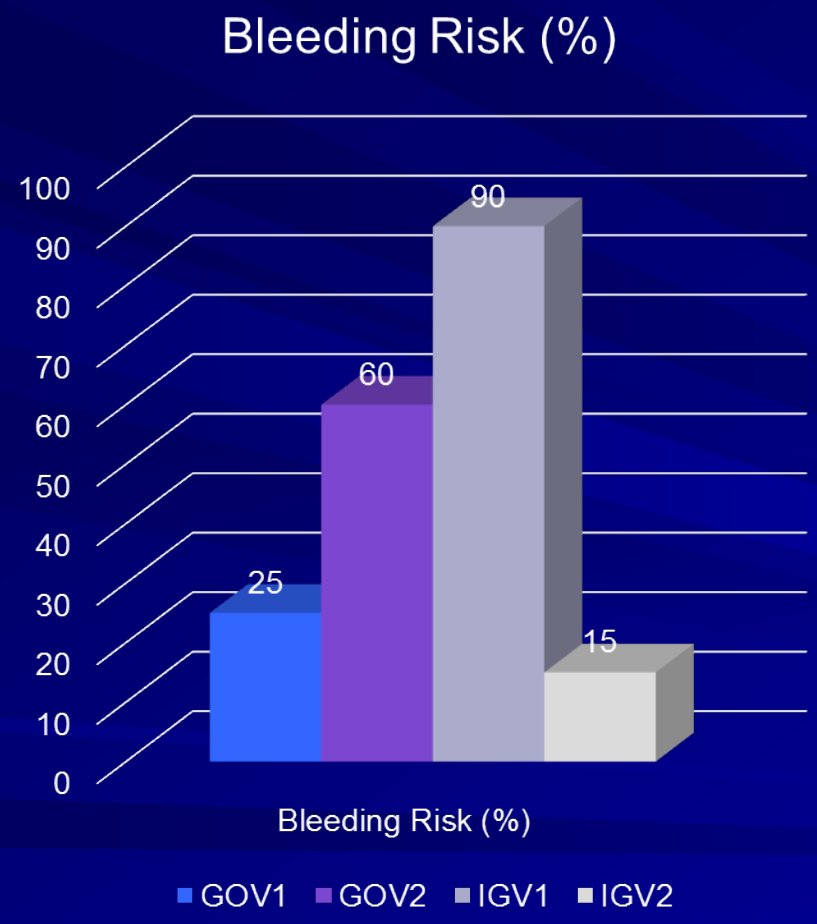
- *Liver Transplant eval.*
- TIPS if MELD < 15
- Banding + Beta-blocker
- Banding
- TIPS if MELD 15-18 or Shunt (+/-)
- Sclerotherapy (-)

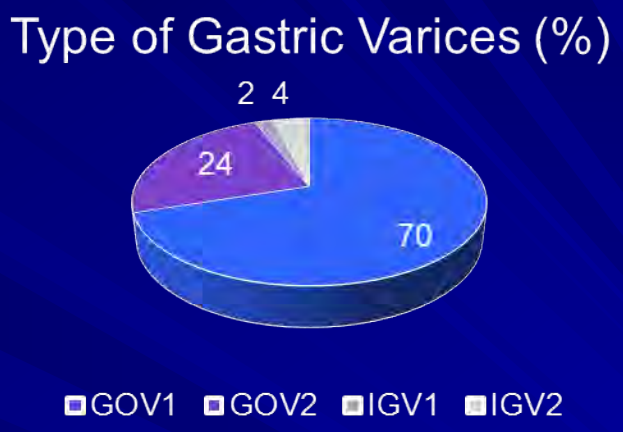
Gastric Varices Classification

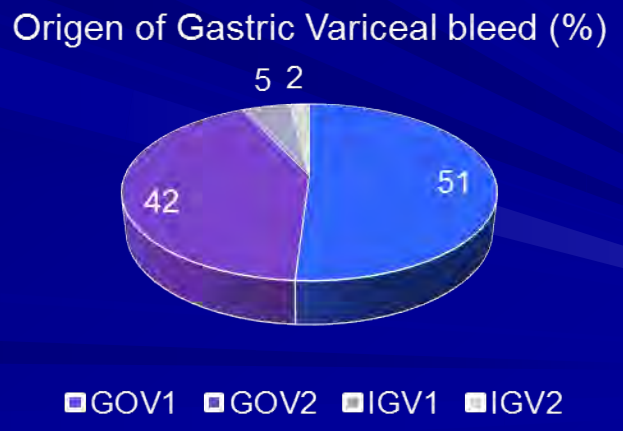
- **GOV1**: (**70% of GV**; 25% of them will bleed)
  - continuous with esophageal varices in **lesser curvature**;
  - treat as esophageal
- **GOV2**: (**24% of GV**; 60% of them will bleed);
  - extend from **esophagus to fundus**;
  - +/- cyanoacrylate +/- TIPSS
- **IGV1**: (**2% of GV**; 90% of them will bleed);
  - **isolated fundic** varices;
  - likely splenic vein thrombosis = splenectomy after vaccination (if possible)
- **IGV2**: (**4%of GV**; 15% of them will bleed);
  - **isolated in antrum**;
  - rarely bleed; band or sclerose if bleeding.

Gastric Variceal Bleed

Risk, Frequency & Origen







Gastric Variceal Bleed (GOV2)

- 10-15% of all variceal bleeds.
- Bleeding Risk:
  - At 1 year, 2 years, 3 year, and 5 years, the bleeding risk is 16%, 25%, 36%, and 44% (Kim T et al. Hepatology 1997;25:307-12). Mean bleed 4.8 units.
  - 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.
- Re-bleeding rate post TIPS monotherapy is 20%.

Treatment of Acute Gastric Variceal Bleed

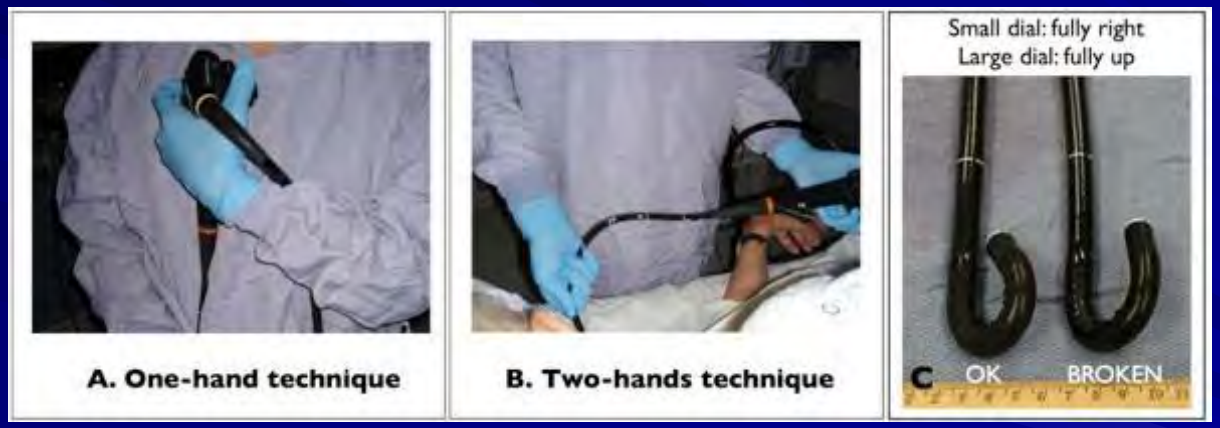
- Intravariceal Cyanoacrylate injection (**Hystoacryl**, Dermabond) q 3-4 weeks until obliteration:
  - hemostasis in 90%;
  - embolization 0.7%;
  - re-bleeding at 3 d, 3 month and 1 year: 6.9%, 10.6%, and 10.0%.
- TIPSS:
  - controls 90% of bleeds (goal HVPG pressure =/< 8 mmHg);
  - re-bleeding at 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)

PROPHYLAXIS

- SECONDARY PROPHYLAXIS: comparison of beta blockade vs n-BCA (at time 0, 2, and 6 months) obliteration gives (Mishra SR et al. Gut 2010;59:729-35):
  - Re-bleeding at 26 weeks: 55% in BB vs 15% with n-BCA
  - Mortality at 26 weeks: 25% in BB vs 3% with n-BCA
  - Addition of beta-blocker to serial cyanoacrylate obliteration does no change re-bleeding rate nor mortality. (Hung HH et al. Journal of Hepatology 2012;56:1025-32).

- PRIMARY PROPHYLAXIS: In mostly GOV2 (some IGV1); first bleeding rate after 26 weeks of follow up:
  - No treatment = 45% vs
  - Propranolol = 28%, vs
  - Cyanoacrylate (n-BCA) = 13%

Best is “One-Hand” Technique



Material Needed

- Goggles for eye protection (endoscopist(s), assistants, patient).
- Three to four 3cc syringes with Luer-lock fitting filled with each with 1 cc n-BCA (each amp of n-BCA has 0.5 mL).
- Three to four 3 cc syringes with 3 cc of sterile water each (to flush with1.6 cc, then remove and retract needle and flush the rest; DO NOT SUCTION)
- n-butyl-2-cyanoacrylate preparation (**Hystoacryl** or Indermil): 6-8 amps.
- Therapeutic endoscope (2-T or 6mm for active bleeding and 3.7 mm for elective cases)
- Silicon oil (or Olive oil) to coat endoscope tip and distal end of the working channel
- Water irrigation pump
- Additional suction unit for the 6mm channel endoscope
- Injection needles (25-gauge Carr-Locke needles) primed with > 1.6 cc sterile water (1.6 cc death space); attach n-BCA syringe and inject only after sure needle is intra-variceal).

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

- 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.
  - Portacaval 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 angiomas associated with cirrhosis

Gastric Antral Vascular Ectasia (GAVE) Watermelon Stomach

- Significance:
  - Causes 0.5% of nonvariceal upper gastrointestinal bleeding; 31% 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 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.

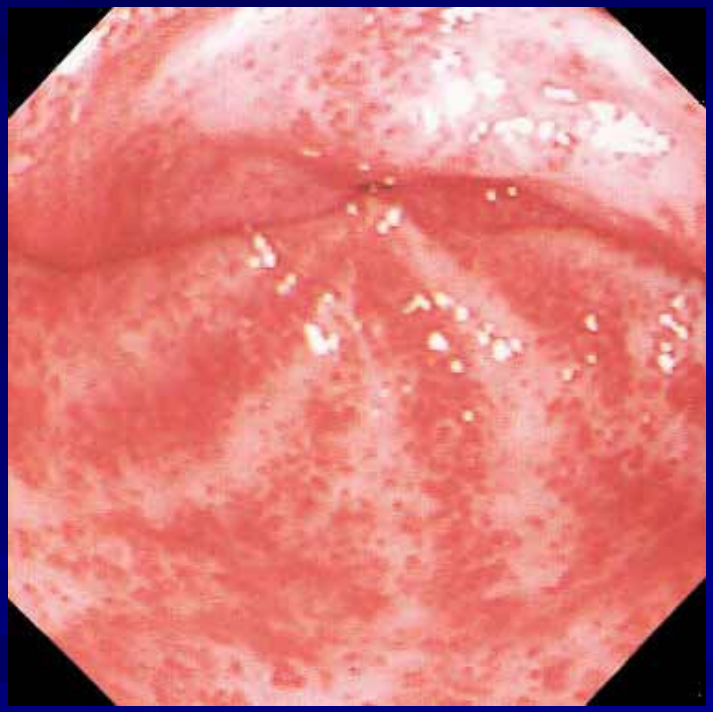
Gastric Antral Vascular Ectasia (GAVE) Watermelon Stomach

- 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, 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.

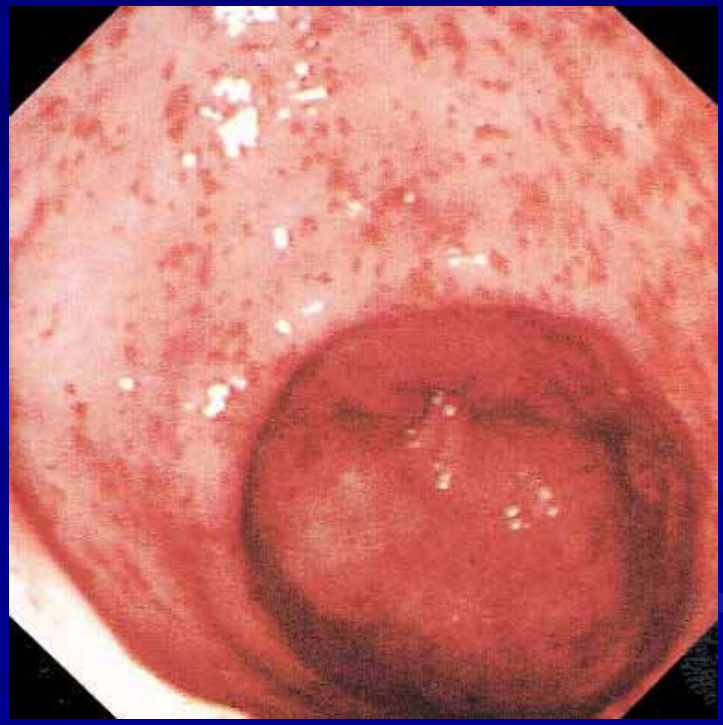
Endoscopic Types of GAVE

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

Classic GAVE
(cirrhosis & non-cirrhosis)



Punctate GAVE
(cirrhosis)



Portal HTN Gastropathy (PHG) vs GAVE

	PHG	GAVE
Mosaic Pattern	Present	Absent
Distribution	Proxim > Distal	Distal > Proxim
Red signs/spots	If severe	Always
Thrombi (Bx)	-	+++
Fibrohyalinosis (Bx)	+	+++
Spindle cell prolif (Bx)	+	++
Treatment	Beta-blocker, Fe, TIPSS	APC

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.
  - May be found in all areas of the gastrointestinal tract, including the esophagus and duodenum.
  - Bleeding is often self-limited, although it is usually recurrent and can be profuse
- Etiology is unknown, likely congenital.
- Causes of bleeding are 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.

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 aortoenteric fistulas, followed by the jejunum and ileum .
- Presentation:
  - Repetitive herald bleed with 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 — Aortoenteric 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

- Treatment:
  - Exploratory laparotomy is indicated for patients with suspected aortoenteric fistula and severe ongoing bleeding.
  - The mortality rate of an untreated aortoenteric 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 aortoenteric 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.

Hemobilia

- Bleeding from the hepatobiliary tract;
  - rare cause of acute UGI bleeding.
- 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,
  - Angioembolization (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

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: pancreaticoduodenectomy or pseudocyst resection and ligation of the bleeding vessel.

Cameron Lesions

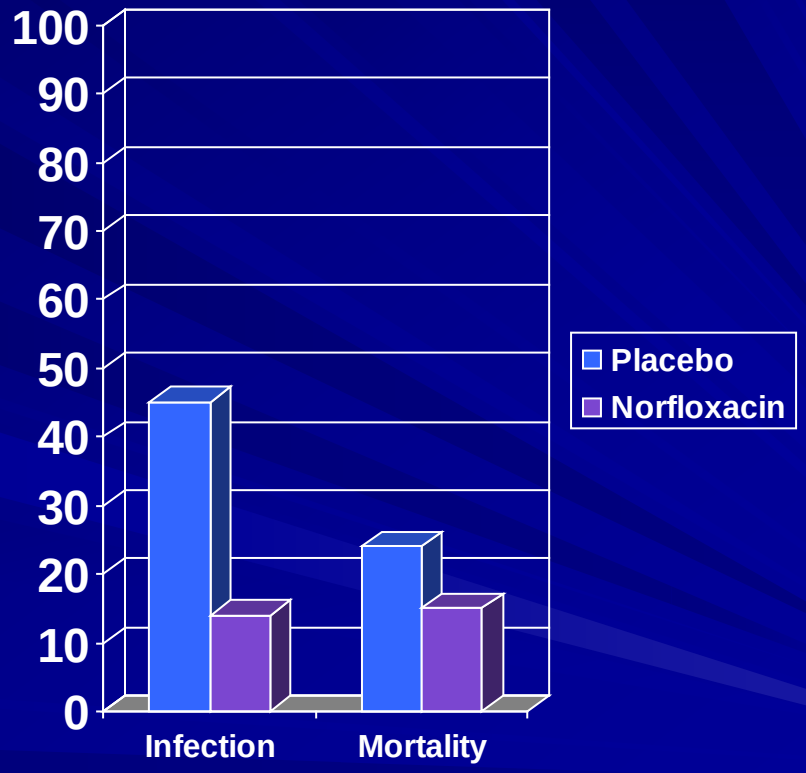
- **Definition:** erosions or ulcers occurring in the sac of a hiatal hernia.
- **Frequency:** up to 5 percent of patients with a hiatal hernia having EGD.
- **Significance:**
  - usually an incidental finding
  - rarely causes acute or chronic upper gastrointestinal bleeding and iron deficiency anemia.
- 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.

QUESTIONS ?

Effect of Antibiotic Prophylaxis on Infection & Mortality Risk

Bernard et al. Hepatology 1999;1655-1661

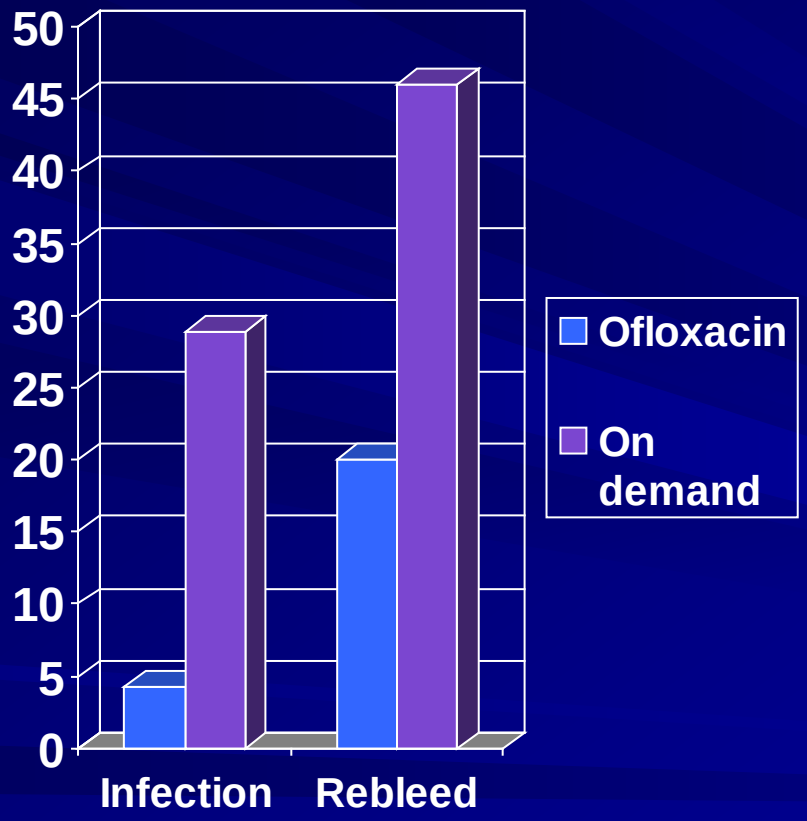
- Prospective, controlled, & randomized.
- Norfloxacin 400 mg q 12 hours, p.o. vs. Placebo.
- Started at Hospital admission.
- Duration: 7 days



Effect of Antibiotic Prophylaxis on Rebleeding rate after Endoscopic treatment of Variceal bleed (283)

- Prospective, randomized.
- 91 cirrhotic patients with variceal bleed receiving endoscopic treatment
- Outcome: rate of rebleeding and infection
- Intervention: Ofloxacin 200mg BIDx 7d vs antibiotic for infection only (46 vs 45)
- No difference on: age, sex, etiology, endoscopic finding, time to EGD, hepatoma, severity of bleed.

Results (%)



- ***CONCLUSION***
- Prophylactic antibiotics in variceal bleed decrease rebleeding rate and transfusion needs (0.7 vs 2.7 Units)

Causes of UGI Bleeding
UCLA & West LA VAMC

- Peptic Ulcer Disease: 55%
- Esophago-Gastric Varices: 14%
- AVM's: 6%
- Mallory-Weiss tear 5%
- Tumors & Erosions: 4%
- Dieulafoy's lesions: 1%
- Other: 11%

Causes of UGI Bleeding

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

- Mucosal abnormalities: 42%
- Esophagitis: 15%
- Gastric Ulcers: 13%
- Esophageal/Gastric Varices: 12%
- Duodenal Ulcers: 11%
- Angiodysplasia: 4%
- Mallory-Weiss tear: 3%
- Tumors: 2%
- Healed Ulcer: 1%

Prognosis by Endoscopic Stigmata of Recent Hemorrhage

Characteristic	Rebleeding %	Surgery %	Mortality %
Clean base	5 (0-10)	0.5 (0-3)	2 (0-3)
Flat spot	10 (0-13)	6 (0-10)	3 (0-10)
Adherent clot	22 (14-36)	10 (5-12)	7 (0-10)
Visible vessel	43 (0-81)	34 (0-56)	11 (0-21)
Active bleeding	55 (17-100)	35 (20-69)	11 (0-23)

Injectable Solutions

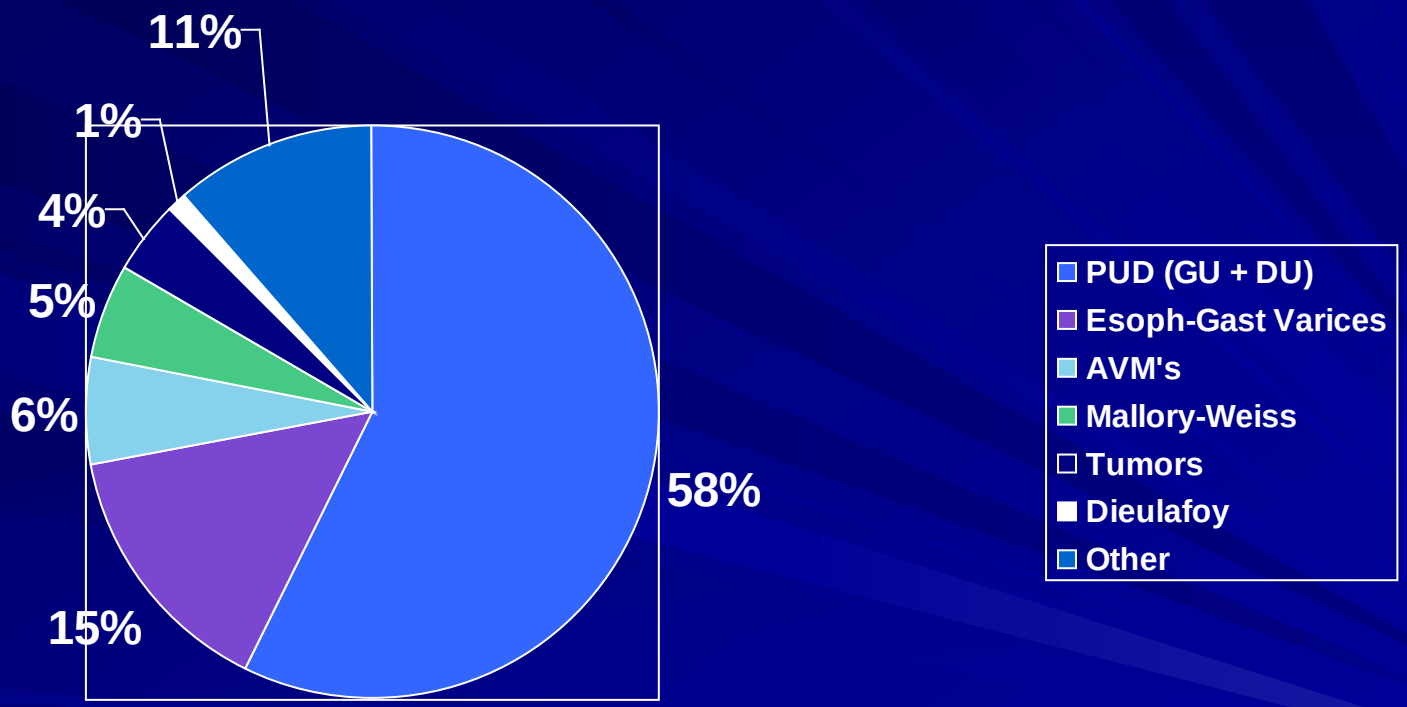
- **Submucosal "pillow"** for polypectomy or mucosectomy : Hypertonic, 50% Dextrose, or colloid (hialuronic acid) solutions improve duration of pillow; low dose epinephrine decreases bleed. Color enhances contrast.
  - 9.75 ml 5% NaCl + 0.25 ml 1/1000 epi + 1 drop methylene blue = **4.8% NaCl 1/40000 epi**
  - Inject as needed to lift lesion; inject first away from endoscope, and then closer, to make the lesion to "face you".

Risk of Rebleeding after EGD

- Age > 60
- Systolic pressure < 100
- Co-morbidity: Hepatic failure, renal failure, disseminated cancer, CHF, CAD
- UGI malignancy
- Stigmata of recent bleed & rebleeding risk:
  - Clean base: 5 %
  - Flat spot: 10%
  - Adherent clot: 22 %
  - Visible vessel: 43 %
  - Active bleed or oozing: 55 %

Causes of UGI Bleeding

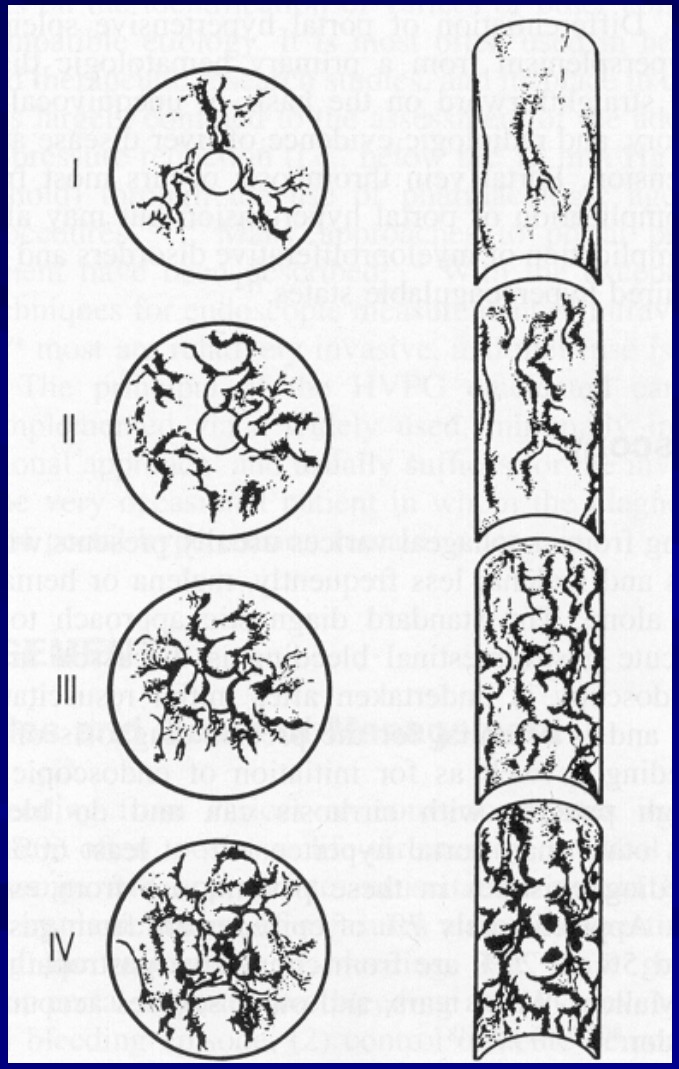
UCLA & West LA VAMC

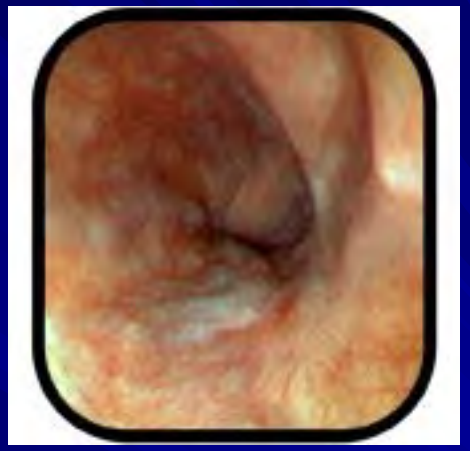


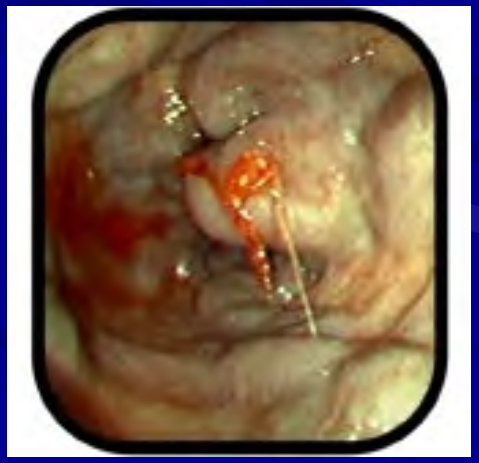
Minnesota Tube

- Change from “baseline” gastric balloon “volume to pressure” relation (outside the body vs inside the stomach) of 15 mm Hg or more, suggest misplacement (esophagus or duodenum) or small stomach (partial gastrectomy). STOP.
- First inflate only the gastric balloon to full size, and then place well fitting and properly strapped football helmet.
- Pull M-tube to “snug” tension and tape it to helmet’s face-frame. Keep scissors at bedside.

Endoscopic Grading System







InScope Multi-Clip Applier

Minnesota Tube

- Treat with Octreotide/Somatostatin drip and “intestinal decontamination”
- Lavage through esophageal port to see if bleeding persists.
  - **Inflate esophageal balloon to 40 mm Hg if bleeding persists.**
  - **Deflate for 5 min every 6 hours, and retest if bleeding returns.**
  - **Repeat EGD if needed.**
- Correct coagulopathy (FFP 80 cc/h, rFVII).
- Consult Surgery and Invasive Radiology

Tattooing

- To mark area in need of surgical removal, or in need of endoscopic follow up to asses completeness of treatment.
- Should be done with permanent tattoo (india ink/ carbon particles). Indocianine green or methylene blue, last only hours or days.
- Tattoo opposite wall to the lesion with 0.2 to 0.3 ml/injection x 2-4 injections; do oblique injection or pull needle back partially to avoid deep injection. Larger volume injections can cause severe inflammatory reaction.

TIPSS Mortality Risk by MELD

(Based on: Bilirubin, Creatinine and INR)

MELD	3-month mortality (%)
<10	2-8
10-19	6-29
20-29	50-76
30-39	62-83
> 40	100