

Updates in Management of Acute Variceal Bleeding

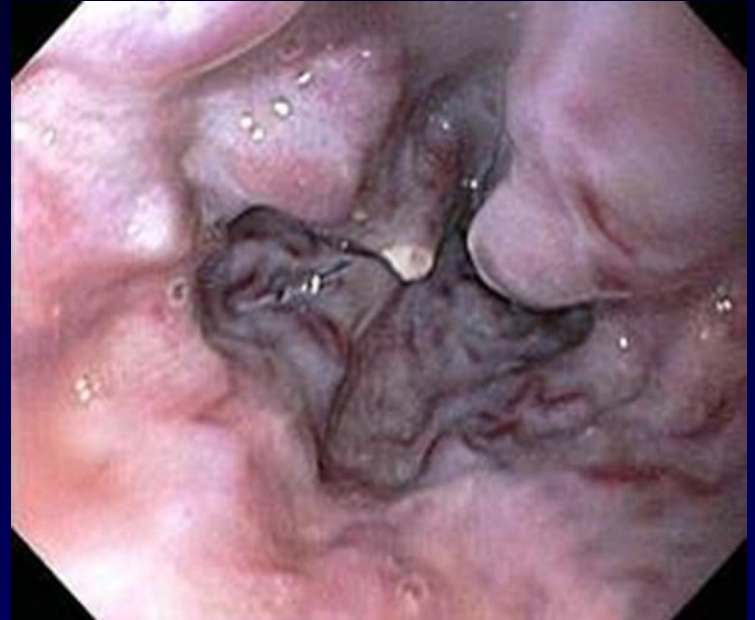
Dr. Raymond S.Y. Tang
Institute of Digestive Disease
The Chinese University of Hong Kong
Prince of Wales Hospital

16th April, 2013



Outline

- **Significance**
- **Management**
 - Key issues
 - Established therapies
 - Emerging technologies



The Problem

- **Gastroesophageal Varices**
 - ~ 40% in Child's A cirrhosis
 - ~ 85% in Child's C cirrhosis
- **Acute Variceal Bleeding**
 - 1-year rate of 1st variceal bleeding ~ 12%
 - 1-year rate of recurrent bleeding ~ 60%
 - 6-week mortality ~ 15 to 20%



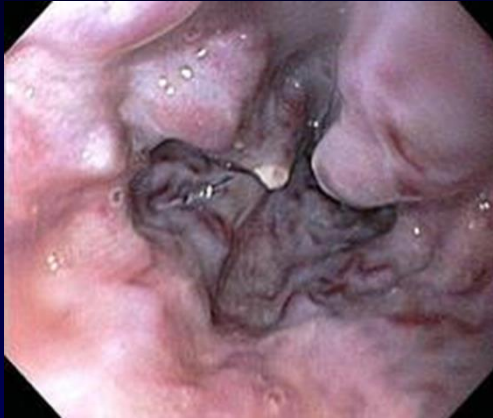
The Problem

- **Although mortality from variceal bleeding has decreased over the past 2 decades due to:**
 - Antibiotic prophylaxis
 - Improved endoscopic therapy and pharmacological therapy
- **Still a major potentially lethal complication of cirrhosis**

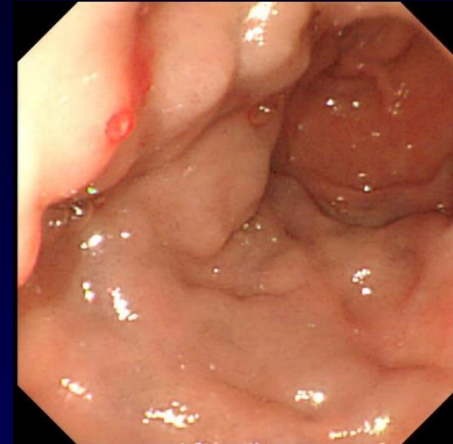


Varices

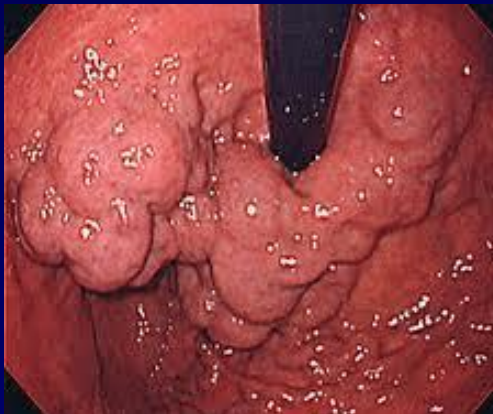
Oesophageal



Duodenal



Gastric



Rectal



Management of Acute Variceal Bleeding

**Initial Assessment &
Resuscitation**

Pharmacological Therapy

Endoscopic Therapy

Rescue / Alternative Therapy



Initial Assessment & Resuscitation

- **Presentation:**
 - ? Hematemesis ? Melena ? PR bleeding
- **Hemodynamic Stability:**
 - ? Shock ? Tachycardia
- **Hemoglobin Level:**
 - ? Target Hb (avoid over-transfusion)



Initial Assessment & Resuscitation

- **Level of Care:**
 - ICU vs general ward
- **Airway Protection:**
 - Consider intubation for patient with significant hepatic encephalopathy



Blood Volume Resuscitation

- **Maintain hemodynamic stability**
- **Avoid over-aggressive transfusion**
 - *Over-aggressive transfusion*
 - → *Increase in portal pressure*
 - → *More re-bleeding & mortality*
 - Target Hb ~ 8 g/dL



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

JANUARY 3, 2013

VOL. 368 NO. 1

Transfusion Strategies for Acute Upper Gastrointestinal Bleeding

Càndid Villanueva, M.D., Alan Colomo, M.D., Alba Bosch, M.D., Mar Concepción, M.D.,

- **Restrictive transfusion strategy (Tx if Hb < 7) vs Liberal transfusion strategy (Tx if Hb < 9) in 921 patients with UGIB**
- **In subgroup analysis of 277 patients with cirrhosis**
 - Reduced rate of re-bleeding & mortality in the restrictive transfusion group in Child's A or B patients
 - No difference in Child's C patients



Management of Coagulopathy

- **FFP and/ or Platelets**
 - Can be considered in patients with significant coagulopathy and/or thrombocytopenia
- **Recombinant Factor VIIa**
 - No benefit in cirrhotic patients with UGIB in general
 - But post hoc analysis data shows reduced failure to control variceal bleeding in Child's B, C patients



Garcia-Tsao G et al. Hepatology 2009
Bosch J et al. Gastroenterology 2004



Pharmacological Therapy

- Vasoactive drugs
- Antibiotic prophylaxis



Vasoactive Drugs

- **Somatostatin & Analogues**

- Octreotide & Vapreotide
- Inhibits vasodilator hormones e.g. glucagon, +/- direct vasoconstricting property
 - Splanchnic vasoconstriction

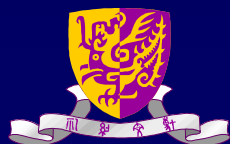
- **Vasopressin & Analogues**

- Terlipressin
- Non-specific arteriolar vasoconstriction
 - Splanchnic vasoconstriction

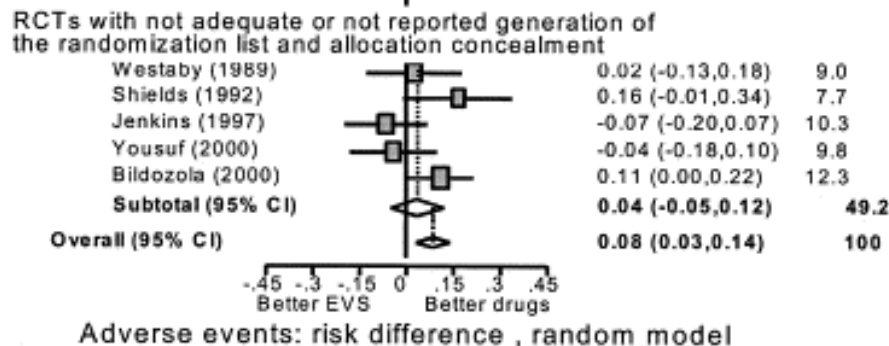
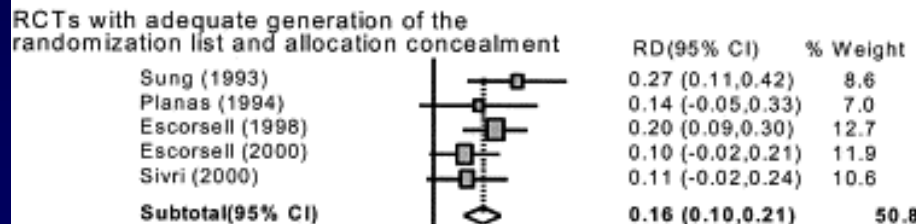
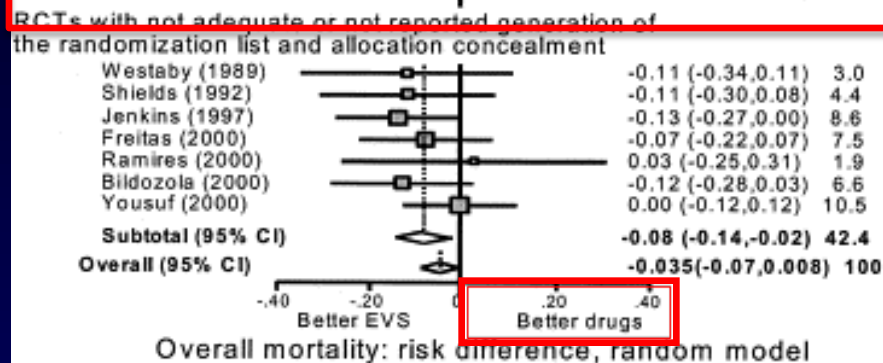
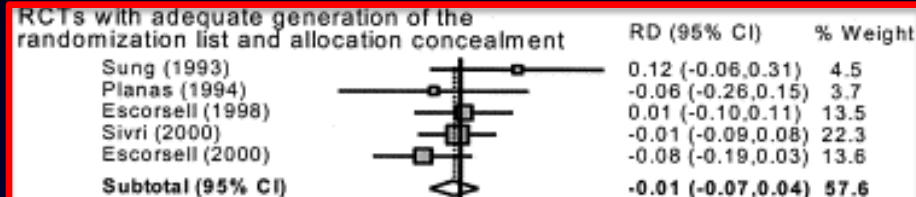


Vasoactive Drugs

Regimen	Dose	Duration
Octreotide	IV 50ug bolus, followed by IV infusion of 50ug/h	2 – 5 days
Terlipressin	2mg IV Q4h x 48h, then 1mg IV Q4h	2 – 5 days



Vasoactive Drugs as 1st line therapy



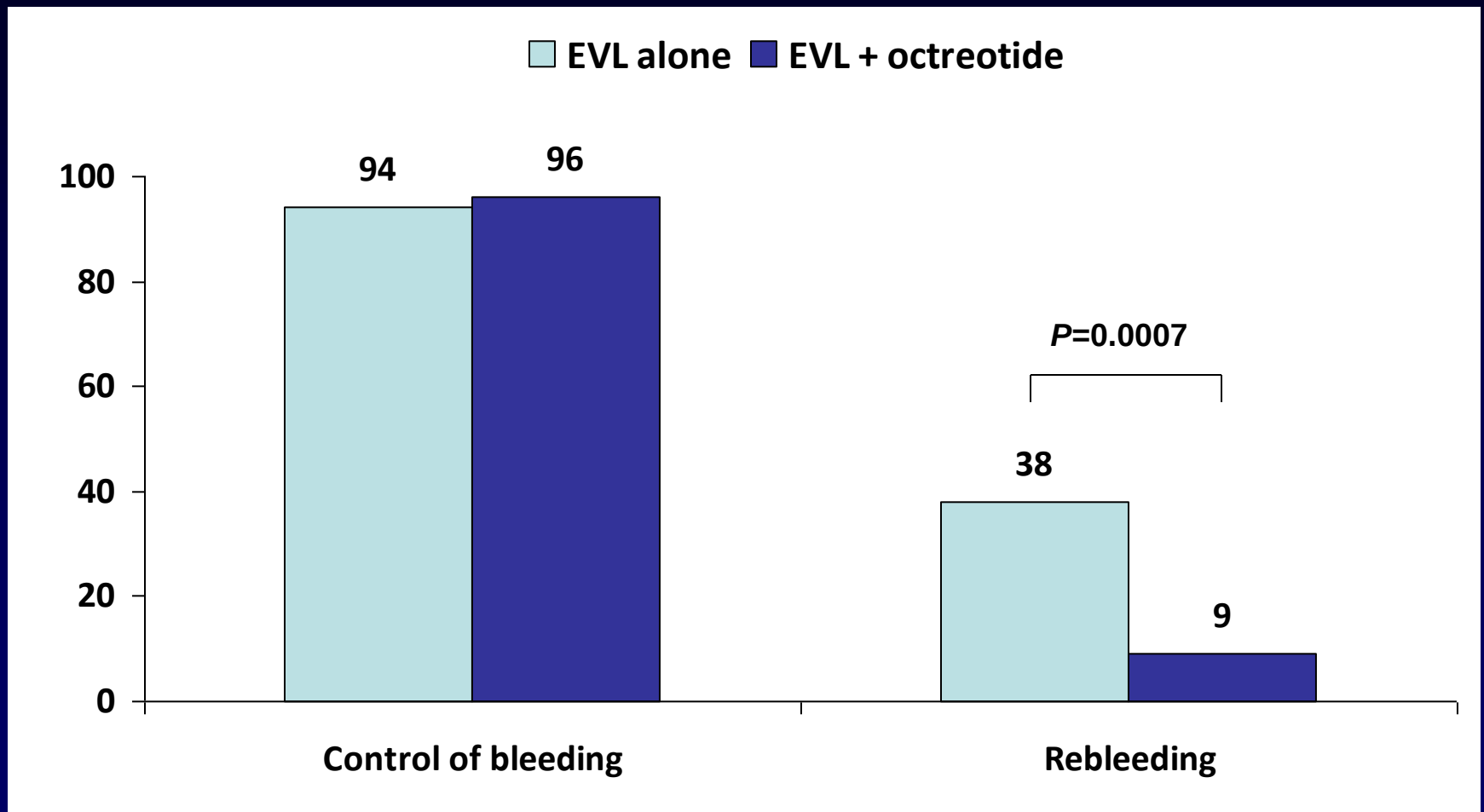
- A Cochrane meta-analysis of 15 RCTs
 - Sclerotherapy vs Vasoactive drugs as 1st line therapy
 - Vasoactive drugs is better, controlling bleeding in 83% of patients

Early use of Vasoactive Drugs

Author	Treatment	Control	Timing	Results
Levacher Lancet 95	Terlipressin+ TNG	Nil	At home	Rebleeding Mortality
Averginos Lancet 97	Somatostatin	Placebo	Before endoscopy	Rebleeding Mortality
Cales NEJM 01	Vapreotide	Placebo	<6h before endoscopy	Survival & control of bleeding

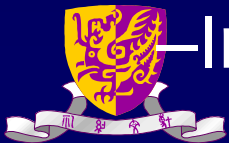


Endoscopic Variceal Ligation (EVL) vs Octreotide + EVL



Antibiotic Prophylaxis

- **Cirrhotic patients with UGIB → high risk of bacterial infection**
 - Higher risk of recurrent variceal bleeding
 - Higher mortality
- **Antibiotic prophylaxis x 5 – 7 days**
 - Ceftriaxone, Quinolones
 - Reduced bacterial infections (with or without ascites)
 - Increased survival



Timing of Endoscopy

- **OGD within 12 hours of admission in cirrhotic patients with suspected variceal bleeding**
- **Vasoactive drugs should be given before endoscopy if variceal bleeding is highly suspected**

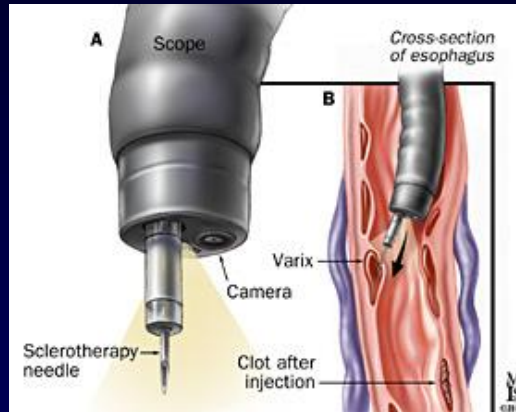


Endoscopic Therapy

Banding Ligation



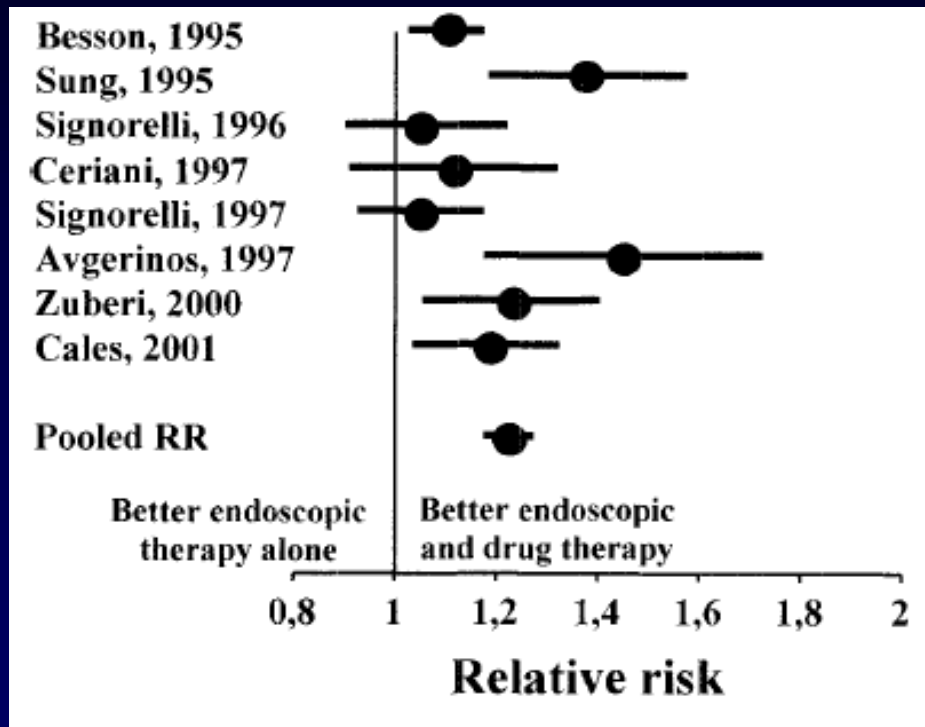
Injection Sclerotherapy



Cyanoacrylate Obturation



Endoscopic Therapy + Pharmacological Therapy

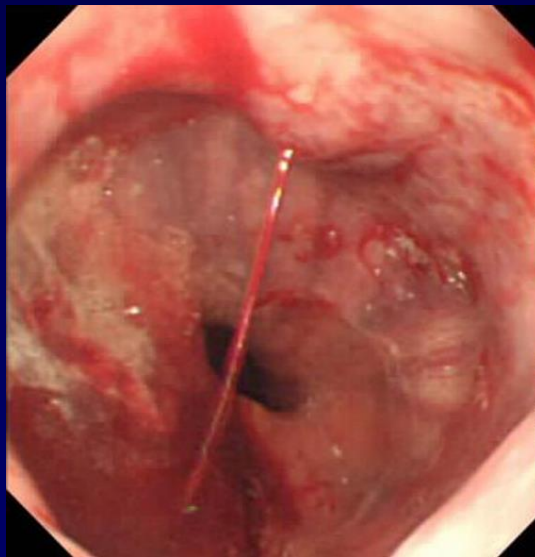


Meta-analysis of 8 trials

- Improve initial & 5-day hemostasis
- No difference in mortality or severe adverse events



Oesophageal Varices (OV)



Endoscopic Banding Ligation (EBL) vs Injection Sclerotherapy

- **Data from RCTs and Meta-analysis support EBL as the preferred therapy**
 - Better initial control of bleeding
 - Less adverse events
 - Improved mortality



Lo G et al. Hepatology 1997

Villanueva et al. J Hepatol 2006

Garcia-Pagan et al. Nat Clin Pract Gastroenterol Hepatol 2005



Endoscopic Banding Ligation (EBL) vs Injection Sclerotherapy

- **Sclerotherapy can be used in patients in whom EBL is not feasible**



Lo G et al. Hepatology 1997

Villanueva et al. J Hepatol 2006

Garcia-Pagan et al. Nat Clin Pract Gastroenterol Hepatol 2005



Endoscopic Banding Ligation (EBL) vs Cyanoacrylate Obturation

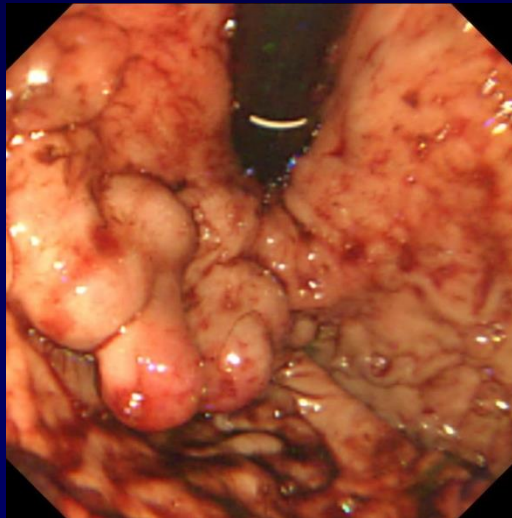
- **Conflicting data from 1 small prospective case series & 2 small randomized studies**
 - Ljubicic et al reported no significant difference in terms of acute OV bleeding control, re-bleeding rate, and mortality
 - Santos et al reported more minor complications, OV recurrence, and a trend towards more re-bleeding in Cyanoacrylate group



Cipolletta L et al. Dig Liver Dis 2009
Ljubicic N et al. Hepatogastroenterology 2011
Santos M et al. Eur J Gastroenterol Hepatol 2011



Gastric Varices (GV)



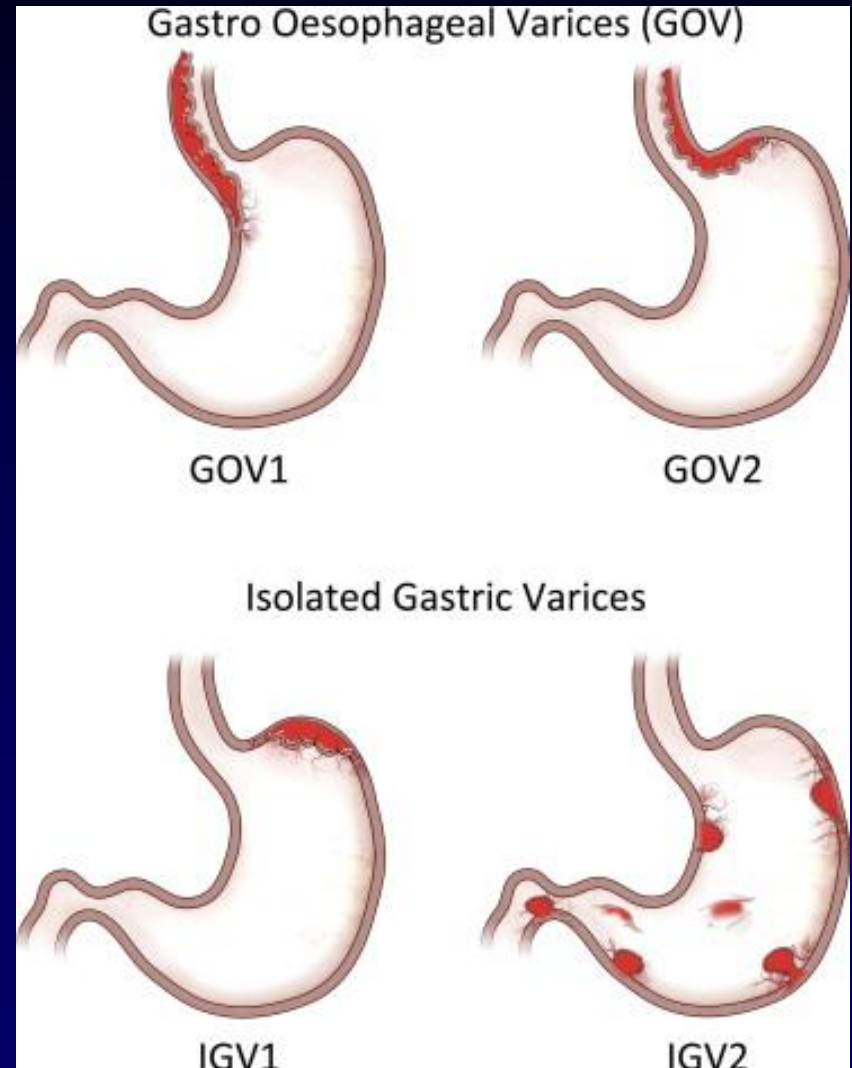
Gastric Varices (GV)

- **Present in 20% of patients with cirrhosis**
 - Isolated or in combination with OV
- **More severe bleeding than OV bleeding**
- **Higher mortality than OV bleeding**



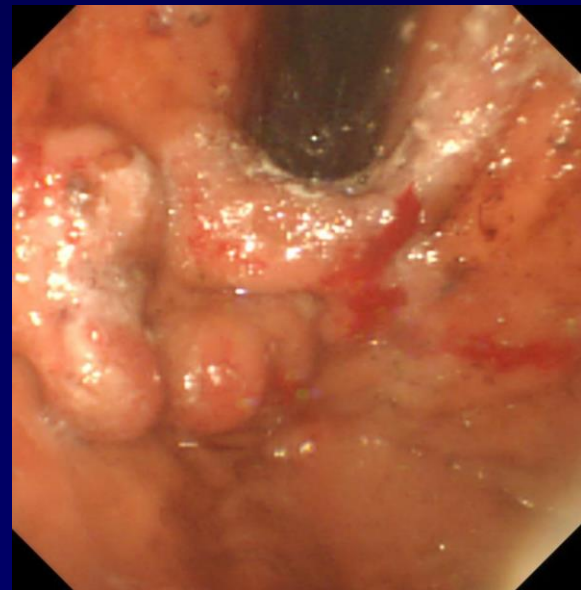
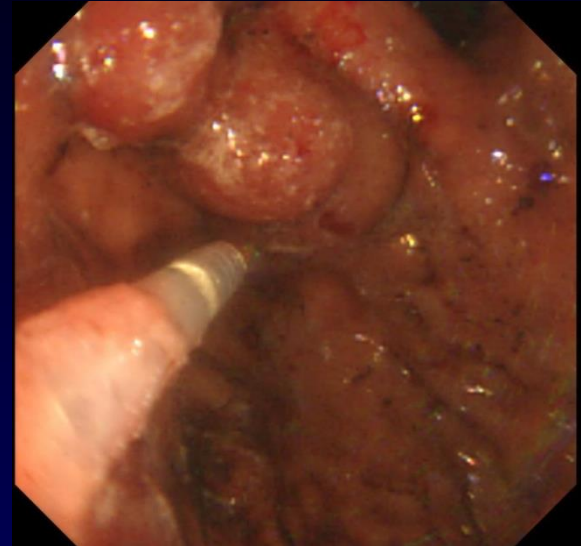
Classification of GV

- **GOV1:**
 - GV is a continuation of OV along lesser curve
 - Same treatment as OV
- **IGV1:**
 - If this is from splenic vein thrombosis, then splenectomy



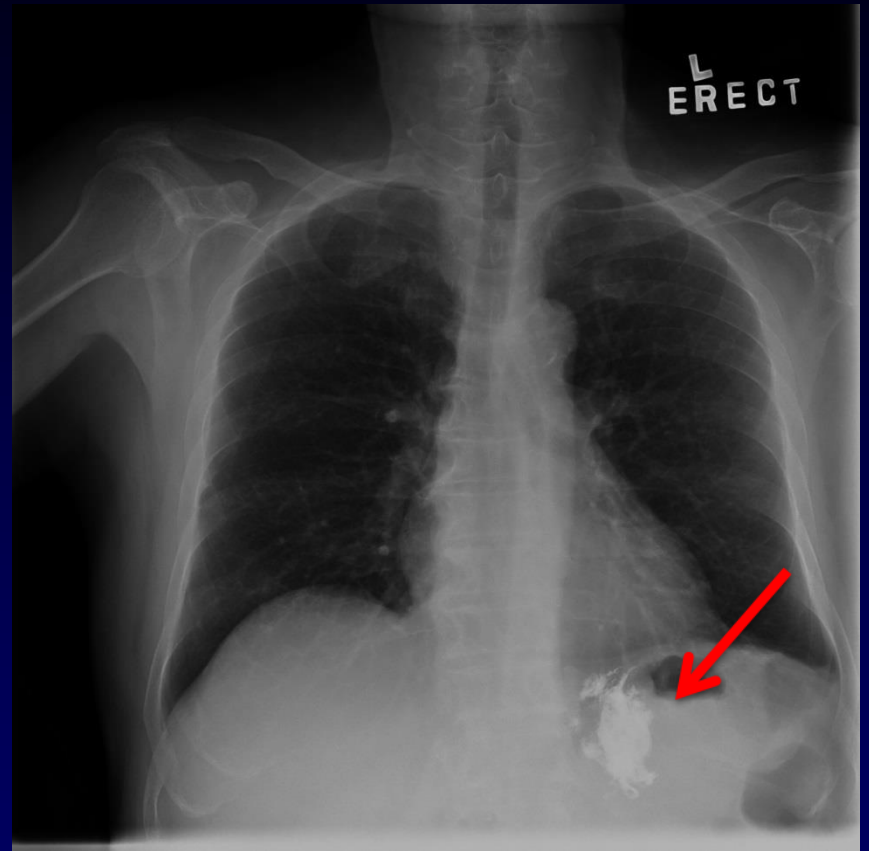
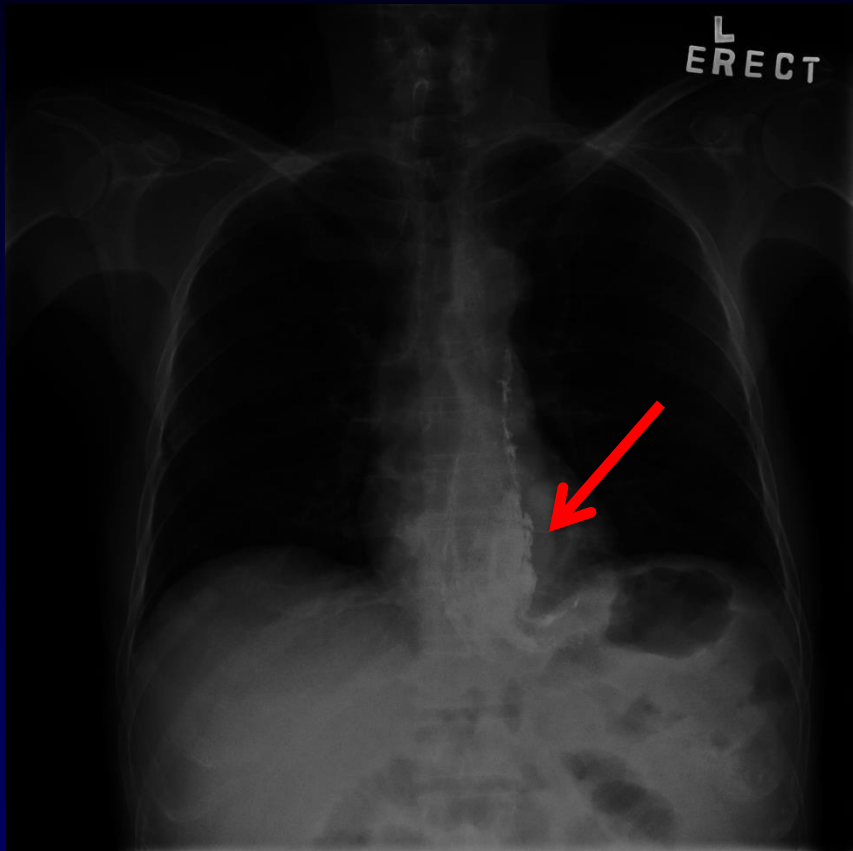
Cyanoacrylate Obturation

- **Tissue adhesive**
 - N-butyl-cyanoacrylate
 - Isobutyl-2-cyanoacrylate
 - Thrombin
- **Acute fundal GV bleeding**
 - Better initial control of bleeding
 - Lower re-bleeding rate



Sarin S et al. Am J Gastro 2002
Lo G et al. Hepatology 2001





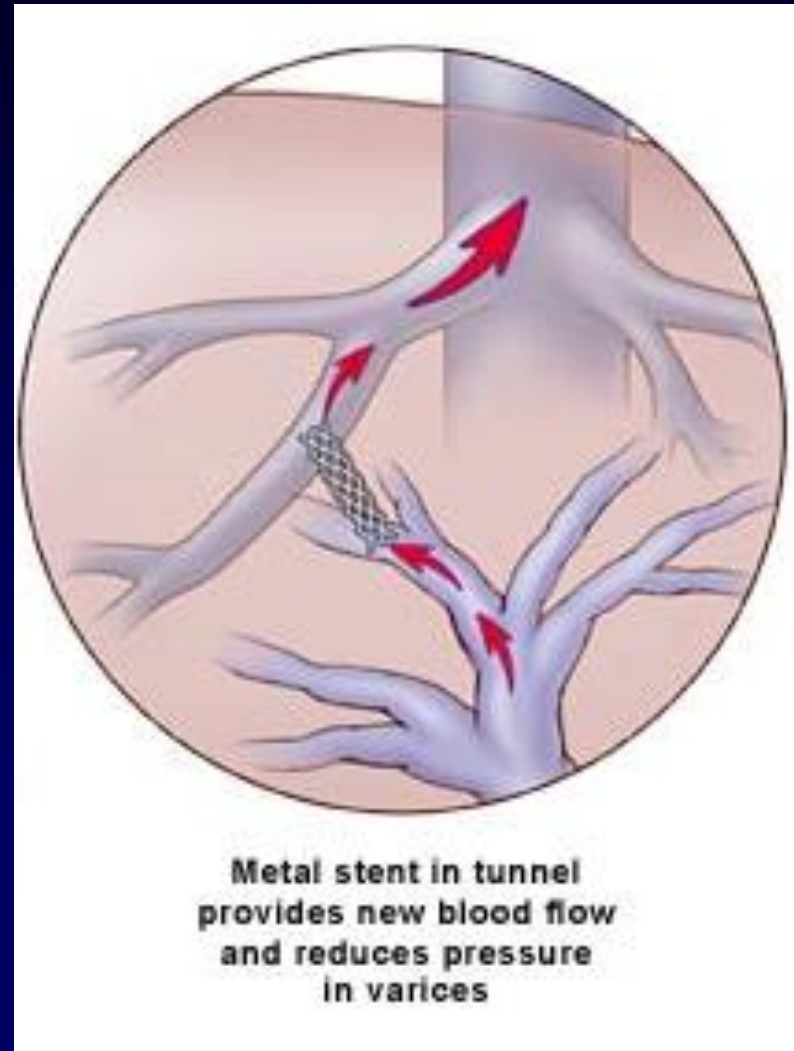
Cyanoacrylate Obturation vs Endoscopic Banding Ligation (EBL)

- **Acute GV bleed:**
 - Similar initial control of bleeding by both
 - Less re-bleeding in the Cyanoacrylate Obturation group (23% vs 47%)



Transjugular Intrahepatic Portosystemic Shunt (TIPS) for GV

- Can be 1st line therapy for uncontrolled GV bleeding if Cyanoacrylate obturation is not available
- Initial hemostasis success ~ 90%



TIPS vs Cyanoacrylate Obturation in Prevention of GV re-bleeding

- **35 patients in TIPS group vs 37 patients in Cyanoacrylate group**
- **Less re-bleeding in TIPS group**
 - 4 TIPS patients (11 %) and 14 cyanoacrylate patients (38 %) ($P = 0.014$)
- **No difference in survival or complication rate**



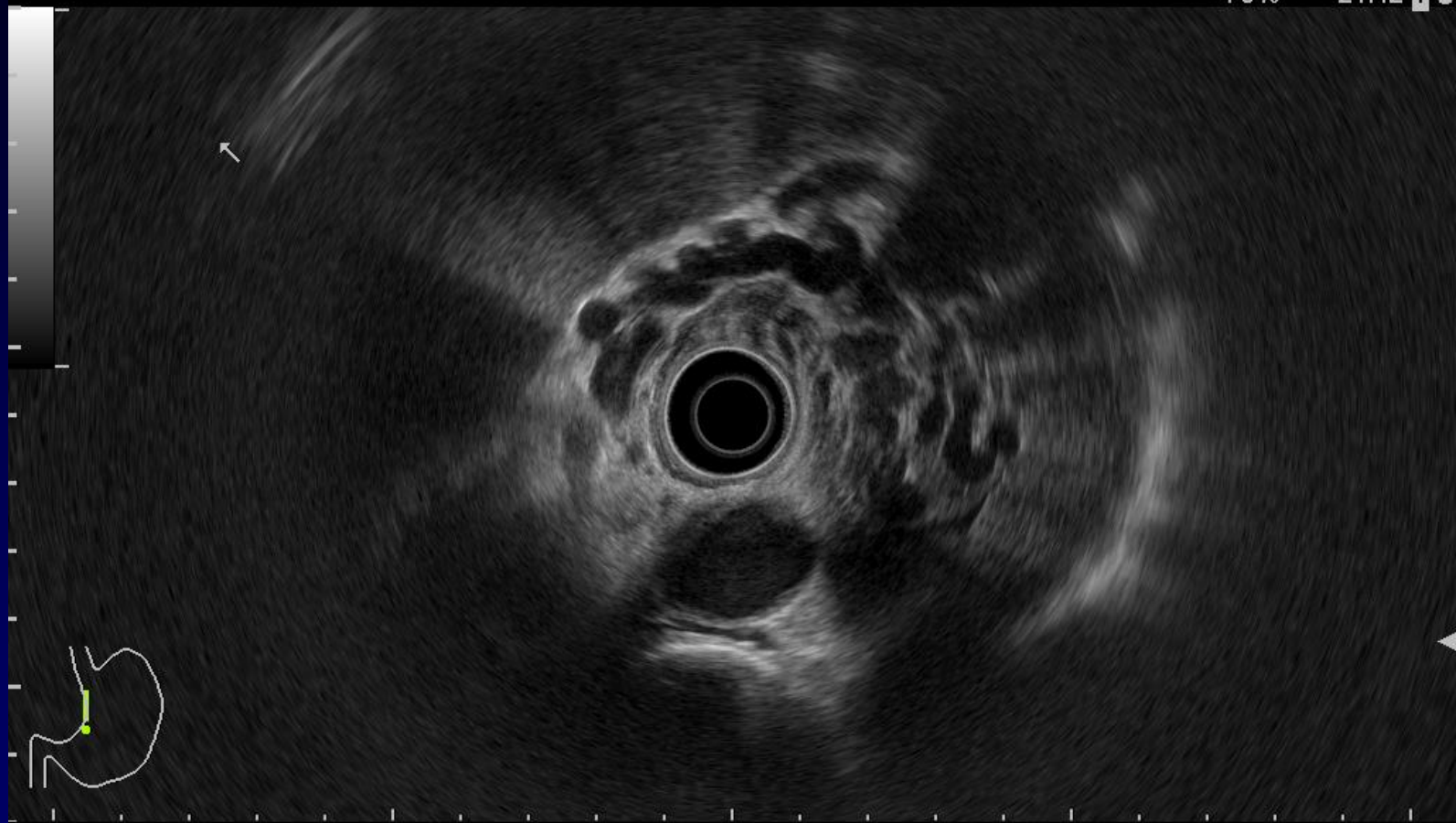
EUS guided Cyanoacrylate Injection

- **Advantages of EUS**

- Allow detection of “deep” varices not seen on luminal view
- Allow treatment of bleeding varix even if luminal view is obscured by blood clot
- Ensure intra-variceal injection
- Allow real-time monitoring of variceal obturation



70% 21Hz 1 ●



7.50M R12.0 G65 D68 A1

49/50

27:Contrast EUS Probe:OLY-R5R1



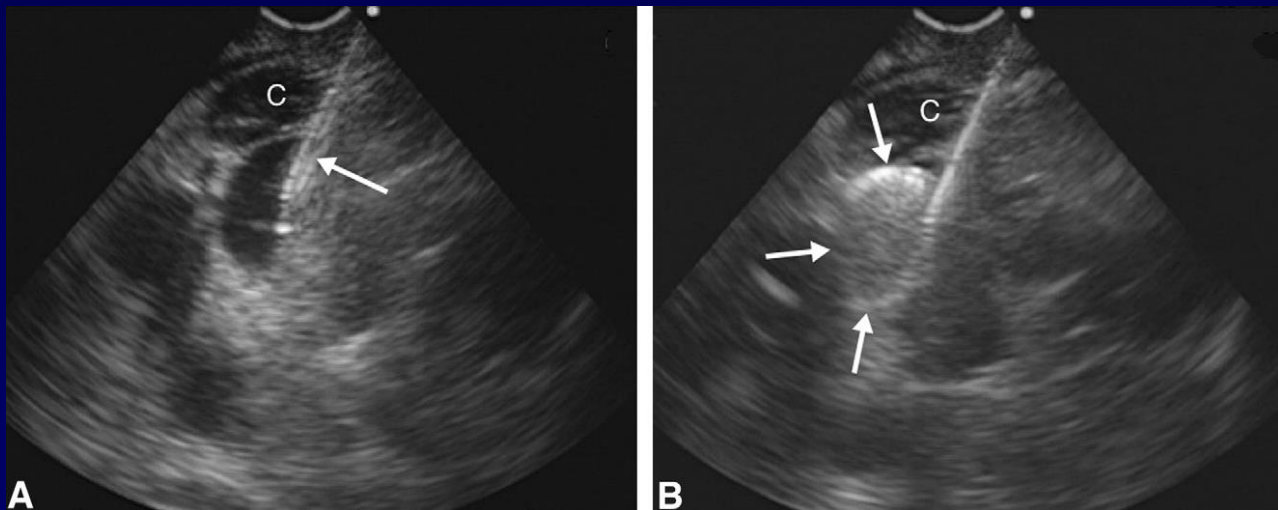
EUS guided Cyanoacrylate Injection

- **Lee YT et al. GIE 2000**
 - 54 patients with GV bleeding treated with biweekly Cyanoacrylate injection under EUS monitoring
 - Less recurrent bleeding compared to “on-demand” Cyanoacrylate injection group
- **Romero-Castro R et al. GIE 2007**
 - 5 patients with GV bleeding successfully treated with EUS-guided FNA needle injection of Cyanoacrylate



EUS guided Cyanoacrylate Injection + Coil Embolization

- **Binmoeller K et al. GIE 2011**
 - 30 patients with fundal GV bleeding
 - Control of acute bleeding 100%
 - 4 patients had re-bleeding from non-variceal source
 - No distant “glue” embolization



GV Bleeding treated with EUS guided Cyanoacrylate Injection

C3465282

Name :

Sex : Age :

D.O.Birth :

17/09/2012

11:23:00

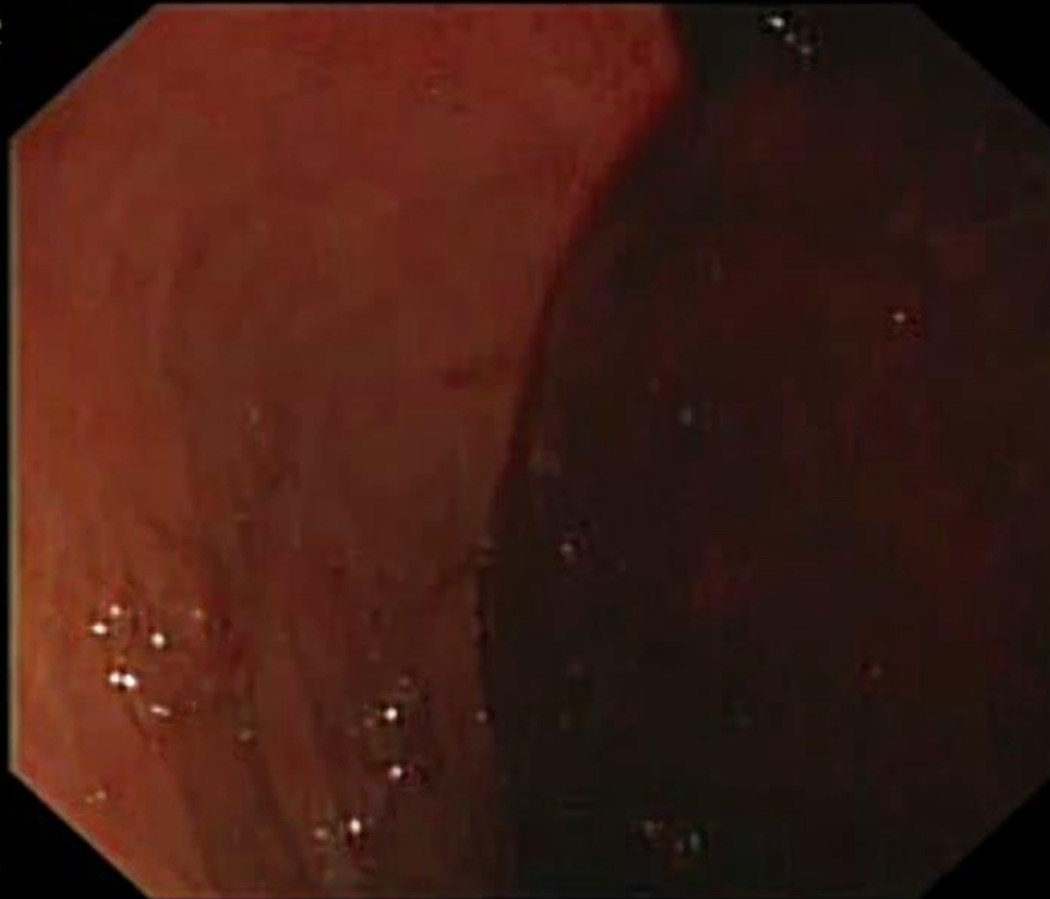
SCV:92

Cr: N Ec: B1

Cr: D Z: 1.0

Physician :

Comment :



Rescue / Alternative Therapy

- TIPS
- Shunt Surgery
- Balloon Tamponade
- Self-Expandable Metal Stents
- Balloon-Occluded Retrograde Transvenous Obliteration
- Liver Transplant



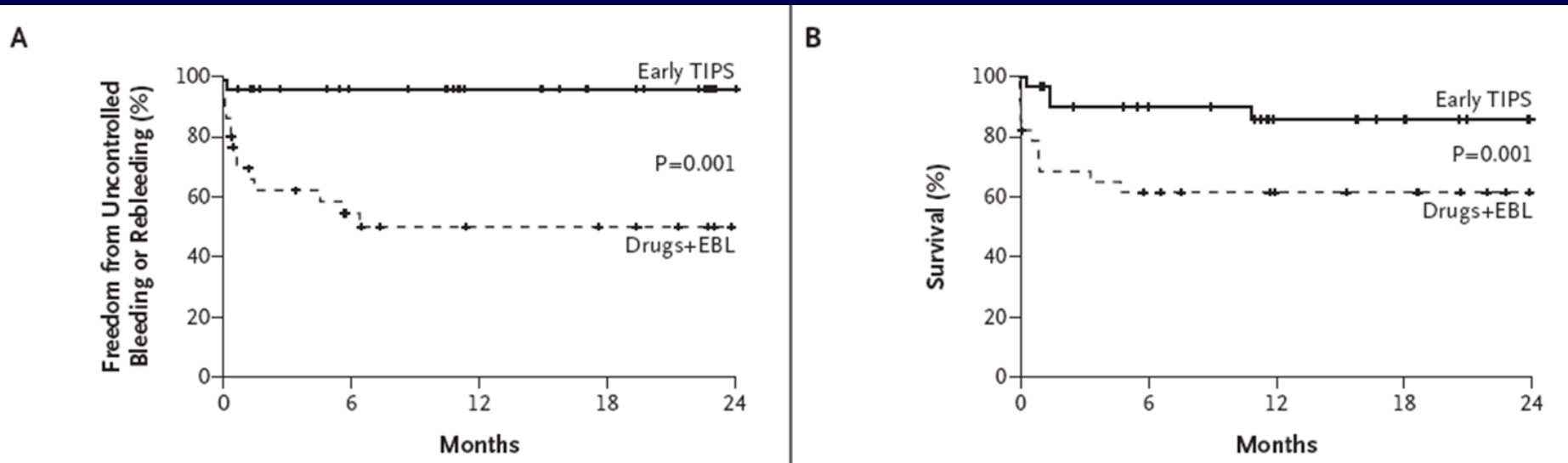
TIPS

- Modern covered TIPS stents usually have longer patency
- Usually a bridge to more definitive therapy (e.g. liver transplant)



? Early Use of TIPS in Variceal Bleeding

- **Garcia-Pagan et al. NEJM 2010**
 - 63 patients with Child's C or Child's B cirrhosis and persistent variceal bleeding
 - Early TIPS (within 72h) vs EBL + B-blocker, after initial treatment with vasoactive drug + endoscopy



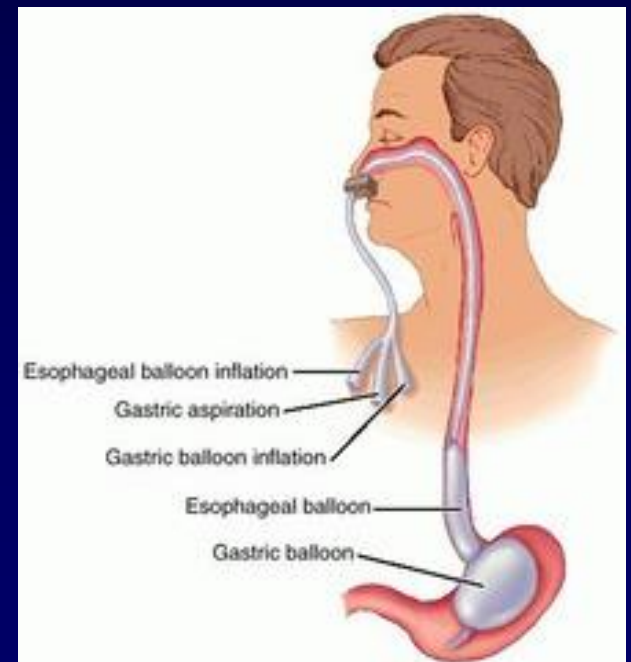
Shunt Surgery

- **Child's A and B cirrhosis with uncontrolled variceal bleeding**
- **Non-cirrhotic portal hypertension related variceal bleeding**
- **Effective in preventing re-bleeding, but higher rates of hepatic encephalopathy**



Balloon Tamponade

- Sengstaken–Blakemore tube
- Minnesota tube
- Linton tube
 - Temporary measure for uncontrolled variceal bleeding
 - Complications:
 - Aspiration, migration, necrosis/ perforation of esophagus



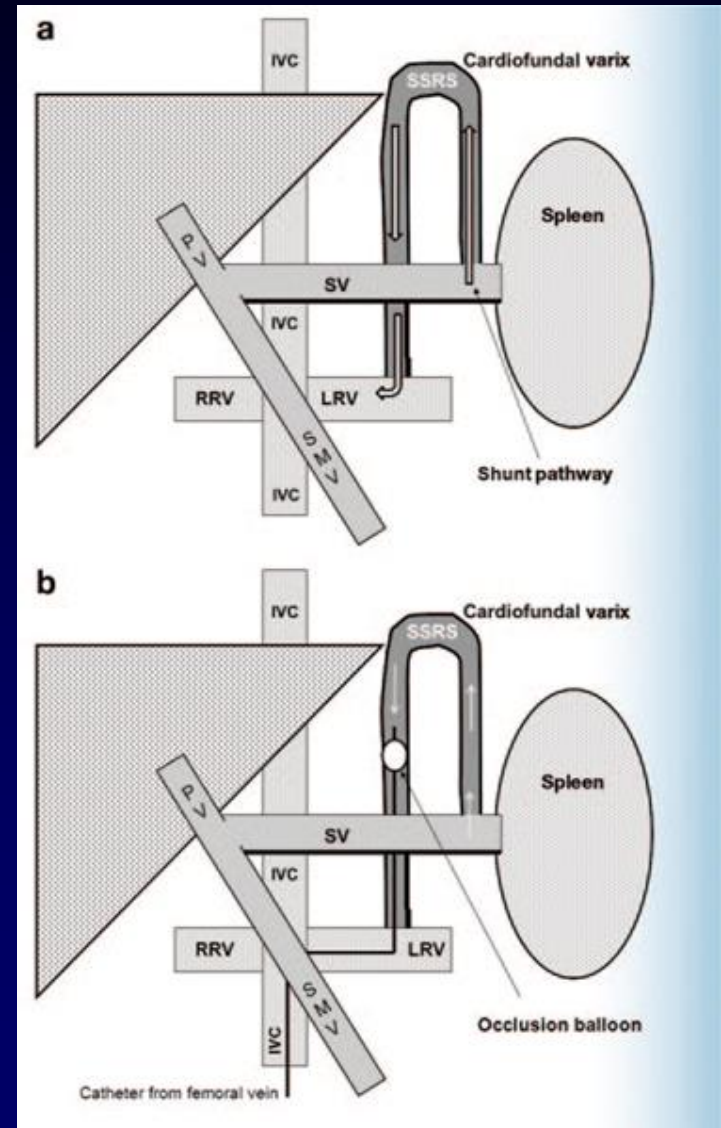
Self-Expandable Metal Stents

- Alternative to Balloon Tamponade or TIPS (contraindications to TIPS) in uncontrolled OV bleeding
- Usually as a temporary measure (removable stents)
- Not very useful for GV bleeding



Balloon-Occluded Retrograde Transvenous Obliteration

- For cardiofundal GV with dominant tributaries from the splenic vein or splenic hilum and terminate in the left renal vein (spontaneous splenorenal or gastrosplenic shunts)
- GV treated with sclerosants
- However, may aggravate OV, ascites



Summary

- **Variceal bleeding is still a major potentially lethal complication of cirrhosis**
- **Early use of vasoactive drugs**
- **Timely endoscopy**
- **Tailor endoscopic therapy to the type of varix**
- **Becoming familiar with benefits and risks of rescue / alternative therapies for uncontrolled variceal bleeding**

