



# Gastrointestinal Bleeding in Patients with Decompensated Cirrhosis

Andrés Cárdenas, MD, MMSc, PhD, AGAF, FAASLD

GI / Liver Unit, Hospital Clinic

Institut de Malalties Digestives i Metabòliques

University of Barcelona, Spain

# CASE

- 56 yr old man - HCV cirrhosis, type 2 diabetes and obesity without prior decompensations.
- Previous large varices on EGD - on nadolol, metformin and low dose aspirin.
- 3 day history of malaise, weakness, melena and one episode of copious hematemesis.
- Admitted to hospital.

## PHYSICAL EXAM

- Alert & oriented X 2
- BP: 79/52, HR 112 bpm, O2 sat 96%
- Pale , clammy extremities
- Heart and lungs – no murmurs , no S3 or gallop, no rales
- Abdomen – non tender, grade 2 ascites, palpable spleen
- Positive flap

## BLOOD TESTS

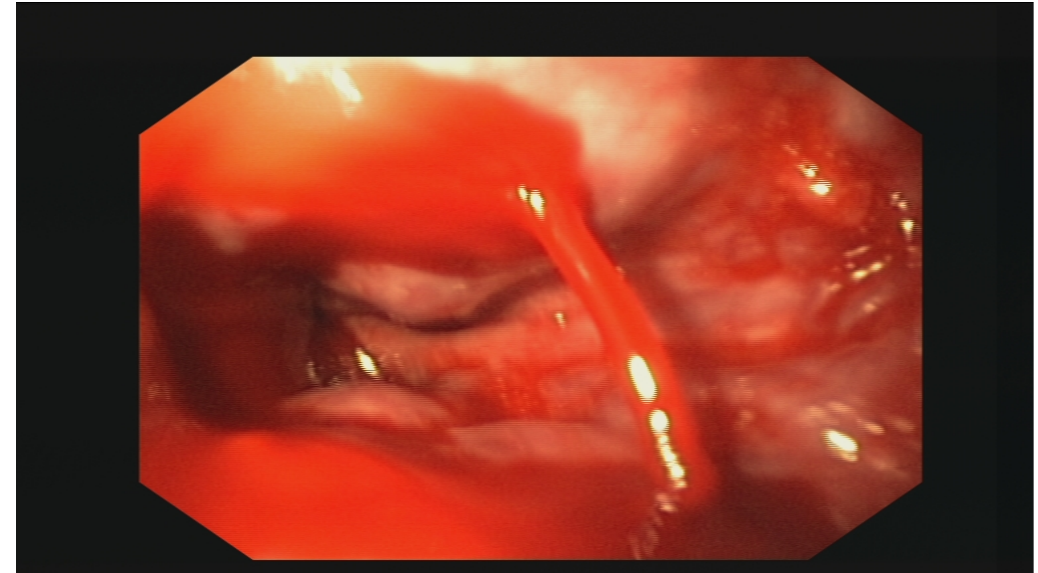
- Hemoglobin 8g/dL
- WBC 5400
- Platelets 165,000, INR 1.8
- Total Bilirubin 3.1 mg/dl
- Serum Creatinine 1.4 mg dl,
- Albumin 3.2 g
- AST 66, ALT 49 IU
- Alk Phosphatase 159 IU
- Serum Sodium 134 mEq/L

Child C

MELD score 23

## Most common causes of upper gastrointestinal bleeding in cirrhosis

1. Esophageal varices
  2. Gastric Varices
  3. Portal Hypertensive Gastropathy
  4. Peptic ulcer disease
  5. Erosive esophagitis
  6. GAVE
  7. AVM's
  8. Malignancy
- } 80-85%



# Acute Variceal Bleeding - 2019 Must Haves

---

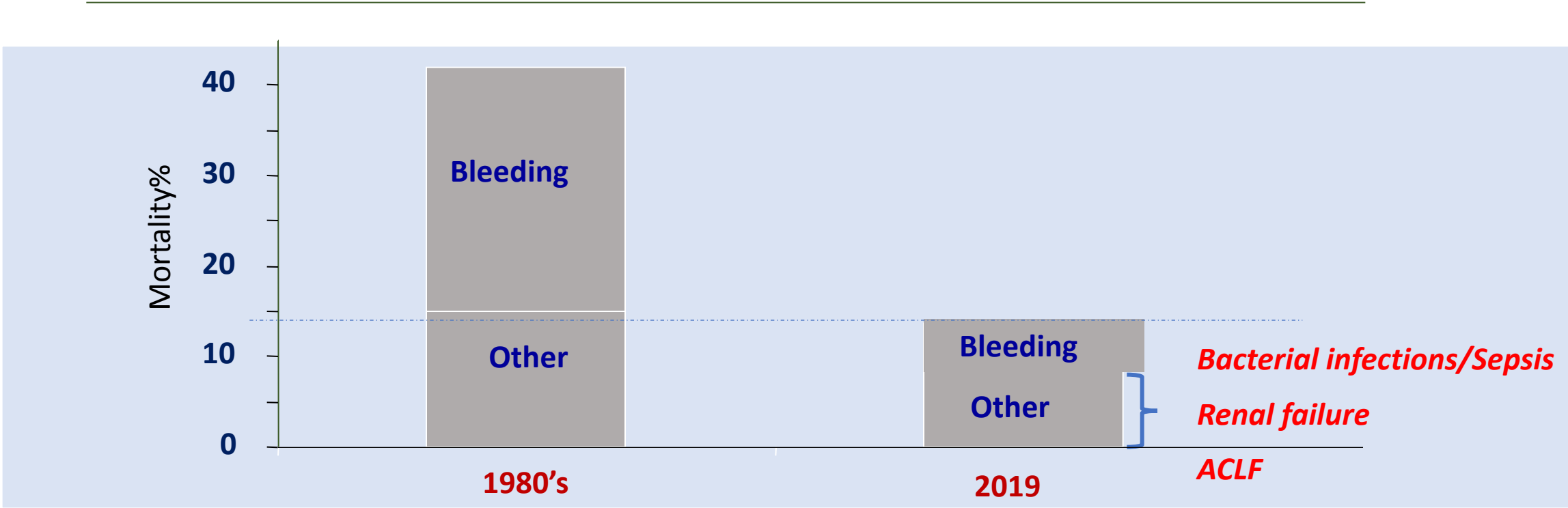
1. ICU or closely monitored setting
2. ABC's – careful volume repletion
3. Intubation (selected cases)
4. I.V. vasoactive therapy
5. Antibiotics
6. Prokinetics
7. Adequate blood transfusion
8. Prompt endoscopic therapy
9. Possibility of tamponade
10. Possibility of TIPS



*AASLD Guidance, Hepatology 2017  
EASL Guidelines 2018*

# Acute Variceal Bleeding

## 6-week mortality



- Protect the liver - Protect the kidney - Prevent infections

*Abraldes et al. J Clin Gastroenterol 2007; 41: S312-317*  
*Conejo I et al. Clin Gastroenterol Hepatol. 2018 Jan;16(1):132-139*

# *Initial Management*

---

- 1. IV access and volume expansion (crystalloids)**
- 2. Prophylactic antibiotics**
- 3. Vasoactive therapy**
4. Do not over-transfuse
5. Avoid shock (prevents acute kidney injury)
6. IV erythromycin 250 mg (30 min before endoscopy)
7. Avoid the systematic and long-term use of PPI's (i.e omeprazole)
8. Consider intubation
9. No recommendation in regards to coagulopathy
10. Stratify patient- (identify those that will re-bleed)

# Effect of erythromycin before endoscopy in patients with variceal bleeding: a prospective, randomized, double-blind, placebo-controlled trial

**TABLE 3. Effects of erythromycin and placebo in the study population**

Variables	Erythromycin	Placebo	P value
No. of patients	47	43	
Empty stomach, no. (%)	23 (48.9)	10 (23.3)	<.012
Endoscopic score, mean (SD)	12.5 (3.6)	9.8 (4.2)	<.05
Endoscopy duration, min, mean (SD)	19.0 (9.8)	26.0 (13.4)	<.005
Hospital stay, d, mean (SD)	3.4 (2.4)	5.1 (2.9)	<.002
No. of units of blood transfused in 24 h, mean (SD)	3.0 (1.8)	3.6 (2.8)	.64
Transfusion of PRBCs, no. (%) of patients	12 (25.5)	11 (25.6)	.99
Second-look endoscopy, no. (%)	2 (4.3)	4 (9.3)	.33
Aspiration pneumonia, no. (%)	0.0	2 (4.7)	.23
In-hospital mortality, no. (%)	4 (8.5)	6 (13.9)	.41

PRBCs, Packed red blood cells; SD, standard deviation.



# Orotracheal Intubation?

*No clear guidelines*

---

## Pros

- Protects airway
- Can administer deep sedation
- Can take longer with the procedure
- May extubate right after

## Cons

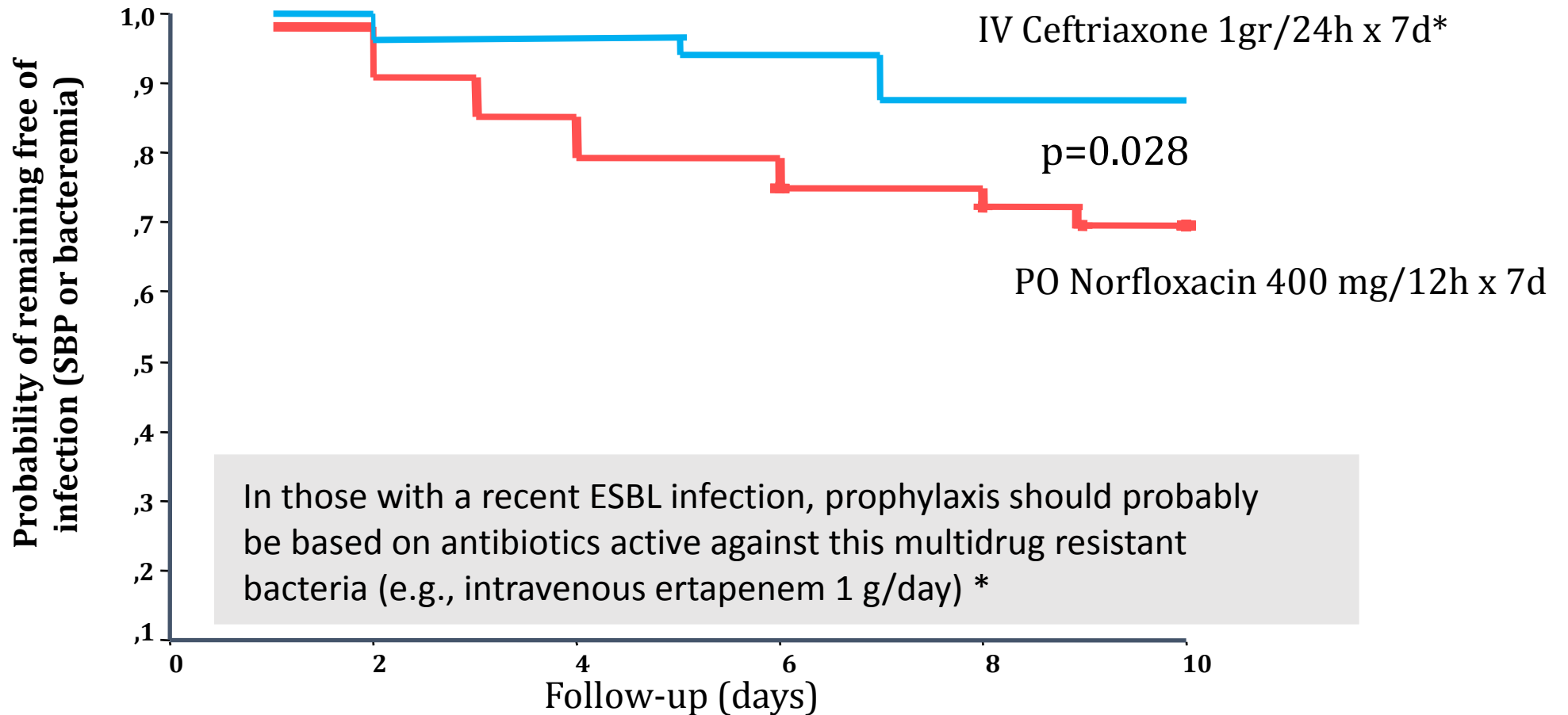
- Increase rate of cardiopulmonary unplanned events (pneumonia)
- May worsen outcome
- Can cause trauma / more bleeding
- No good data to support intubation

*Massive hematemesis or obtunded patient: intubate for procedure*

*Dig Dis Sci. 2007  
Gastrointest Endosc. 2003  
BAVENO VI. 2015  
Gastrointest Endosc 2017*

# Antibiotic prophylaxis in AVB & advanced cirrhosis

(malnutrition, Bili>3, Ascites, HE, massive bleed)



# Prospective, multicenter, randomized, noninferiority trial – Terlipressin, Somatostatin, and Octreotide in AVB

*n= 780 patients (all with EBL)- randomized to 3 groups*

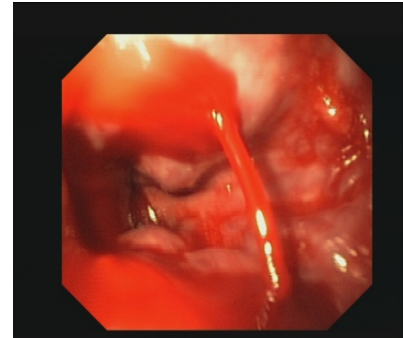
Treatment Response	All Patients (n = 780)	Terlipressin Group (n = 261)	Somatostatin Group (n = 259)	Octreotide Group (n = 260)	P Value
Control of index bleeding without rescue therapy, n (%)	690 (88.5)	234 (89.7)	227 (87.6)	229 (88.1)	0.752
Time interval from T0 to bleeding control, hours	9.8 ± 10.3	9.6 ± 10.7	10.1 ± 10.1	9.7 ± 10.2	0.839
Time interval from commencement of vasoactive drug to bleeding control, hours	8.0 ± 10.3	7.8 ± 10.6	8.2 ± 10.1	8.1 ± 10.3	0.899
Patients with rebleeding, n (%)*	29 (4.2)	8 (3.4)	11 (4.8)	10 (4.4)	0.739
Time interval from T0 to rebleeding, hours <sup>†</sup>	66.8 ± 23.6	70.0 ± 27.5	69.0 ± 19.6	61.9 ± 26.0	0.730
Time interval from bleeding control to rebleeding, hours <sup>†</sup>	62.1 ± 24.4	64.7 ± 26.4	64.2 ± 22.4	57.9 ± 26.8	0.801
Mortality, n (%)	67 (8.6)	21 (8.0)	23 (8.9)	23 (8.8)	0.929
Cause of mortality					0.920
Uncontrolled index bleeding, n (%)***	60 (89.6)	19 (90.5)	20 (87.0)	21 (91.3)	
Uncontrolled rebleeding, n (%) <sup>‡</sup>	2 (3.0)	1 (4.8)	1 (4.3)	0 (0)	
Liver failure, n (%) <sup>‡</sup>	3 (4.5)	1 (4.8)	1 (4.3)	1 (4.3)	
Infection, n (%) <sup>‡</sup>	2 (3.0)	0 (0)	1 (4.3)	1 (4.3)	
5-day treatment success, n (%)	659 (84.5)	225 (86.2)	216 (83.4)	218 (83.8)	0.636

# Endoscopy

*Allows diagnosis and therapy*

---

- When?
  - At least within the first 12 hours of admission.
  - Actively vomiting blood ? As soon as safely possible
- Diagnosis ?
  - Active blood spurting or oozing from a varix
  - White nipple or clot adherent to a varix
  - Varices without other potential sources of bleeding

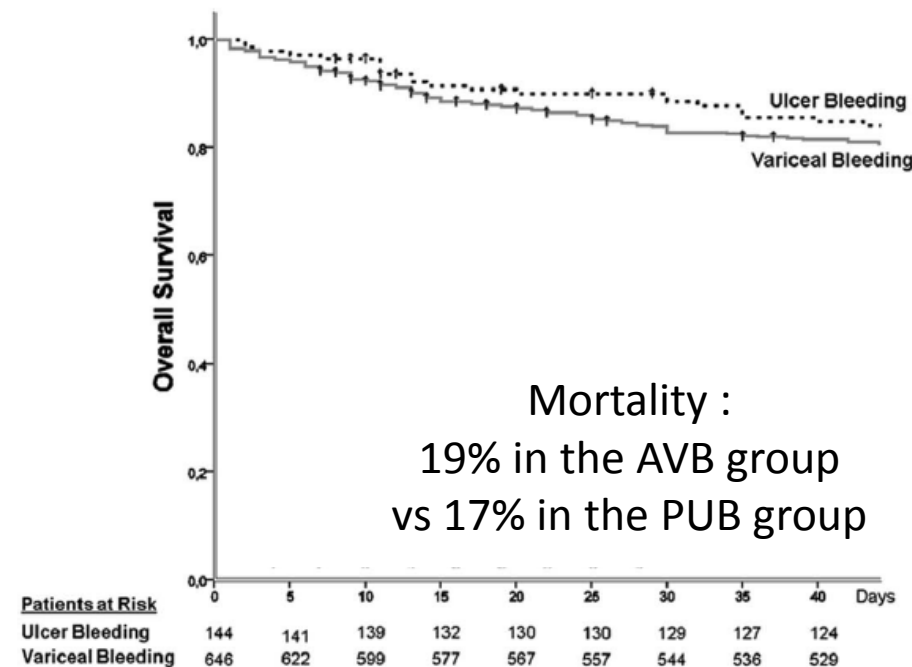


*Chen, et al J Hepatol 2012 Dec;57(6):1207-13.  
Cardenas Clin Liv Dis 2014  
Baveno VI J Hepatol 2015  
Garcia-Tsao, et al, AASLD Guidance 2017*

# Peptic Ulcer Bleeding in Patients With Cirrhosis

- Multicenter study of 646 patients with AVB and 144 patients with PUB.
- Child-Pugh and MELD similar between both.
- Rebleeding rate : **26% in AVB vs. 10% in PUB**
- Less than 3% in both groups died of uncontrolled bleeding.
- The causes of death were usually related to hepatic failure or comorbidities.

*Up to 20% of cases of UGIB in cirrhosis.*



# 6-week re-bleeding and survival stratified by hematemesis and door-to-endoscopy time (hrs).

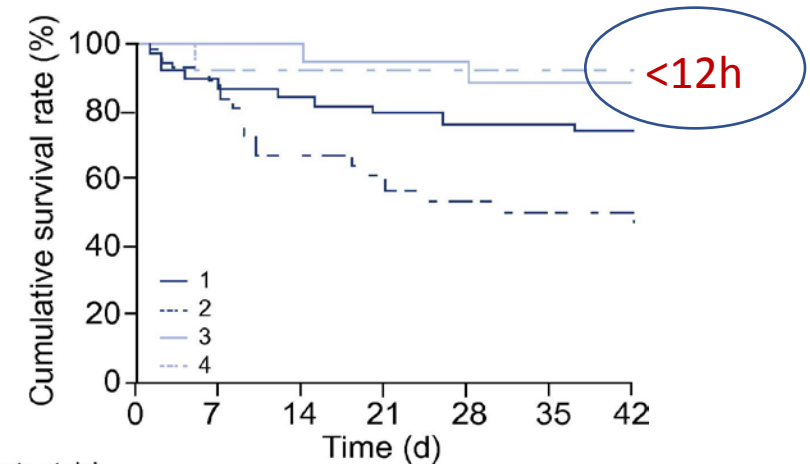
6-week re-bleeding

<12h

6-week survival

**B**

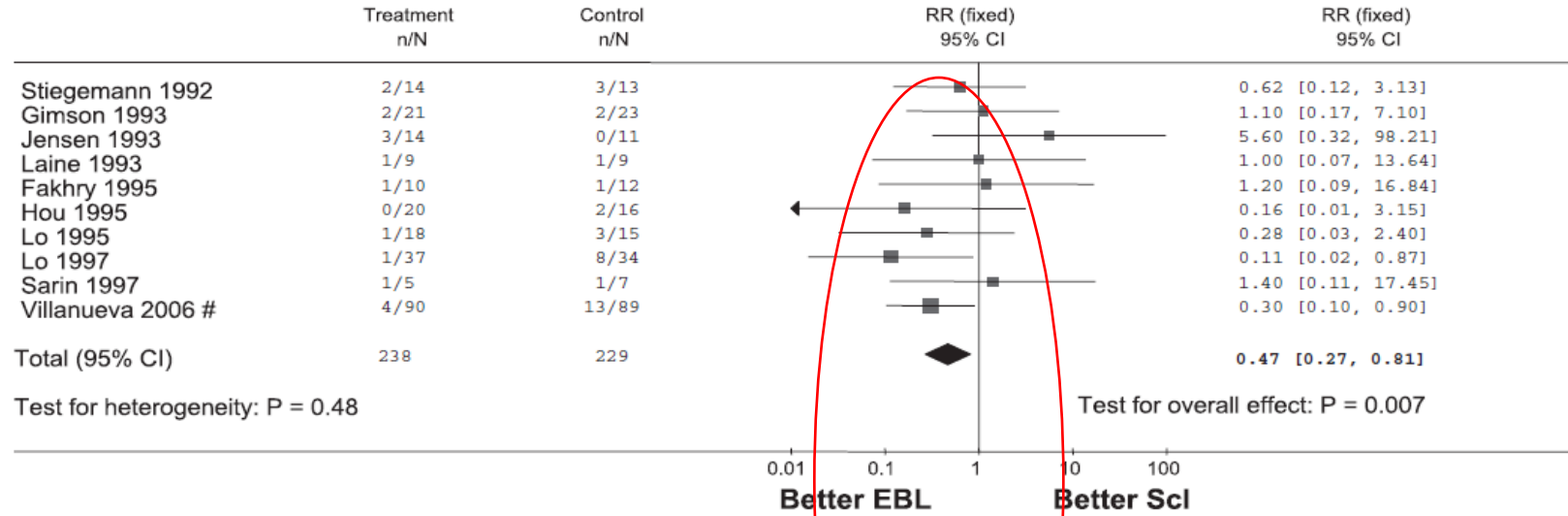
Log rank test	
	<i>p</i> value
1 vs. 2	0.031
1 vs. 3	0.203
1 vs. 4	0.238
2 vs. 3	0.005
2 vs. 4	0.022
3 vs. 4	0.861



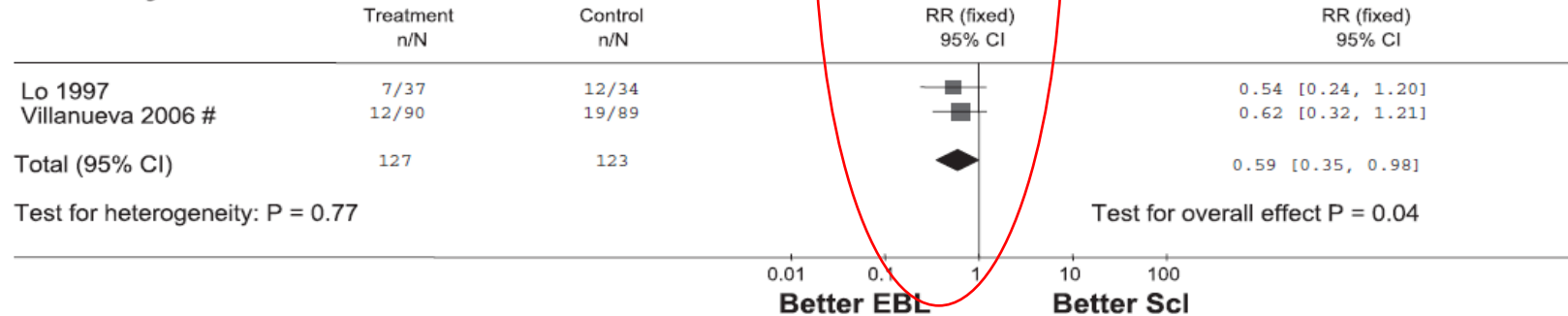
		Patients at risk						
		0	7	14	21	28	35	42
1	Hematemesis + ≤12 h (—)	37	32	31	29	28	28	27
2	Hematemesis + >12 h (···)	36	30	24	20	19	18	16
3	Non-hematemesis + ≤12 h (---)	17	17	16	16	15	15	15
4	Non-hematemesis + >12 h (-·-·)	11	10	10	10	10	10	10

# Endoscopic therapy AVB - Meta-analysis of ligation vs sclerotherapy

## Initial Control of Bleeding



## Mortality

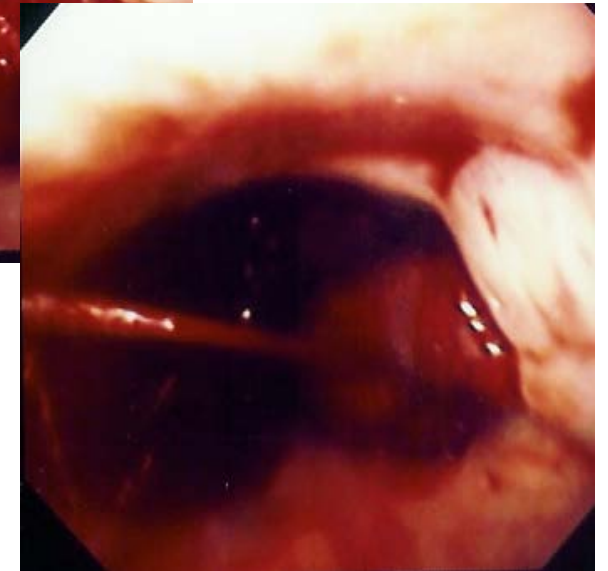
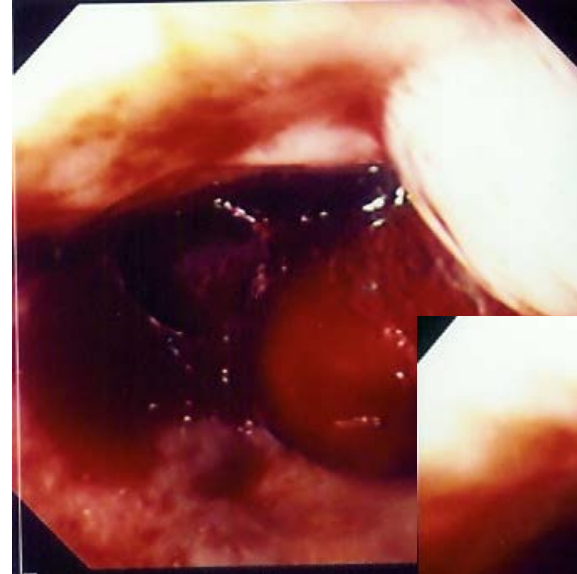


# Refractory bleeding

*The time frame for AVB is 5 days*

---

- In 10-15 % of cases, patients are not controlled with therapy
- There are two types:
  - Patients bleed profusely despite EBL
  - Fresh hematemesis >2 hr after therapy, hypovolemic shock, or 3 g drop in Hb
- Left untreated mortality rates > 50%
- Several approaches
  - *Repeat EGD*
  - *Tamponade (balloon or stent)*
  - *TIPS*



*Baveno V J Hepatol 2010/2015  
D'Amico M, et al Clin Liver Dis. 2010  
Ibrahim. Gastroenterology. 2018*

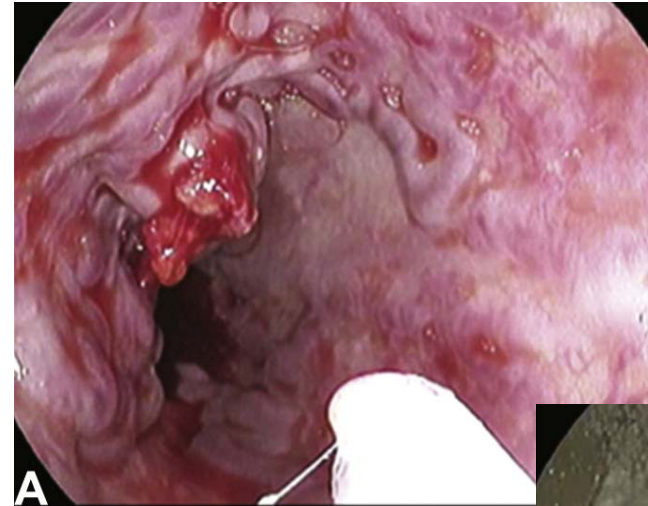


# Hemospray

*Acute bleeding and/or post EBL ulcers*

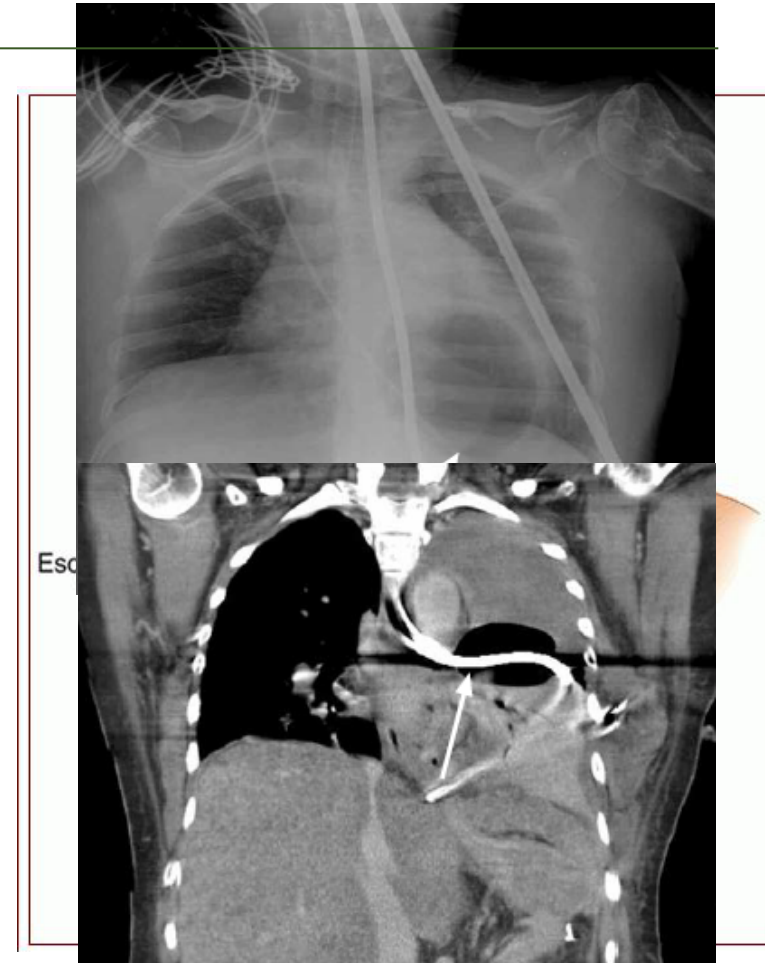
---

- Hemostatic powder
  - Easy to apply , forms cohesive barrier, non-contact method,
- No controlled studies
- Case reports :
  - Successfully stopped bleeding in all after 1 attempt
- Follow-up requires EBL or TIPS



# Tamponade

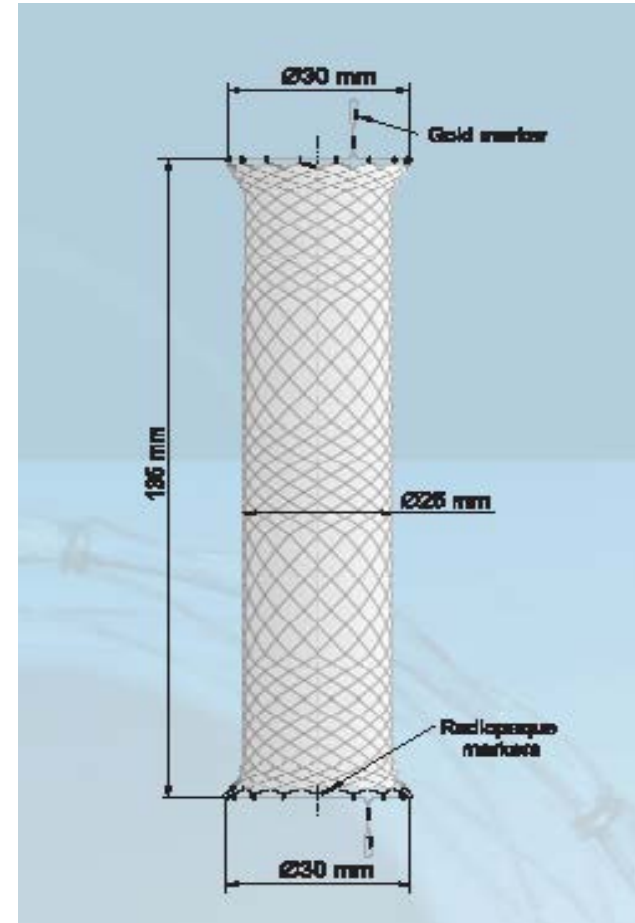
- Ballon tamponade
  - Inflate gastric balloon first
  - Esophageal balloon ( if bleeding perisists)
  - Intubation required
- Temporary “bridge” (for a maximum of 24 -48 h)
- Beware of complications!
  - Perforation ~ 5-10%
  - Aspiration neumonia ~25 -35%
  - Ulcers / necrosis ~ 10 -15%



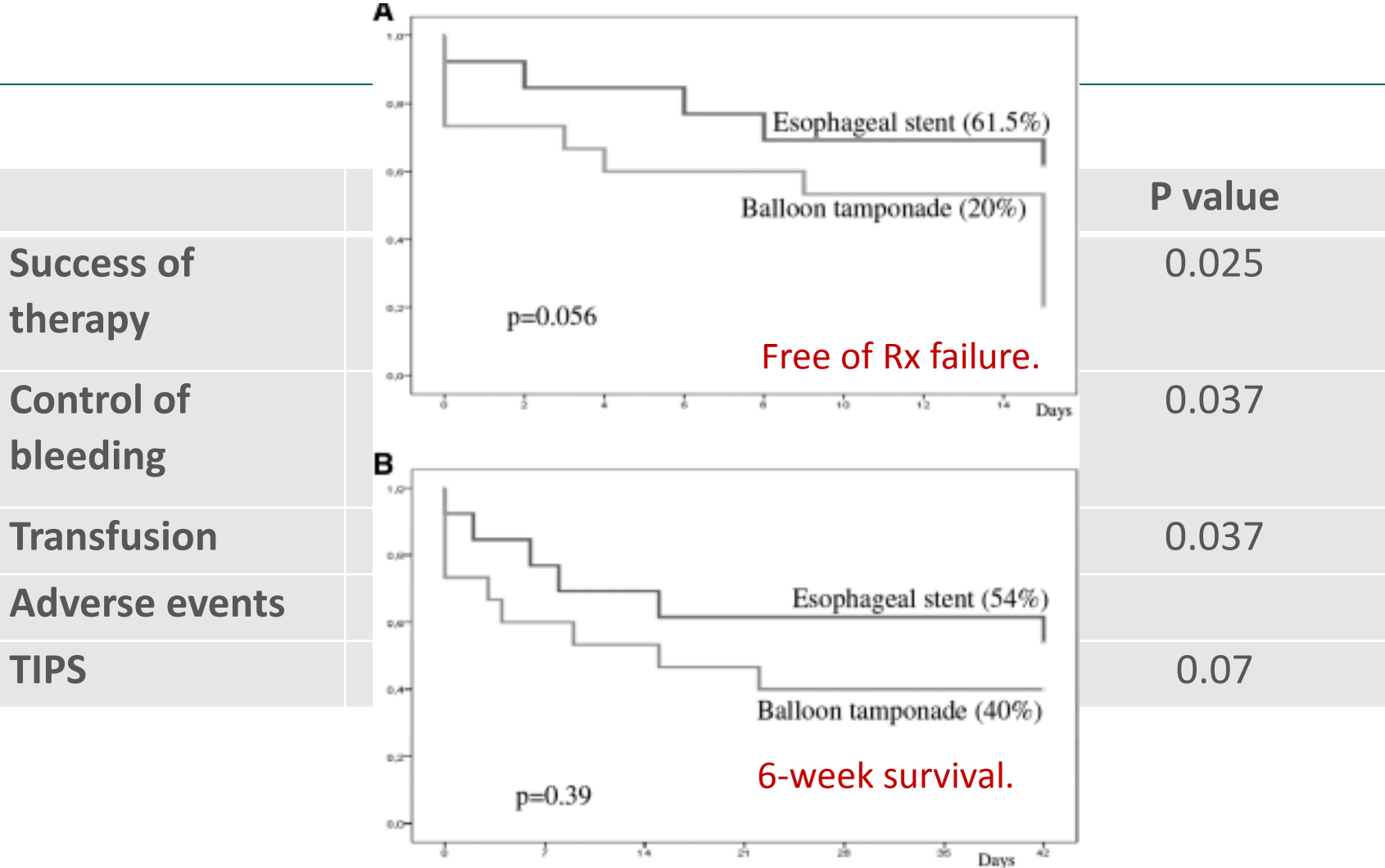
# Fully covered expandable esophageal metallic stents

- Easily implanted
- With or without endoscopy
- Direct compression of varices
- Non-traumatic edges
- Highly effective and safe
- Oral intake soon afterwards
- Remove after 7 days
- **BRIDGE TO TIPS OR LT**

*Rodrigues, Cardenas, Escorsell, Bosch. Semin Liv Dis 2019*



# Self-Expandable Esophageal Metal Stent vs Balloon Tamponade in Esophageal Variceal Bleeding Refractory to Medical and Endoscopic Treatment: A Multicenter RCT



# Rescue TIPS in Treatment Failures

Author	N pts	% Pugh's C	Immediate control (%)	Previous endoscopic therapy	% rebleeding	Interval of rebleeding (days)	Site of rebleeding <sup>a</sup>	Mortality (%)
LaBerge et al. [3]	32	NG	97	Sclerotherapy	NG	NG	NG	NG
Haag et al. [4]	19	68	100	NG	11	10	SU	26 (30 days)
Helton et al. [5]	23	78	NG	Sclerotherapy	NG	NG	NG	56 (in hospital)
Le Moine et al. [6]	4	NG	NG	Sclerotherapy	NG	NG	NG	75 (30 days)
Rubin et al. [7]	12	NG	75	Sclerotherapy Band ligation	NG	NG	NG	NG
Jalan et al. [8]	19	68	100	Sclerotherapy	15.6	30	V-SU	42 (30 days)
Jabbour et al. [9]	25	48	96	Sclerotherapy	NG	NG	V-SU-DU	44 (30 days)
Sanyal et al. [10]	30	73	100	Sclerotherapy	7	14	V-GU	40 (6 weeks)
Perarnau [11]	48	56	92	Sclerotherapy	8.5	NG	NG	25 (30 days)
Banares et al. [12]	56	41	95	Sclerotherapy	14	30	V	15 (30 days)
Gerbes et al. [13]	11	64	91	Sclerotherapy Band ligation	27	14	NG	27 (30 days)
Chau et al. [2] <sup>b</sup>	112	71	96	Sclerotherapy	13 EV 14 GV	7	EV-GV-SU	37 (30 days) EV 34 GV 42
Barange et al. [14] <sup>c</sup>	32	47	90	Sclerotherapy	14		NG	25 (30 days)
Bizollon et al. [15]	28	61	96	Sclerotherapy Band ligation	8	14	V-SU	25 (40 days)
Azoulay et al. [1]	58	81	90	Sclerotherapy	6	14	V-GU	29 (30 days)

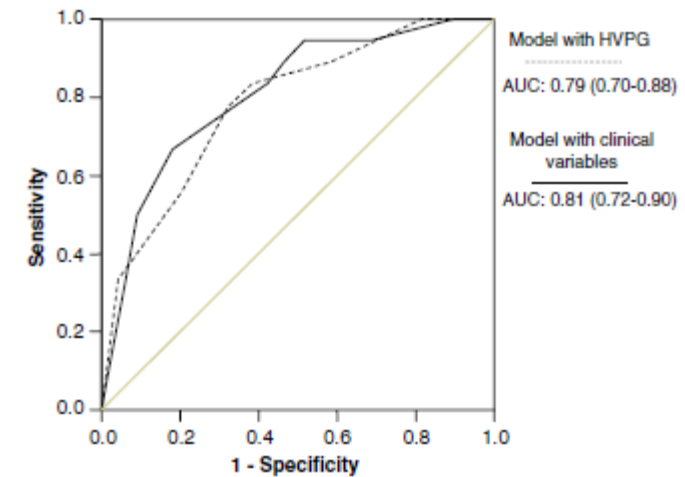
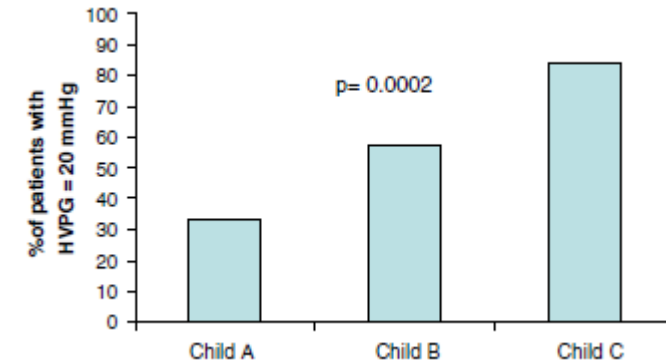
Should high risk patients have a *preemptive* TIPS?

# High Risk Criteria for therapeutic failure- Stratification

- 117 patients with AVB in whom HVPG was measured within 48 h of admission
- Multivariate analysis identified three variables independently associated with 5-day failure:

Multivariable models for 5-day failure

	OR (90% CI)
<b>Model with all variables</b>	
HVPG $\geq 20$ mm Hg	5.44 (1.67–17.69)
Systolic blood pressure $<100$	4.94 (1.88–13.02)
Non-alcoholic etiology	4.96 (1.73–14.27)
<b>Model excluding HVPG</b>	
Child class	
Child B vs A	6.41 (1.01–40.75)
Child C vs A	17.61 (2.37–130.89)
Systolic blood pressure $<100$	5.54 (2.03–15.17)
Non-alcoholic etiology	6.66 (2.00–22.17)

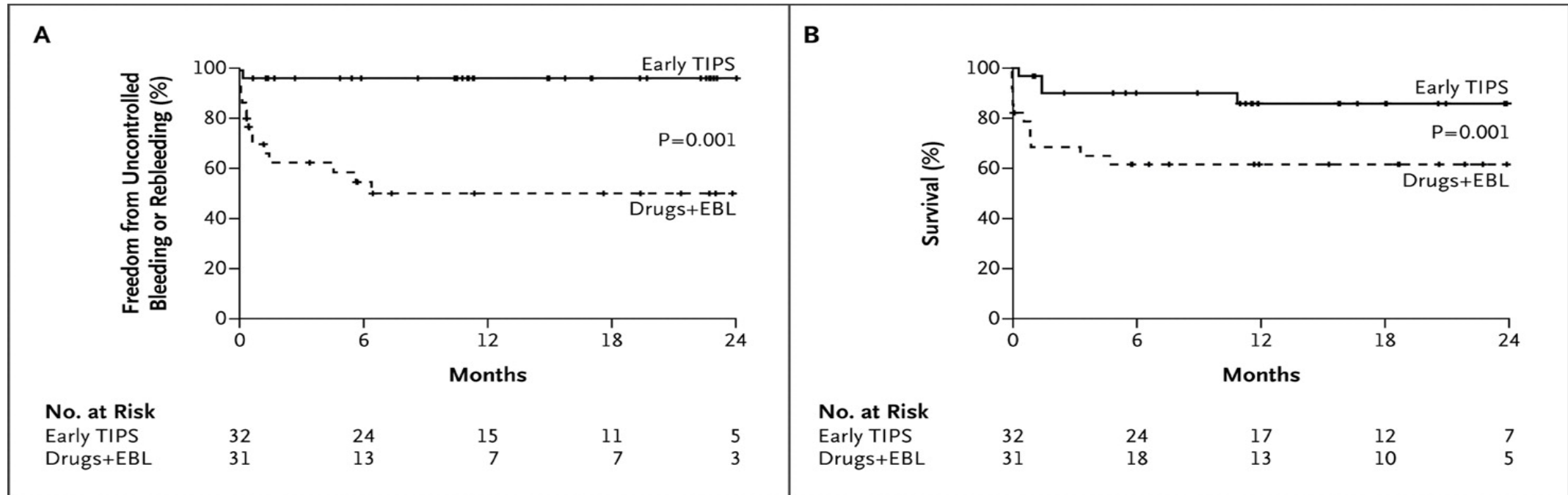


# Multicenter RCT of Early TIPS (1<sup>st</sup> 72 hrs) vs Band Ligation In Patients with Acute Variceal Bleeding

(Child B with active bleed and Child C ≤ 13)

Primary end-point

Survival

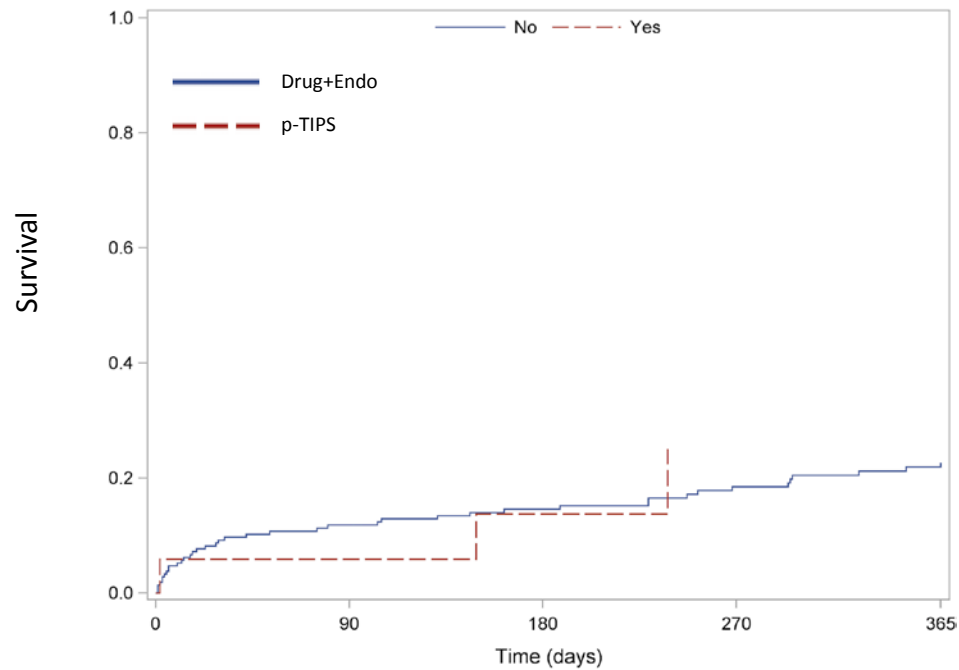


# Preemptive-TIPS improves outcome in high-risk variceal bleeding: (Propensity score matched analysis)

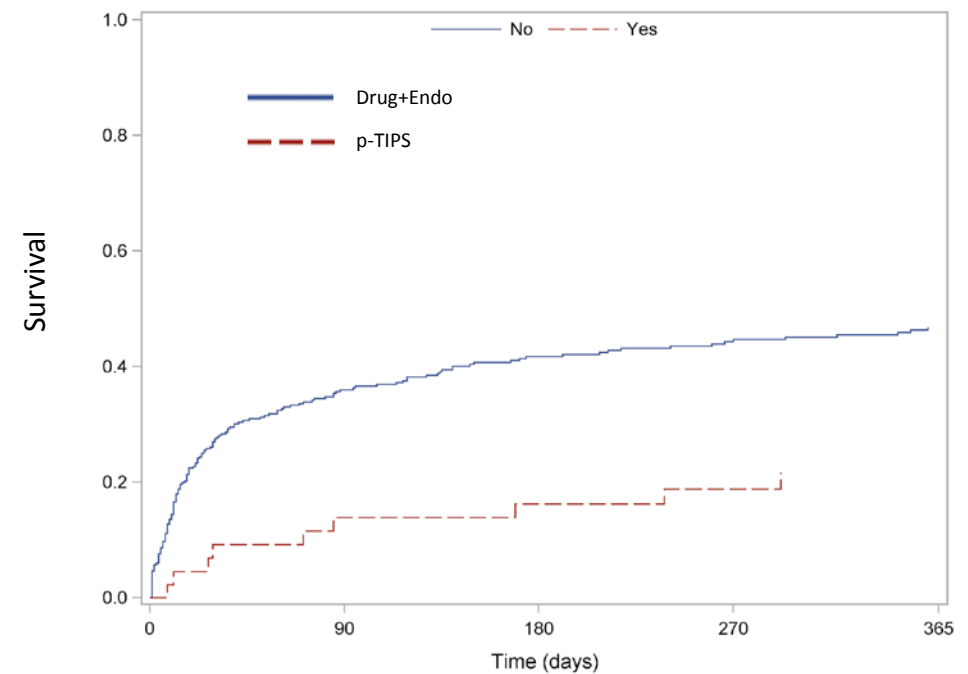
Multicenter, international study in 34 centers ( April 2013 – 2015 )

66 Early TIPS vs 605 Drugs and EBL

Child-Pugh B + Active Bleeding



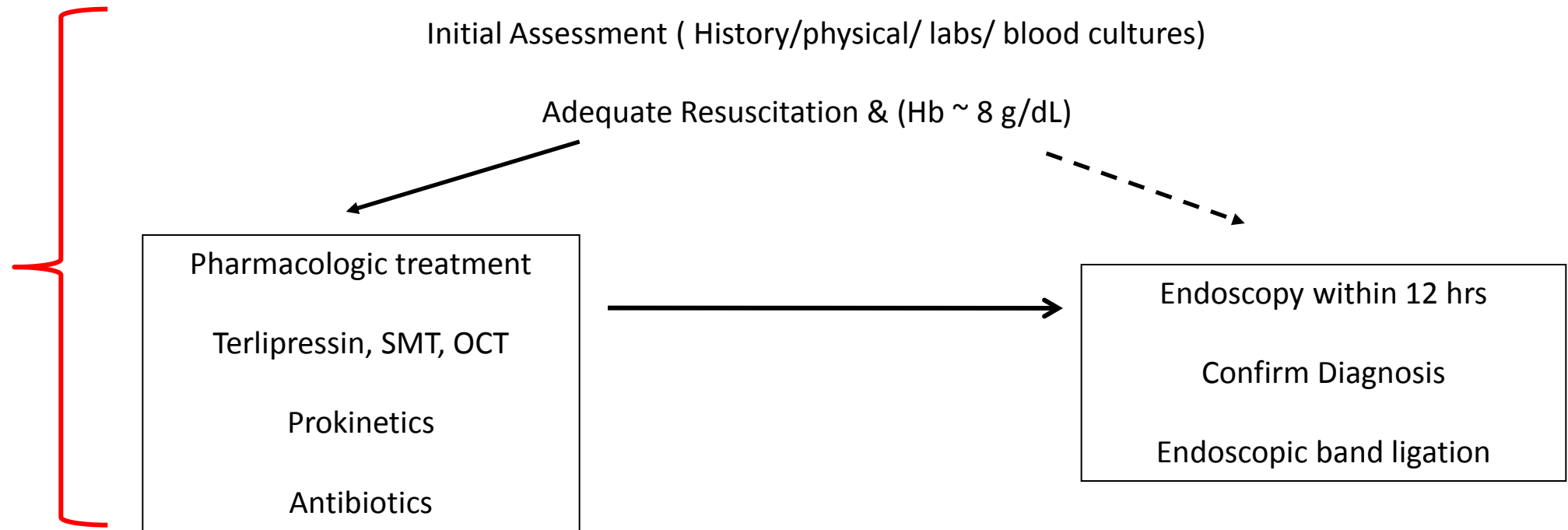
Child-Pugh C





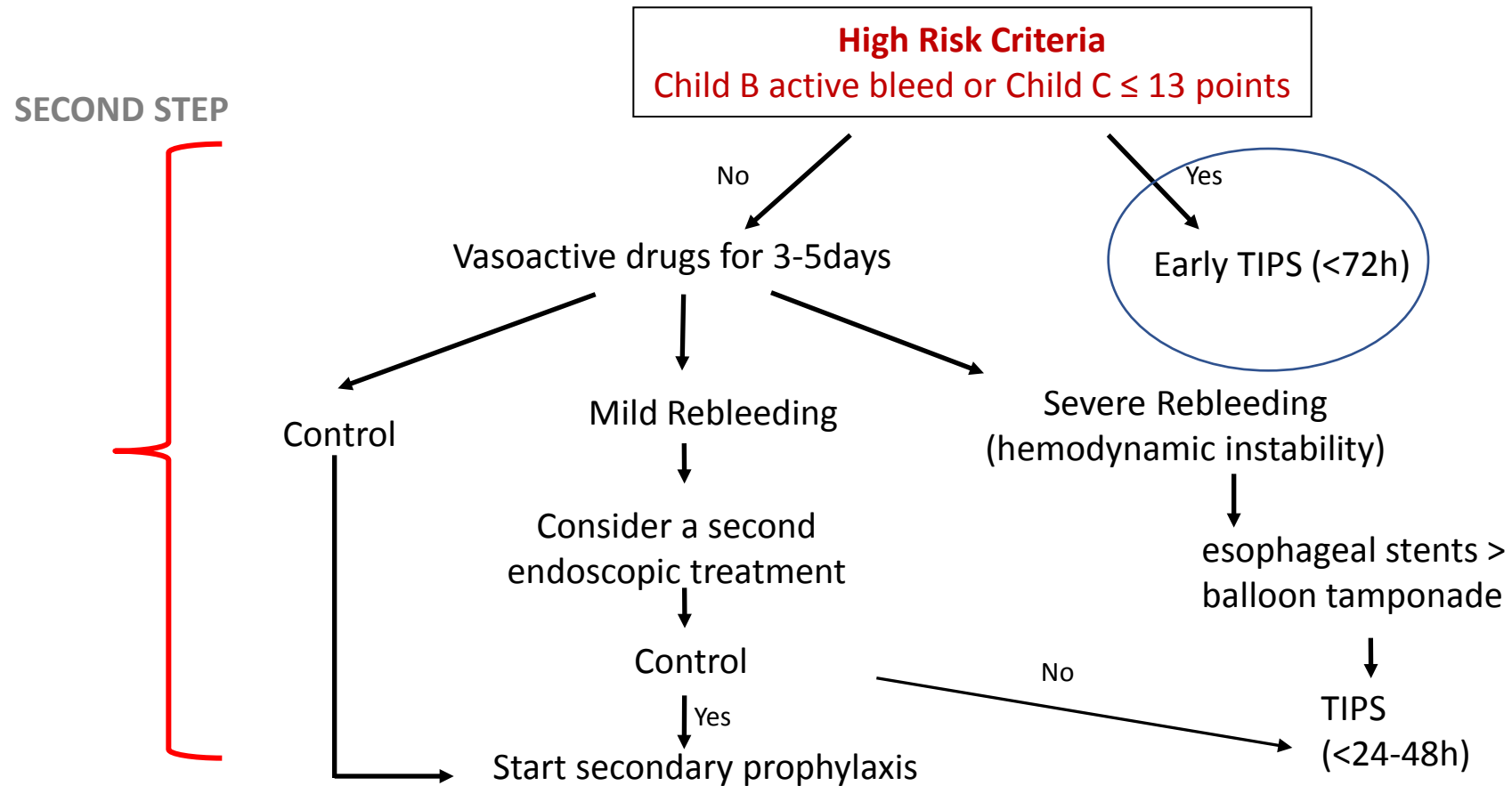
## TAKE AWAY POINTS - ACUTE VARICEAL BLEEDING IN CIRRHOSIS

FIRST STEP



*AASLD Guidance, Hepatology 2017  
EASL Guidelines, J Hepatol 2018*

## TAKE AWAY POINTS - ACUTE VARICEAL BLEEDING IN CIRRHOSIS



*AASLD Guidance, Hepatology 2017  
EASL Guidelines, J Hepatol 2018*

# Acknowledgements

- **Mentors**

- ***Boston:***

- Nezam Afdhal
- J Thomas Lamont

- ***Barcelona:***

- Pere Gines
- Vicente Arroyo

- **Hepatic Hemodynamic Unit**

- Juan Carlos Garcia-Pagan
- Virginia Hernandez-Gea
- Anna Baiges
- Fanny Turón
- Jaime Bosch

- **Liver Intensive Care Unit**

- Angels Escorsell
- Enric Reverter
- Javier Fernandez