Overview of the Clinical Manifestations of Cirrhosis

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Singapore Hepatology Conference

Preceptorship Programme

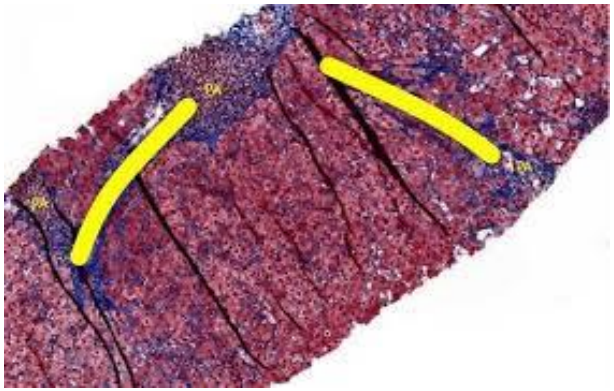
25th May 2021

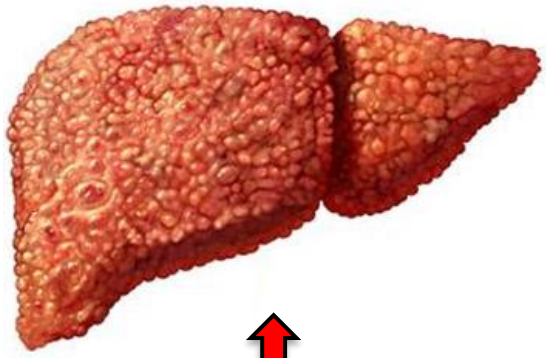
Disclosures

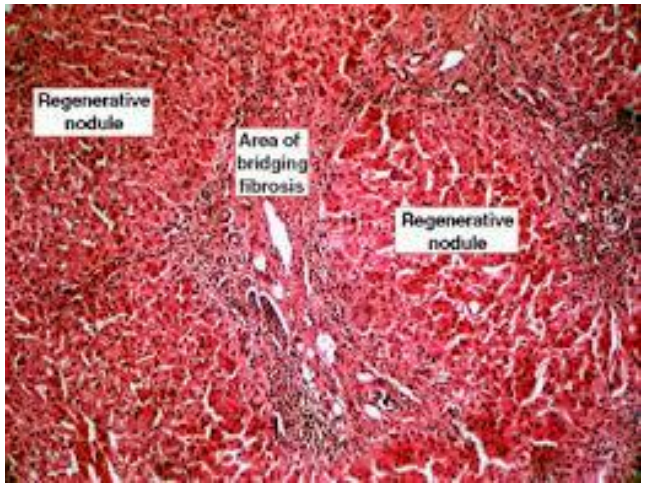
- No disclosures

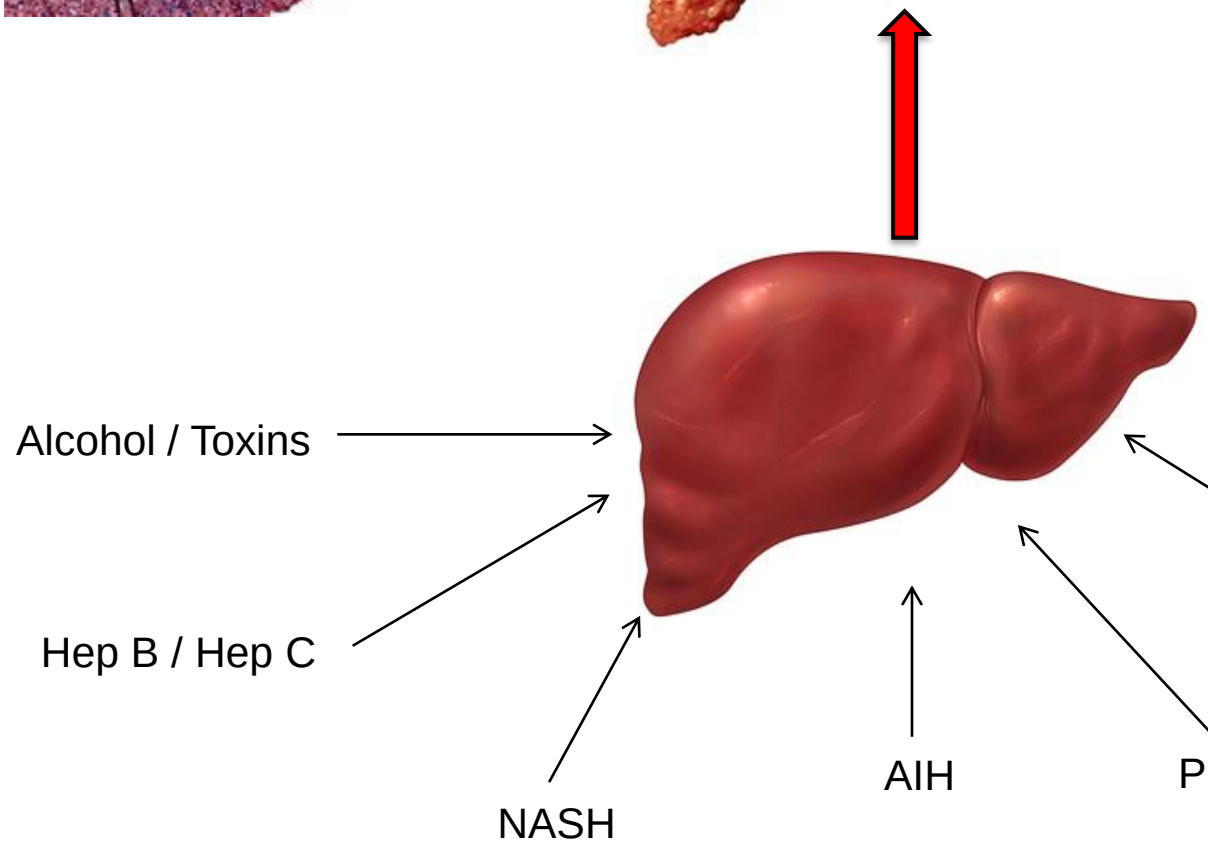
Outline

- Advanced Liver Disease
  - Compensated Advanced Chronic Liver Disease (cACLD)
  - Decompensated disease
  - Complications of decompensated disease






Regenerative nodule
Area of bridging fibrosis
Regenerative nodule

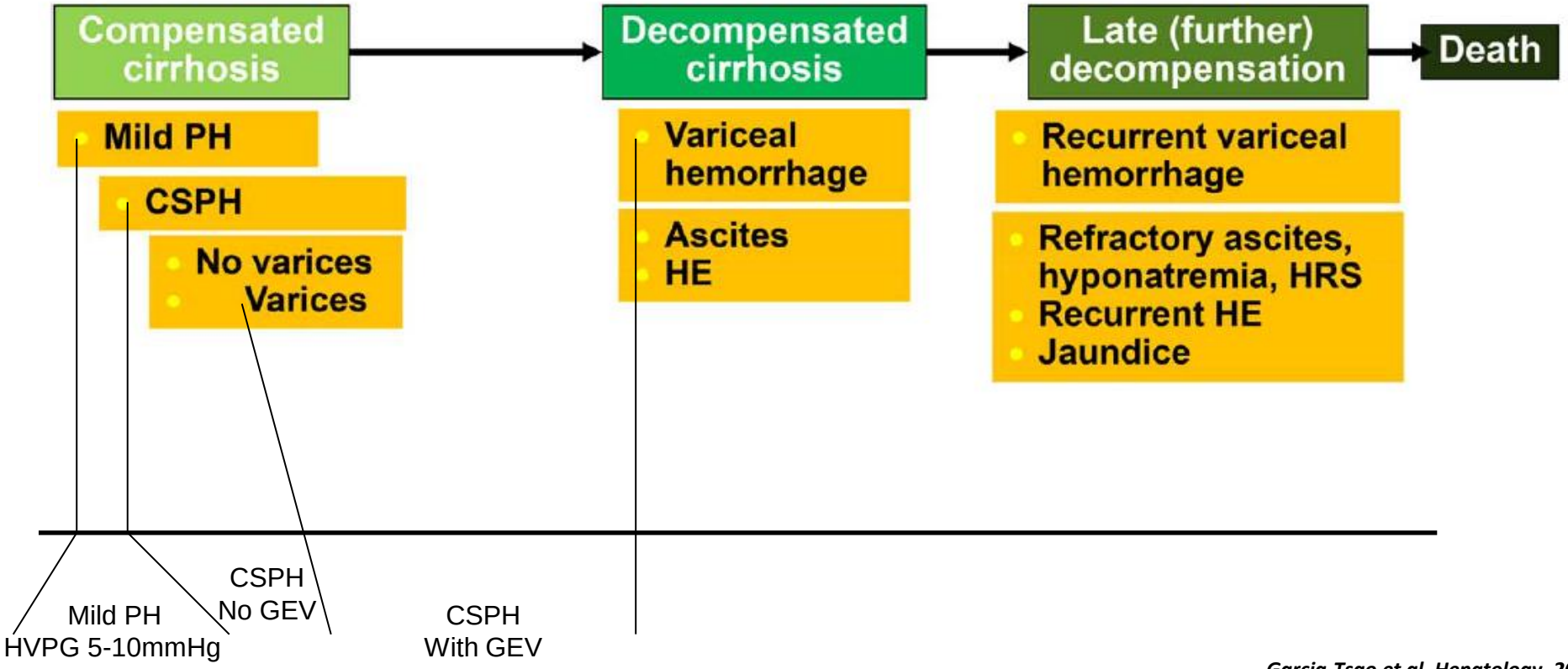

Alcohol / Toxins
Hep B / Hep C
NASH
AIH
PBC
Wilsons
Chronic biliary obstruction

Cirrhosis and cACLD

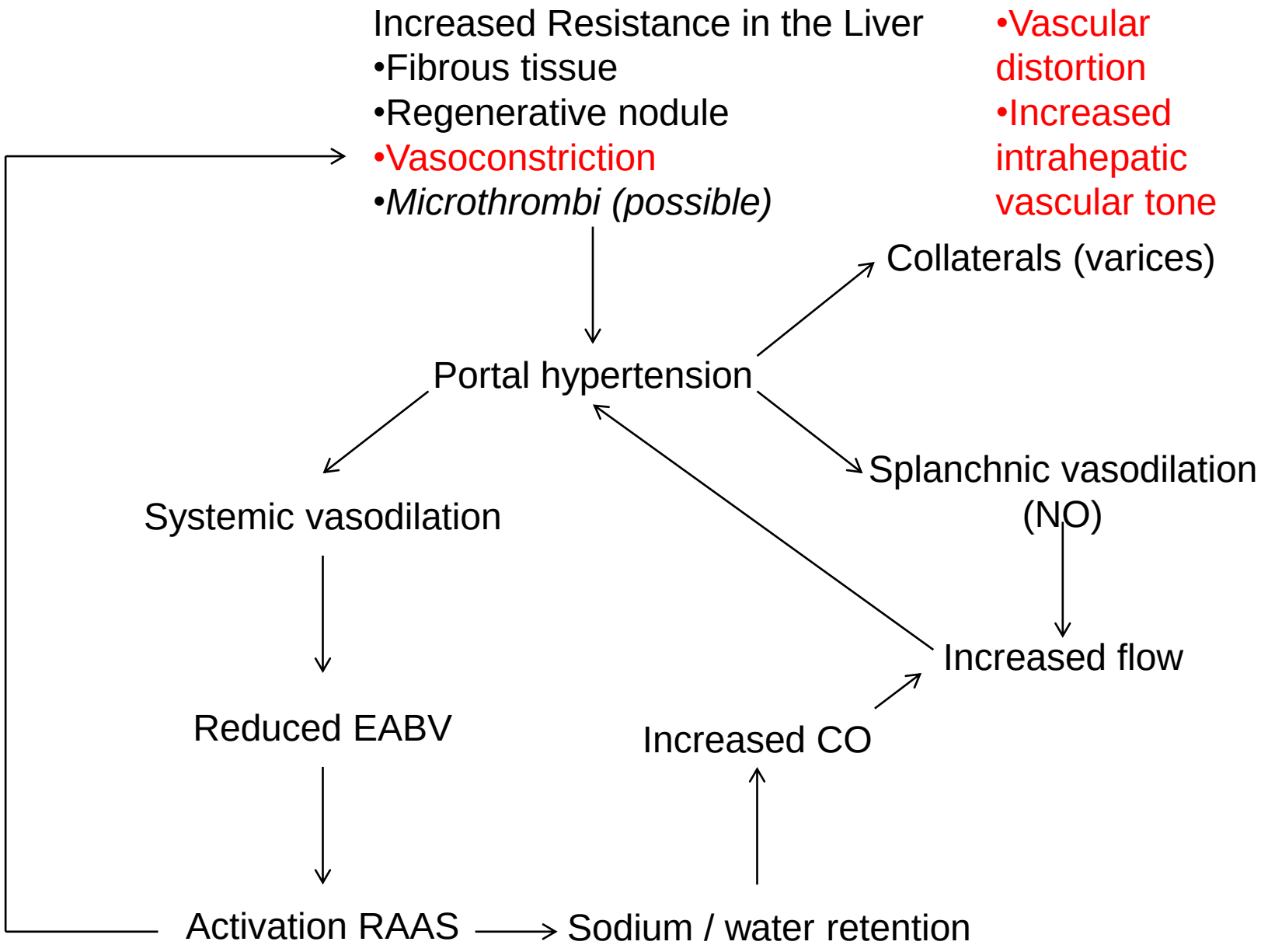
1. Liver cirrhosis is a histological diagnosis.
2. Cirrhosis is not histologically present in every patient classified as F4 by non-invasive methods.
3. There is no consensus in a clinical definition of liver cirrhosis.
4. Patients in pre-cirrhotic stages may have portal hypertension
5. Hepatocellular carcinoma surveillance might be indicated in pre-cirrhotic stages
6. Non-invasive tests have changed the clinical scenario of chronic liver disease.

Augustin et al, de Franchis R. (eds) Portal Hypertension VI. Springer, Cham. 2016

What is advanced liver disease?



Garcia-Tsao et al, Hepatology. 2017


Increased Resistance in the Liver
•Fibrous tissue
•Regenerative nodule
•Vasoconstriction
•Microthrombi (possible)
•Vascular distortion
•Increased intrahepatic vascular tone
Collaterals (varices)
Portal hypertension
Systemic vasodilation
Splanchnic vasodilation (NO)
Increased flow
Reduced EABV
Increased CO
Activation RAAS
Sodium / water retention

cACLD / CSPH

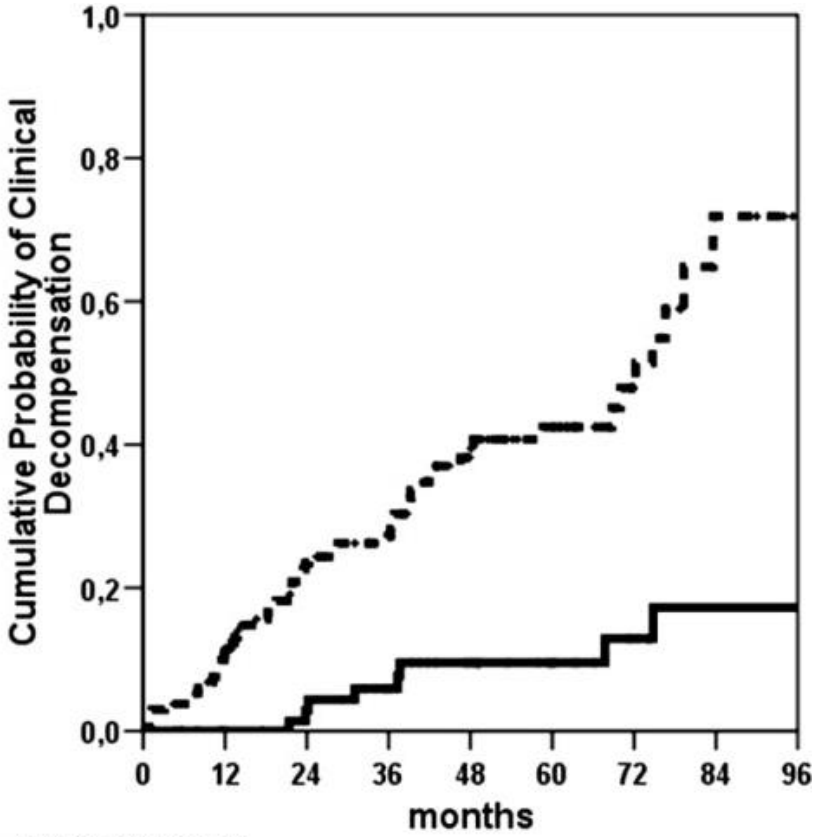
Classification	Mild PH	CSPH no varices	CSPH with varices
HVPG	5-10	>10	>10
Mortaliy (p/a)	1%	1%	3%
Aim of treatment	Prevent CSPH	Prevent decompensation	Prevent decompensation (first bleeding episode)
Annual progression of varices	7-8%	7-8%	Size: 10-12% VH: 10-15%

- Patients with cirrhosis should have a diagnostic endoscopy for variceal surveillance
- Endoscopy can be avoided in patients with a liver stiffness of <20 kPa and platelet > 150 with a >95% probability
- Yearly fibroscan and platelet count

D'Amico J Hep 2006
Garcia-Tsao et al, Hepatology. 2017

Significance of CSPH

- Ascites
- Variceal haemorrhage
- Hepatic encephalopathy



HVPG <10 mmHg							
At risk	79	72	66	55	44	32	14
Events	0	0	2	4	6	6	8
HVPG ≥ 10 mmHg							
At risk	134	112	86	73	49	34	3
Events	0	15	29	33	44	47	54

Log rank test: $p<0.01$

HR: 3.95 (2.29-6.83)

Ripoll et al, Gastrpenterology 2007

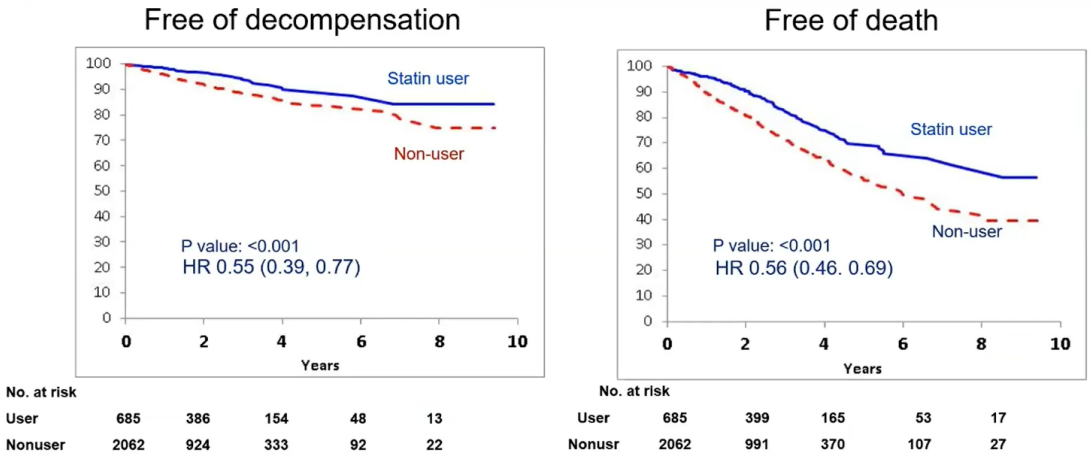
Patients with mild PH – preventing CSPH

- Treat underlying disease (eg. Hep B)
- Weight loss – obesity worsens the natural history of cACLD
- Alcohol abstinence
- Vaccinations
- Screening for HCC
- *Improve diet and nutrition – extrapolated data on sarcopaenia*
- *Consideration of the use of statins*
- *Anticoagulants*

Bosch J et al, J Hep 2015
De Franchis et al, J Hep. 2015

:ins for improvement of portal pressure / improved function

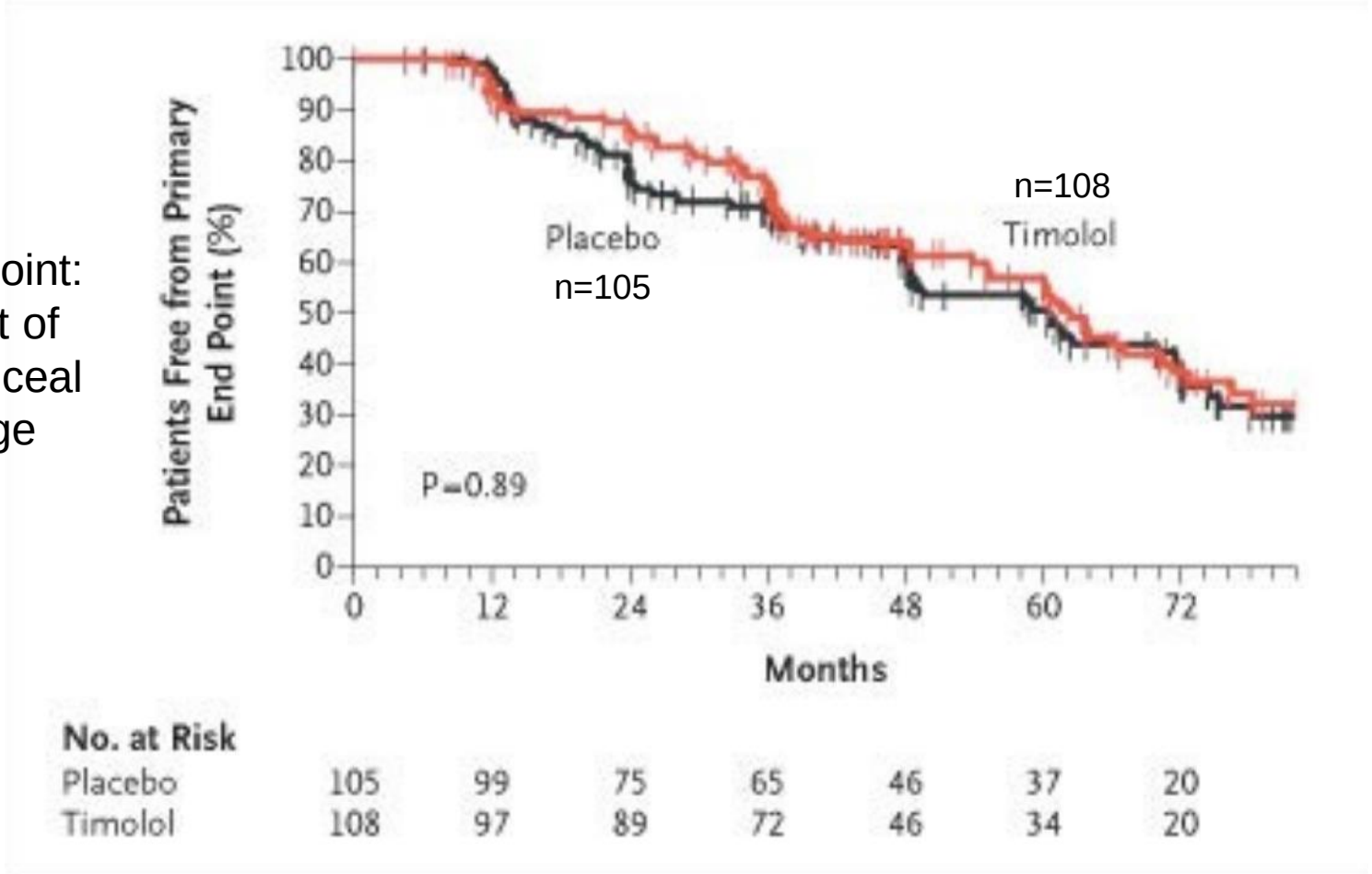
	Placebo (n=29)			Statins (n=30)		
	Baseline	4/52	p	Baseline	4/52	p
HVPG (mmHg)	19.8	19.4	0.47	18.5	17.1	**0.003**
ICG (mL/min)	237	222	0.44	221	276	**0.017**



Abraldes et al, Gastroenterology 2009
Mohanty et al, Gastroenterolgy 2016

Primary prophylaxis of varices in mild cACLD?

Primary end point: Development of varices or variceal haemorrhage



Groszmann RJ et al, NEJM 2005

Identification of CSPH

- Only in compensated cirrhosis
- LSM ≥ 25 rules in (but not in obese NASH)
- Presence of varices or collaterals

Pons et al, AJG 2021
Garcia Tsao et al, Gastroenterology 2021

Patients with CSPH– preventing decompensation

- Variceal surveillance scopes
- Other management as per mild cACLD
- Consideration of beta blockers in all CSPH

De Franchis et al, J Hep. 2015

Variceal Surveillance (cACLD)

Size of varices / Underlying insult	No varices	Small #	Medium / Large
Present	2 years	1 year	Primary prophylaxis
Absent	3 years*	2 years*	Primary prophylaxis

primary prophylaxis for small varices only if decompensated disease, or red wale signs
*provided no co-factors (EtOH / obesity)

(Baveno VI) De Franchis et al, J Hep. 2015

Primary Prophylaxis Varices

TABLE 3. Management of Patients With Moderate/Large Varices That Have Not Bled

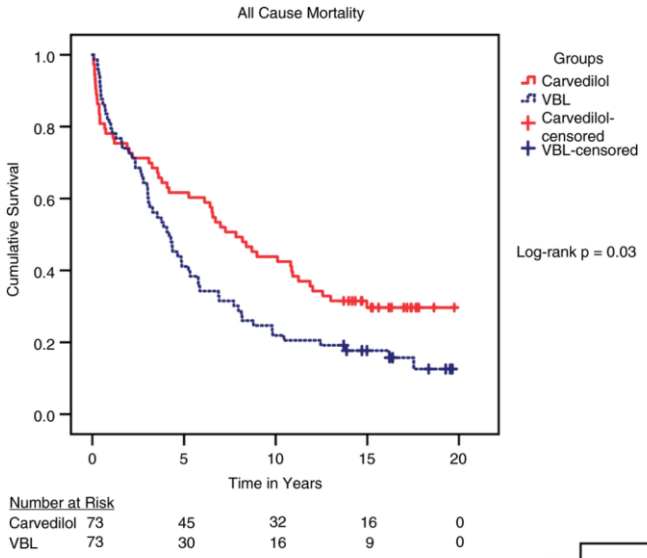
Therapy	Recommended Dose	Therapy Goals	Maintenance/Follow-up
Propranolol	• 20-40 mg orally *twice* a day • Adjust every 2-3 days until treatment goal is achieved • Maximal daily dose: ○ 320 mg/day in patients without ascites ○ 160 mg/day in patients with ascites	• Resting heart rate of 55-60 beats per minute • Systolic blood pressure should not decrease <90 mm Hg	• At every outpatient visit make sure that heart rate is on target • Continue indefinitely • No need for follow-up EGD
Nadolol	• 20-40 mg orally *once* a day • Adjust every 2-3 days until treatment goal is achieved • Maximal daily dose: ○ 160 mg/day in patients without ascites ○ 80 mg/day in patients with ascites	• Resting heart rate of 55-60 beats per minute • Systolic blood pressure should not decrease <90 mm Hg	• At every outpatient visit make sure that heart rate is on target • Continue indefinitely • No need for follow-up EGD
Carvedilol	• Start with 6.25 mg *once* a day • After 3 days increase to 6.5 mg twice-daily • Maximal dose: 12.5 mg/day (except in patients with persistent arterial hypertension)	• Systolic arterial blood pressure should not decrease <90 mm Hg	• Continue indefinitely • No need for follow-up EGD
EVL	• Every 2-8 weeks until the eradication of varices	• Variceal eradication (no further ligation possible)	• First EGD performed 3-6 months after eradication and every 6-12 months thereafter

Any of these four therapies can be used, but current data do not support the use of combination therapy.

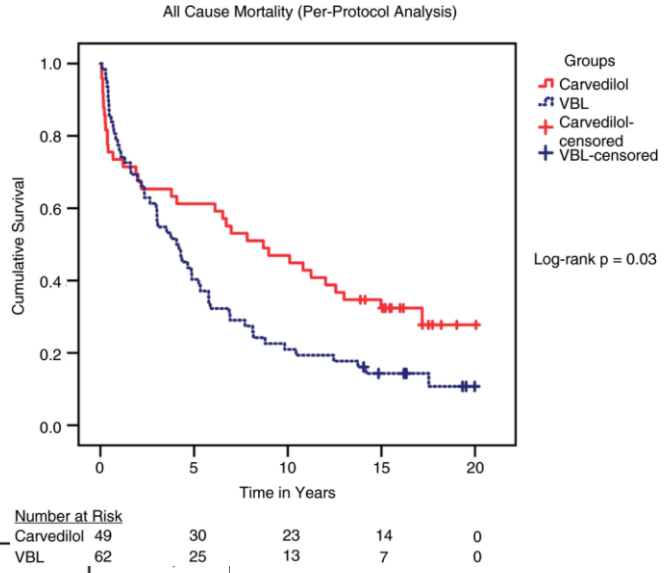
Garcia-Tsao et al, Hepatology 2017

Carvedilol has improved mortality

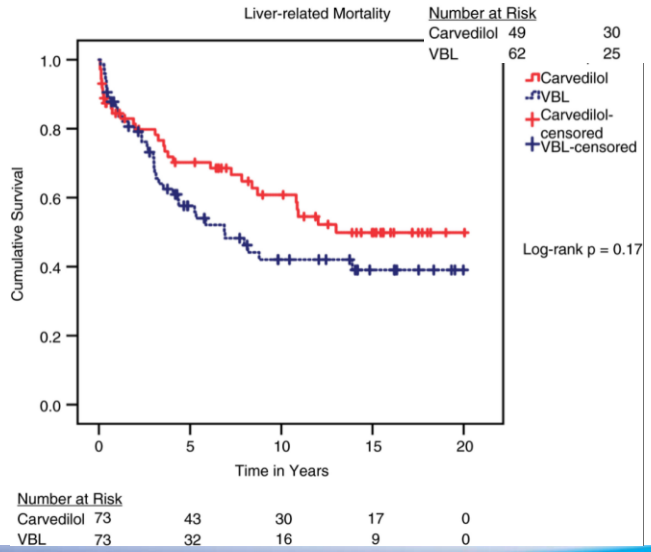
All cause mortality ITT, p=0.03



All cause mortality PP, p=0.03

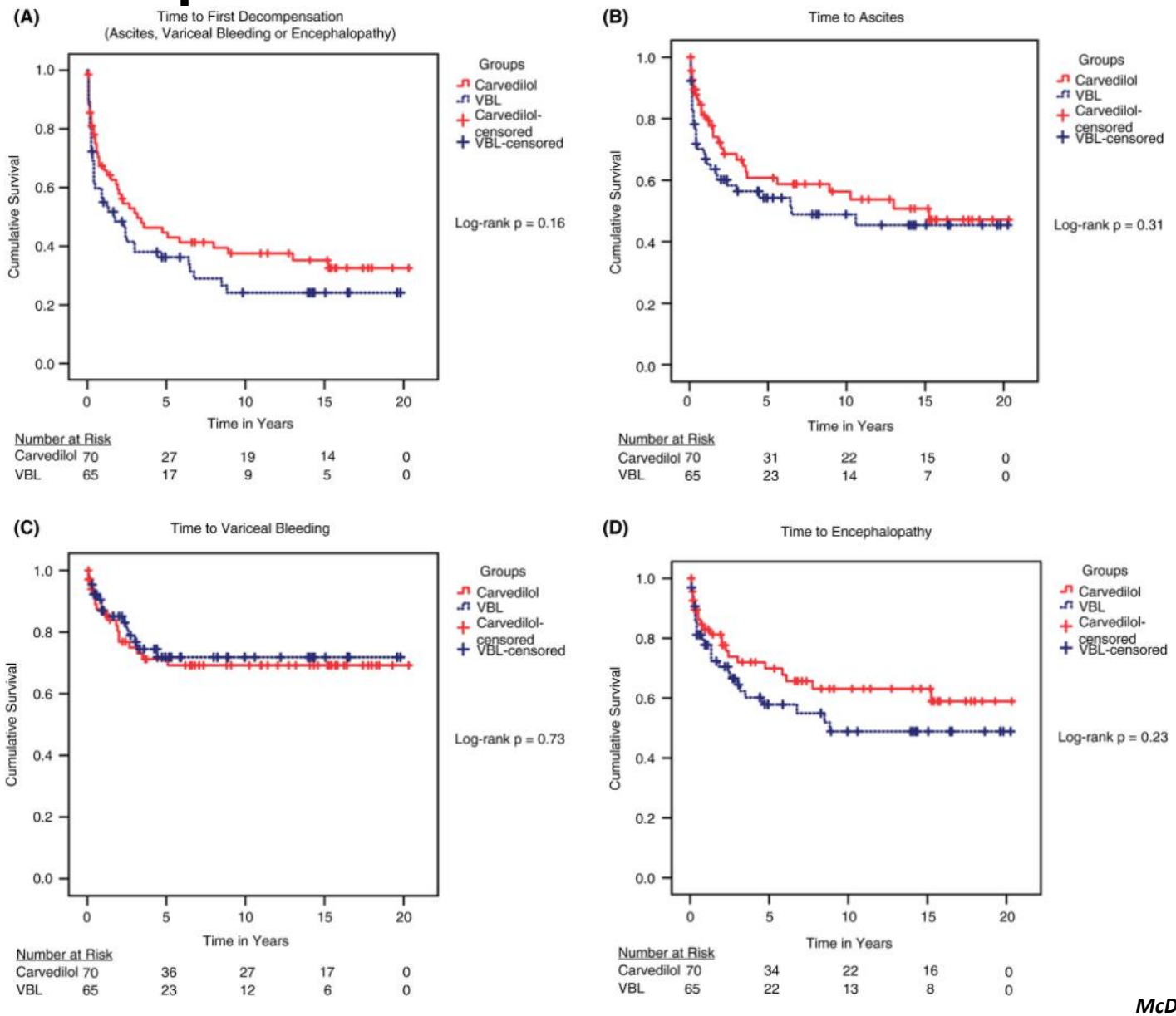


Liver related mortality, p=0.17

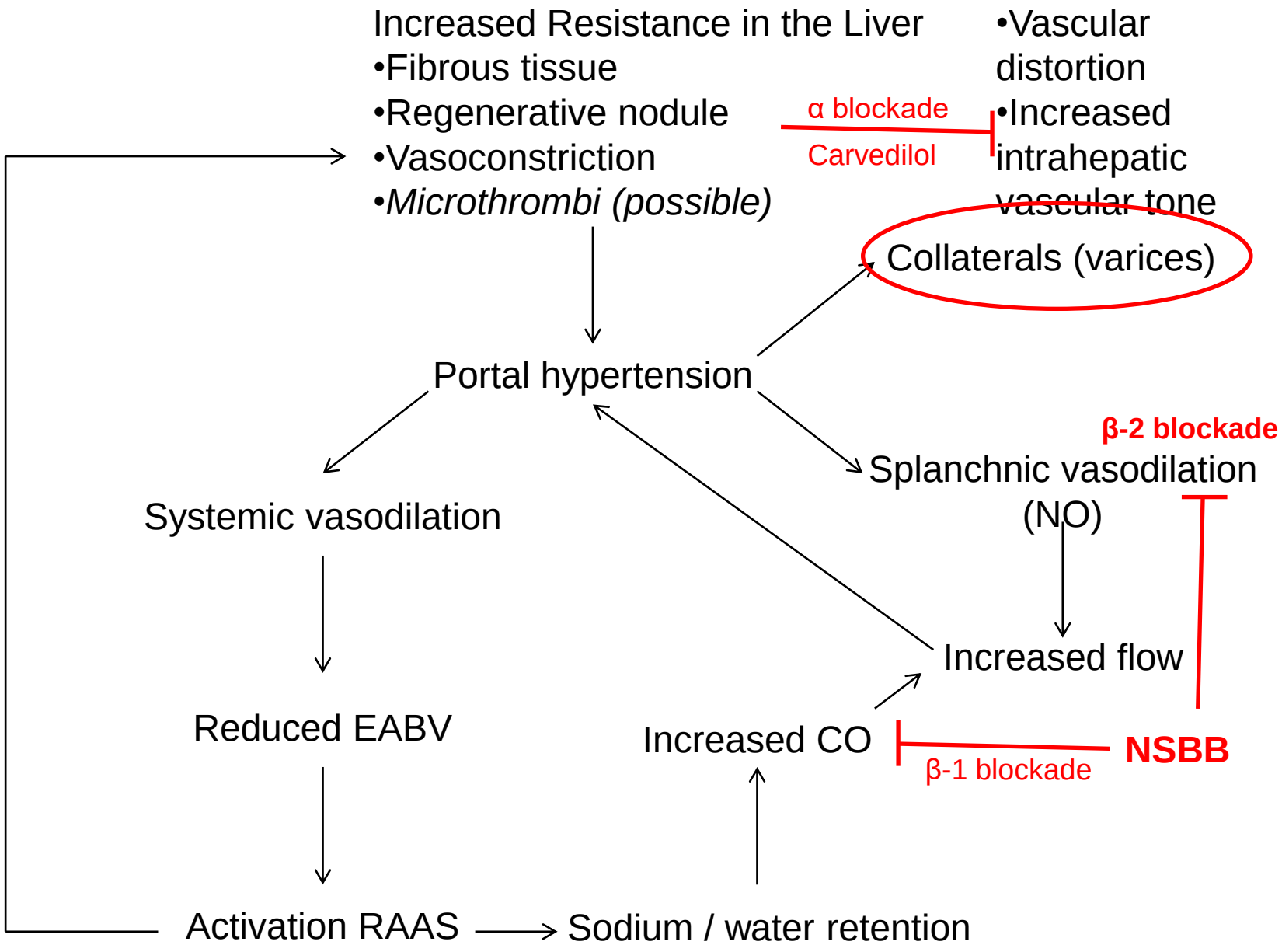


McDowell et al, APT 2020

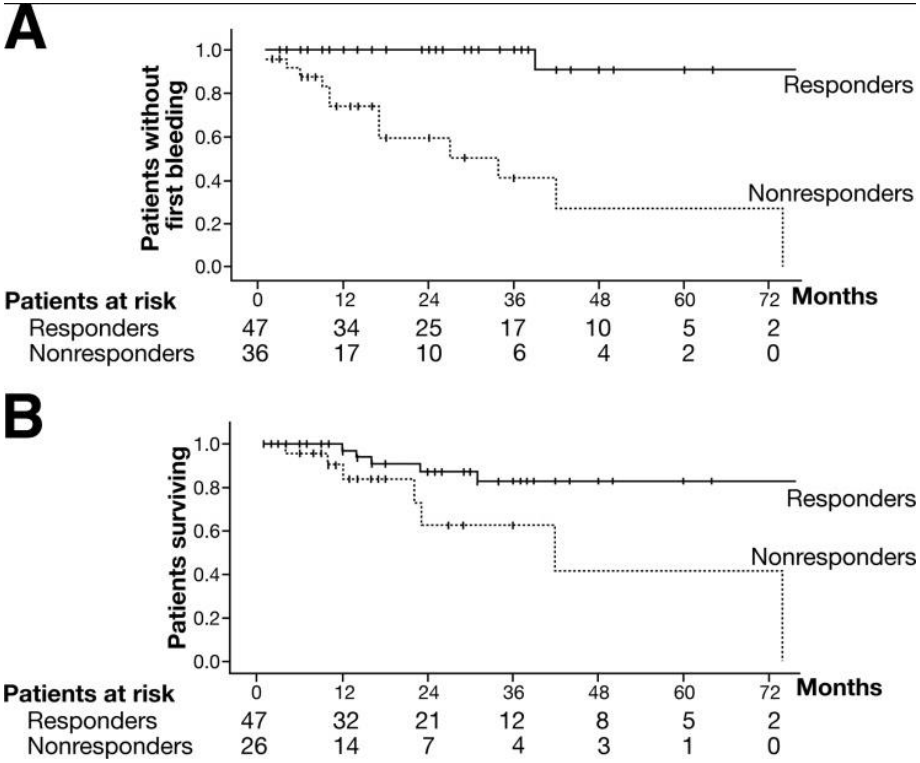
Specific liver outcomes



McDowell et al, APT 2020


Increased Resistance in the Liver
•Fibrous tissue
•Regenerative nodule
•Vasoconstriction
•Microthrombi (possible)
α blockade
Carvedilol
•Vascular distortion
•Increased intrahepatic vascular tone
Collaterals (varices)
Portal hypertension
β-2 blockade
Splanchnic vasodilation (NO)
Systemic vasodilation
Increased flow
Reduced EABV
Increased CO
β-1 blockade
NSBB
Activation RAAS
Sodium / water retention

NSBB – more than varices?



p<0.001

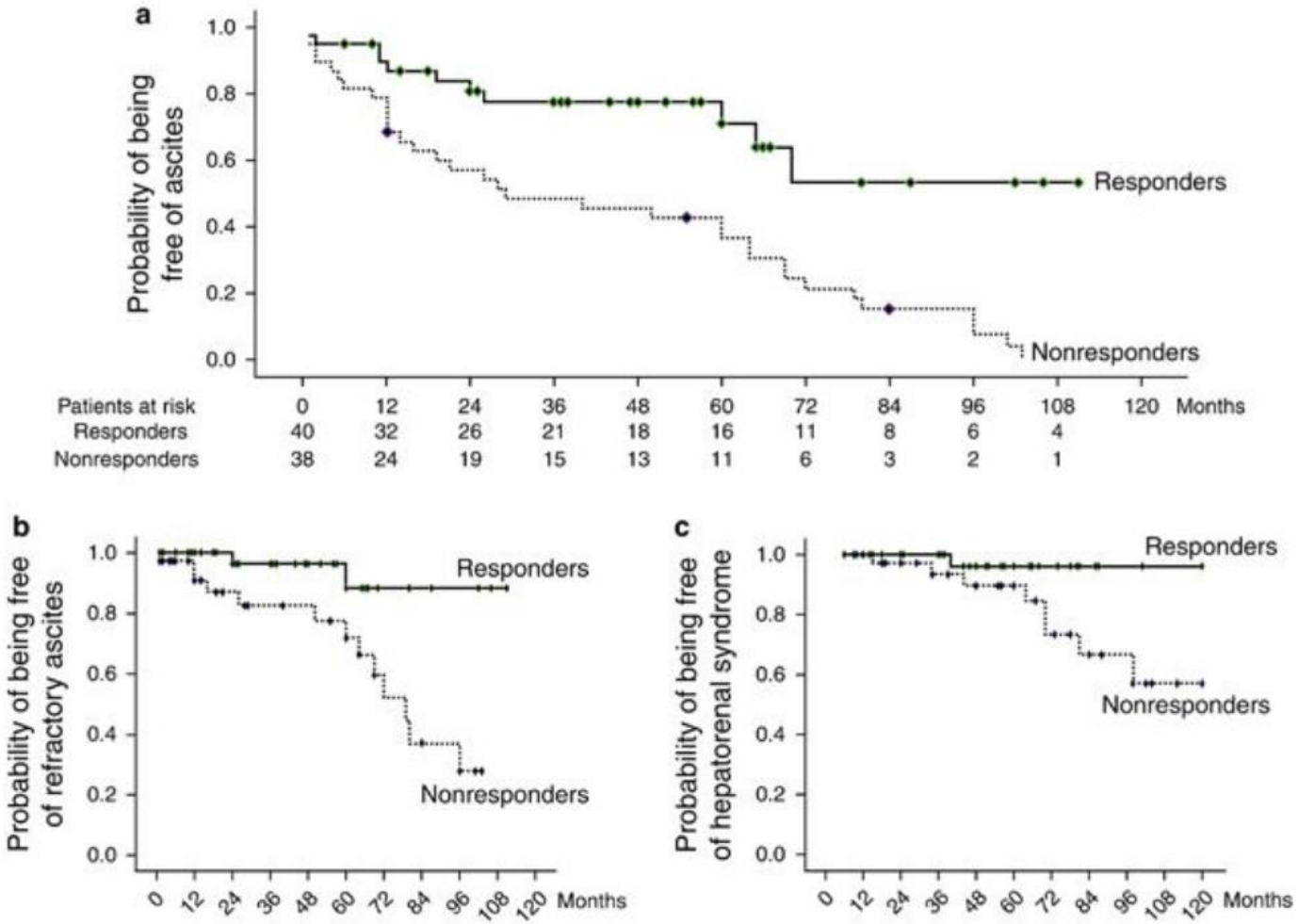
Ascites	Responders	Non-responders	p
1 year	11%	42%	<0.001
2 year	23%	70%	<0.001

P=0.01

n=105, 75 (71%) responders

Villanueva et al, Gastroenterology 2009

NSBB – more than varices?



Hernandez-Gea et al, AJG 2012

Comparison of trials

Trial	Timolol	PREDESCI
Patients	HVPG > 5	HVPG ≥ 10
Endpoint	Development of varices	Decompensation (ascites / VH / HE)
Beta blocker	Timolol	Nadolol (with carvedilol NR)
Exclusion	Varices	Varices on screening
Outcome	N/S	Clinical decompensation (HR 0.51) Reduced large varices (HR 0.5) Reduced death (HR 0.54)
Side notes		Greater HVPG lowering in carvedilol even though only non-responders got it

Villanueva et al, Lancet 2019
Groszmann RJ et al, NEJM 2005

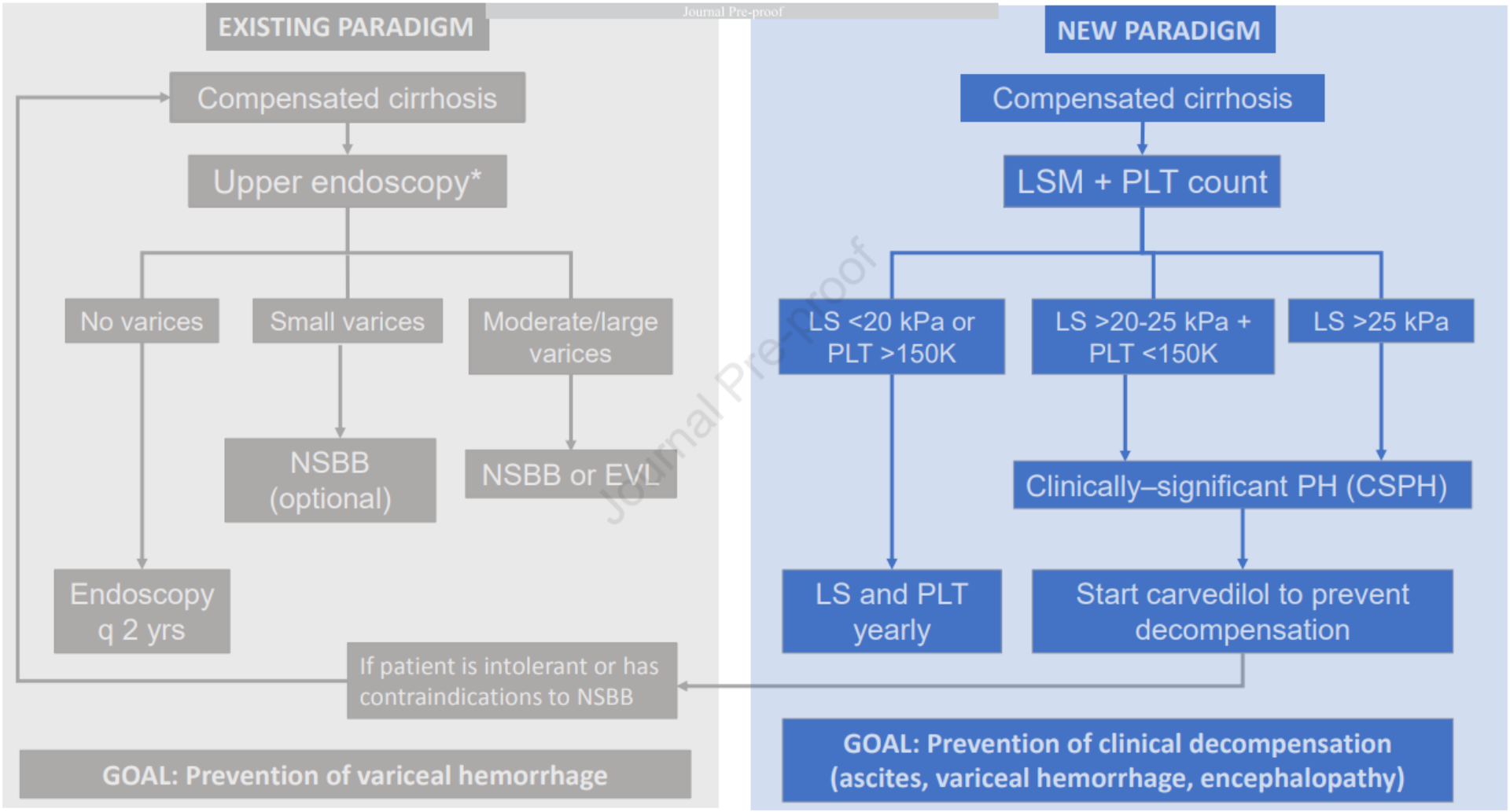
CLD

	Stages of chronic liver disease				
	No cirrhosis	**Compensated cirrhosis**			**Decompensated cirrhosis**
Clinical features (ascites, VH or HE)	No	No			Yes
Liver fibrosis on biopsy	None/mild	Advanced (cACLD)			Biopsy not needed
HVPG (mmHg)	3-5	5-10	>10 higher likelihood of decompensation		>10; >20 worse outcomes in VH
Portal hypertension	None	Mild	Clinically significant (CSPH)		CSPH by definition
Varices/collaterals	No	No	± (if +, CSPH by definition)		± or VH
Liver stiffness (kPa)	<5 to 10	10-20 (grey zone)	>20-25	>25	Not necessary
Platelet count (K/mm^3)	Any	Any	<150	Any	Usually <150

Journal Pre-proof

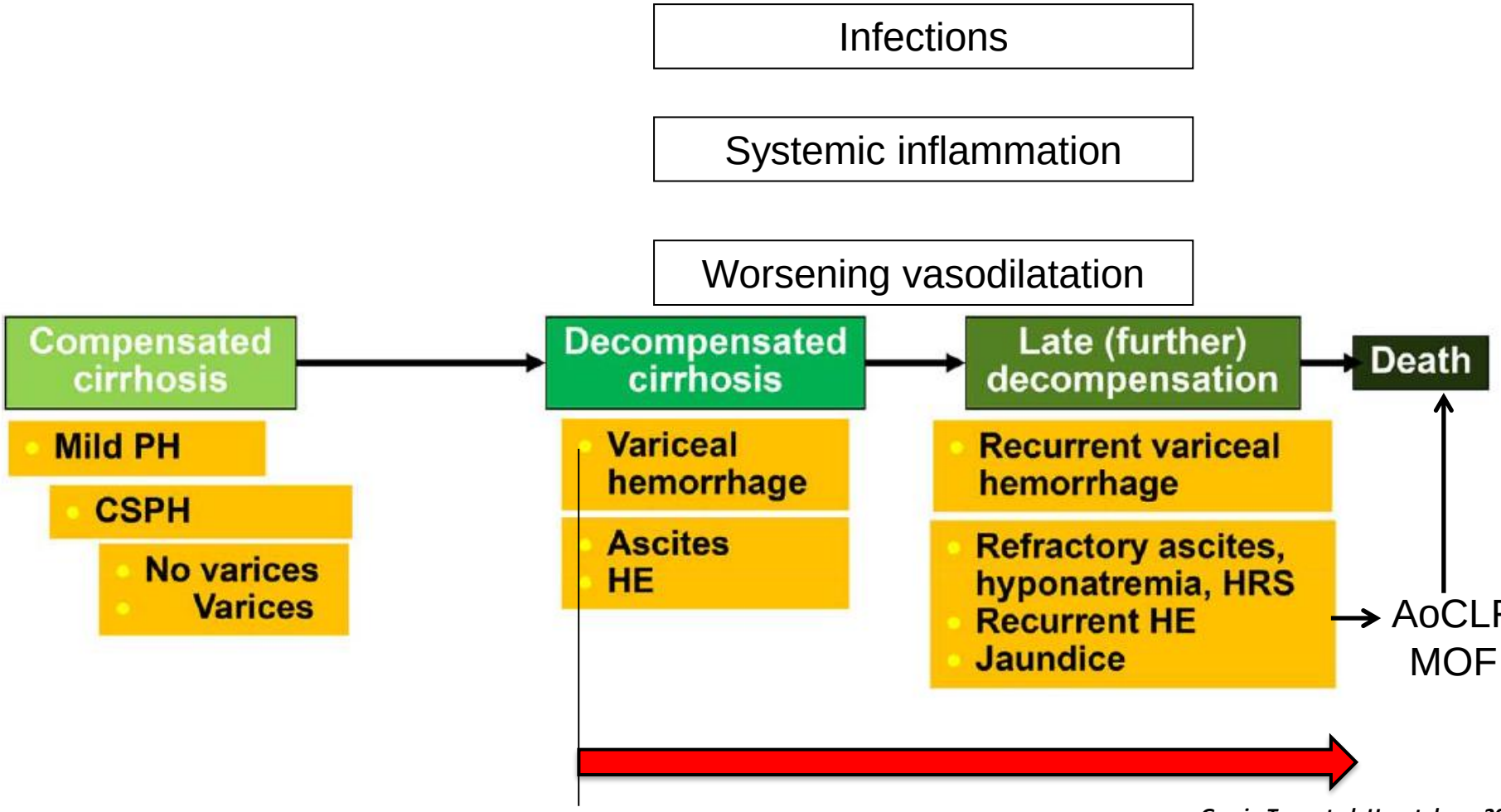
Garcia Tsao et al, Gastroenterology 2021

Proposed aims



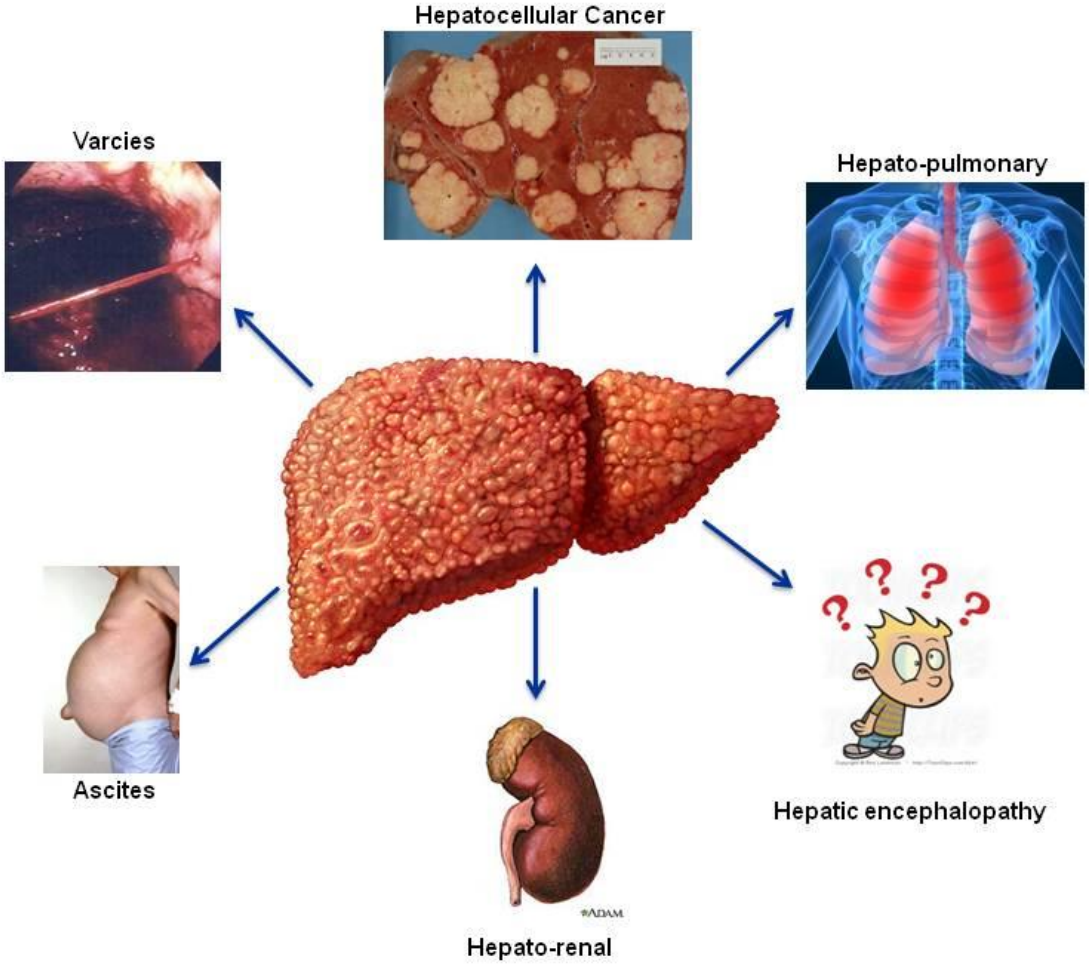
Garcia Tsao et al, Gastroenterology 2021

Decompensated Advanced Liver Disease

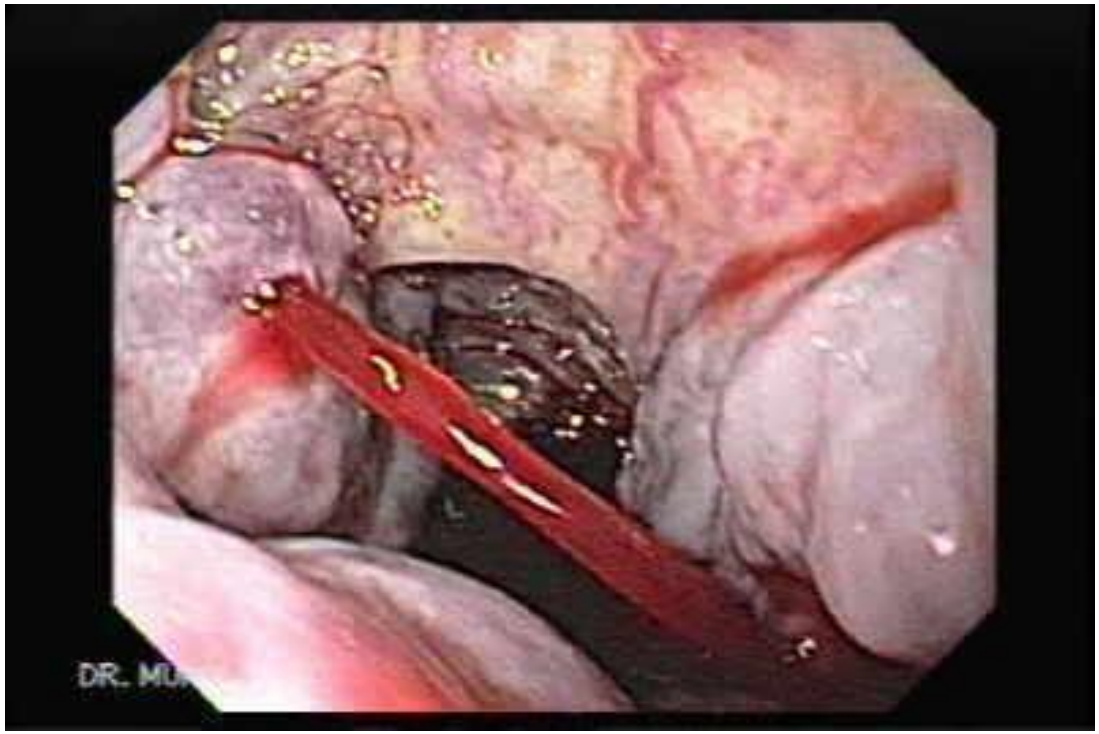


Garcia-Tsao et al, Hepatology. 2017

Decompensated Advanced Liver Disease



Acute Esophageal Variceal Bleeding



HVPG > 12mmHg

Image courtesy of El Salvador Atlas of Gastrointestinal Video Endoscopy

Considerations

- ICU setting
- ABC's
- Intubation
- Vasoactive agents
- Antibiotics
- Prokinetics (QTc)
- Blood transfusion (~7)
- Endoscopy (12hrs / ASAP)
- Possible early TIPSS
- Consideration of esophageal stents

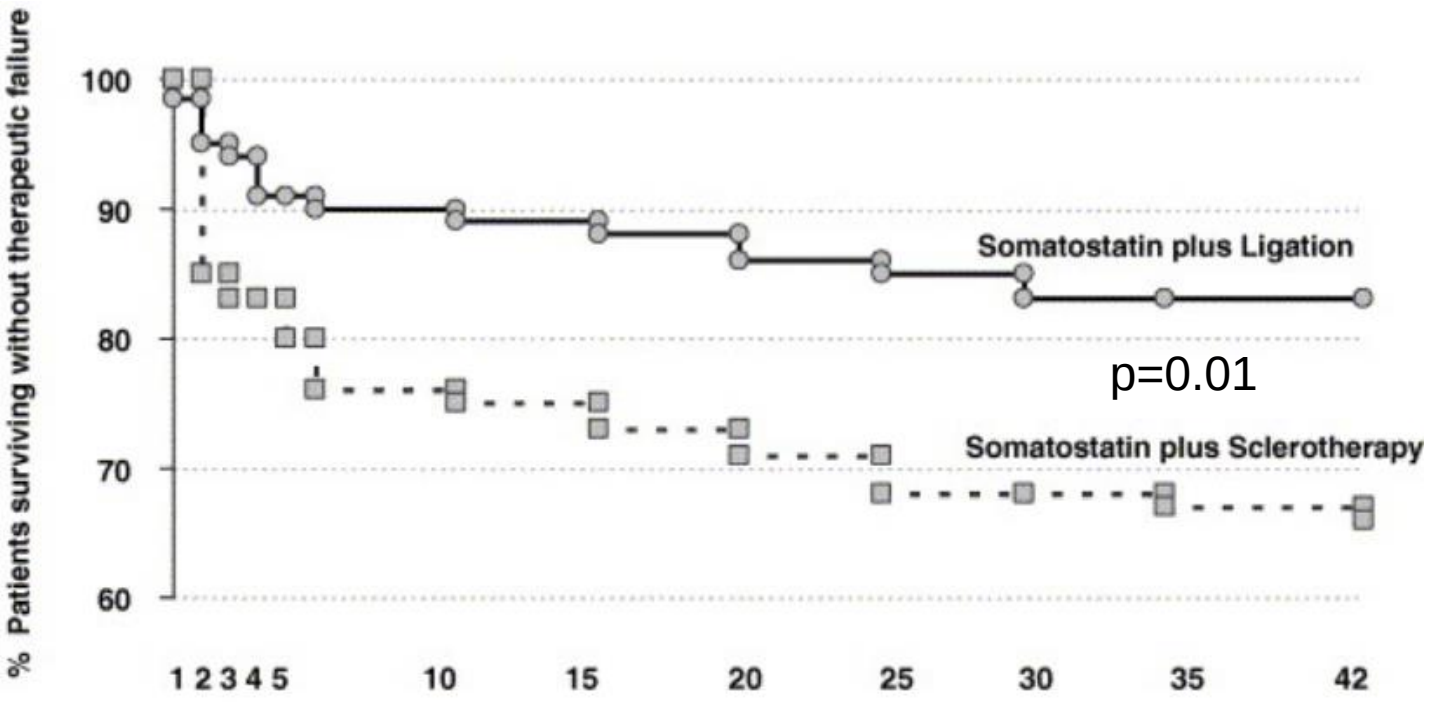
Villanueva et al, NEJM 2013
Chen et al, J Hep 2012
Garcia-Tsao et al, Hepatology 2017
Cardenas et al, Clin Liv Dis 2014

Easy to scope… But…

"Although pooled rates of timely endoscopy and vasoactive medication use were high (85.8% and 83.0%, respectively), ***only half of patients received prophylactic antibiotics(52.8%; 95% CI, 40.0%–66.2%)***"

Tapper et al, CGH 2017

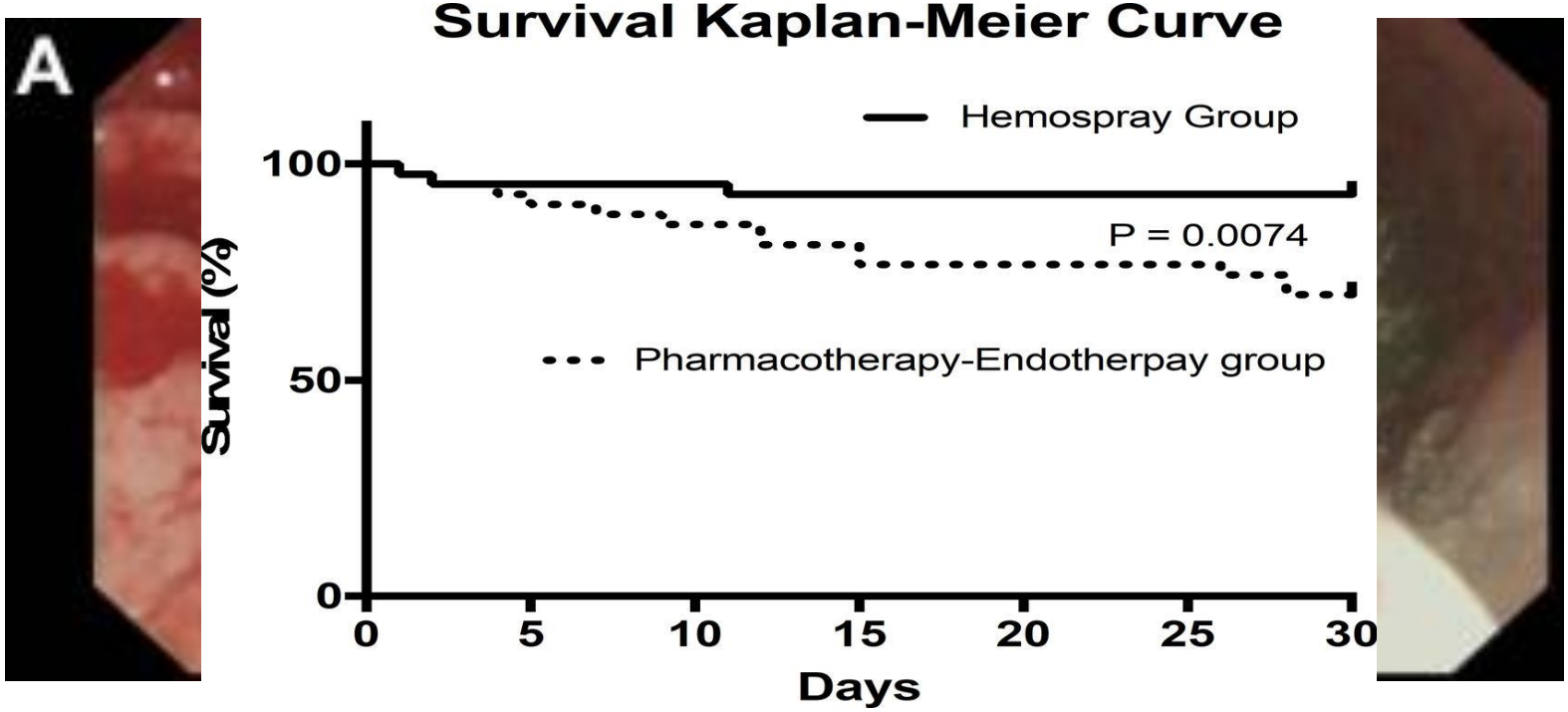
EVL vs sclerotherapy



Nº AT RISK									
SMT+EVL Group	90	81	80	79	77	76	74	72	72
SMT+EST Group	89	68	67	64	61	57	57	55	53

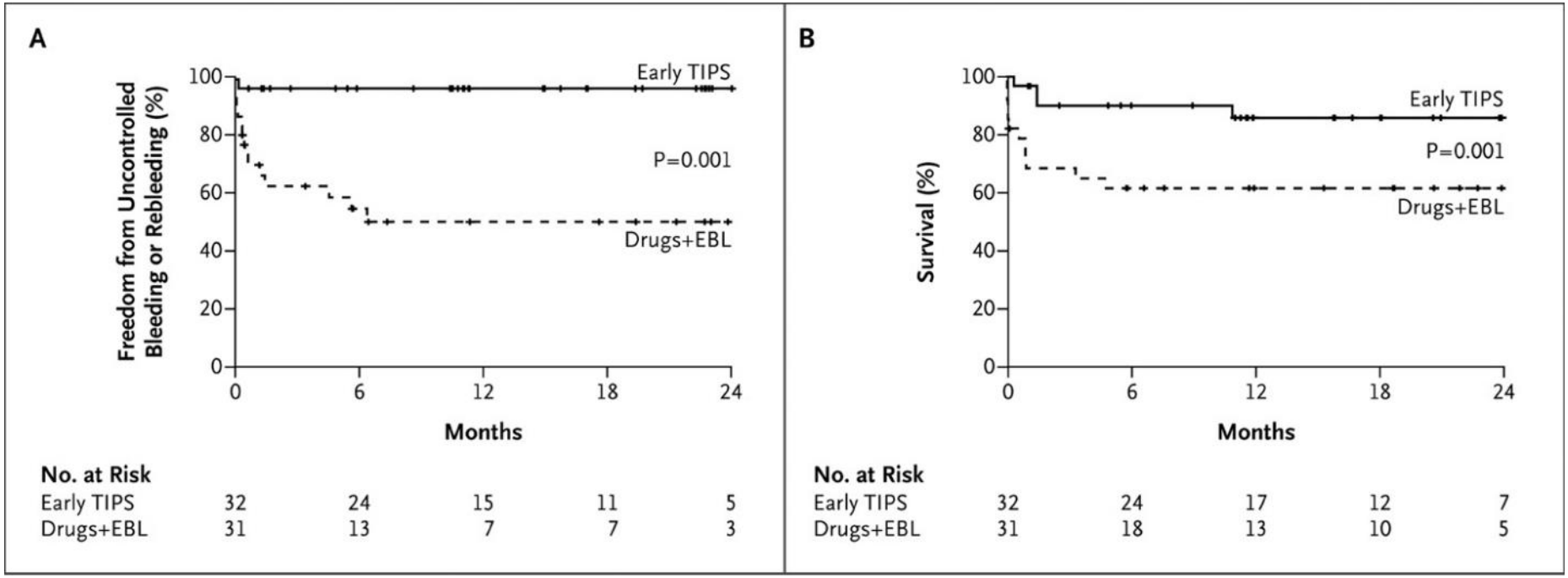
Vilanueva et al, J Hep 2006

Hemospray?



Smith et al, J Hep 2014
Ibrahim et al, Gut 2018

Consideration of early TIPSS



CPT B: 7-9 (8-9 with active bleeding)
CPT C: 10-13
Vasoactive drugs / NSBB can be stopped

Nicoara-Farcau et al, Gastroenterology 2021
Garcia-Pagan et al, NEJM 2010

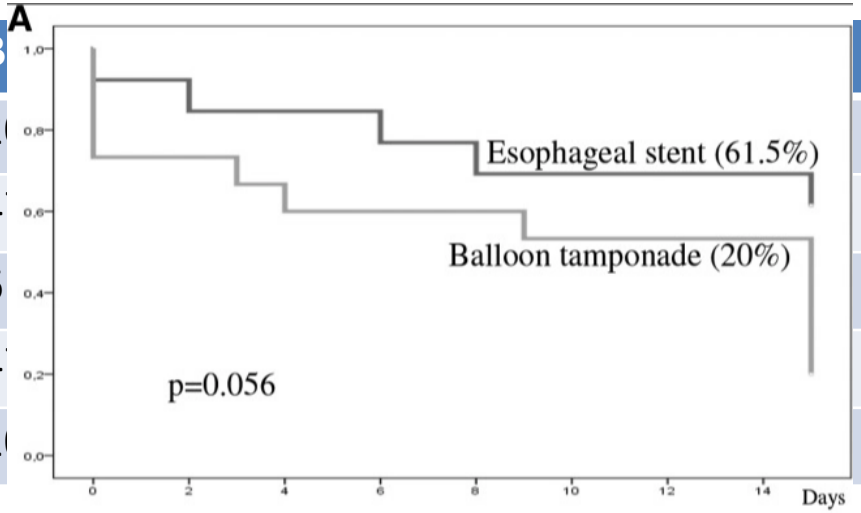
SB Tube?

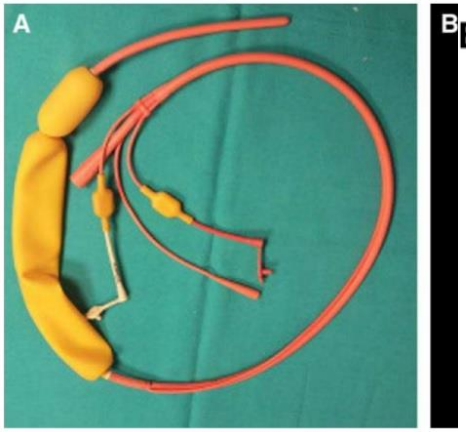
Outcome	No. (%)
Initial hemostasis with SB tube (n = 66)	50 (75.8)
Rebleeding after successful hemostasis with SB tube (n = 50)	11 (22.0)
Esophageal perforation (n = 66)	4 (6.1)
Death (n = 66)	28 (42.4)
Causes of death (n = 28)	
After failed successful initial hemostasis with SB tube (n = 16)	
Failure of successful hemostasis	12 (42.9)
Esophageal perforation	4 (14.3)
After successful initial hemostasis with SB tube (n = 12)	
Among patients with rebleeding (n = 6)	
Failed successful hemostasis	5 (17.9)
Multi-organ failure	1 (3.6)
Among patients without rebleeding (n = 6)	
Multi-organ failure	6 (21.4)

Choi et al, KJIM 2017

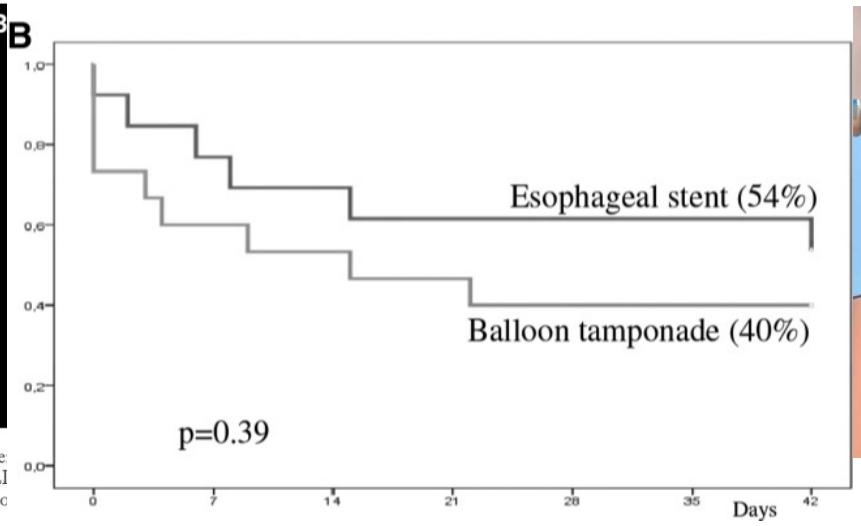
SB Tube vs SEMS

	B	p
Success of therapy	2(	0.025
Control of bleeding	4	0.037
Transfusion	6	0.037
Adverse events	4	
TIPS	1(	0.07





G. 1. Devices used in the study. (A) Four-lumen Sengstaken-Blake
l balloon, gastric aspiration, and supraglottic aspiration. (B) SX-ELI
npletely expanded (25 mm of diameter). There were two retrieval loc



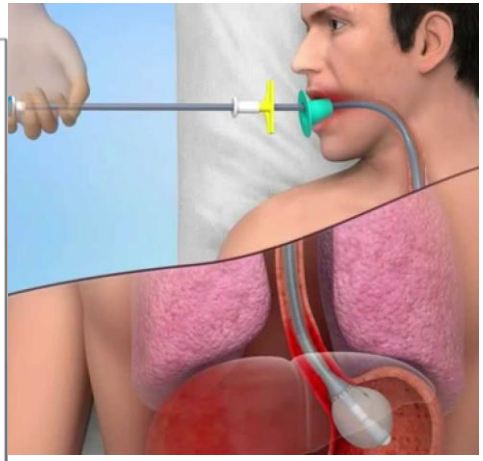
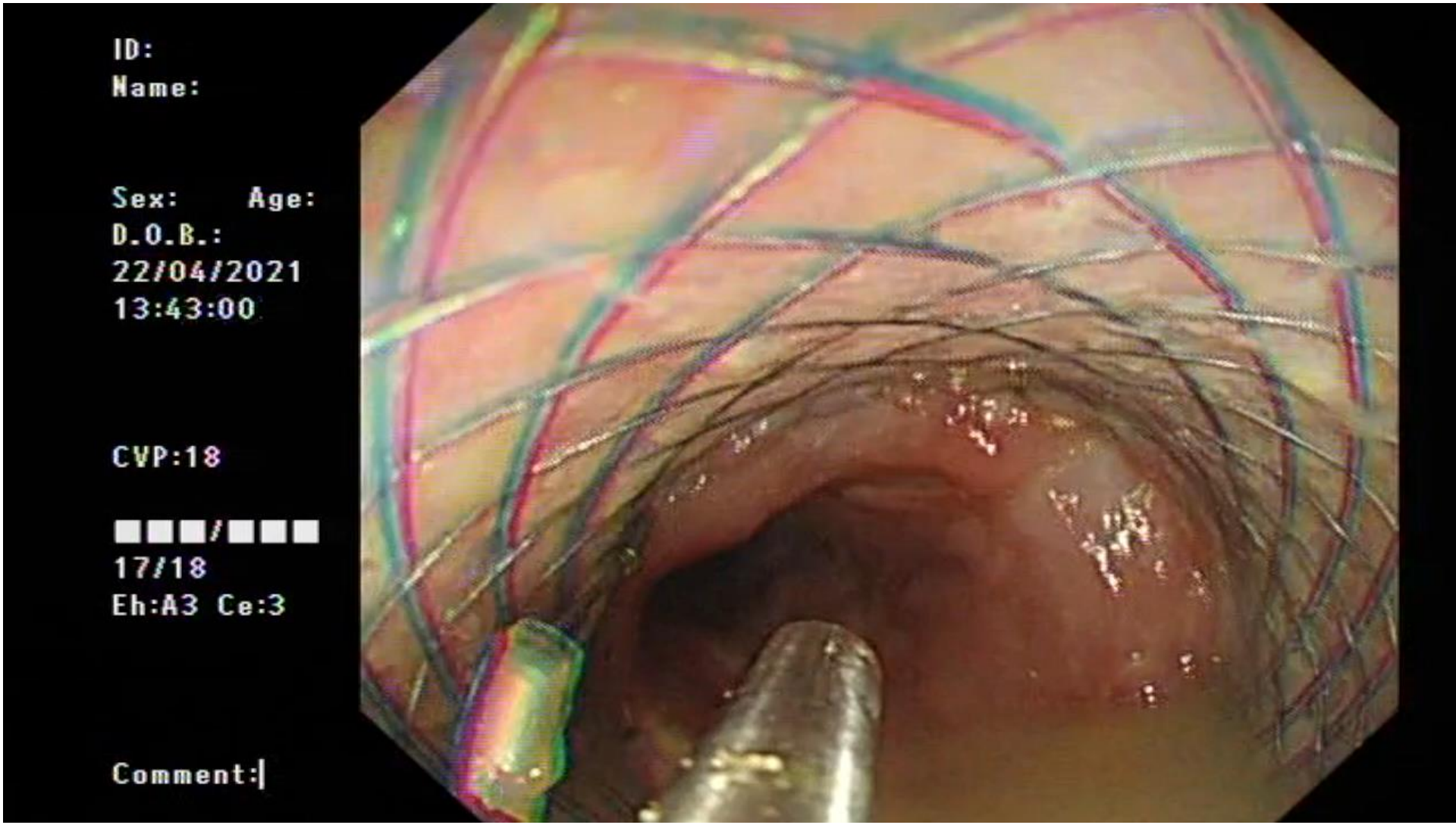


Image courtesy of Ella-CS
Image courtesy of EndoToday
Escorsell et al, Hepatology 2016

Danis Stent Deployment



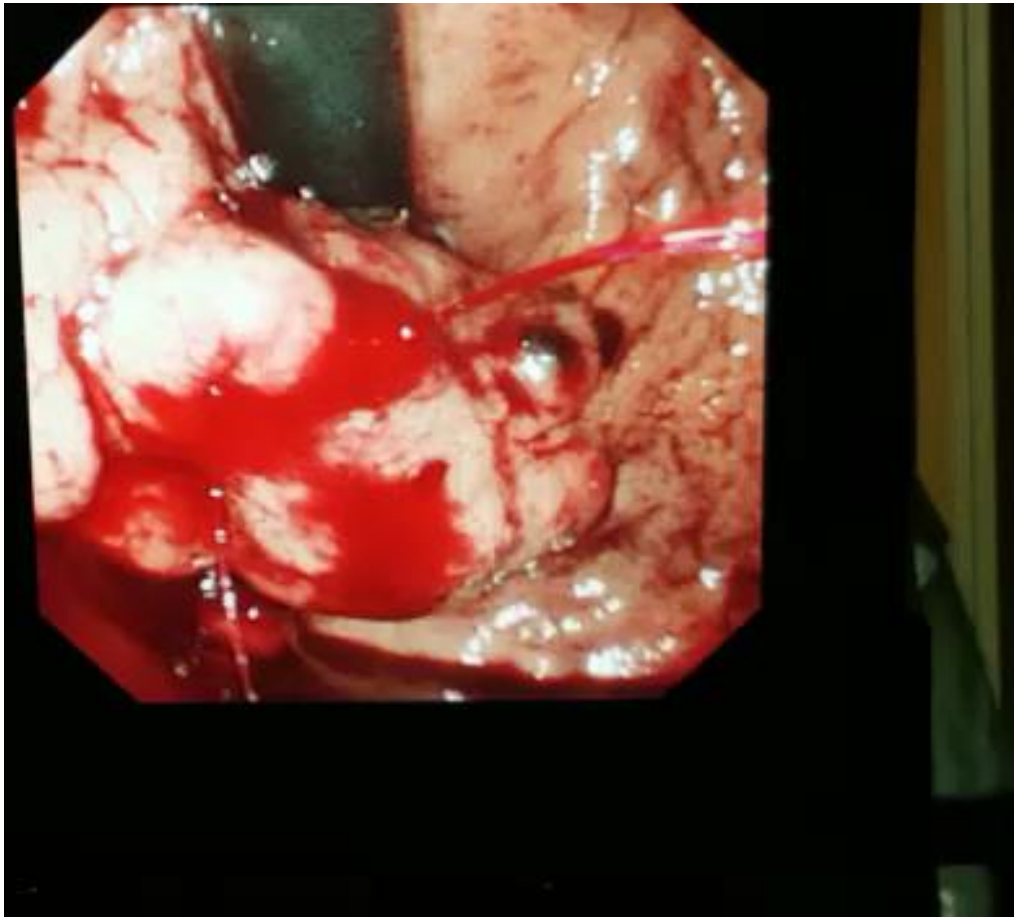
Danis Stent Removal



Post bleed

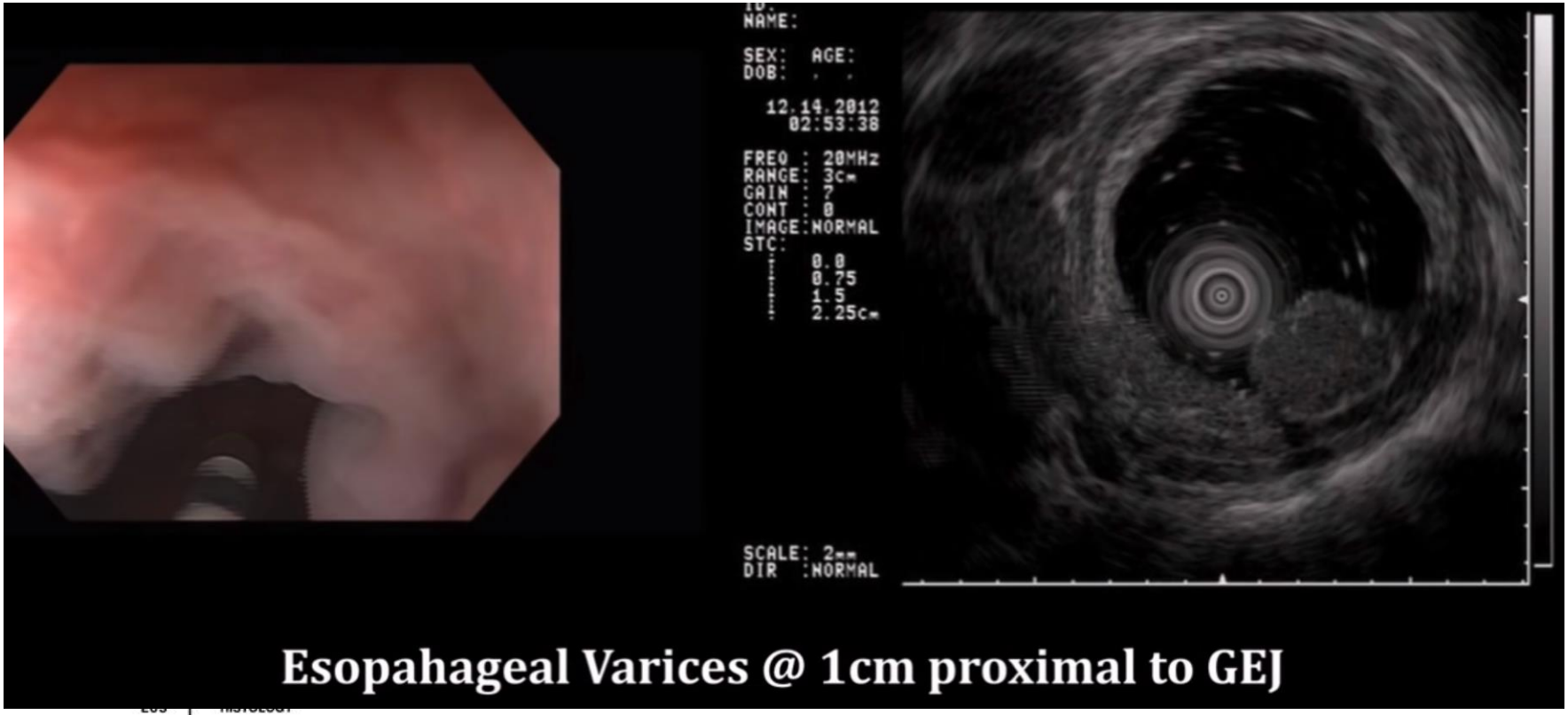
- Watch for infections (SBP / pneumonia)
- NSBB + EVL
- Optimization of underlying disease
- Other causes for decompensation (HCC, PVT)
- Other strategies for cACLD
- KIV pre-emptive TIPSS

Acute Gastric Variceal Bleeding

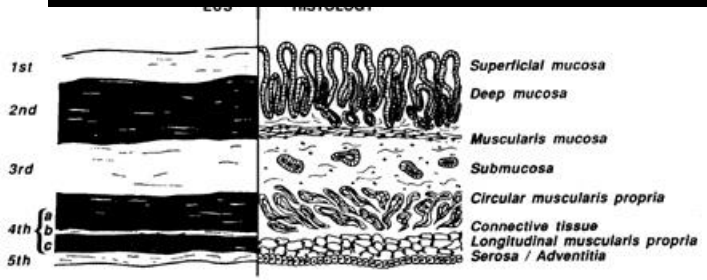


HVPG > 12mmHg

Acute Gastric Variceal Bleeding

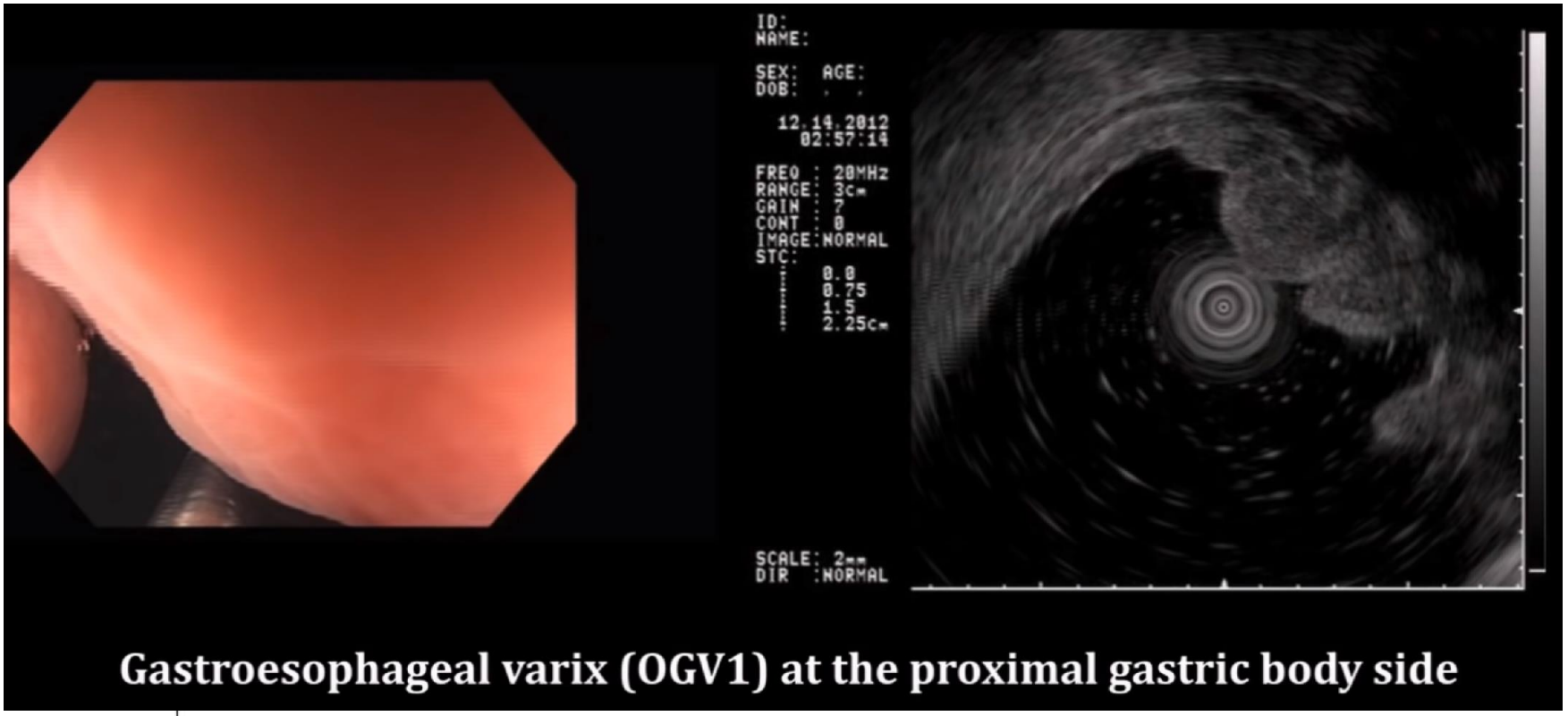


Esopahageal Varices @ 1cm proximal to GEJ

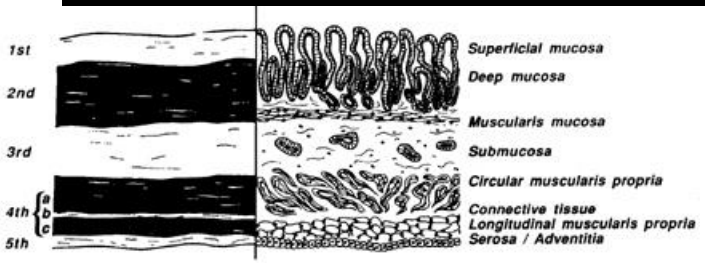


Kaltenbach / Soetiknoe, ASGE Video Library

Acute Gastric Variceal Bleeding

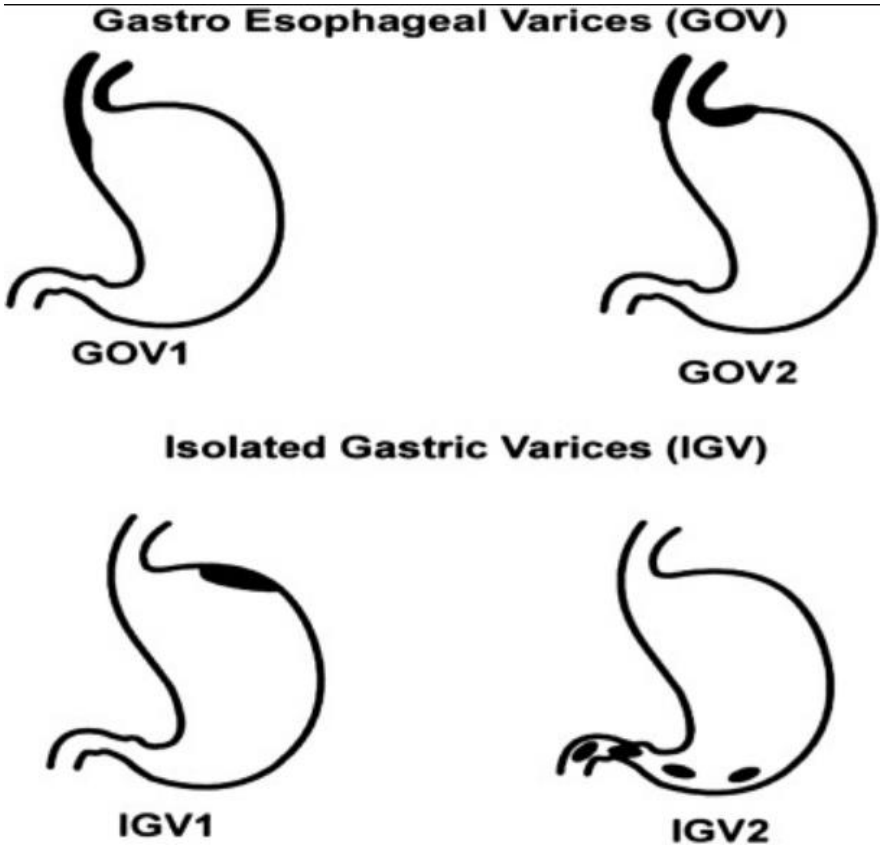


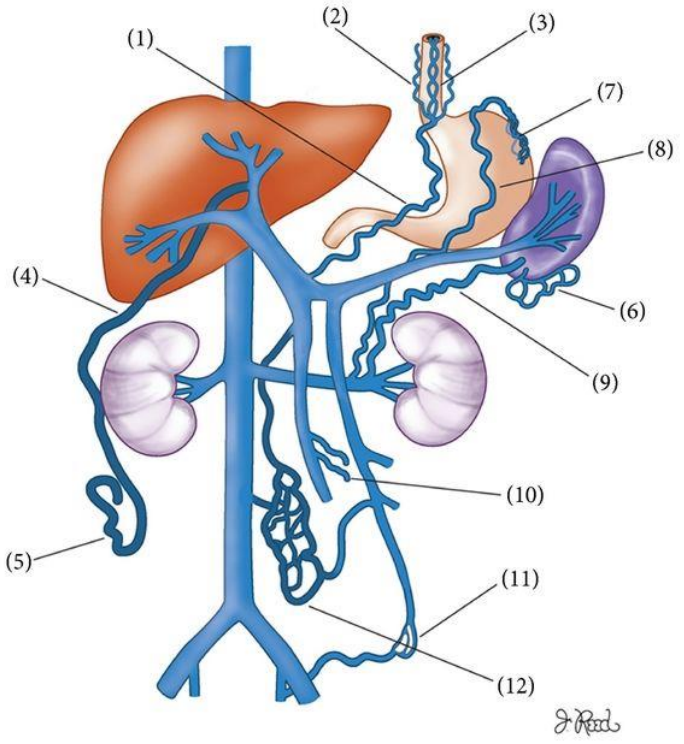
Gastroesophageal varix (OGV1) at the proximal gastric body side



Kaltenbach / Soetiknoe, ASGE Video Library

Acute Gastric Variceal Bleeding

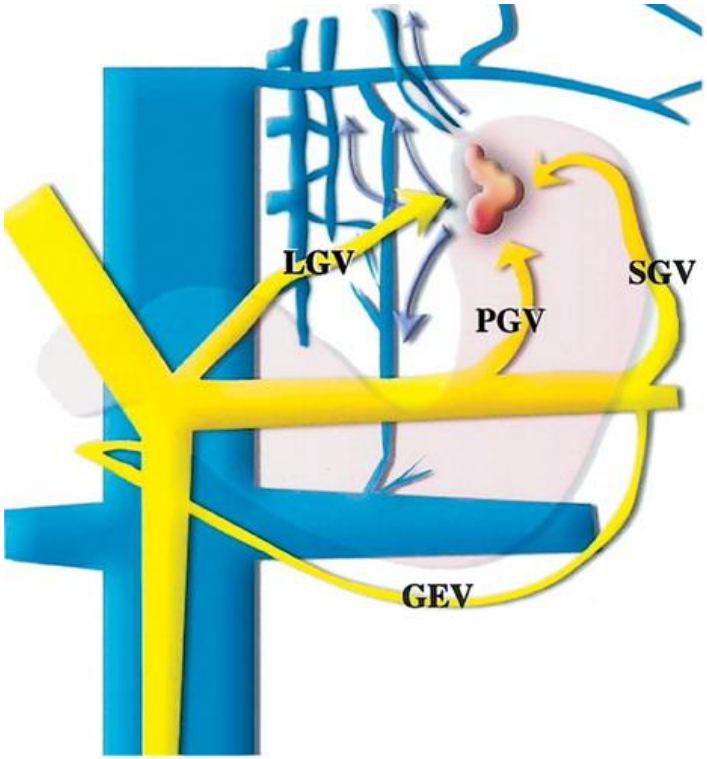


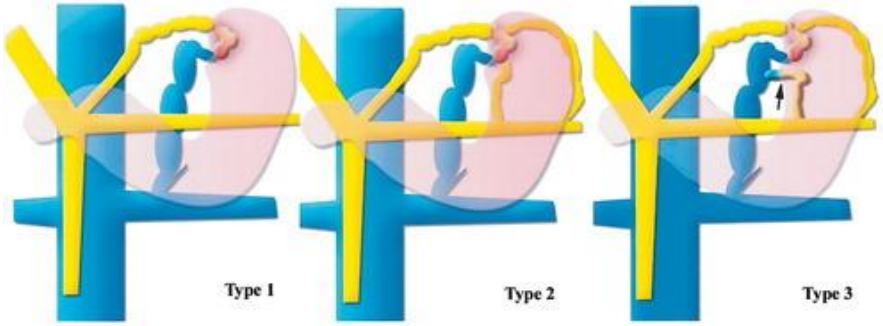


(1) Coronary
(2) Paraesophageal
(3) Esophageal
(4) Paraumbilical
(5) Caput medusae
(6) Perisplenic
(7) Retrogastric
(8) Gastrorenal shunt
(9) Splenorenal shunt
(10) Mesenteric
(11) Hemorrhoidal
(12) Retroperitoneal paravertebral

Sarin et al, Clin Liv Dis 2014

Classification by vascular afferents - Arakawa

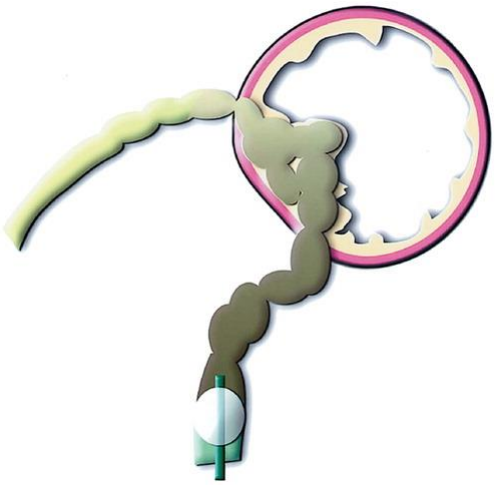




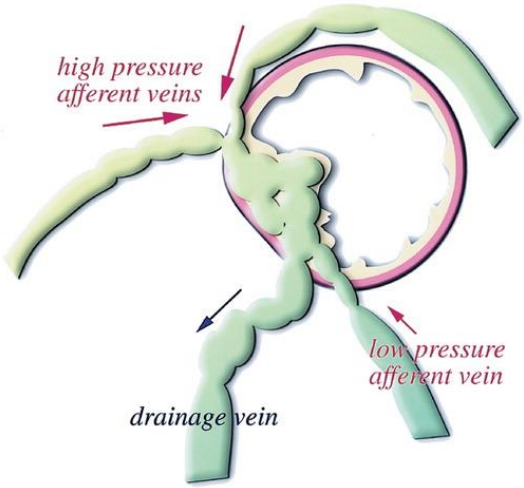
Kiyosue et al, Radiographics 2003

BRTO – technical issues with afferents

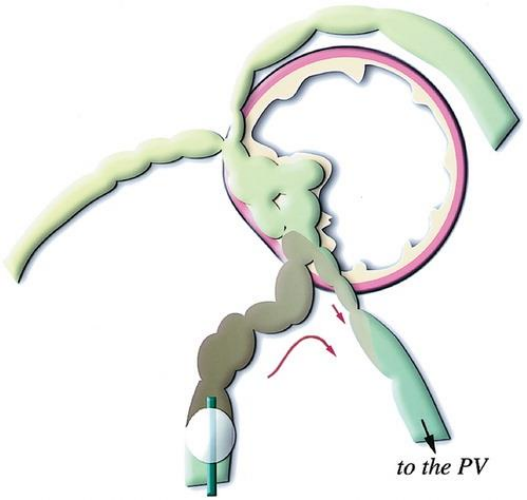
Type 1



Type 2

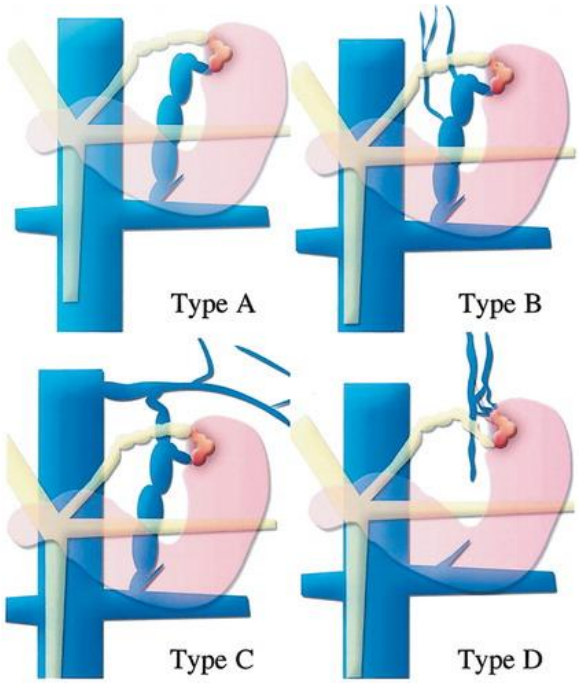


Type 3

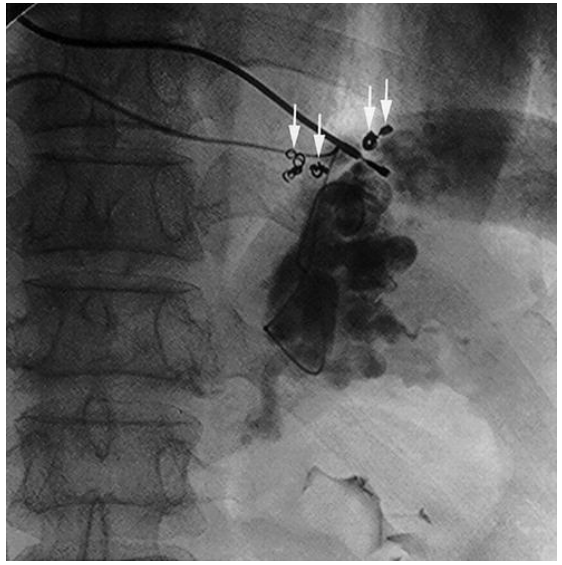


Kiyosue et al, Radiographics 2003

Classification by efferents







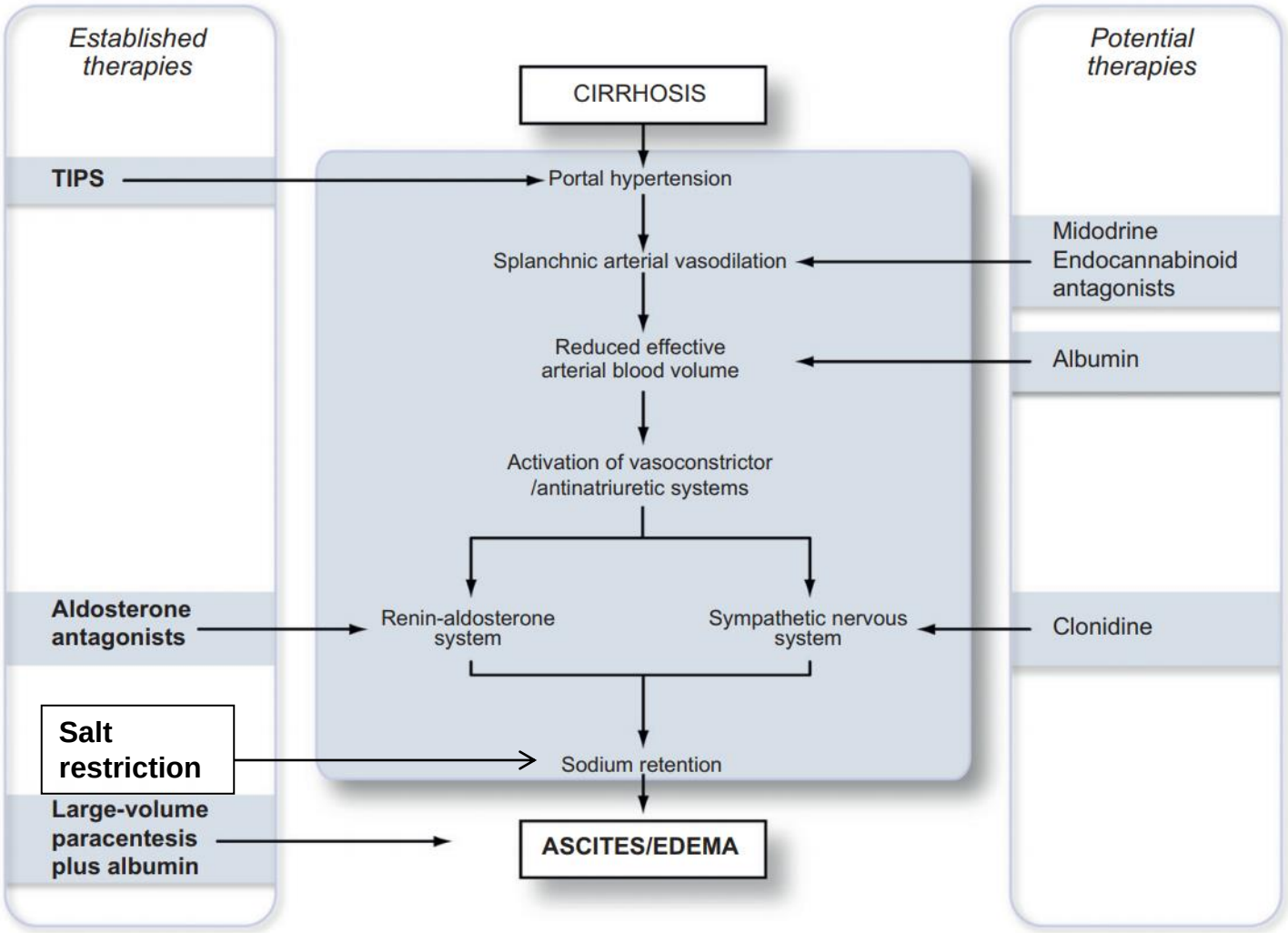
Kiyosue et al, Radiographics 2003

Treatment of Bleeding

- EVL or tissue adhesive (sclerotherapy) for GOV1
- Cyanoacrylate glue for GOV2 and IGV1
  - N-butyl-2-cyanoacrylate
- 21G or 23G needle (6-8mm long)
- Use of lipiodol
- Consideration of early TIPS
- Consider repeat glue injection after 2 weeks in combination with beta blockers (vs TIPS)

de Franchis et al, J Hep 2015
Sarin et al, Clin Liv Dis 2014

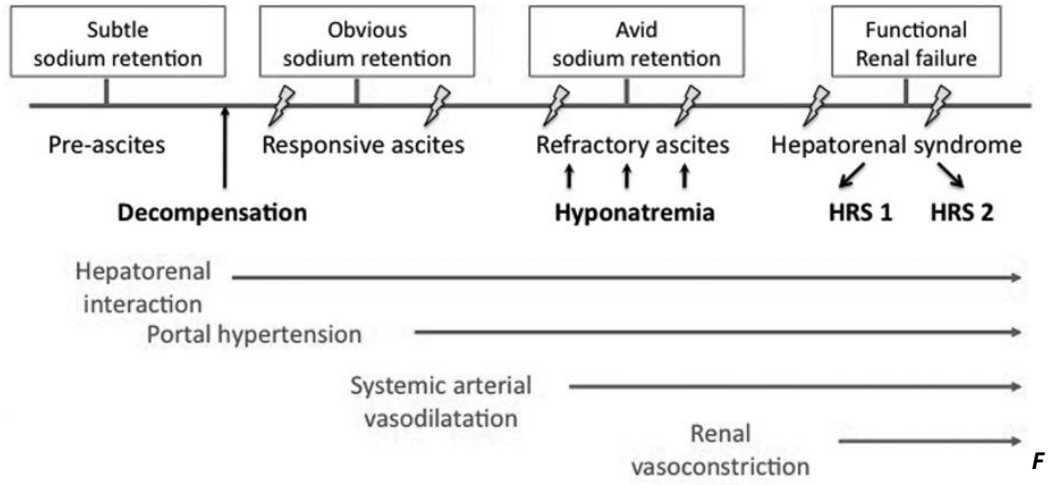
Ascites



Sola et al, J Hep 2010

Management of Ascites

- Dietary Na restriction (88mmol/day)
  - Insensible Na loss 10mmol/day
- Diuretic therapy
- *Albumin*
- Regular large volume paracentesis
- TIPSS



F Wong et al, JGH 2011

Diuretics: Sequential vs combined

3 of 6

sequential diuretic therapy (Group A) and combined diuretic therapy (Group B)

	Group A (n= 50)	Group B (n= 50)	p Value
Number of patients who did not reach the effective diuretic step (%)	6 (12%)	2 (4%)	NS
because of the development of adverse effects	5	2	
because of resistant ascites	1	0	
Number of patients with excessive diuretic response while on treatment with the effective diuretic step (%)	2 (4%)	2 (4%)	NS
Number of patients with adverse effects while on treatment with the effective diuretic step (%)	14 (32%)	8 (17%)	<0.05
Total number of treatment failures	22 (44%)	12 (24%)	<0.05

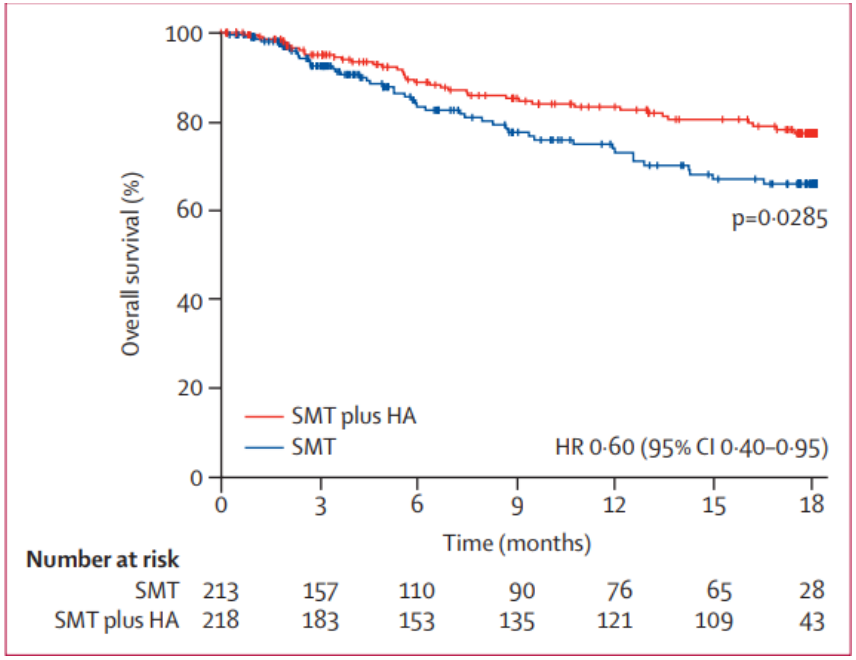
Angeli et al, Gut 2010

Diuretics: Caution

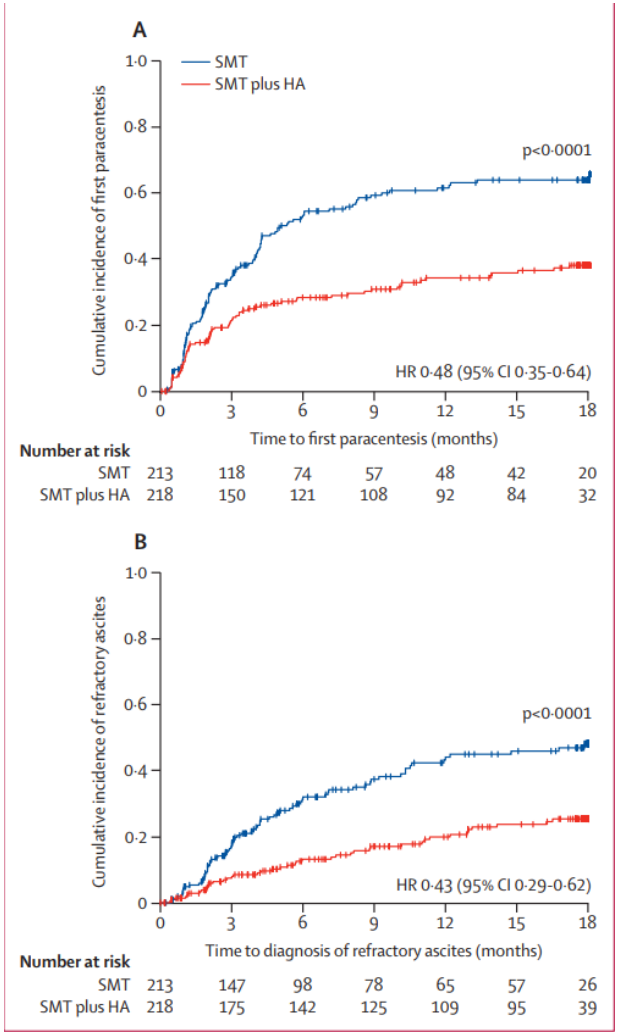
- Maximum 0.5kg/day weight loss
  - Maximum ascites absorption 400ml/day
- Urine sodium to potassium ratio > 1
- Lack of response: wt loss <0.8kg over 4 days and urine Na output less than intake
- Electrolytes (Na / K) and renal function

F Wong et al, JGH 2011

Ascites: Albumin?



Weekly albumin



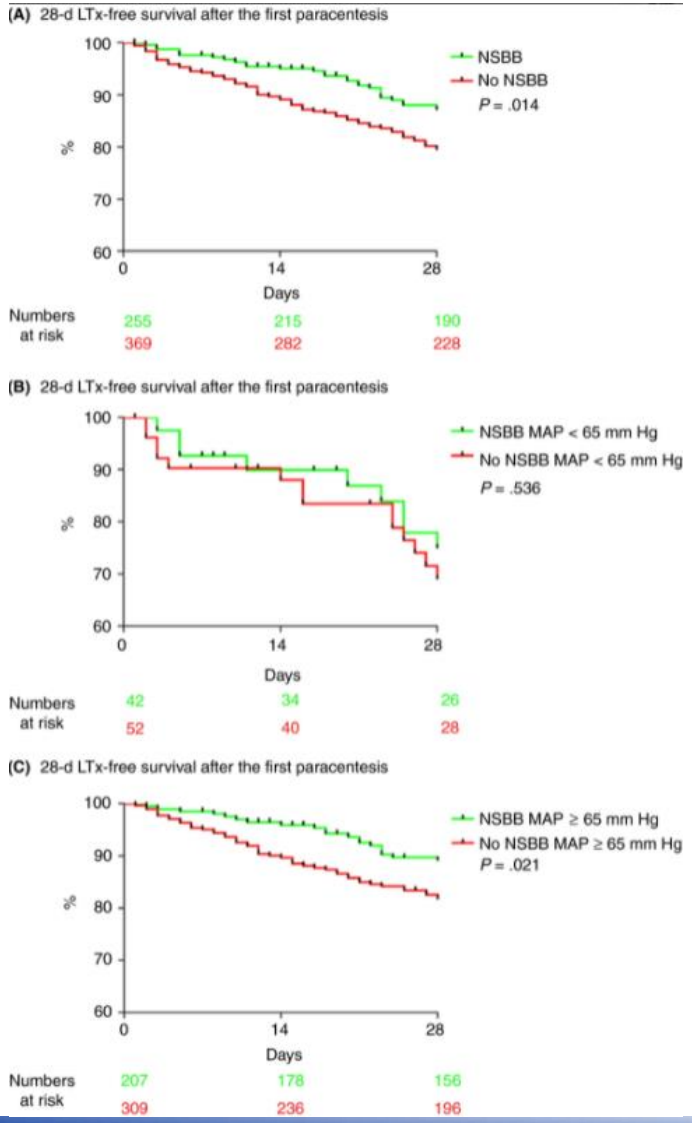
Caraceni et al, Lancet 2018

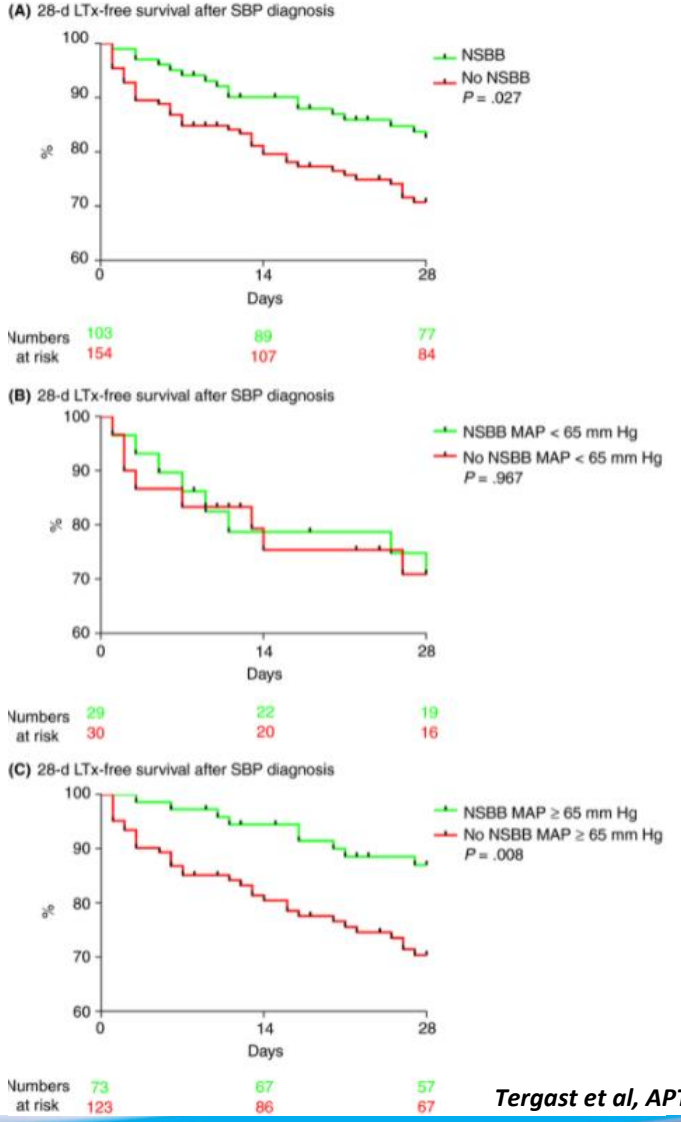
NSBB Controversy

- Refractory ascites and SBP are not absolute contraindications
- High doses (>160mg/day) propranolol should be avoided
- In refractory ascites and severe circulatory dysfunction (SBP < 90 / MAP <65 or Na <130 or HRS), dose of NSBB decreased or drug held
- NSBB can be reintroduced if improves

Garcia-Tsao et al, Hepatology. 2017

NSBB safety is dependent on SBP





Tergast et al, APT 2019

Spontaneous Bacterial Peritonitis

- Low index of suspicion (infection, decompensation)
- PMN >250cells/mm3
- Presence of bacteria in the ascites

Runyon et al, Hepatology. 2013

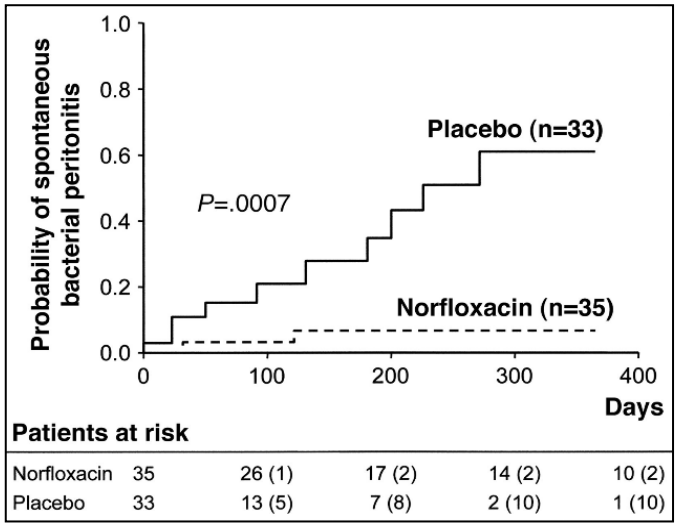
IV Albumin for SBP

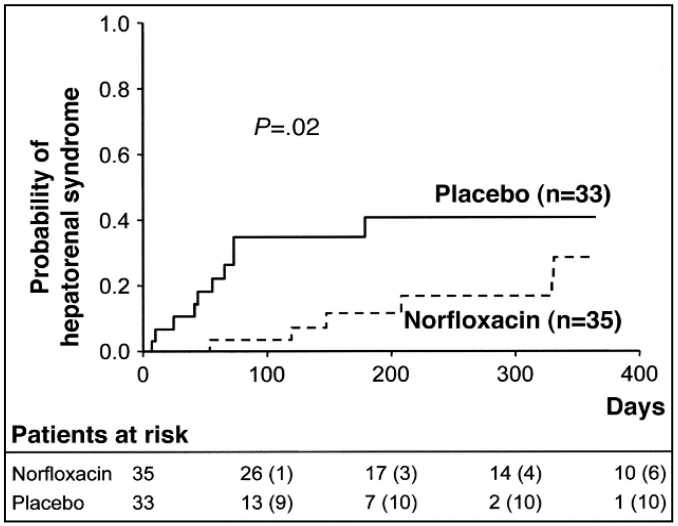
Outcome Variable	Cefotaxime (N=63)	Cefotaxime plus Albumin (N=63)	P Value
Resolution of infection — no. (%)†	59 (94)	62 (98)	0.36
Duration of antibiotic therapy — days	6±1	5±1	0.48
Paracentesis for ascites after resolution of infection — no. (%)‡	16 (25)	14 (22)	0.83
Hospital stay — days	13±1	14±1	0.48
Renal impairment — no. (%)	21 (33)	6 (10)	0.002
Death — no. (%)			
In hospital§	18 (29)	6 (10)	0.01
At three months¶	26 (41)	14 (22)	0.03

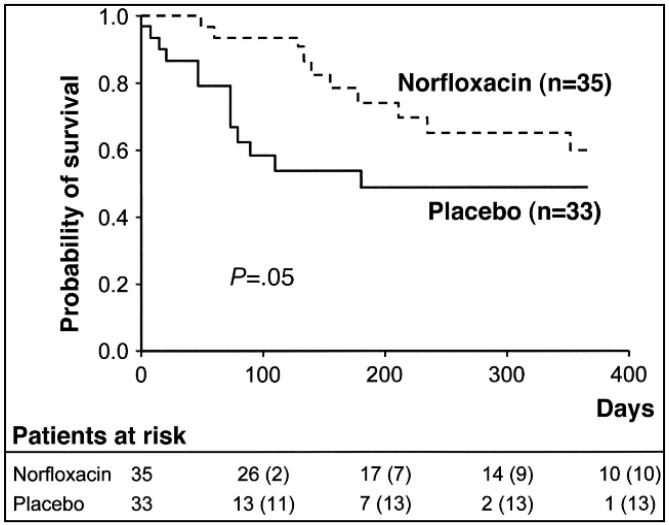
"…albumin was given at a dose of **1.5 g per kilogram of body weight** during **the first six hours** after enrollment, followed by **1 g per kilogram on day 3**…"

Pau Sort et al, NEJM 1999

Primary Prophylaxis for SBP



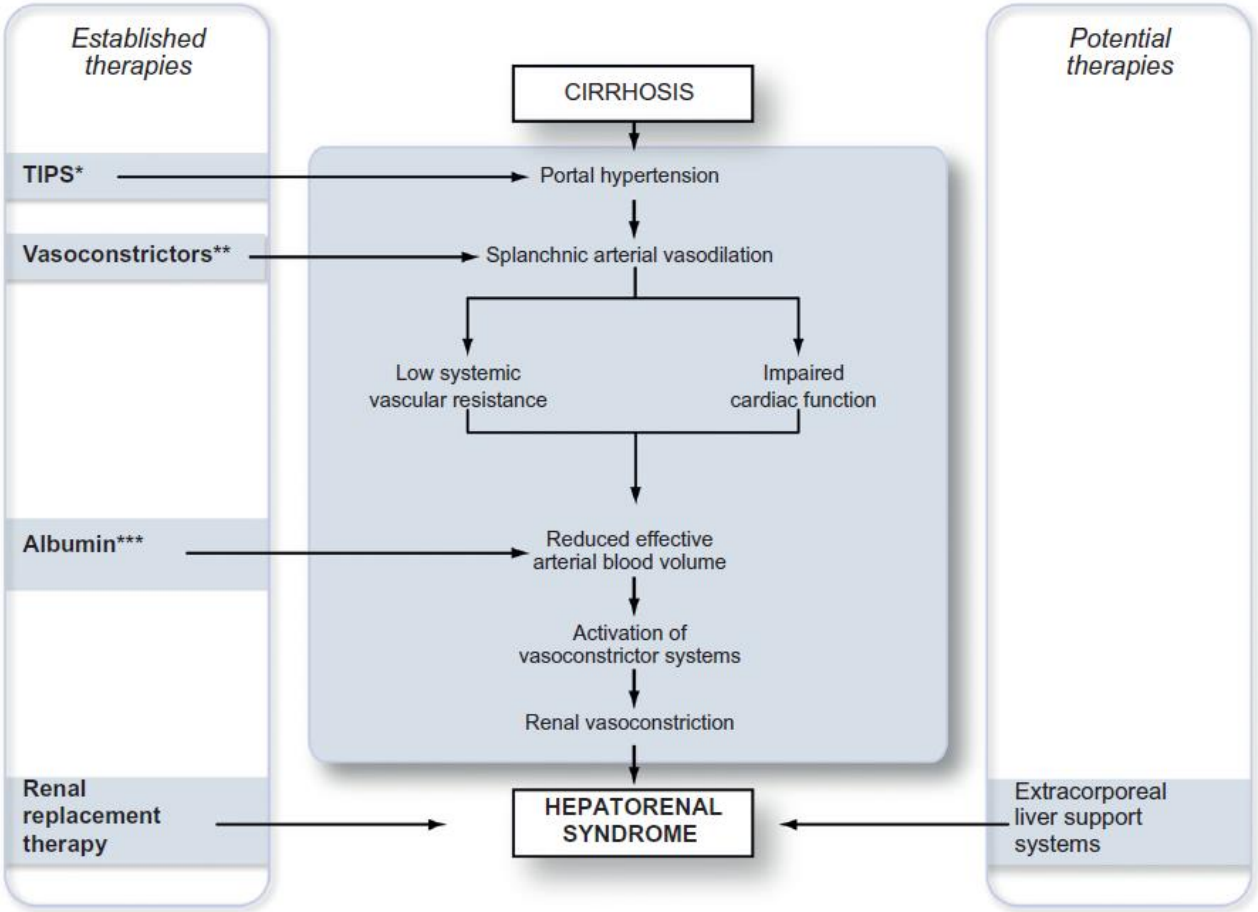




- Fluid protein < 15g/L
- Impaired renal function
  - Cr > 1.2 mg/dL or
  - BUN > 25 mg/dL or
  - Na < 130 or
- Impaired liver function
  - Child's >9 and
  - Bil > 3mg/dL

Fernandez et al, Gastroenterology 2007

Hepatorenal Syndrome – Renovascular



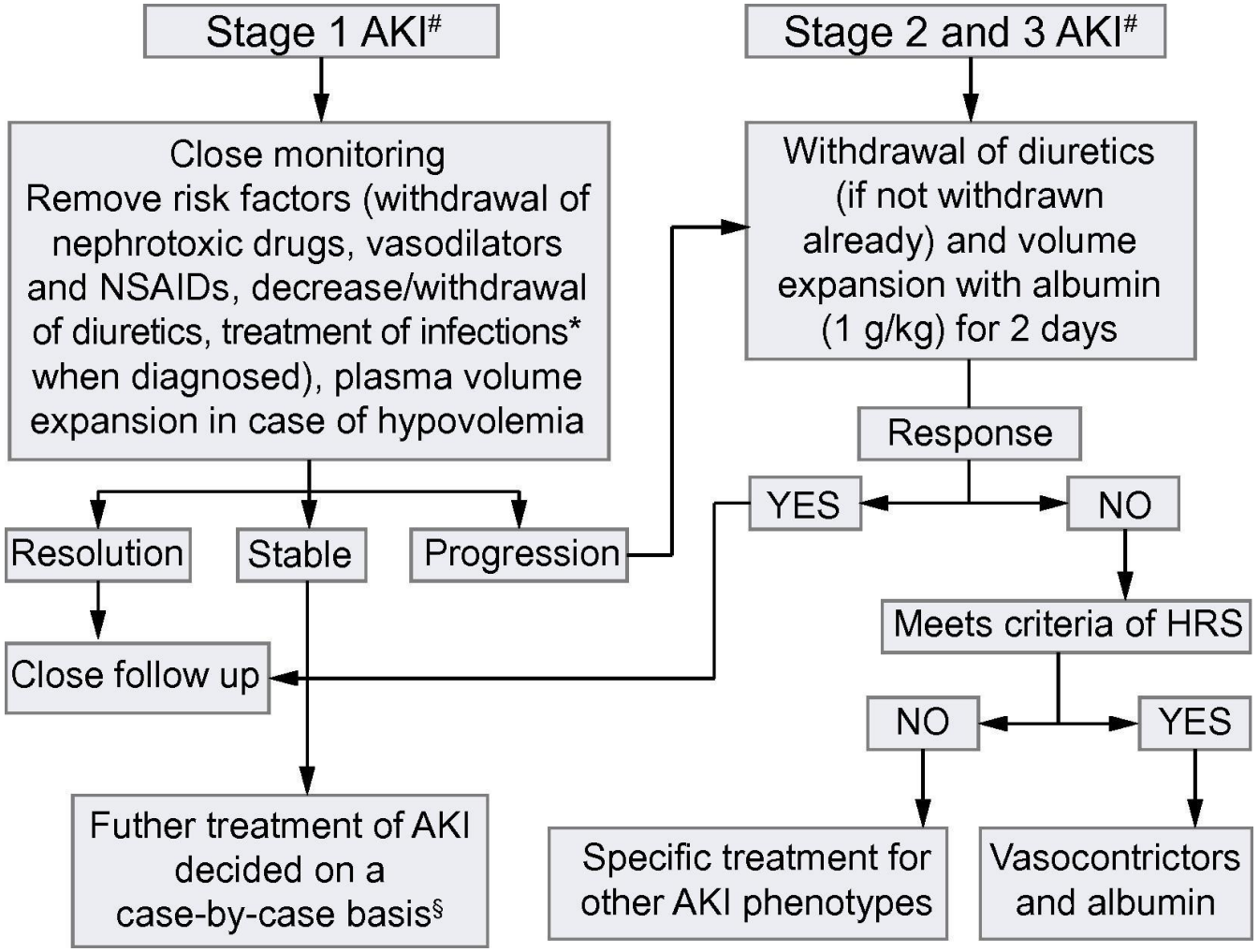
Sola et al, J Hep 2010

HRS1 – Defintions (AKI)

Term	Descriptor
Baseline	Cr within last 3 months
AKI	➢Rise in Cr >26.5umol/L within 48hr ➢Rise of 50% from baseline within last 7 days
Stage 1	26.5umol/L or 1.5-2x baseline
Stage 2	2-3x baseline
Stage 3	>3x baseline ➢353.6umol/L with a rise in >26.5umol/L ➢Initiation of RRT
Progression	Move to a higher stage and/or need for RRT
Regression	Move to a lower stage
Partial resp	Regression, but > 26.5umol/L above baseline
Full resp	Cr within 26.5umol/L of baseline

Angeli P et al, J Hep 2015

HRS1 – Management



Angeli P et al, J Hep 2015

Terlipressin

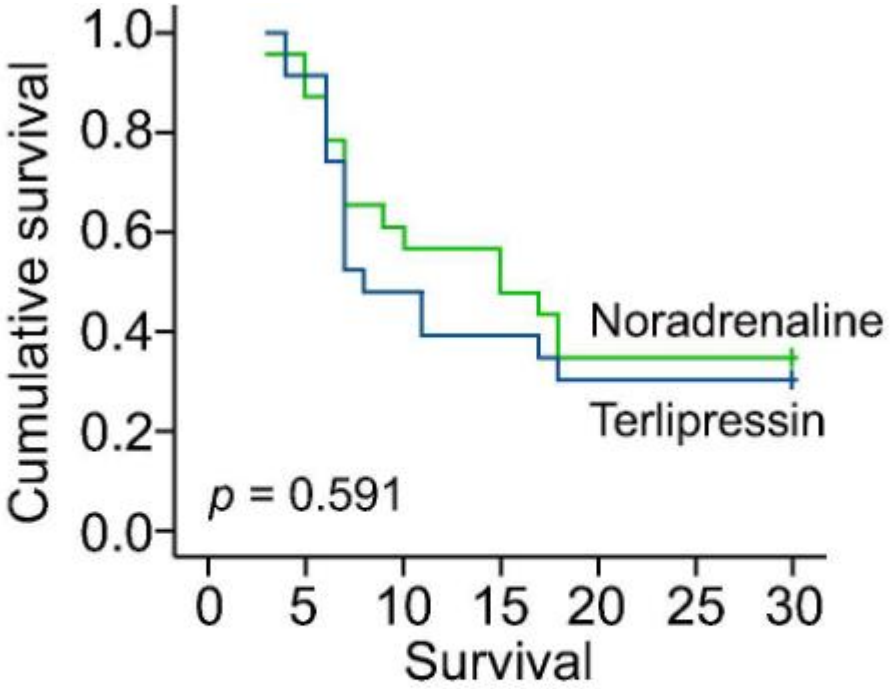
Table 2. Primary and Four Secondary End Points Included in Multiplicity Adjustment.*

End Point	Terlipressin	Placebo	P Value
	number/total number of patients (percent)		
Primary end point of verified reversal of HRS†			0.006
Clinical success	63/199 (32)	17/101 (17)	
Clinical failure	121/199 (61)	81/101 (80)	
Competing event‡			
Liver transplantation	10/199 (5)	2/101 (2)	
Death	5/199 (3)	0/101	

Increased adverse events in Terli arm leading to discontinuation

Wong et al, NEJM.2021

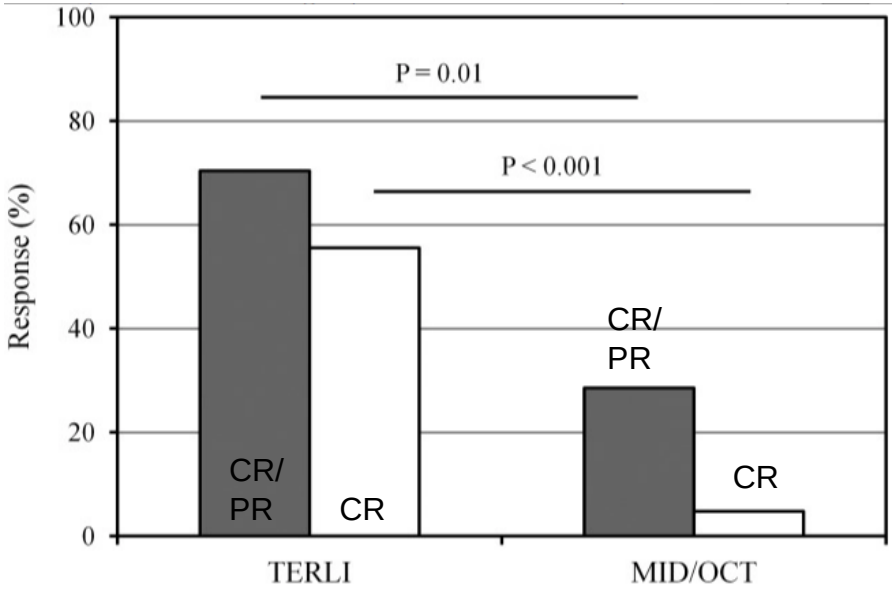
Terlipressin vs NorA?

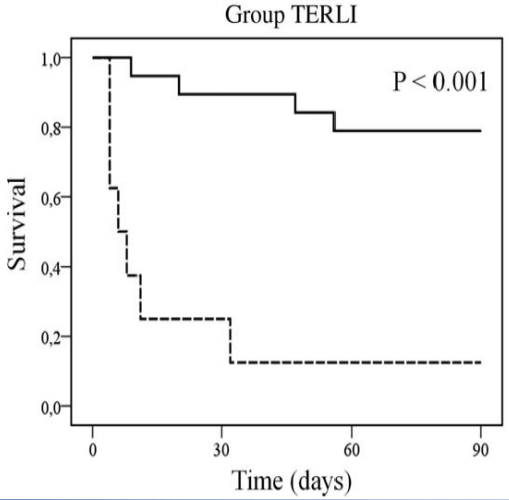


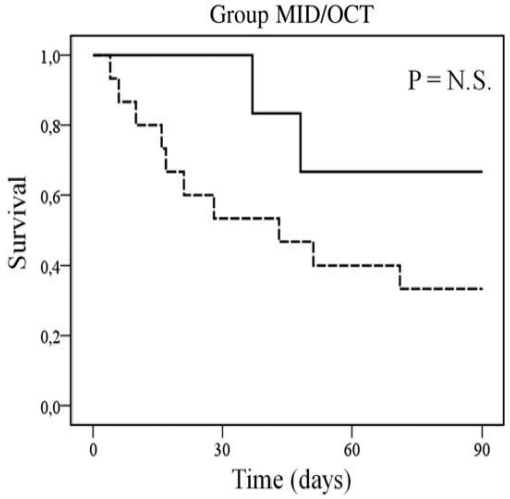
Patients at risk	Day					
	5	10	15	20	25	30
Terlipressin group (n = 23)	20	11	9	7	7	7
Noradrenaline group (n = 23)	21	13	11	8	8	8

Singh V et al, J Hep 2012

Terlipressin vs Mid/Oct?





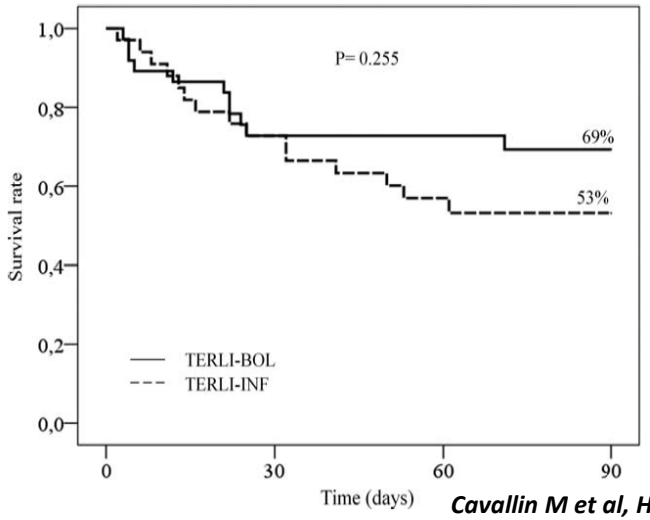


Cavallin M et al, Hepatology 2015

Terlipressin: Bolus vs infusion

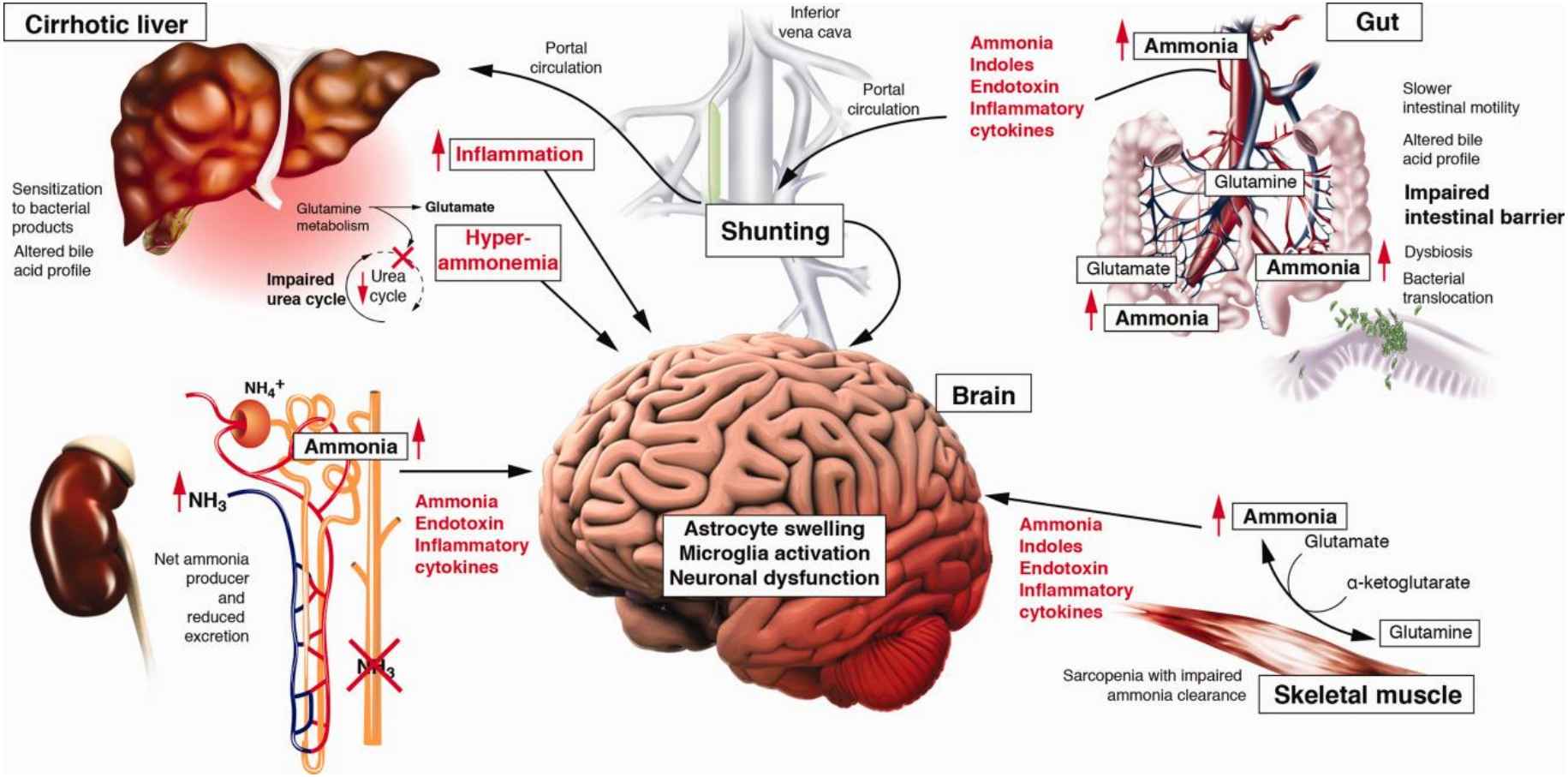
	TERLI-INF Group (n = 26)	TERLI-BOL Group (n = 24)	*P*
Length of treatment, days	9.31 ± 4.06	8.52 ± 3.86	0.4705
Cumulative dose of albumin, g	189.20 ± 91.78	164.38 ± 89.36	0.3311
End of treatment sCr, μmol/L	120.00 ± 33.34	121.25 ± 38.53	1.0000
Maximum daily dose of terlipressin, mg	2.62 ± 1.06	4.50 ± 3.06	0.0001
Mean daily dose of terlipressin, mg	2.23 ± 0.65	3.51 ± 1.77	0.0001
Delta CTP	−0.62 ± 0.65	−0.52 ± 0.79	0.8014
Delta MELD	−7.31 ± 3.70	−6.88 ± 3.48	0.6048
Delta MELD-Na	−7.69 ± 4.27	−5.46 ± 6.88	0.2712
Delta MAP			
Day 3 of treatment versus baseline	9.10 ± 11.32	5.35 ± 12.53	0.5957
Middle of treatment versus baseline	15.04 ± 18.04	10.75 ± 12.54	0.5164
End of treatment versus baseline	12.11 ± 19.34	9.20 ± 12.90	1.0000

	TERLI-INF Group (n = 34)	TERLI-BOL Group (n = 37)	*P*
Patients, no. (%)	7 (20.59)	16 (43.24)	<0.05
Suspected intestinal ischemia	—	3	—
Peripheral ischemia	1	—	—
Circulatory overload	2	5	—
Angina pectoris	3	3	—
Arrhythmia	—	1	—
Arterial hypertension	1	—	—
Persistent diarrhea	—	2	—
Others	—	2	—



Cavallin M et al, Hepatology 2016

Hepatic Encephalopathy



Bajaj et al, Hepatology 2015

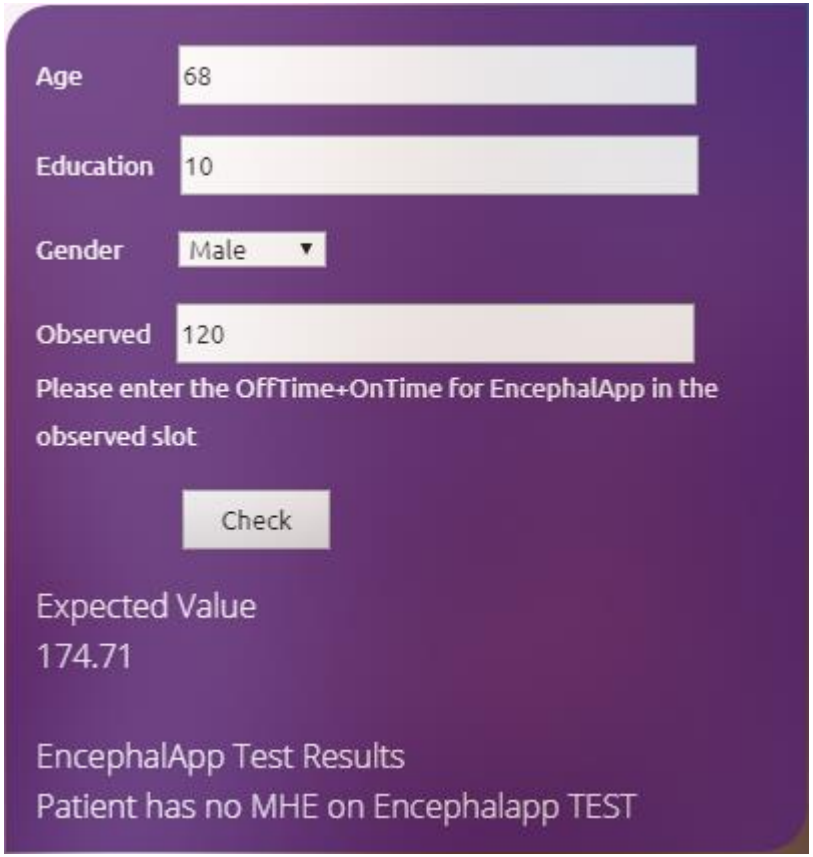
Hepatic Encephalopathy

HEPATIC ENCEPHALOPATHY (HE)		
Patients can change between these states over time	**COVERT HE** ← → **OVERT HE** **Includes minimal HE and grade 1 HE** 40-60% of patients	**Subdivided by** **Time course:** episodic (one epidose/6 months), recurrent: >1/6 months, persistent—never resolved **Factor-associated:** precipitated (associated factors), spontaneous (none))
Diagnosis	• Cannot be diagnosed clinically • Needs combination of paper/pencil/ computerized/neurophysiological tests	• Exclusion of other causes of altered mental status • Obvious clinical manifestations ranging from disorientation through coma without focal deficits
Clinical relevance	• Overt HE development, impaired quality of life • Driving and socioeconomic status • Higher death and hospitalizations	In-hospital death, aspiration, recurrent episodes, disability, burden on caregivers and socioeconomic status, poor survival within 2 years of discharge, persistent cognitive impairment after multiple episodes
Treatment strategies	• Growing evidence base but not standard care • Can treat patients on an individual basis with lactulose, rifaximin, or probiotics	**Acute episode:** care of unconscious patient, identify/treat precipitating factors, and empiric treatment with lactulose, then rifaximin **To prevent recurrence:** after first episode, lactulose; after second episode, rifaximin **Overall:** consideration for liver transplantation

Bajaj et al, Hepatology 2015

MHE





www.encephalapp.com

Acharya C et al, Liver Transpl 2017
Allampati S et al, Am J Gastro 2016
Bajaj et al, CGH 2015
Bajaj et al, Hepatology 2013

Porto-pulmonary Hypertension

Pulmonary Hemodynamics Associated with Advanced Liver Disease (Right Heart Catheterization)

Macitentan for the treatment of portopulmonary hypertension (PORTICO): a multicentre, randomised, double-blind, placebo-controlled, phase 4 trial

Prof Olivier Sitbon, MD • Prof Jaume Bosch, MD • Emmanuelle Cottreel, MSc • Denes Csonka, PhD • Pascal de Groote, MD • Prof Marius M Hoeper, MD • Prof Nick H Kim, MD • Nicolas Martin, MSc • Laurent Savale, MD • Prof Michael Krowka, MD • Show less

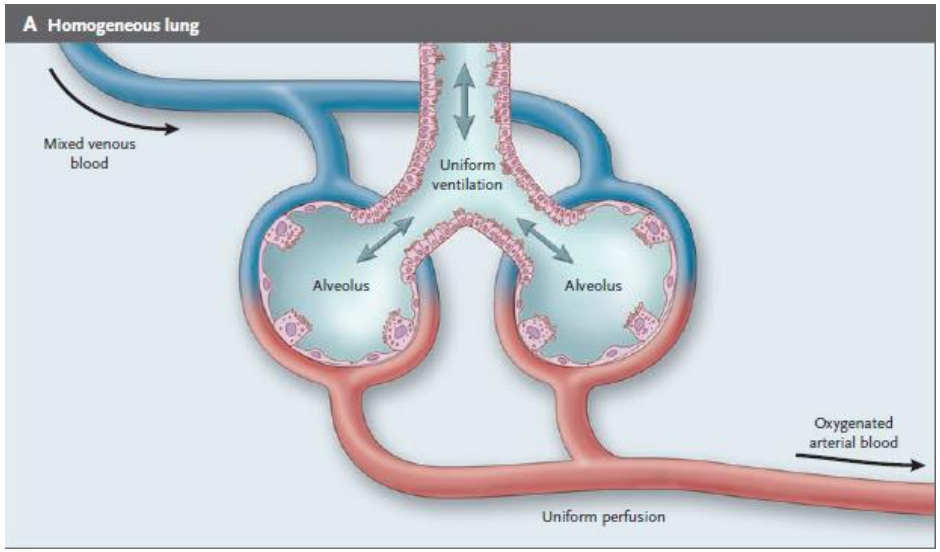
Published: June 06, 2019 • DOI: https://doi.org/10.1016/S2213-2600(19)30091-8 • Check for updates

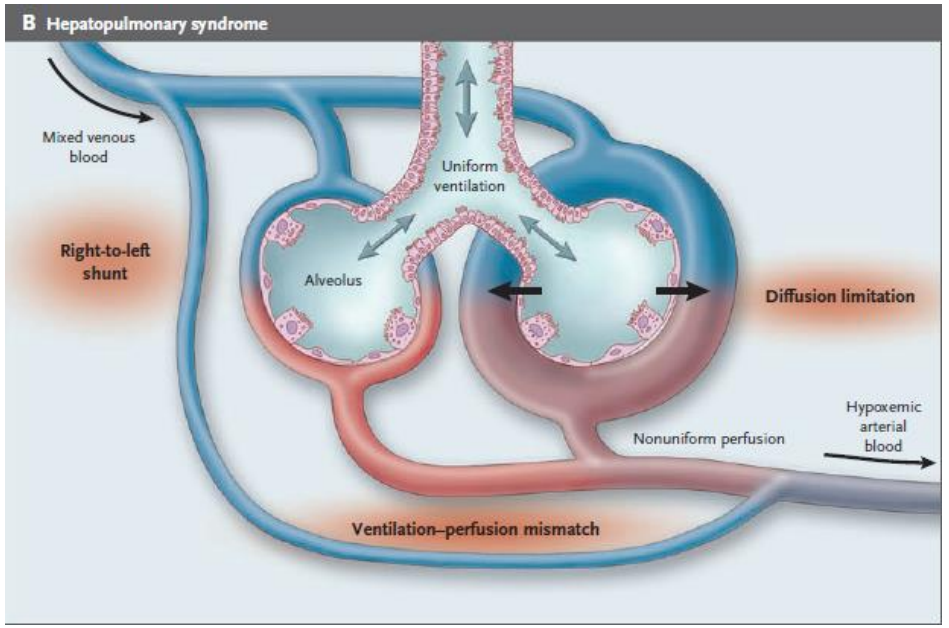


a. Mean pulmonary artery pressure (MPAP) $>$ 25 mm Hg
b. Pulmonary vascular resistance (PVR) $>$ 240 dynes.s.cm^{-5}*
c. Pulmonary capillary wedge pressure (PCWP) $<$15 mm Hg

Krowka, Semin Respir Crit Care Med 2012

Hepatopulmonary Syndrome





Dilated capillaries
Blood flow not uniform
Shunting

→

Ventilation-perfusion mismatch

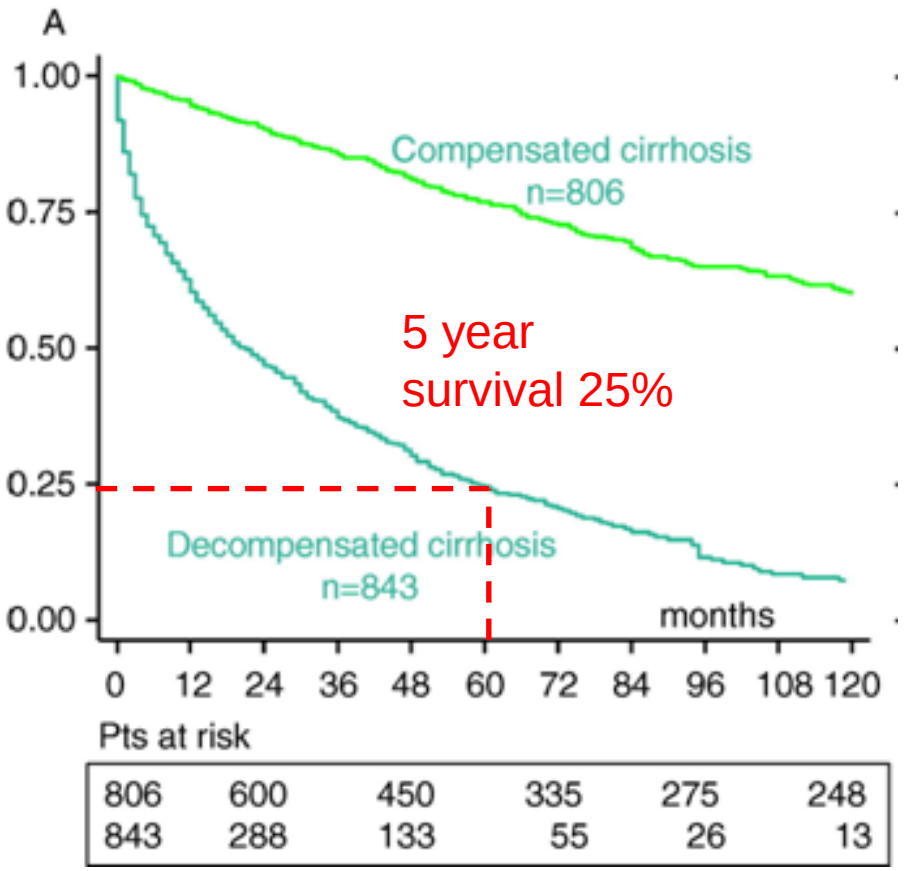
Rodriguez-Roisin, NEJM 2008

Decompensated cirrhosis – when to transplant?



Costs
QoL
Availability of organs

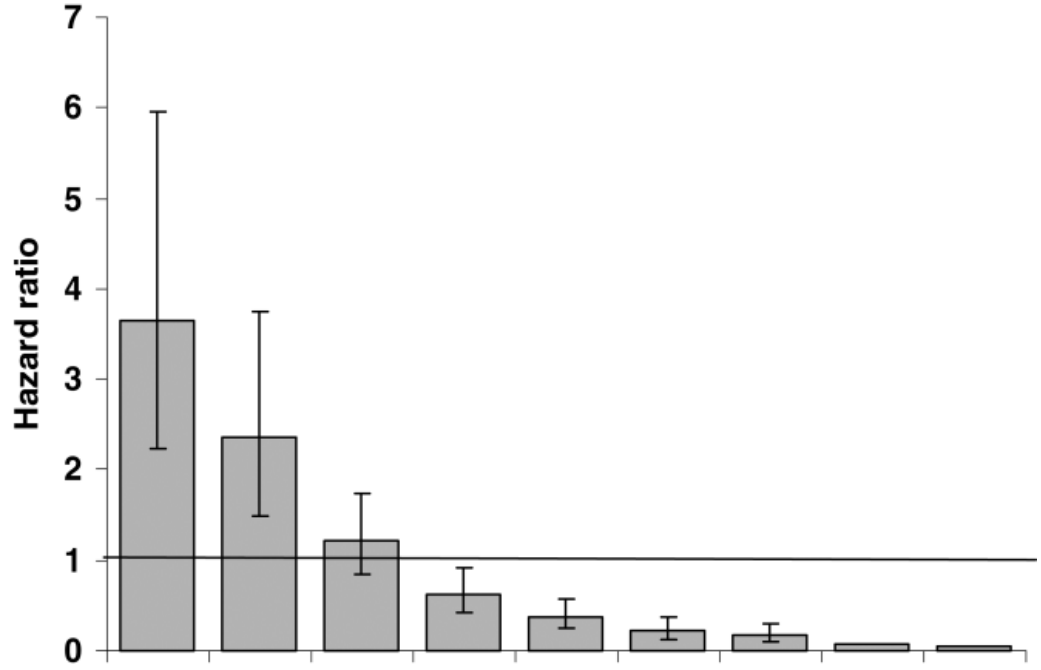
Liver Transplant for Decompensated Cirrhosis



5 year survival of 75% with liver transplant (SRTR data)

D'Amico et al, J Hep 2006
Scientific Registry of Translpant Recipients 2011

Decompensated cirrhosis – when to transplant?



MELD	6-11	12-14	15-17	18-20	21-23	24-26	27-29	30-39	≥40
Hazard Ratio	3.64	2.35	1.21	0.62	0.38	0.22	0.18	0.07	0.04
p-values	<0.001	<0.001	0.41	<0.01	<0.001	<0.001	<0.001	<0.001	<0.001

Merion et al, Am J Transpl 2005

Summary

- Advanced liver disease is the final common pathway of most liver diseases
- It has a wide spectrum of severity, with different targets and complications at each stage
- Intensity of care has to increase with worsening severity of disease
- Good understanding of fluid, hemodynamics, and pressures is key in these patients
- Liver transplantation remains one of the main options for patients with severe disease