

Complications of Cirrhosis: The Sequelae of Portal Hypertension

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Case Study

- 62-year-old female
- Compensated alcohol-associated cirrhosis
 - Alcohol use disorder in remission

What is cirrhosis?

- Final pathway of any chronic liver disease
- Inflammation leads to fibrosis
- Cirrhosis = fibrosis encircling nodules of liver tissue

Case Study

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- Fibroscan, labs & imaging:
 - Liver stiffness measurement (LSM) = 21 kPa
 - Platelet count = 110k
 - Abdominal ultrasound shows nodular liver & splenomegaly
- Does this patient have portal hypertension, and should it be treated?

What is Portal Hypertension?

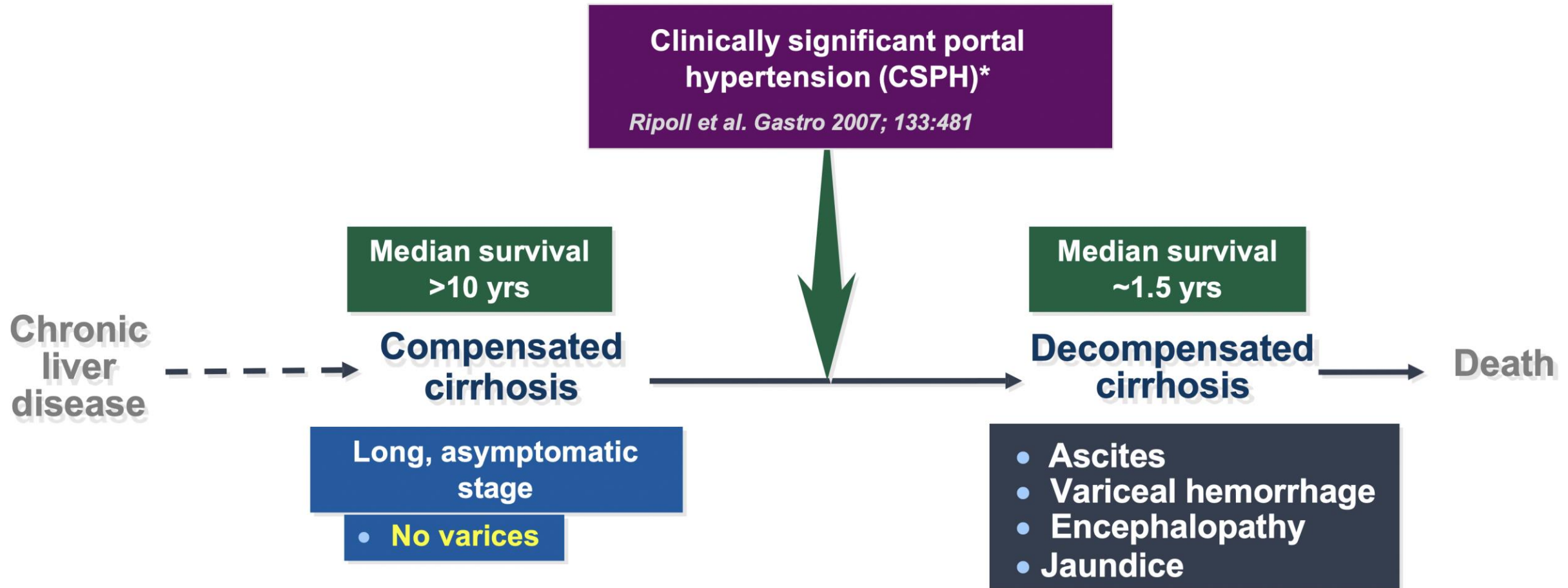
- Elevated venous pressure at any level in the portal system
- Clinical manifestations:
 - Splenomegaly → thrombocytopenia
 - **Ascites**
 - Porto-systemic collaterals
 - Gastro-esophageal varices: **variceal bleeding**
 - Porto-systemic shunting: **hepatic encephalopathy**

Presentation depends on site of increased resistance

Taxonomy of Portal Hypertension

- Pre-hepatic → ex: portal vein thrombus
- Hepatic
 - Pre-sinusoidal – ex: schistosomiasis
 - Sinusoidal – cirrhosis (most common)
 - Post-sinusoidal – ex: veno-occlusive disease
- Post-hepatic → ex: Budd-Chiari

Compensated vs. Decompensated Cirrhosis: CSPH is the Main Driver of Decompensation

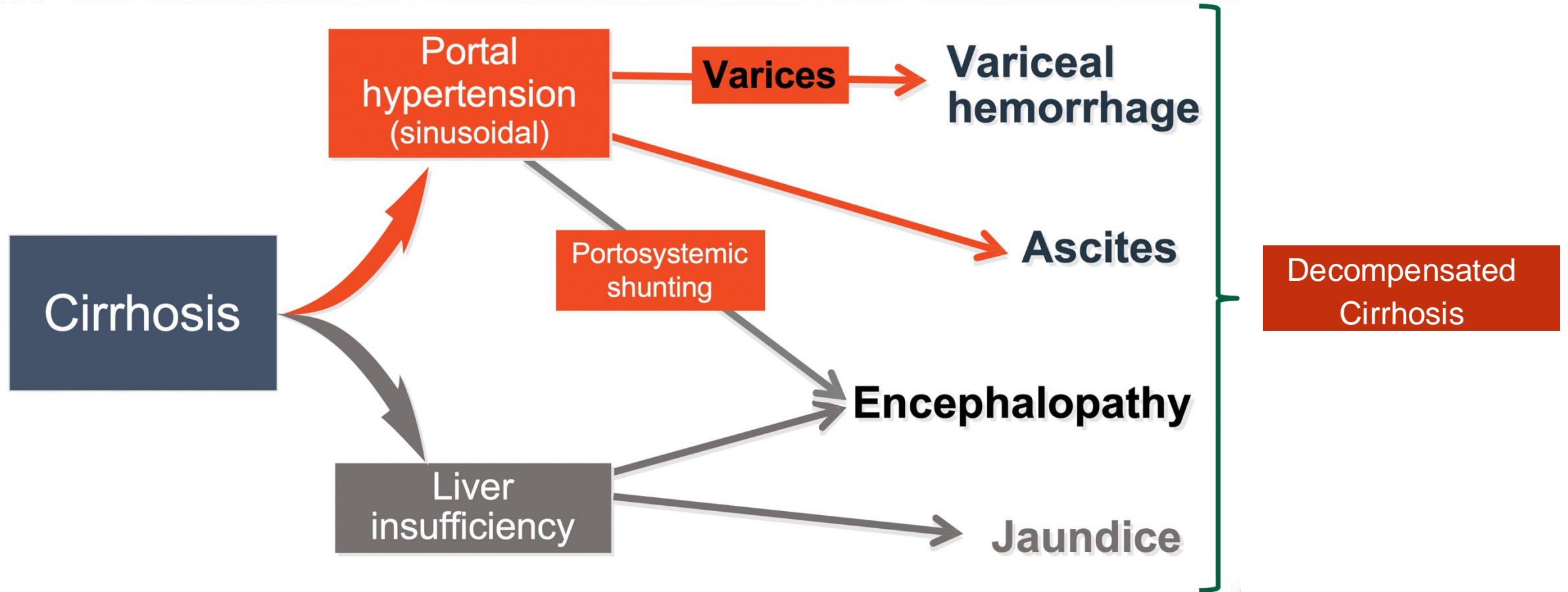


Clinically, making the diagnosis of compensated cirrhosis is more challenging!

Making the diagnosis of a compensated patient is **challenging**

Making the diagnosis of a decompensated patient is **not challenging**

Complications of Cirrhosis Results Mostly From Portal Hypertension



Diagnosis of Portal Hypertension

Clinically!

- Cirrhosis
- Low platelets
- Ascites
- Varices on EGD

Imaging

- Splenomegaly
- Portosystemic collaterals
- Portal flow mean velocity <12 cm/second
- Reversal of flow in the portal vein
- Portal vein diameter >13 mm
- Portal/splenic/superior mesenteric vein thrombosis

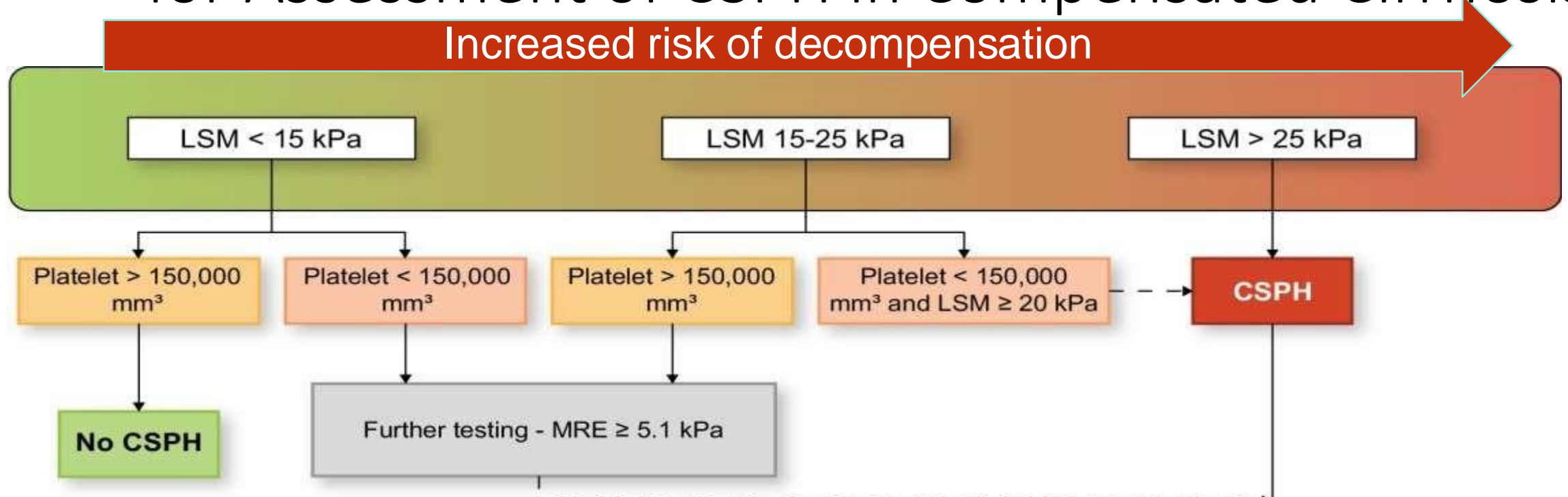
Clinical Manifestations & Complications of Portal Hypertension

- Ascites
- Spontaneous bacterial peritonitis
- Splenomegaly
- Thrombocytopenia
- Variceal hemorrhage
- Portal hypertensive gastropathy
- Hepatorenal syndrome
- Hepatic hydrothorax
- Hepatopulmonary syndrome
- Portopulmonary hypertension
- Portal vein thrombosis

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Liver Stiffness Measurement by Transient Elastography for Assessment of CSPH in Compensated Cirrhosis



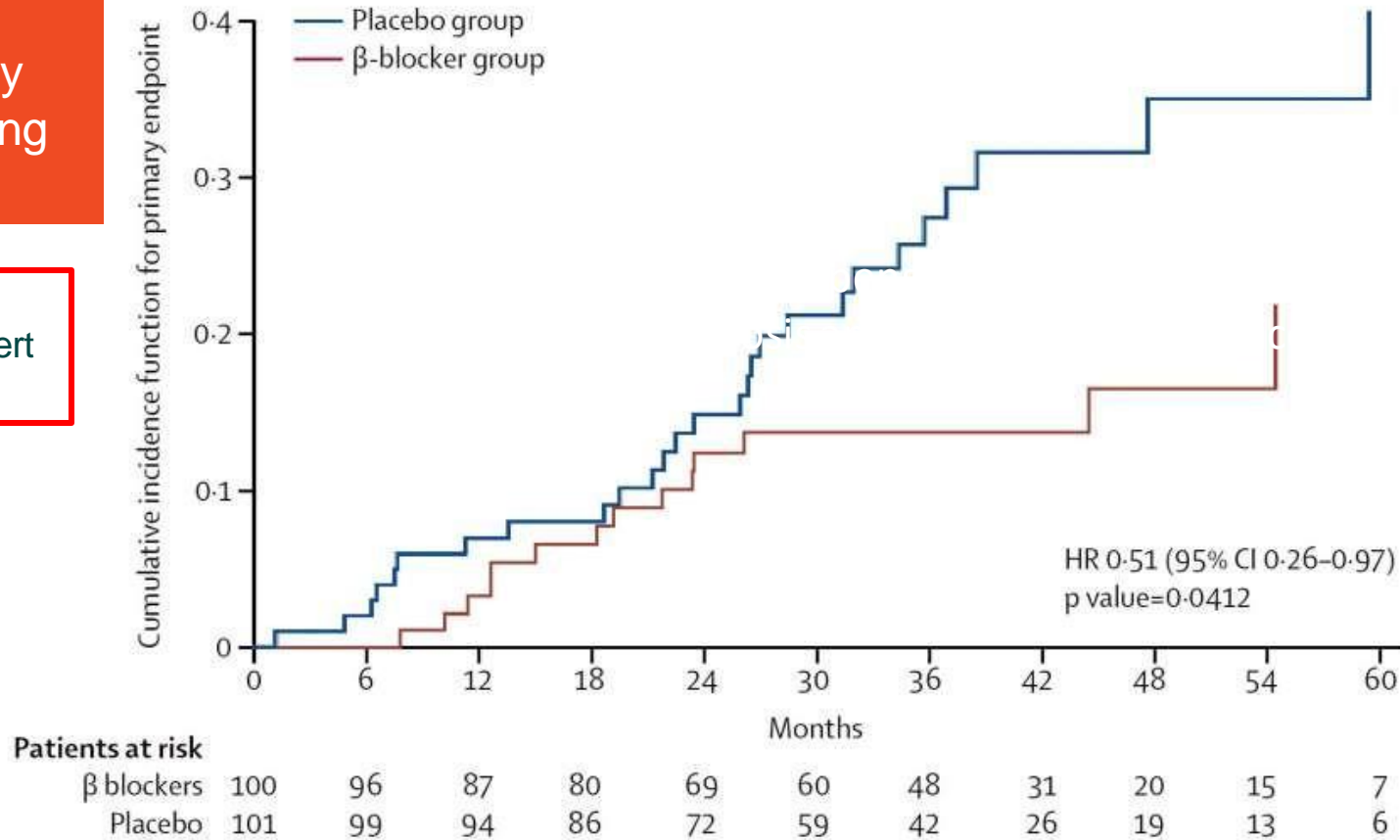
LSM (kPa)	<10	10-15	>15	>20	>25
cACLD <i>Compensated advanced CLD</i>	No	Suggestive (no CSPH)	Highly likely (- or + CSPH)	cACLD + CSPH	
Platelet count	Any	>150	>150 / <110	<150	Any

CSPH = clinically-significant portal hypertension

β -blockers Prevent Decompensation and/or Death in Patients with Compensated Cirrhosis and CSPH

Probability of developing any decompensating event / death

Ascites, variceal hemorrhage or overt encephalopathy



- The primary endpoint occurred in 16% in the BB group vs. 27% in the placebo group
- An absolute risk reduction of 11%
- NNT = 9

NSBB should be considered to prevent decompensation in patients with cirrhosis and CSPH

Baveno VII, 2021

Management of CSPH

Non-Selective Beta-Blockers (NSBBs) in patients with compensated cirrhosis + CSPH

- Prevention of clinical decompensation (ascites, variceal hemorrhage, HE)
- Medications: **Carvedilol**, propranolol, nadolol
- Safety considerations: Systolic BP >90, HR >50
- Contraindications: Severe asthma, bradyarrhythmia, heart block
- Side effects: Dizziness, fatigue, decreased exercise tolerance, sexual dysfunction

Case Study

Our patient has **CSPH** as indicated by **LSM + PLT count**

1. Are there any contraindications to starting NSBB?
2. Discuss with patient the benefits of NSBB for CSPH
3. Start NSBB: **Carvedilol** (or propranolol or nadolol)
4. If unable to tolerate NSBB / refuses NSBB, consider EGD for variceal surveillance
 - No/small varices – EGD in 2-3 years
 - Medium/large varices – EVL until obliteration, EGD at 6 months post obliteration, followed by annual surveillance endoscopy

Primary Goal: Prevent the 1st episode of decompensation in the patient with cirrhosis + CSPH

~~Treatment~~ Management of Decompensated Cirrhosis

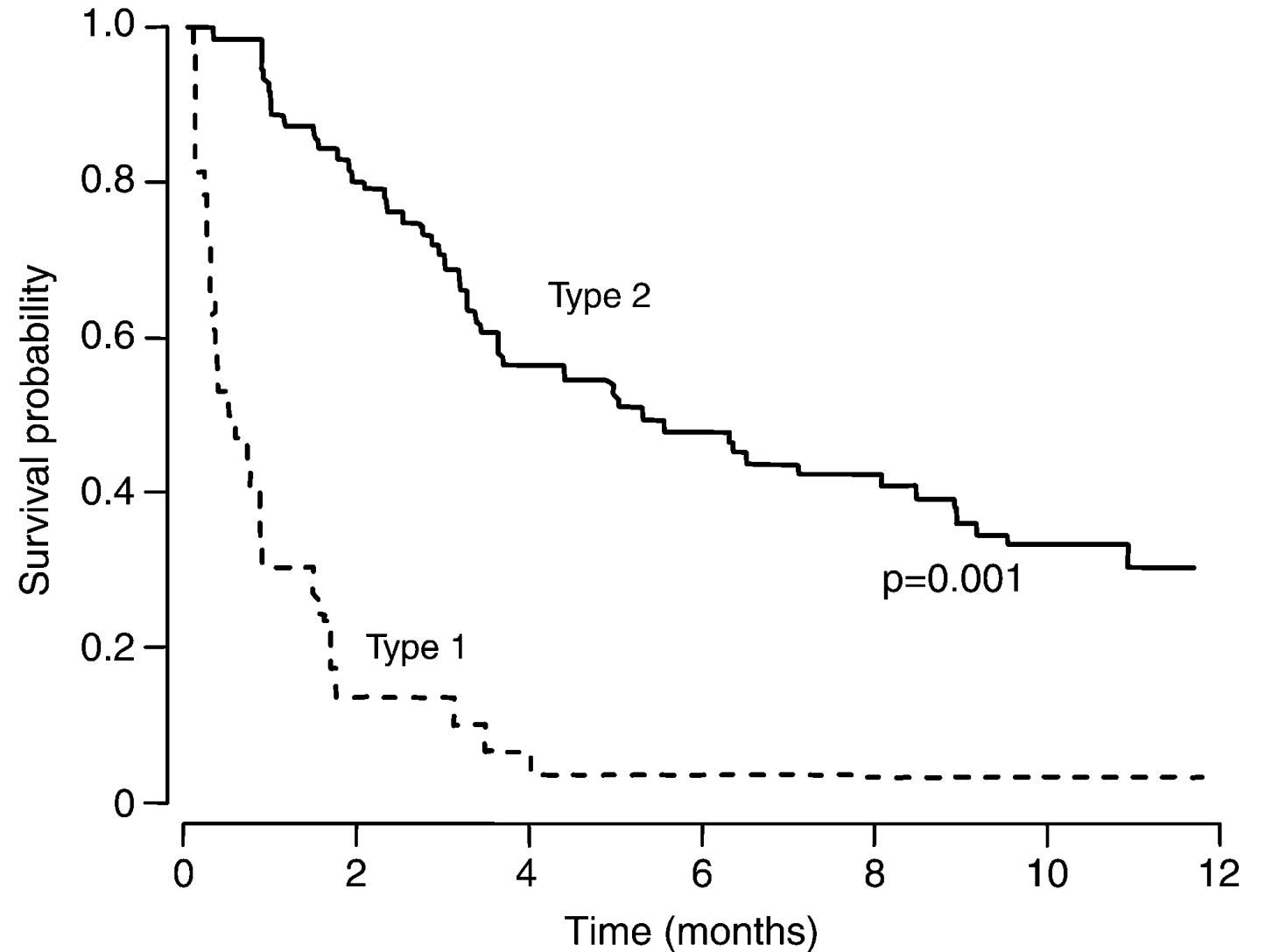
Ascites

- Sodium restriction <2000 mg daily
- Furosemide 40 mg & spironolactone 100 mg
 - Titrate up!
 - Check BMP in 1-2 weeks
- Paracentesis with albumin
 - Antibiotic prophylaxis?
- Refractory ascites
 - TIPS

Goal: Eliminate need for paracentesis

Hepatorenal Syndrome

- HRS-AKI
 - Formerly “Type I”
- HRS-CKD
 - Formerly “Type II”



Diagnosis of HRS-AKI (AASLD & AGA)

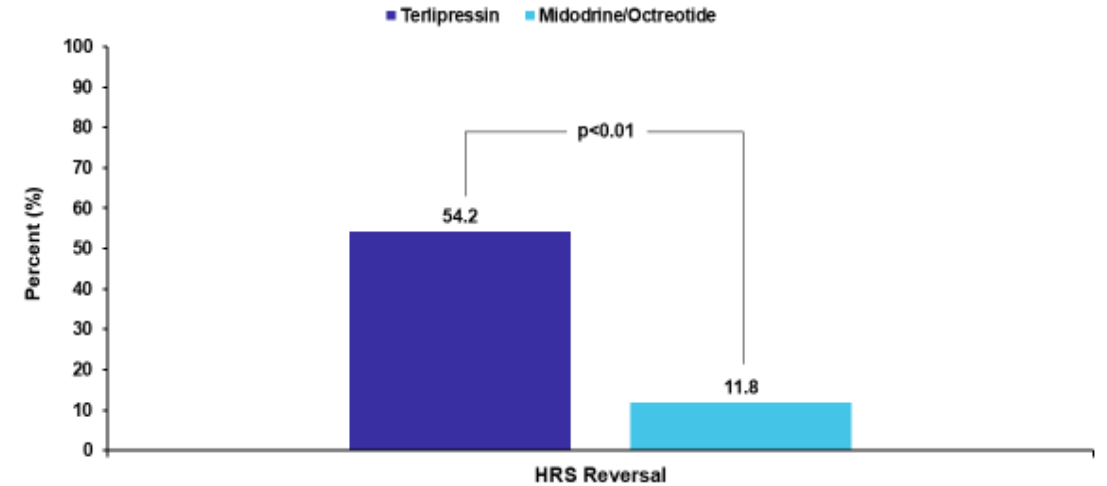
- Cirrhosis with ascites
- No response to withdrawal of diuretics or volume expansion with albumin (max 1 g/kg body weight/day)
- Absence of shock
- No recent use of nephrotoxic drugs (e.g., NSAIDs)
- No signs of structural kidney injury

Management of HRS

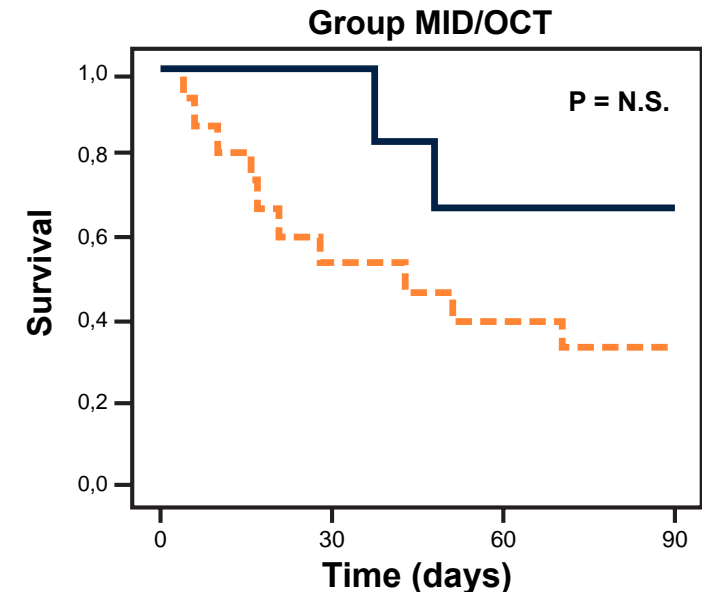
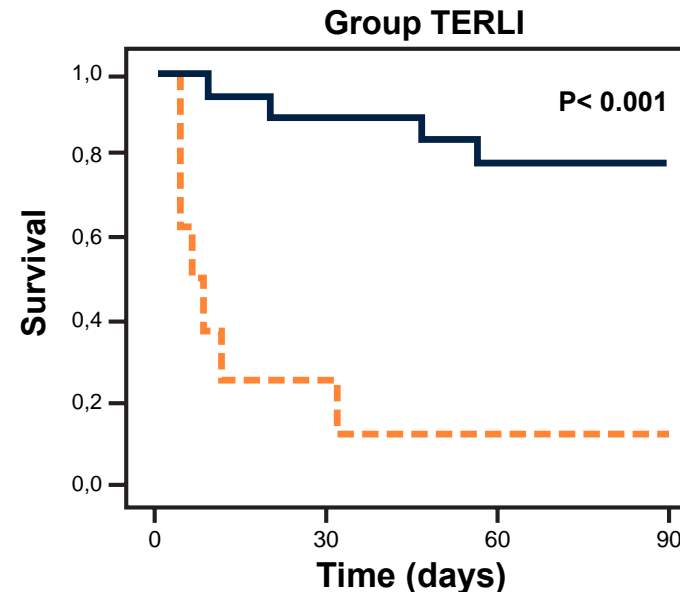
- Definition of HRS-AKI has become much more liberal to help identify those for early intervention
- First line therapy for HRS-AKI is a vasoconstrictor with albumin
 - Terlipressin

Goal: Improve survival

Terlipressin vs Midodrine/Octreotide in a Randomized Controlled Study



Probability of 90-Day, Transplant-Free Survival According to Response to Treatment



Hepatic Encephalopathy

Have you or a loved one experienced any of these symptoms?

Use this checklist to record common symptoms of hepatic encephalopathy (HE)

It is important for you to identify signs of an episode of HE. By paying close attention to the mental and physical symptoms of HE, you can alert your doctor before things get worse.

Whether you are a patient or a caregiver, this easy-to-use checklist can help you identify the symptoms of HE. Check off symptoms below and fill in the date.

If you notice any of the symptoms below, call your doctor immediately. The next time you visit your doctor, bring this checklist to help guide your discussion.

Date ____ / ____ / ____

Mental

- Forgetfulness
- Confusion
- Poor judgment
- Extra nervousness or excitement
- Not knowing where you are or where you're going
- Inappropriate behavior
- Severe personality changes

Physical

- Change in sleep patterns
- Worsening of handwriting
- Loss of small hand movements
- Tremors or shaking of hands or arms
- Slurred speech
- Slowed or sluggish movement
- Breath with a musty or sweet odor
- Other _____

Treatments

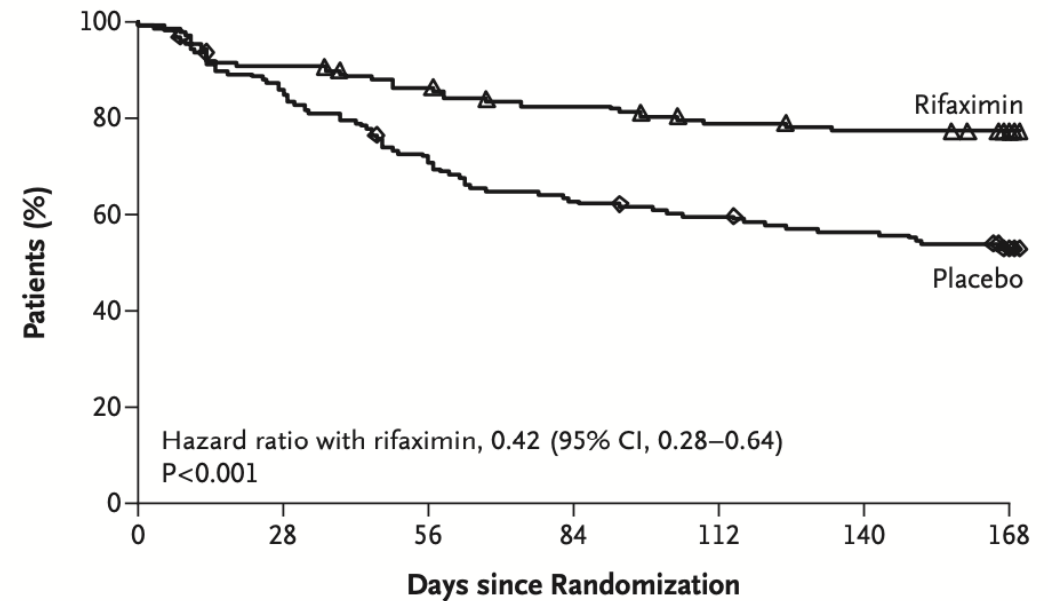
- Lactulose for ~3 BMs daily
- Rifaximin 550 mg BID
- Zinc, LOLA, plant-based diet, probiotics

Goal: Quality of life, reduce hospital admissions

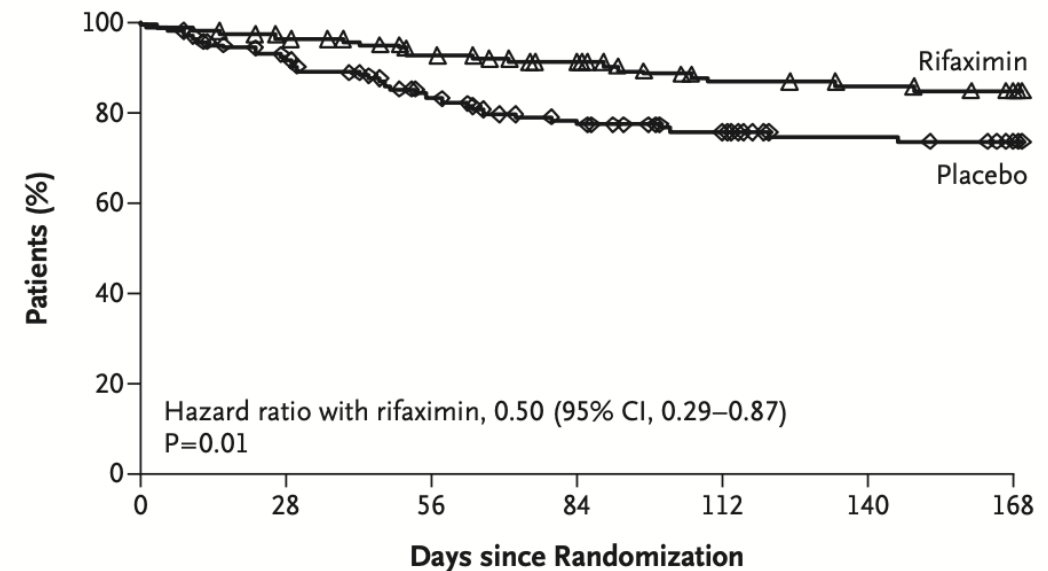
Rifaximin 550mg BID

- Oral, non-systemic, broad-spectrum, rifamycin antibiotic that concentrates in the GI tract
 - Inhibits bacterial growth by inhibiting protein synthesis

A Time to First Breakthrough HE Episode (Primary End Point)



B Time to First HE-Related Hospitalization (Key Secondary End Point)



In Any Patient with *Decompensated* Cirrhosis, it is Important to Screen for Varices!

<p>All patients with ascites and/or HE, but NO prior variceal bleed need EGD</p> <p>Management depends on EGD findings</p>	<p>Small varices on EGD</p>	<p>CTP class B, without red signs</p>	<p>Consider NSBB</p>	<p>If no NSBB: Repeat endoscopy in 1 year</p>
		<p>CTP class C OR varices with red wale signs (high risk for bleeding)</p>	<p>NSBB (propranolol, nadolol), titrate to HR 55-60/min as long as SBP>90 No need to repeat EGD</p>	<p>If no NSBB: EGD for band ligation of varices (ligate every 2-4 weeks until obliteration) Surveillance EGD at 6 months after obliteration, then every 12 months</p>
	<p>Medium/large varices on EGD</p>			

Goal: Prevent variceal hemorrhage

Screening Endoscopy

- No TE, NSBB contraindicated
 - cACLD without varices
 - Ongoing liver injury → Q2 years
 - Quiescent → Q3 years
 - Compensated cirrhosis & CSPH with varices
 - Ongoing liver injury → Q1 year
 - Quiescent → Q2 years
 - Decompensated cirrhosis

Primary Prophylaxis

- 1st choice:
 - Non-selective beta blockers*
 - Carvedilol
 - Propranolol
 - Nadolol
- 2nd choice:
 - Endoscopic variceal ligation
 - Band to obliteration every 2-4 weeks

*Patients on NSBBs do not require monitoring with serial EGD

Goal: Prevent a bleed

Secondary Prophylaxis

- Endoscopic variceal ligation*

AND

- Non-selective beta blockers*
 - Carvedilol
 - Propranolol
 - Nadolol

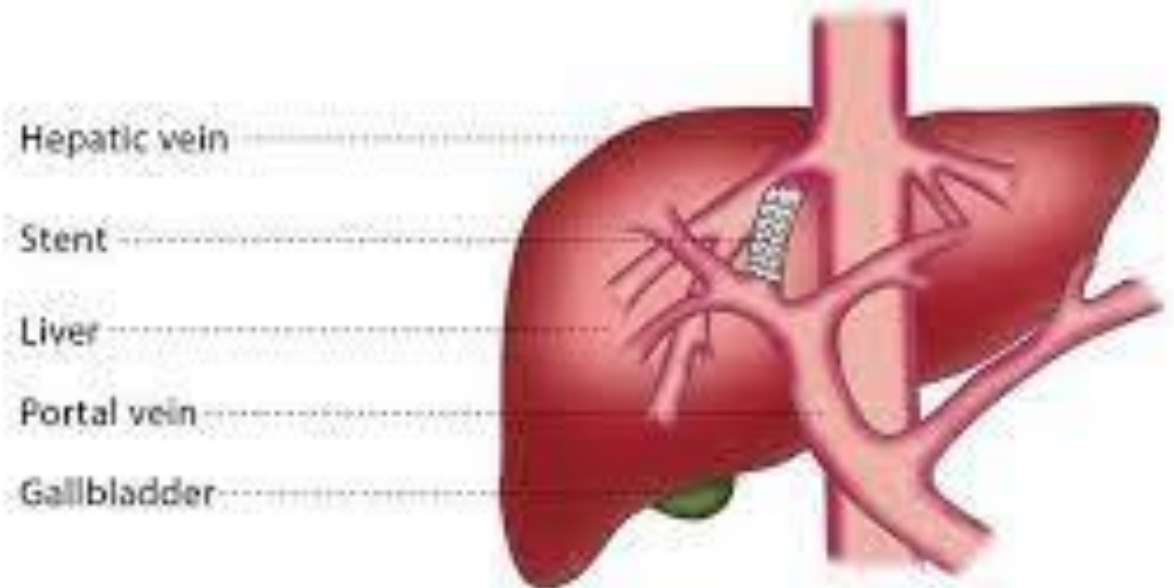
*Not needed if rescue TIPS was performed

Goal: Prevent another bleed

Transjugular intrahepatic portosystemic shunt (TIPS)

- Preemptive TIPS
 - CTP B with bleed or C
- Indications:
 - Hepatic hydrothorax
 - Refractory ascites
 - Variceal bleed
- CT w/wo & Echocardiogram
- Contraindications
 - MELD >20
 - Age >70 (relative)
 - Heart or renal failure
- Warning: Can worsen HE

Transjugular intrahepatic portosystemic shunt (TIPS)



Liver Transplant

- MELD 3.0
 - Total bilirubin, INR, sCr, Na, albumin, sex
- Referral to transplant center
 - Decompensated
 - Living donor
 - HCC

Key Takeaways

- LSM values <15 kPa and PLT >150 k rules out CSPH, while LSM values of ≥ 25 kPa can be used to rule in CSPH
- Starting a patient with CSPH on a non-selective beta blocker such as carvedilol can decrease the risk of hepatic decompensation and death in patients with compensated cirrhosis
- Portal hypertension causes most complications of decompensated cirrhosis such as ascites, variceal bleed, and hepatic encephalopathy
- Refer decompensated liver disease for liver transplant consideration