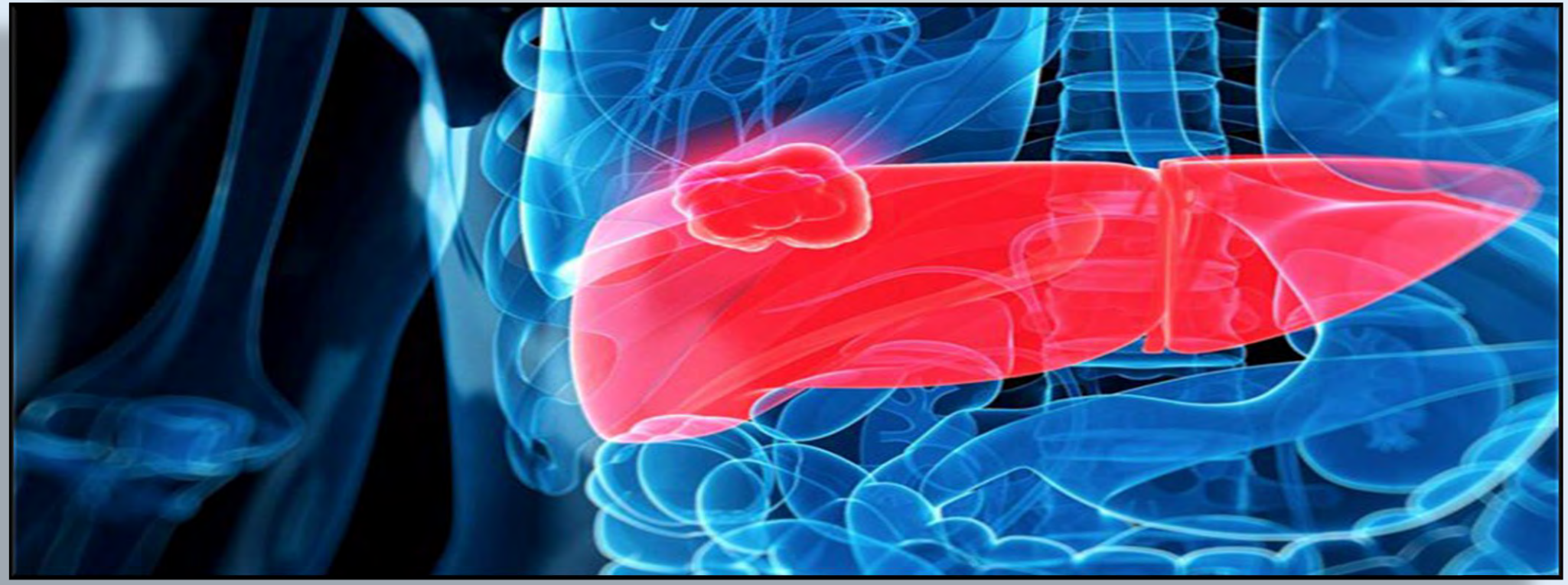
COMPLICATIONS OF CIRRHOSIS



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Project ECHO
Gastroenterology Foundation of sub Saharan Africa

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GI HEPATOLOGY ECHO OF SUB-SAHARAN AFRICA
ESTABLISHED 2020

Clinical Practice Guidelines

JOURNAL OF HEPATOLOGY

EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis☆

European Association for the Study of the Liver*

Summary

The natural history of cirrhosis is characterised by an asymptomatic compensated phase followed by a decompensated phase, marked by the development of overt clinical signs, the most frequent of which are ascites, bleeding, encephalopathy, and jaundice. The following Clinical Practice Guidelines (CPGs) represent the first CPGs on the management of decompensated cirrhosis. In this context, the panel of experts, having emphasised the importance of initiating aetiologic treatment for any degree of hepatic disease at the earliest possible stage, extended its work to all the complications of cirrhosis, which had not been covered by the European Association for the Study of the signs, the most frequent of which are ascites, bleeding, encephalopathy, and jaundice. Following the first appearance of any of these, the disease usually progresses more rapidly towards death or liver transplantation (LT). This phase of the disease has been designated "decompensated cirrhosis".[2] Progression of the decompensated disease may be further accelerated by the development of other complications such as rebleeding, acute kidney injury (AKI), with or without the features of HRS, hepato-pulmonary syndrome (HPS), portopulmonary hypertension (PPHT), cirrhotic cardiomyopathy (CCM), and bacterial infections. Indeed, the development of bacterial infections as well as hepatocellular carcinoma may accelerate

Baveno VII – Renewing consensus in portal hypertension

Roberto de Franchis[1,*], Jaime Bosch[2,3], Guadalupe Garcia-Tsao[4,5], Thomas Reiberger[6,7], Cristina Ripoll[8], on behalf of the Baveno VII Faculty[§]

Summary

To expand on the work of previous meetings, a virtual Baveno VII workshop was organised for October 2021. Among patients with compensated cirrhosis or compensated advanced chronic liver disease (cACLD – defined at the Baveno VI conference), the presence or absence of clinically significant portal hypertension (CSPH) is associated with differing outcomes, including risk of death, and different diagnostic and therapeutic needs. Accordingly, the Baveno VII workshop was entitled "Personalized Care for Portal Hypertension". The main fields of discussion were the relevance and indications for measuring the hepatic venous pressure gradient as a gold standard, the use of non-invasive tools for the diagnosis of cACLD and CSPH, the impact of aetiological and non-aetiological therapies on the course of cirrhosis, the prevention of the first episode of decompensation, the management of an acute bleeding episode, the prevention of further decompensation, as well as the diagnosis and management of splanchnic vein thrombosis and other vascular disorders of the liver. For each of these 9 topics, a thorough review of the

Keywords: Cirrhosis; diagnosis; decompensation; treatment; recommendations.

Received 18 November 2021; received in revised form 10 December 2021; accepted 17 December 2021; available online 30 December 2021

CIRRHOSIS

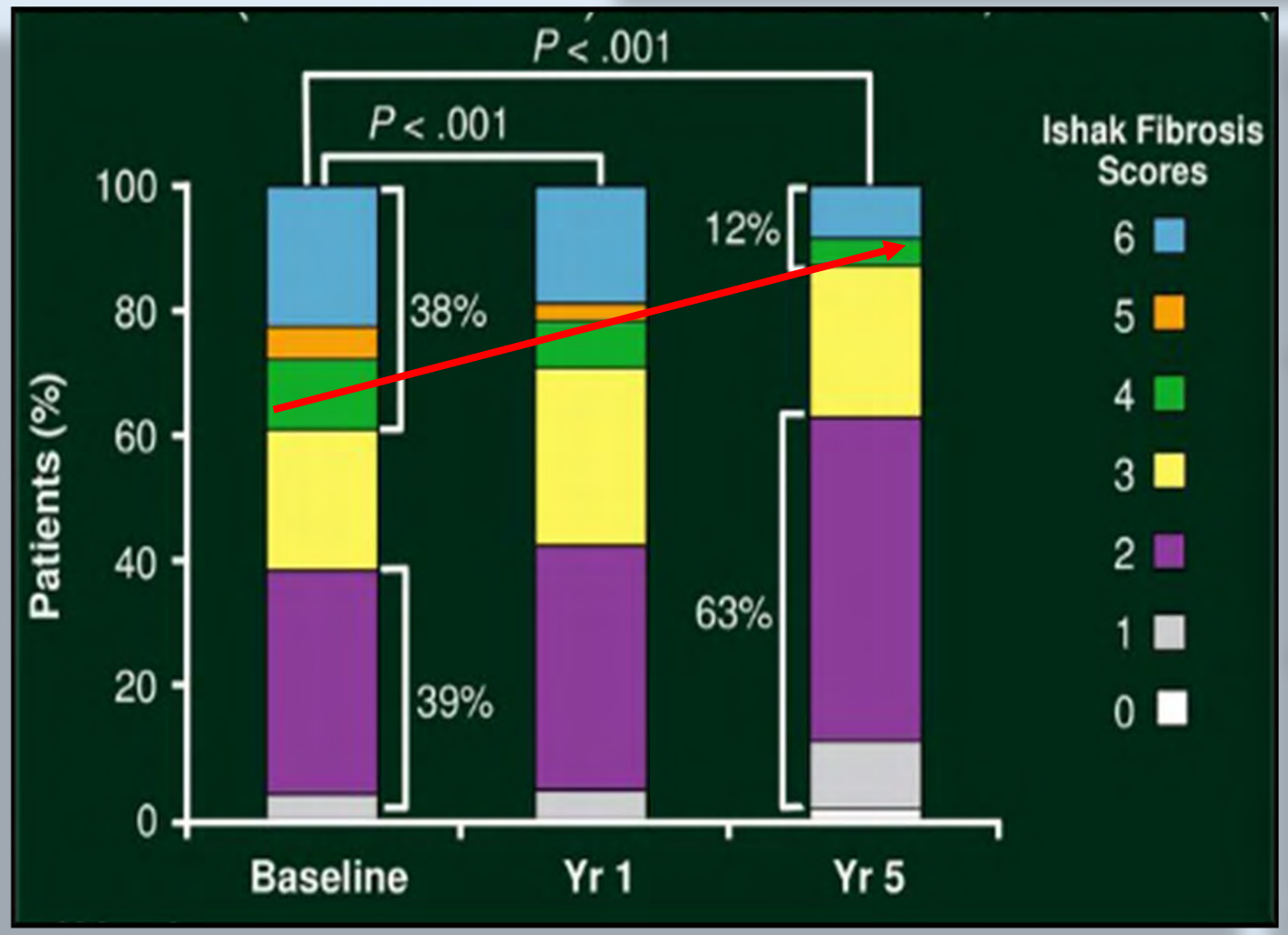
- Histological changes in the liver leading to development of fibrosis.
- Architectural distortion and formation of regenerative nodules.
- Loss of hepatocellular liver mass.
- Loss of Liver function.

Schuppan D, Afdhal NH. Liver cirrhosis. Lancet. 2008.

CAUSES OF LIVER CIRRHOSIS

- Chronic alcohol consumption.
- Chronic viral hepatitis (B, C).
- Metabolic liver disease
  - ✓ Hemochromatosis.
  - ✓ Wilson's disease.
  - ✓ α1-Antitrypsin deficiency.
  - ✓ Nonalcoholic steatohepatitis.
- Immunological
  - ✓ Autoimmune hepatitis.
  - ✓ Primary biliary cholangitis.
  - ✓ Primary sclerosing cholangitis.
- Vascular
  - ✓ Budd-Chiari.
- Drugs
  - ✓ Methotrexate.

AETIOLOGY TREATMENT HEP B AND TDF



- 96% Pts on TDF had stable or improved fibrosis after 5 yrs.
- **Ishak score >/=4**
  - ✓ Baseline: 38%.
  - ✓ Yr 5: 12%.
- **Cirrhosis (Ishak >/=5)**
  - ✓Baseline: 28%.
  - ✓Yr 5: 8%.

Marcellin P, et al. Lancet 2013; 381:468-475

AETIOLOGY TREATMENT HEP C AND DAA

Original Article

Direct-acting antiviral therapy of chronic hepatitis C improves liver fibrosis, assessed by histological examination and laboratory markers

Chun-Han Cheng [a,c], Chia-Ying Chu [b], Huan-Lin Chen [a,c], I-Tsung Lin [a,c], Chia-Hsien Wu [a,c], Yuan-Kai Lee [a,c], Ping-Jen Hu [a,c], Ming-Jong Bair [a,c,*]

[a] *Division of Gastroenterology, Department of Internal Medicine, Taitung Mackay Memorial Hospital, Taiwan*
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[c] *Mackay Medical College, New Taipei, Taiwan*

Received 22 July 2020; received in revised form 24 October 2020; accepted 23 November 2020

Table 3 Histology appearance among study patients.

	Pre-treatment biopsy	Post-treatment biopsy
METAVIR fibrosis score		
F0	0	1 (4.8)
F1	0	1 (4.8)
F2	0	10 (47.6)
F3	19 (90.5)	5 (23.8)
F4	2 (9.5)	4 (19.0)
HAI score (mean ± SD)	6.9 ± 1.9	5.0 ± 2.3

AETIOLOGY TREATMENT NASH AND METFORMIN

Metformin in Nonalcoholic Steatohepatitis: A Randomized Controlled Trial

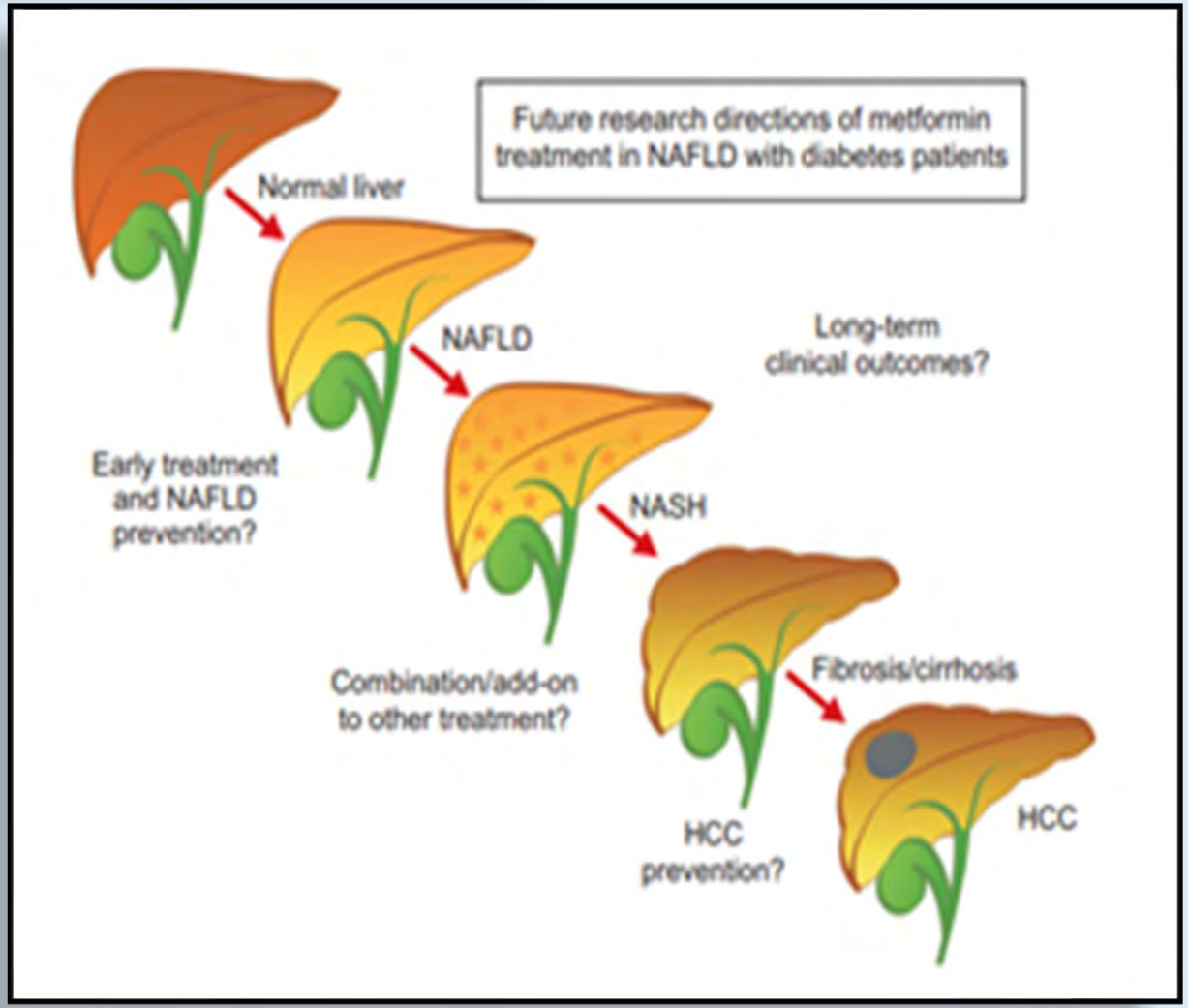
Rozana Kazemi[1], Mohsen Aduli[1], Masoud Sotoudeh[1], Reza Malekzadeh[1], Nahid Seddighi[2], Sadaf Ghajarieh Sepanlou[1], Shahin Merat[1*]

1. Digestive Disease Research Center, Tehran University of Medical Sciences, Tehran, Iran
2. Department of Radiology, Tehran University of Medical Sciences, Tehran, Iran

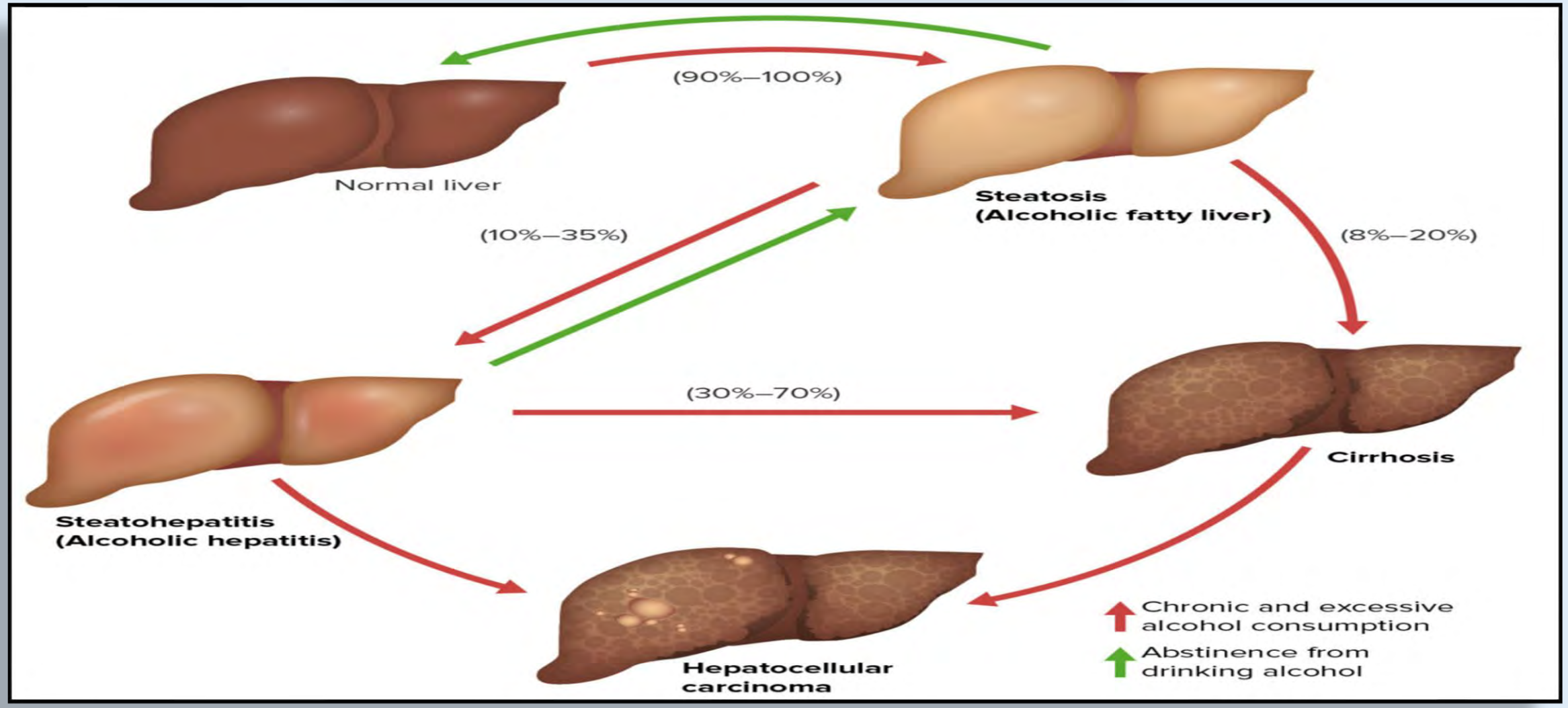
ABSTRACT

BACKGROUND

Nonalcoholic steatohepatitis (NASH) is a common liver disease that can progress to cirrhosis or hepatocellular carcinoma. It is estimated that up to 3% of the Iranian population have this condition. Although the pathogenesis of NASH is incompletely understood, there is significant evidence pointing to the importance of insulin resistance. Metformin is an oral hypoglycemic agent known to improve insulin resistance. This study examines the effectiveness of metformin on biochemical and histological



ALCOHOL ABSTINENCE



STATINS AND CIRRHOSIS

SCIENTIFIC REPORTS
nature research

OPEN

Guideline-conform statin use reduces overall mortality in patients with compensated liver disease

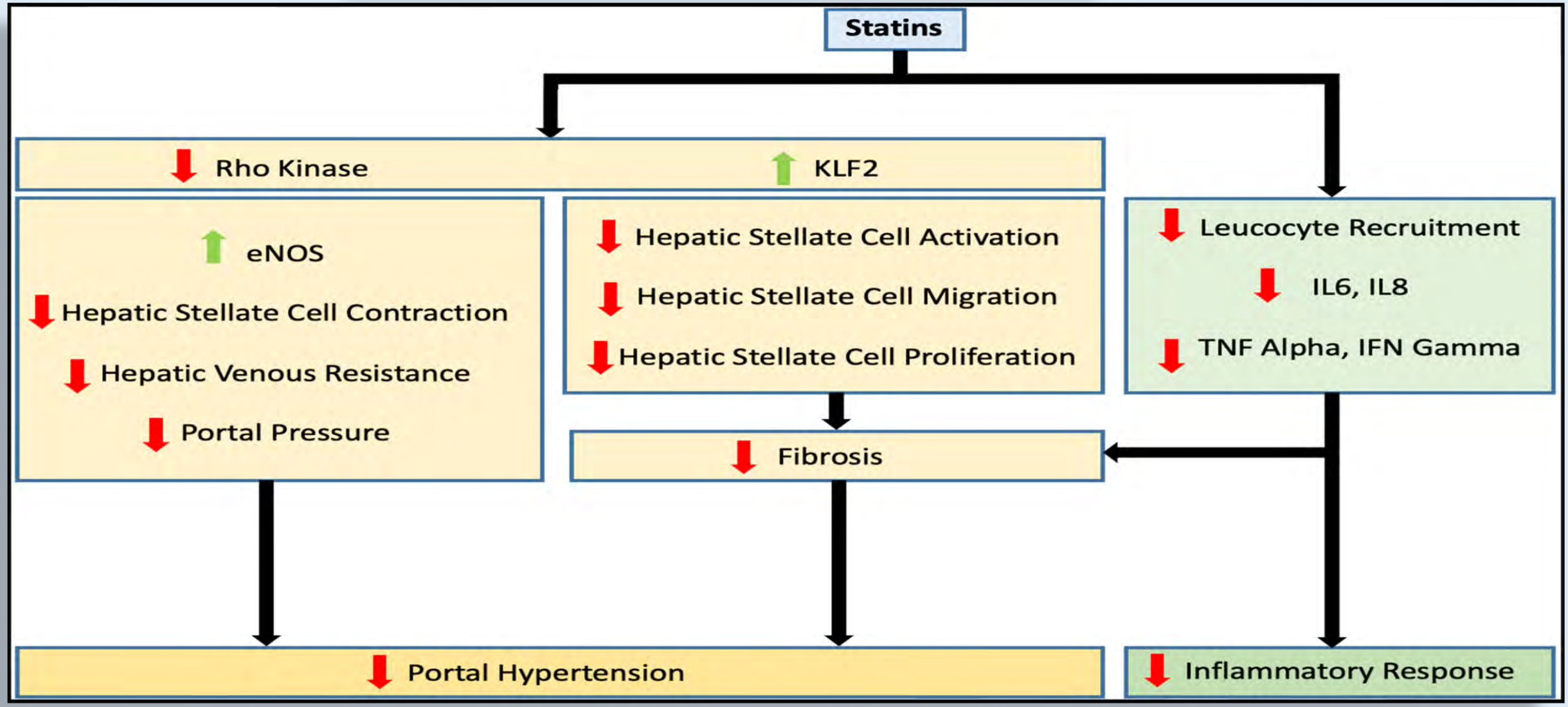
Received: 28 November 2018
Accepted: 10 July 2019
Published online: 12 August 2019

Lukas W. Unger[1,4], Bernadette Forstner[1], Stephan Schneglberger[1], Moritz Muckenhuber[1], Ernst Eigenbauer[2], David Bauer[3,4], Bernhard Scheiner[3,4], Mattias Mandorfer[3,4], Michael Trauner[3] & Thomas Reiberger[3,4]

- **Statins decrease risk of decompensation and death in cirrhosis. To be safe use Simvastatin 20mg/day.**

Mohanty, A et al. Gastroenterology 2016;150:430Ç440).

STATINS AND CIRRHOSIS



COMPLICATIONS OF CIRRHOSIS

PORTAL HYPERTENSION RELATED

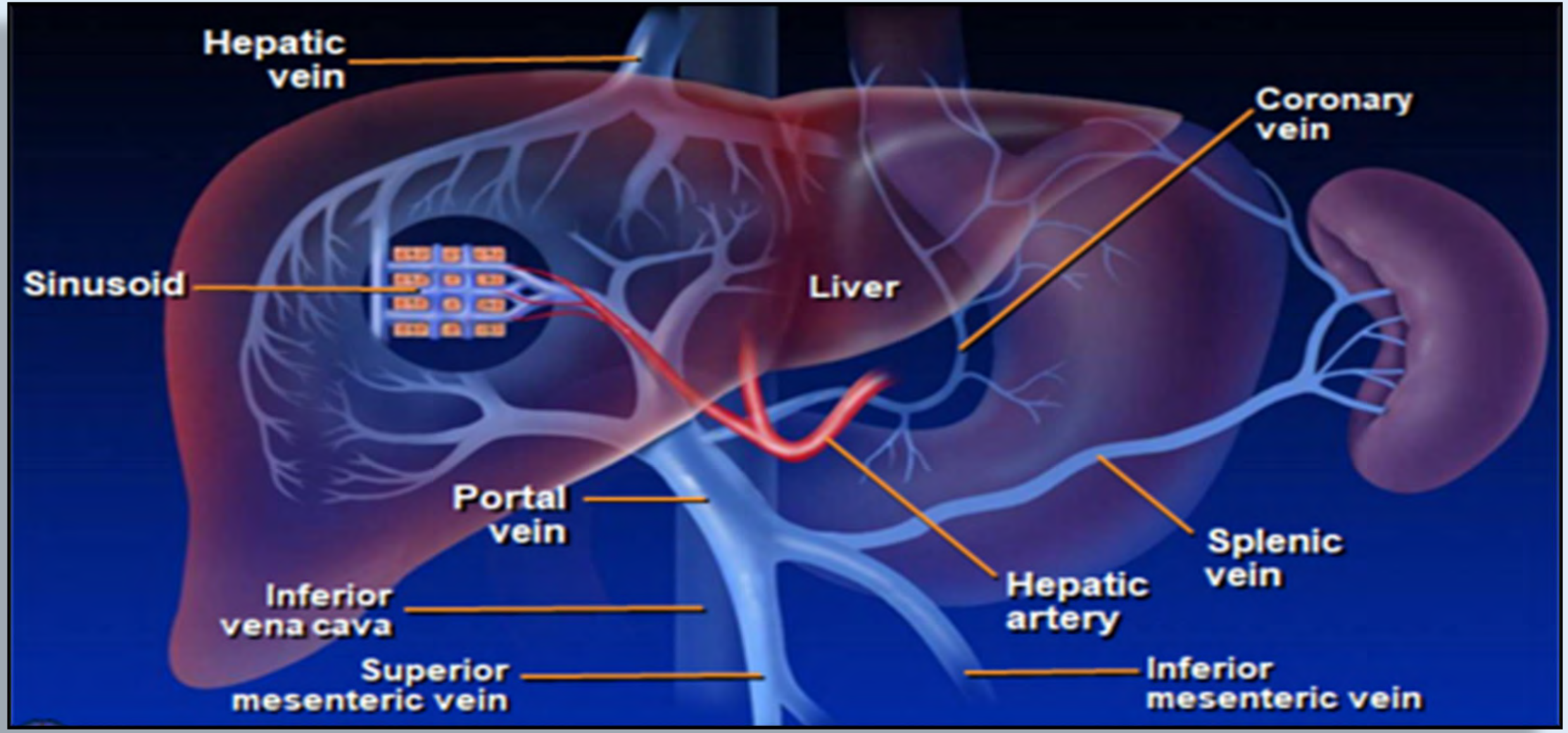
- Ascites
  - ✓Spontaneous bacterial infections.
- Bleeding varices (Esophageal, gastric and ectopic).
- Portal hypertensive gastropathy.
- Hepatorenal syndrome.
- Hepatic hydrothorax.
- Hepatopulmonery syndrome.
- Portopulmonery hypertension.
- Cirrhotic cardiomyopathy.
- Hepatic encephalopathy.
- Relative adrenal insufficiency.

COMPLICATIONS OF CIRRHOSIS

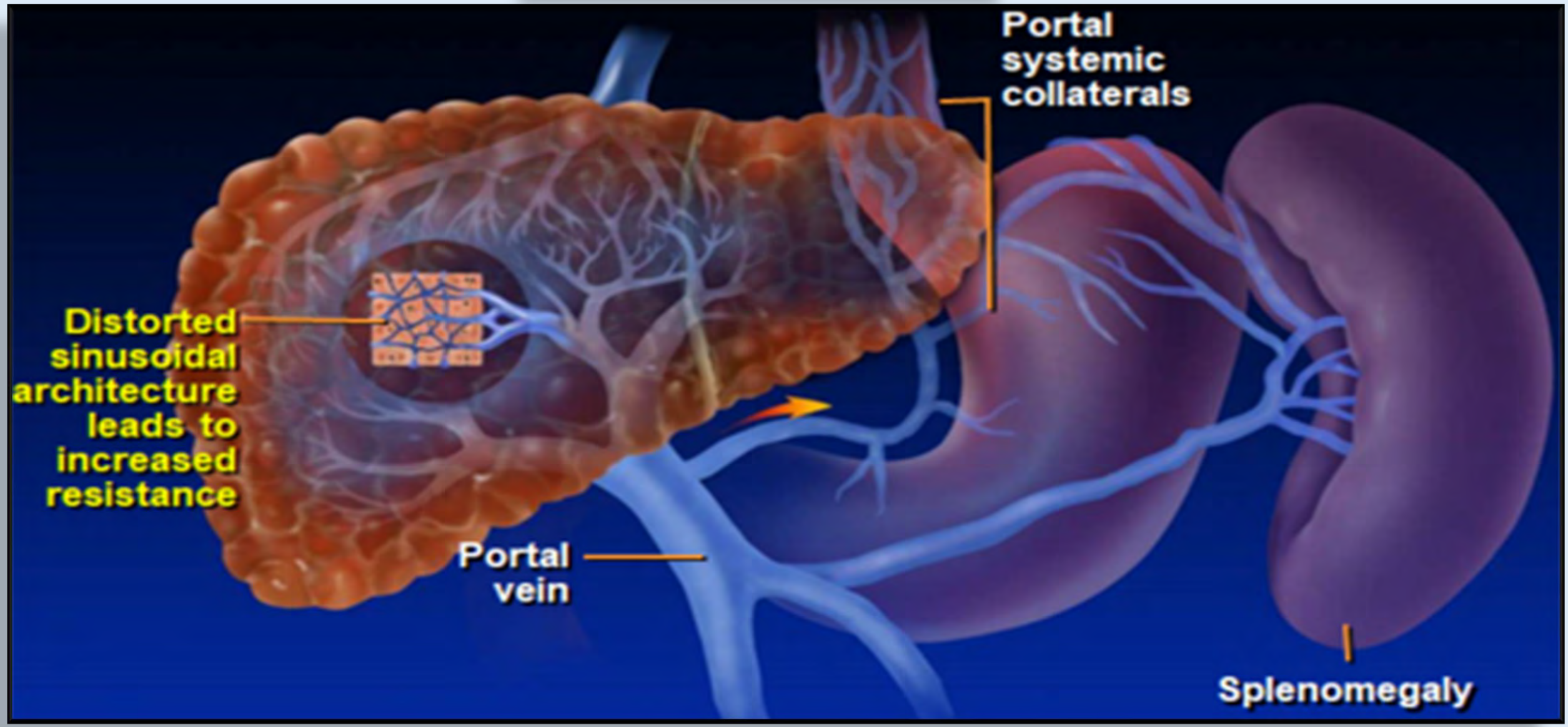
NON-PORTAL HYPERTENSION RELATED

- Altered drug metabolism.
- Malnutrition/Sarcopenia.
- Hepatic osteodystrophy.
- Hypogonadism/Feminization.
- Hyponatremia.
- Coagulopathy.
- Hepatocellular carcinoma.

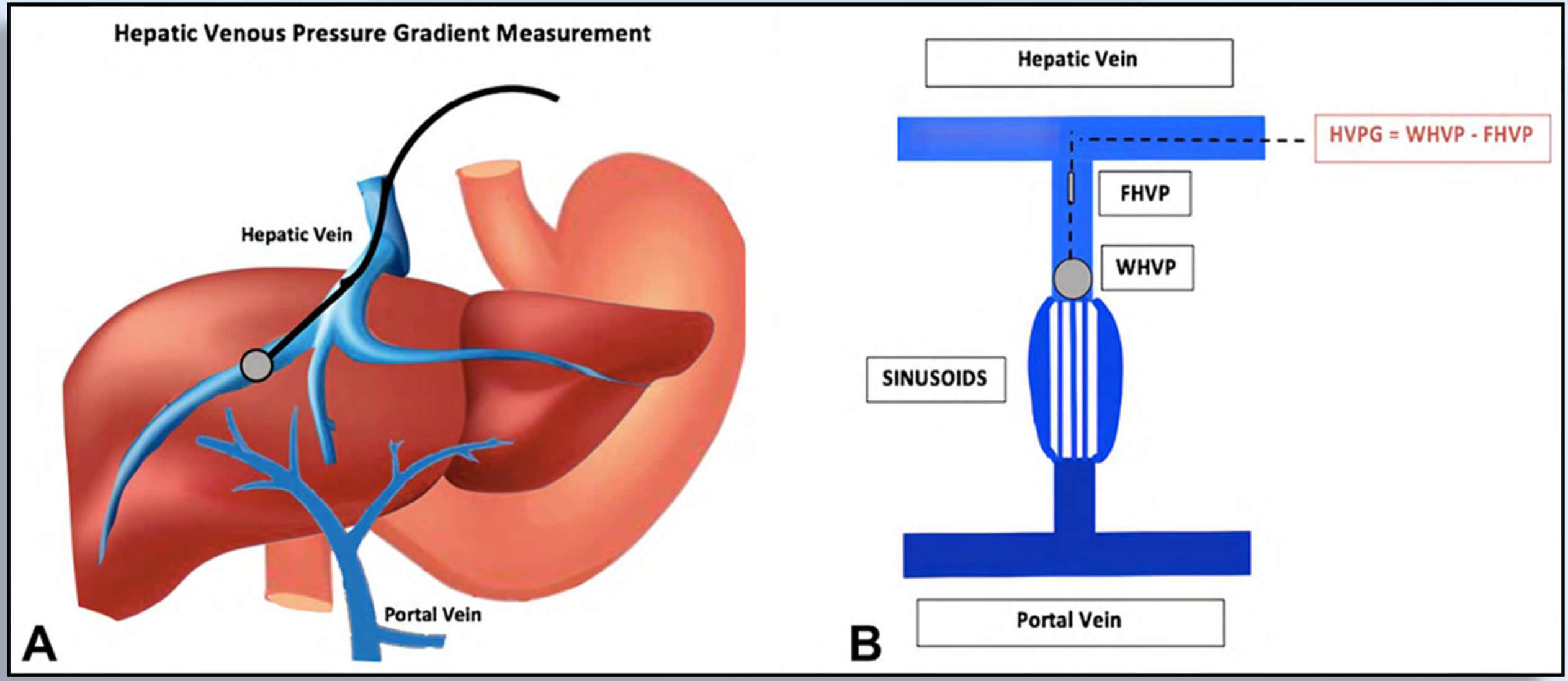
NORMAL VASCULAR ANATOMY



CIRRHOTIC LIVER



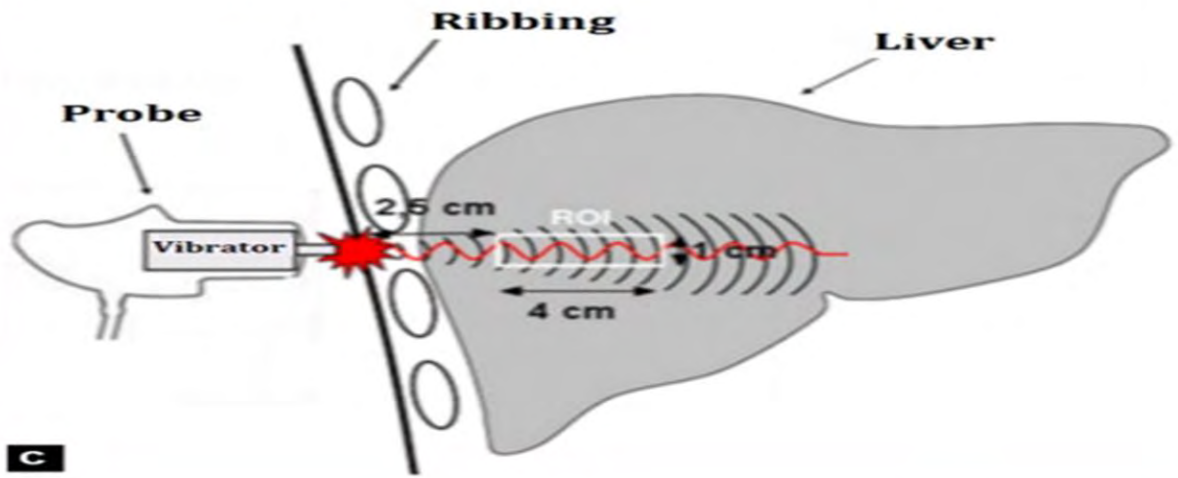
HVPG AS A GOLD STANDARD

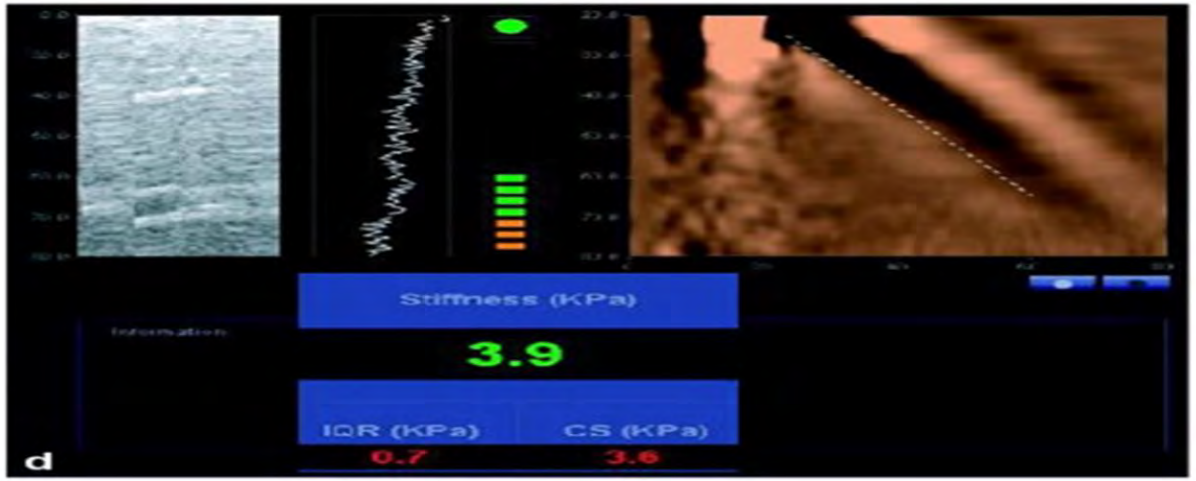


HVPG AS A GOLD STANDARD

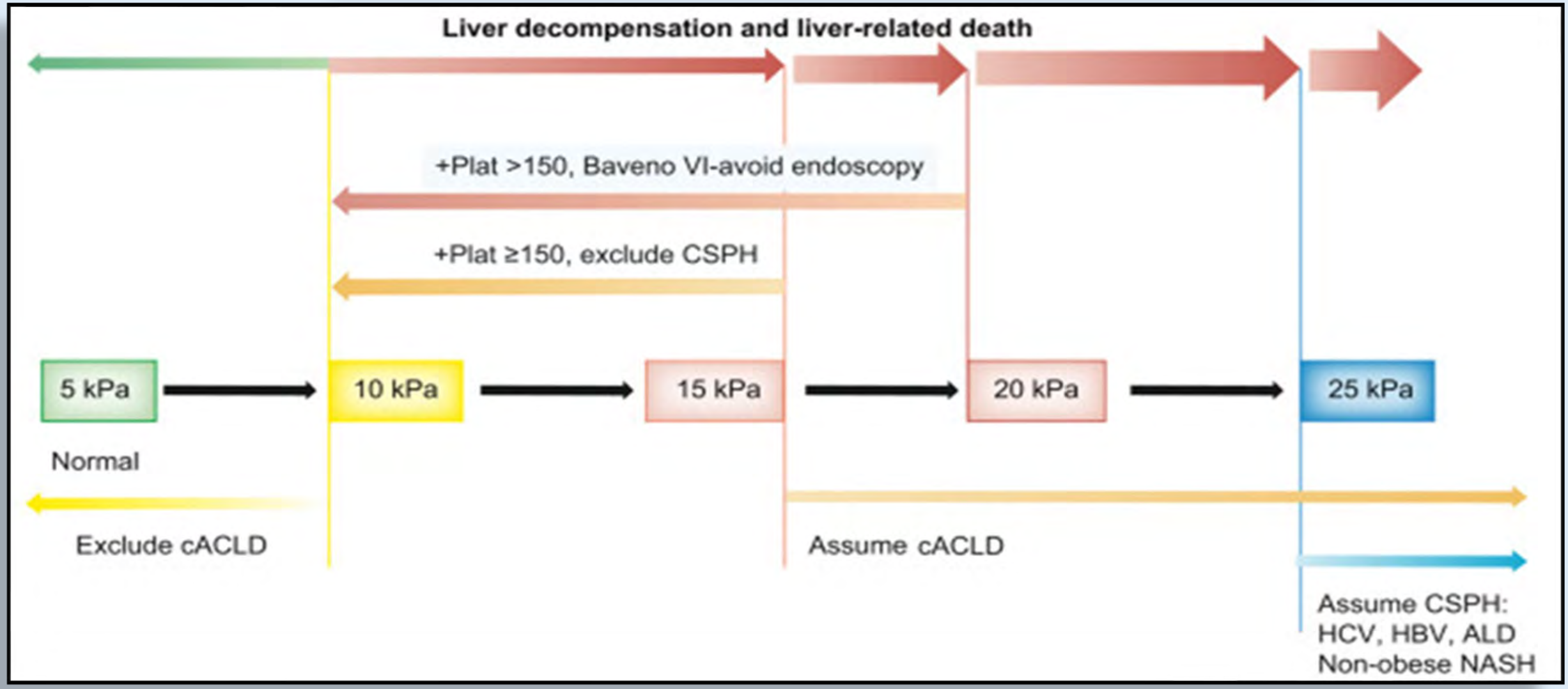
Measurement	Significance
1-5 mm Hg	Normal
≥ 6 mm Hg	Risk of disease progression in persons with HCV recurrence after liver transplantation
≥ 10 mm Hg	Clinically significant portal hypertension
≥ 12 mm Hg	Increased risk for rupture of varices
≥ 16 mm Hg	Increased risk of mortality
≥ 20 mm Hg	Treatment failure and mortality in acute variceal bleeding

NON-INVASIVE TOOLS FOR PHT





CLINICAL COURSE OF CIRRHOSIS



Baveno VII: Renewing consensus in portal hypertension

CLINICAL COURSE OF CIRRHOSIS

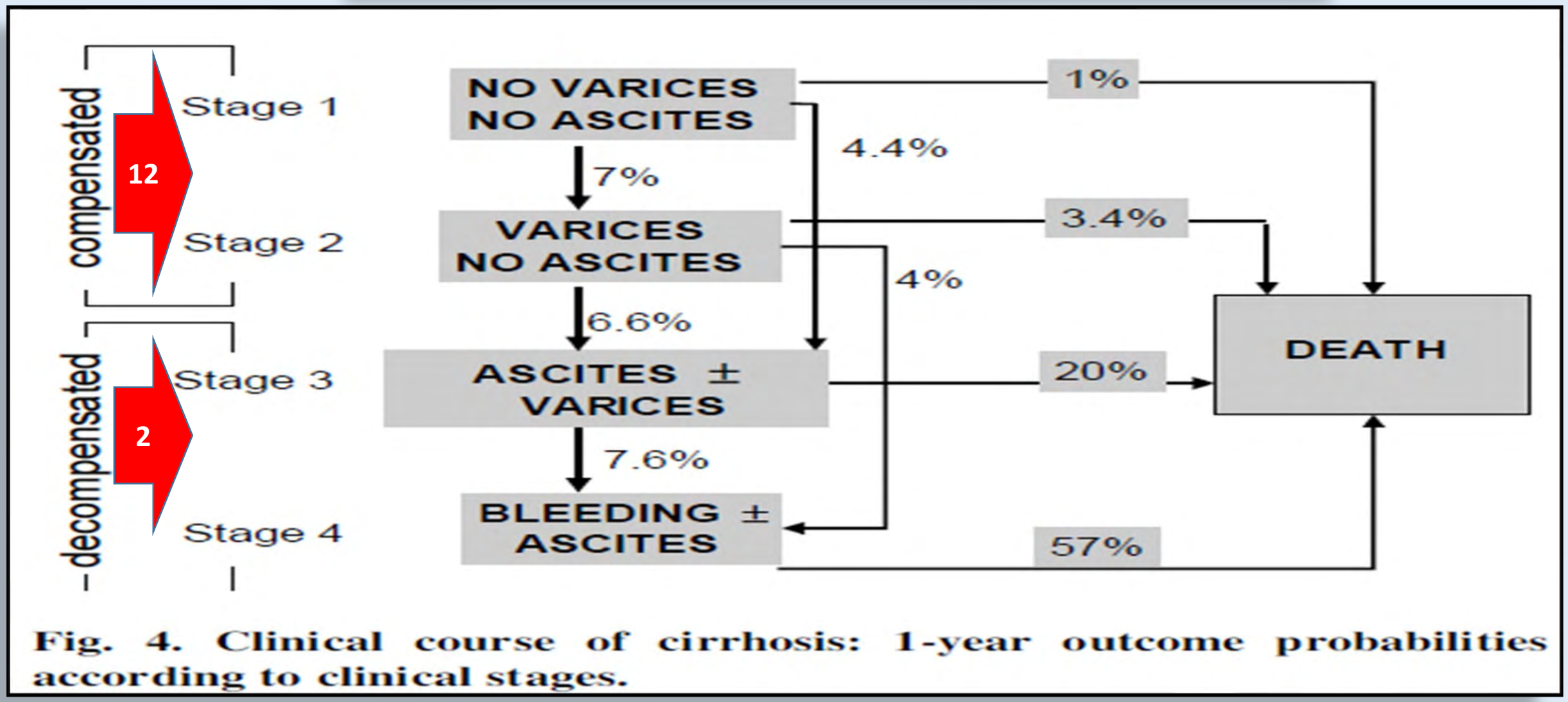


Fig. 4. Clinical course of cirrhosis: 1-year outcome probabilities according to clinical stages.

G. D'Amico et al. / Journal of Hepatology 44 (2006) 217–231

Child-Turcotte-Pugh Classification for Severity of Cirrhosis

Clinical and Lab Criteria	Points*		
	1	2	3
Encephalopathy	None	Mild to moderate (grade 1 or 2)	Severe (grade 3 or 4)
Ascites	None	Mild to moderate (diuretic responsive)	Severe (diuretic refractory)
Bilirubin (mg/dL)	< 2	2-3	>3
Albumin (g/dL)	> 3.5	2.8-3.5	<2.8
Prothrombin time			
Seconds prolonged	<4	4-6	>6
International normalized ratio	<1.7	1.7-2.3	>2.3

***Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)**

Class A = 5 to 6 points (least severe liver disease)

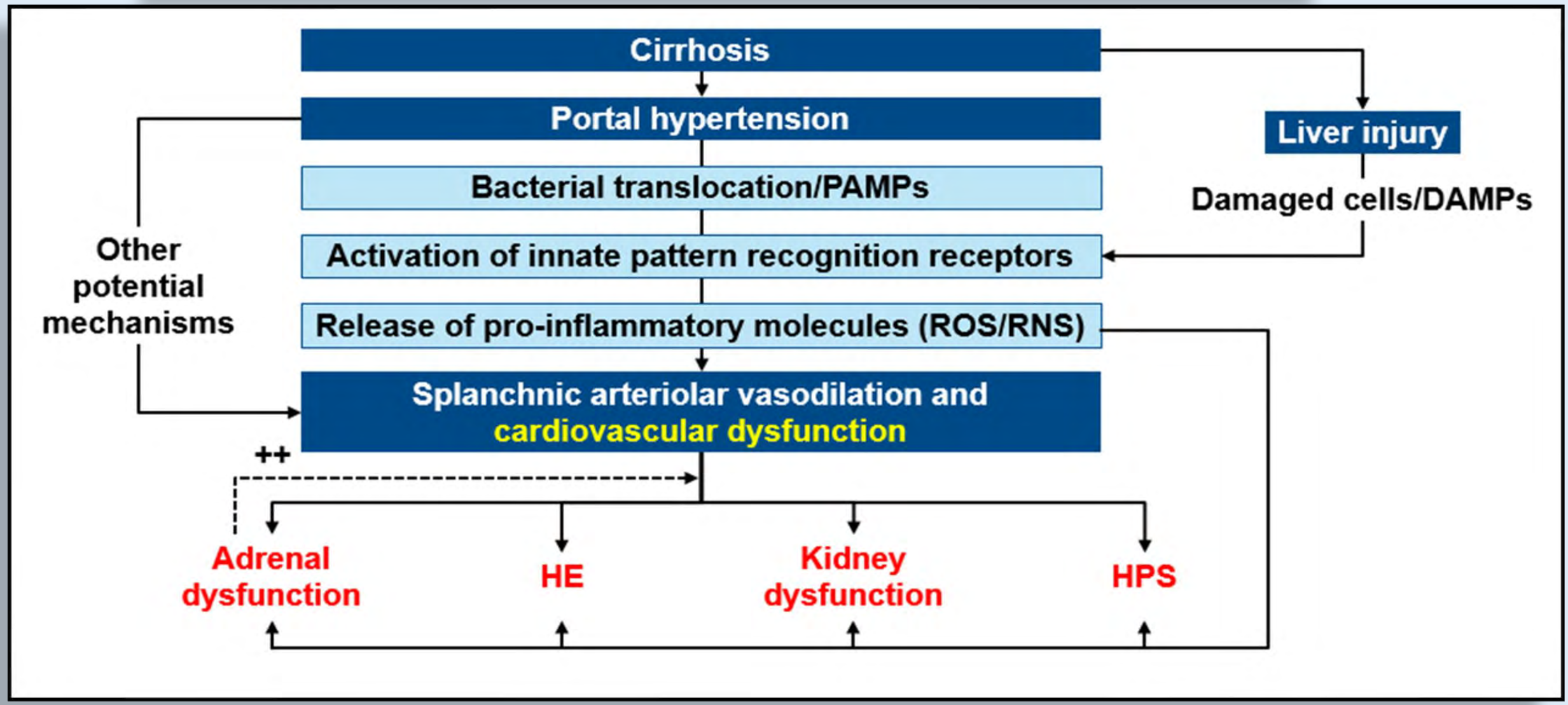
Class B = 7 to 9 points (moderately severe liver disease)

Class C = 10 to 15 points (most severe liver disease)

One and two year survival based on CTP Score

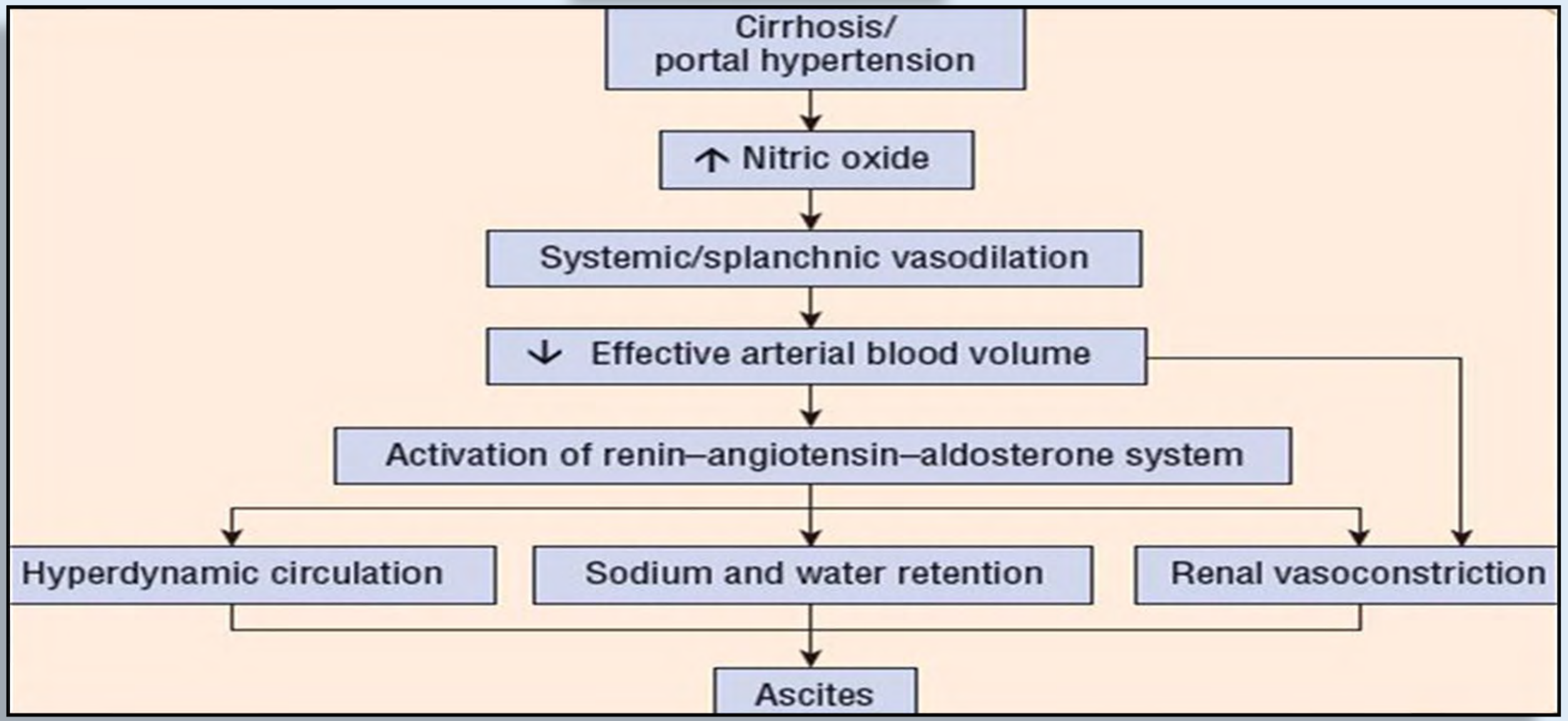
Class	1 yr	2 yr
A (5-6 points)	100 %	85 %
B (7-9 points)	80%	60%
C (10-15 points)	45%	35%

PATHOPHYSIOLOGY



EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024

ASCITES



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ASCITES

- Cirrhosis accounts for 80% of cases of ascites.
- Ascites can be uncomplicated or refractory.
- Significant impact on quality of patients.
- Poor prognosis.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024

UNCOMPLICATED ASCITES
Evaluation and diagnosis

- History
- Physical examination
- Abdominal ultrasound
- Ascites grading
- Laboratory assessment

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024

UNCOMPLICATED ASCITES
Evaluation and diagnosis

Grade of ascites	Definition
Grade 1 ascites	Mild ascites only detectable by ultrasound
Grade 2 ascites	Moderate ascites evident by moderate symmetrical distension of abdomen
Grade 3 ascites	Large or gross ascites with marked abdominal distension

International ascites club grading system for ascites.

UNCOMPLICATED ASCITES
Evaluation and diagnosis

- **Diagnostic paracentesis**
  - ✓Neutrophil count
  - ✓Culture
  - ✓Ascitic total protein
  - ✓SAAG
  - ✓Cytology

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024

UNCOMPLICATED ASCITES Management

➢ Grade 2 or moderate ascites

- Hospitalization not required.

- Correct sodium imbalance:
  - ✓Dietary restriction.
  - ✓Diuretics:
    - Anti-mineralocorticoid drugs, Loop diuretics.
    - Considerations prior to initiating.
    - Monitoring.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024

UNCOMPLICATED ASCITES Management

- **Grade 3 or large ascites**
  - LVP
  - Contraindications
  - LVP should be followed with plasma volume expansion
  - After LVP, minimum dose of diuretics necessary

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024

REFRACTORY ASCITES

International Ascites Club:

- Ascites that cannot be mobilized or the early recurrence of which (after LVP) cannot be satisfactorily prevented by medical therapy.

- **Diuretic resistant:** Lack of response to sodium restriction and diuretic treatment.

- **Diuretic intractable:** Development of diuretic-induced complications that preclude the use of an effective diuretic dosage.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024

REFRACTORY ASCITES
Diagnostic criteria

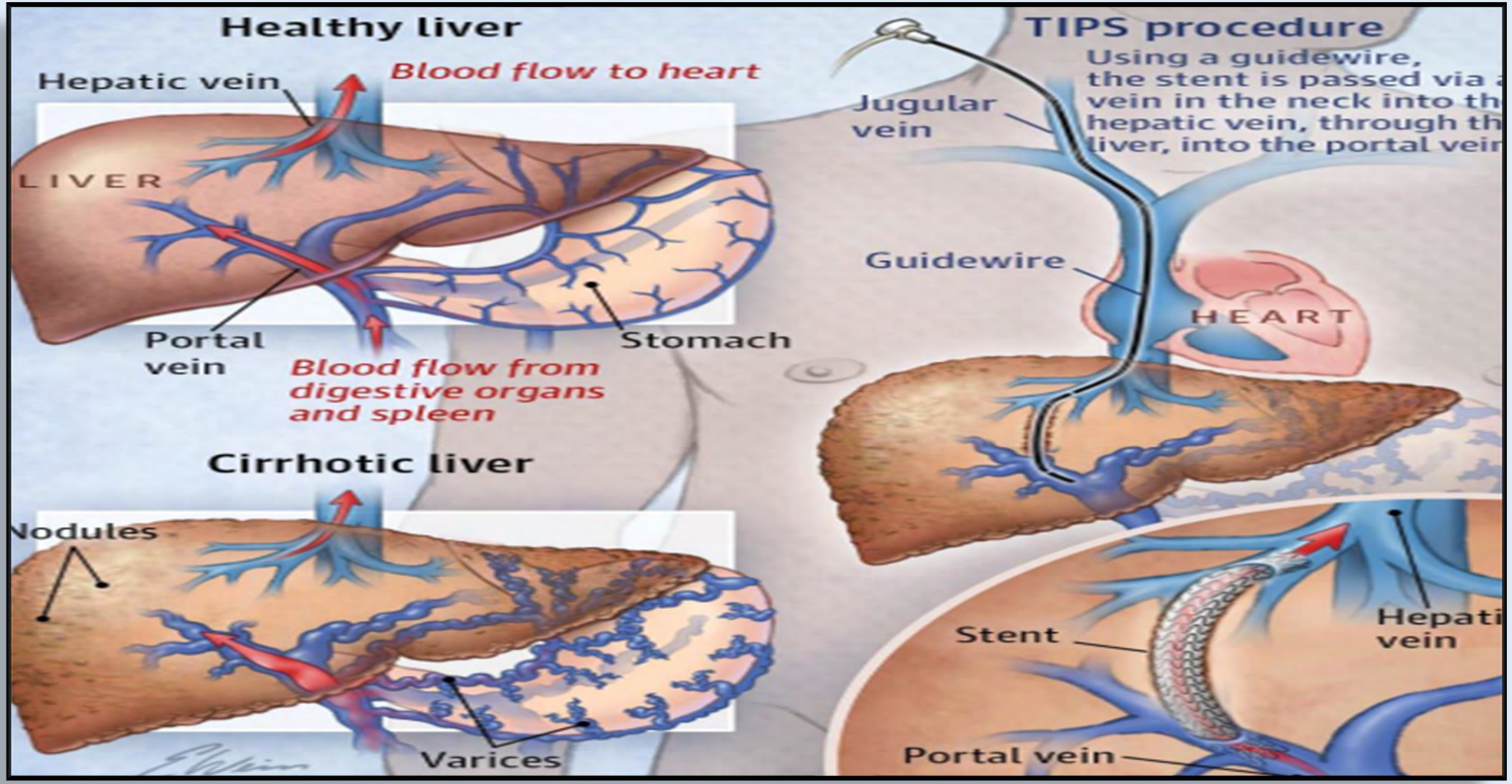
- **Treatment duration:** Intensive diuretic therapy for at least 1 week and on a salt-restricted diet of less than 90 mmol/day.
- **Lack of response:** Mean weight loss of <0.8 kg over 4 days and urinary sodium output less than the sodium intake.
- **Early ascites recurrence:** Reappearance of grade 2 or 3 ascites within 4 weeks of initial mobilization.
- **Diuretic-induced complications:** HE, Renal impairment, Hyponatremia, Hypo/hyperkalemia, Incapacitating muscle cramps.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024

REFRACTORY ASCITES
Management

- LVP is a safe and effective treatment.
- Should be associated with albumin administration to prevent PPCD.
- Drug treatments are controversial or inadequately studied.
- TIPS

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.


Healthy liver
Hepatic vein
Blood flow to heart
LIVER
Portal vein
Stomach
Blood flow from digestive organs and spleen
Cirrhotic liver
Nodules
Varices
TIPS procedure
Using a guidewire, the stent is passed via a vein in the neck into the hepatic vein, through the liver, into the portal vein
Jugular vein
Guidewire
HEART
Stent
Hepatic vein
Portal vein

REFRACTORY ASCITES
Prognosis

- Refractory ascites is associated with a poor prognosis.
- Median survival around 6 months.
- Patients with refractory ascites should be evaluated for LT

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

BACTERIAL INFECTIONS

Multifactorial Factors

- Liver dysfunction.
- Portosystemic shunting.
- Gut dysbiosis.
- Increased Bacterial translocation.
- Cirrhosis-associated immune dysfunction.
- Genetic factors.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

SPONTANEOUS BACTERIAL PERITONITIS

- Bacterial infection of ascitic fluid without any intra-abdominal surgically treatable source of infection.
- All patients with cirrhosis and ascites are at risk.
- **Prevalence**: 1.5–3.5% in outpatients; 10% in hospitalized patients.
- **Prognosis**: more than 90% mortality when first described. Reduced to ~20% with early diagnosis and treatment

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024

SPONTANEOUS BACTERIAL PERITONITIS
Diagnosis

- Diagnosis is based on diagnostic paracentesis.
- 50% of SBP episodes are present at hospital admission.
- Signs/symptoms of peritonitis.
- Signs of systemic inflammation.
- Worsening liver function, HE, shock, renal impairment, GI bleeding.
- SPB may be asymptomatic, particularly in outpatients.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

SPONTANEOUS BACTERIAL PERITONITIS
Management

- Empirical IV antibiotics should be started immediately following diagnosis.
- Several factors should guide empirical antibiotic use.
- Antibiotic therapy should be carefully controlled and monitored.
- The administration of albumin is recommended in patients with SBP.

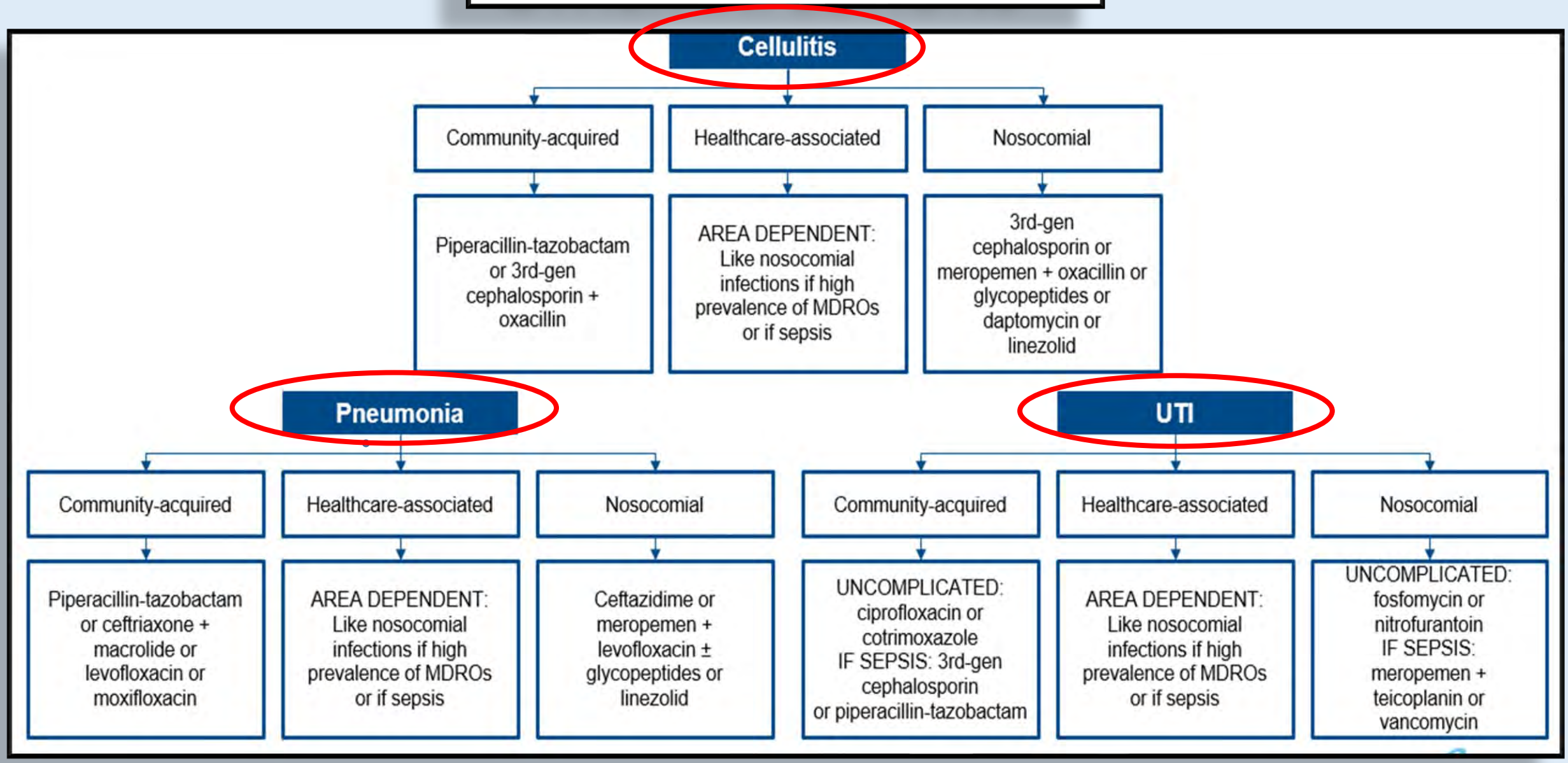
EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

SPONTANEOUS BACTERIAL PERITONITIS
Management

- Primary prophylaxis.
- Secondary prophylaxis.
- PPIs and SBP.
- Liver transplant.

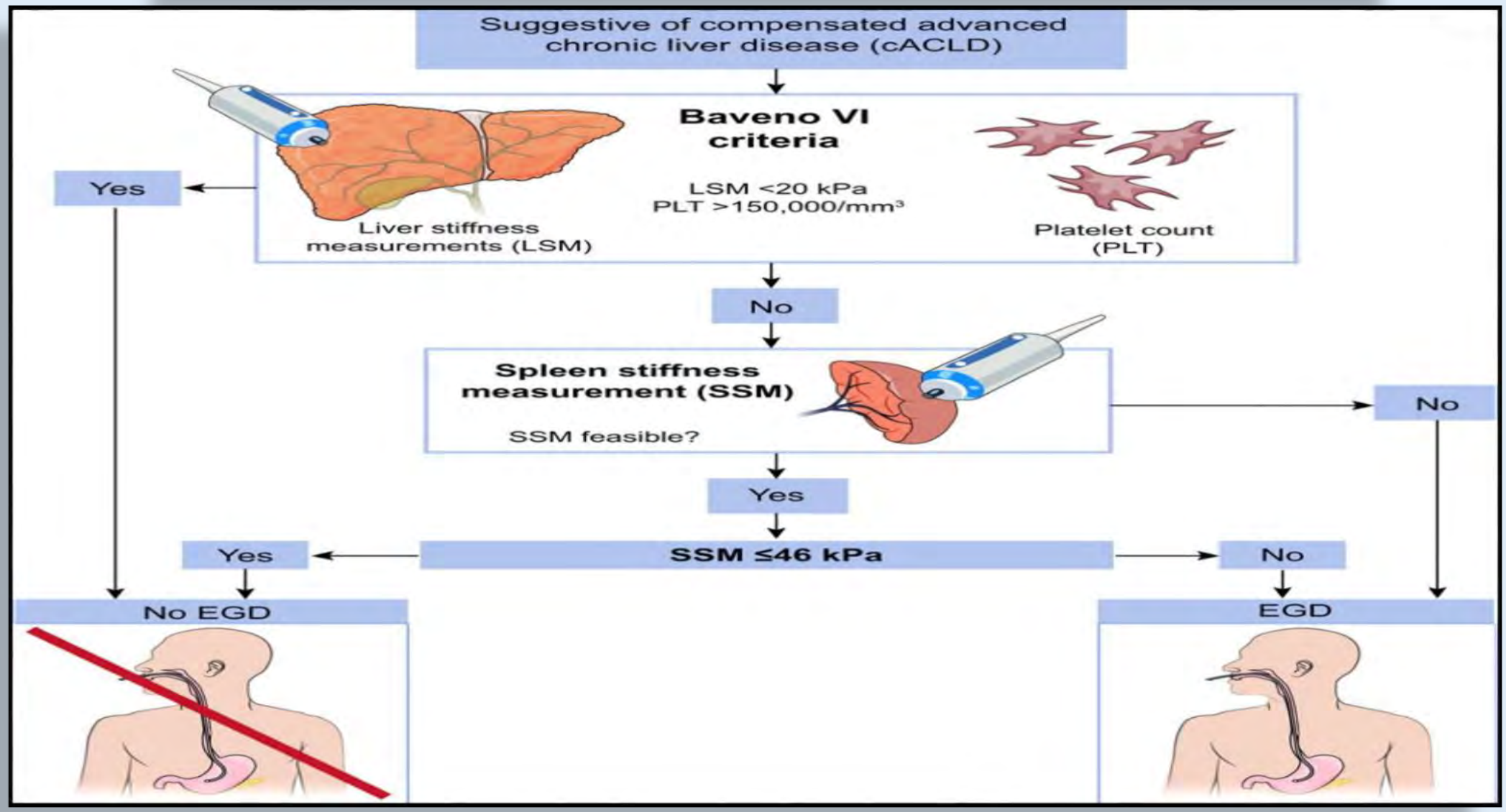
EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

OTHER INFECTIONS



EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

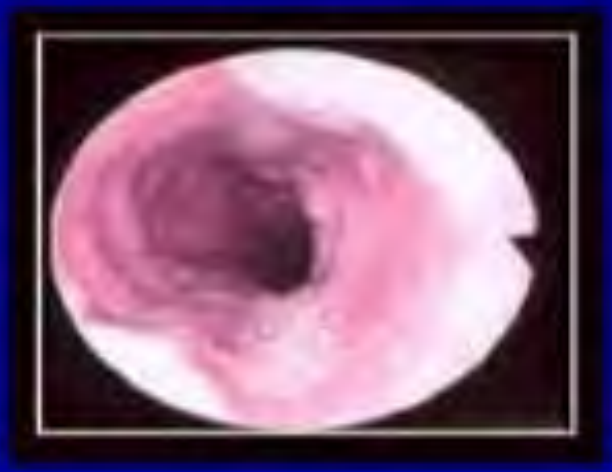
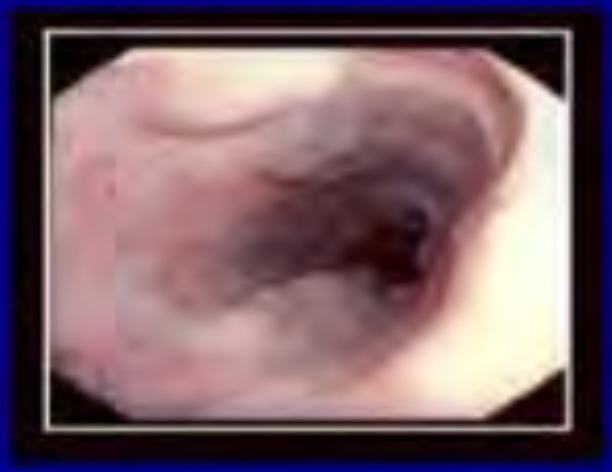
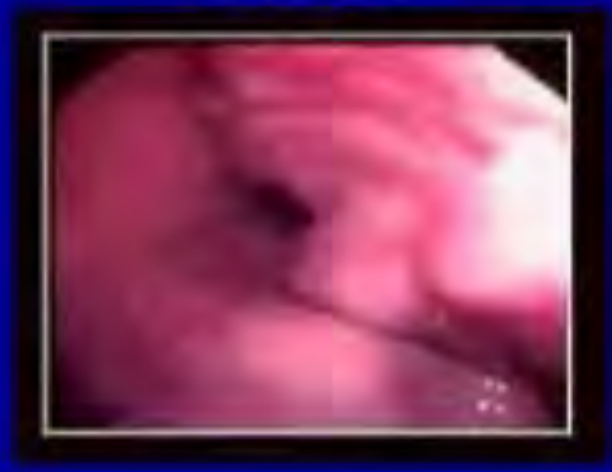
ESOPHAGEAL VARICES: SCREENING OGD



Baveno VII: Renewing consensus in portal hypertension

ESOPHAGEAL VARICES

Modified Paquet classification of Esophageal varices

Grade 1 Small	Grade 2 Medium	Grade 3 Large
		
Minimally elevated veins above surface	Tortuous veins occupying < 1/3 of esophageal lumen	Occupying > 1/3 of esophageal lumen

AASLD practice guidelines: Prevention and management of esophageal varices, Hepatology 2007.

ESOPHAGEAL VARICES

- **Low risk**
  - ✓Small varices without red color signs.

- **High risk**
  - ✓Medium to large varices.
  - ✓Small varices with red color signs.
  - ✓Small varices with CTP class C cirrhosis.

AASLD practice guidelines: Prevention and management of esophageal varices, Hepatology 2007.

ESOPHAGEAL VARICEAL HAEMORRHAGE

- Occurs when variceal wall ruptures due to excessive wall tension.
- Portal pressure is a key factor in both rupture and severity of bleeding.
- 70% of GI bleeding events result from VH in patients with portal hypertension.
- Most severe and immediate life threatening complication.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

ESOPHAGEAL VARICEAL HAEMORRHAGE

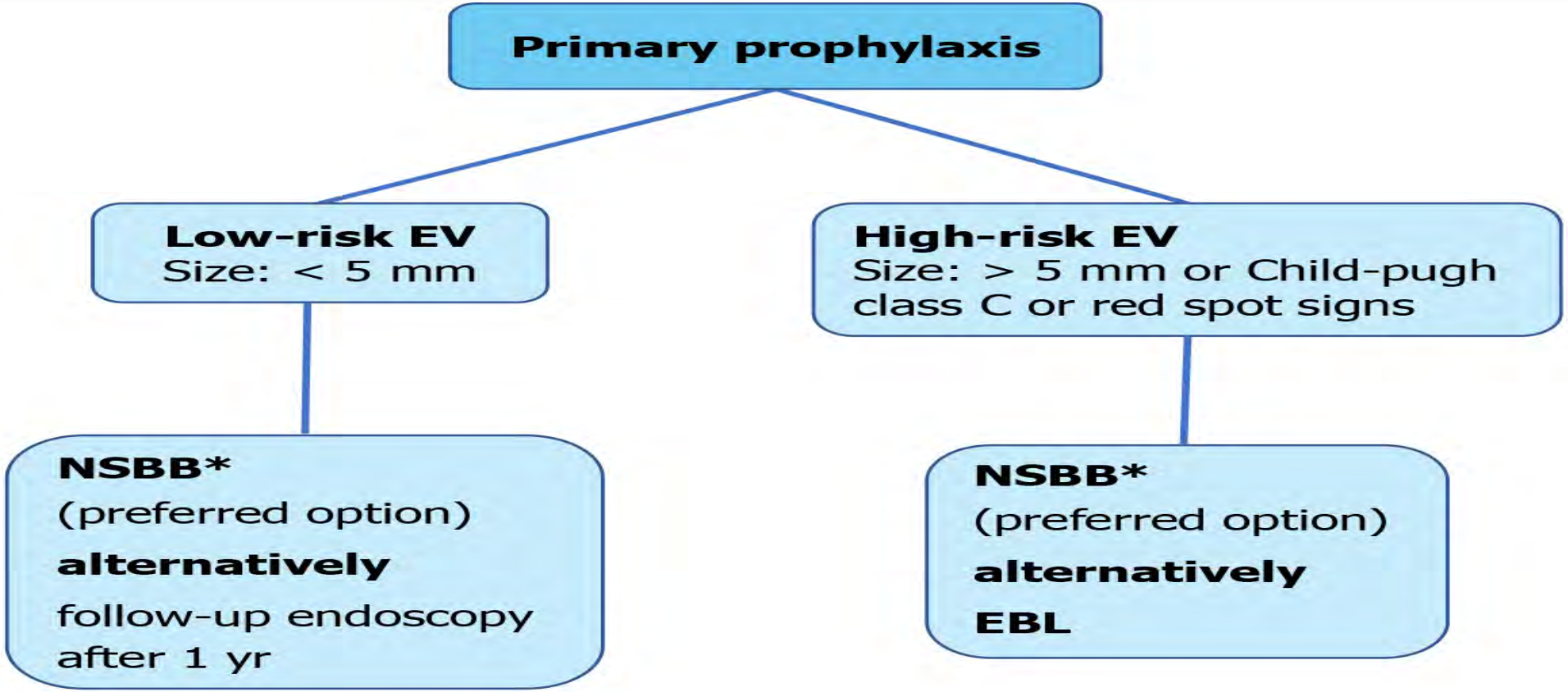
HIGH RISK PATIENTS

- HVPG > 20mmHg.
- CTP class C cirrhosis.
- CTP class B with active bleeding on endoscopy.
- Age >75 years.
- Hepatocellular carcinoma outside Milan criteria.
- High creatinine.
- Previous combination therapy.
- Portal-vein thrombosis.
- Heart failure.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

ESOPHAGEAL VARICEAL HAEMORRHAGE

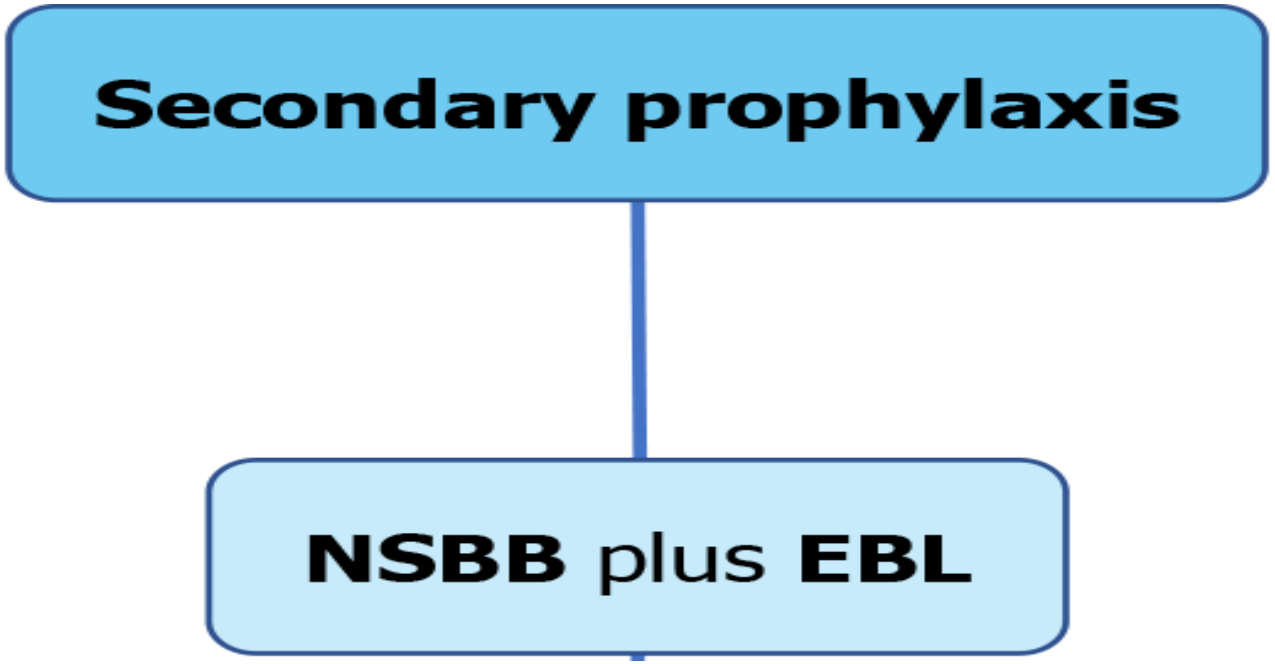
- **Primary prophylaxis**: Prevention of the first variceal bleeding in patients with liver cirrhosis.



EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

ESOPHAGEAL VARICEAL HAEMORRHAGE

- **Secondary prophylaxis**: Preventing recurrent variceal bleed.



EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

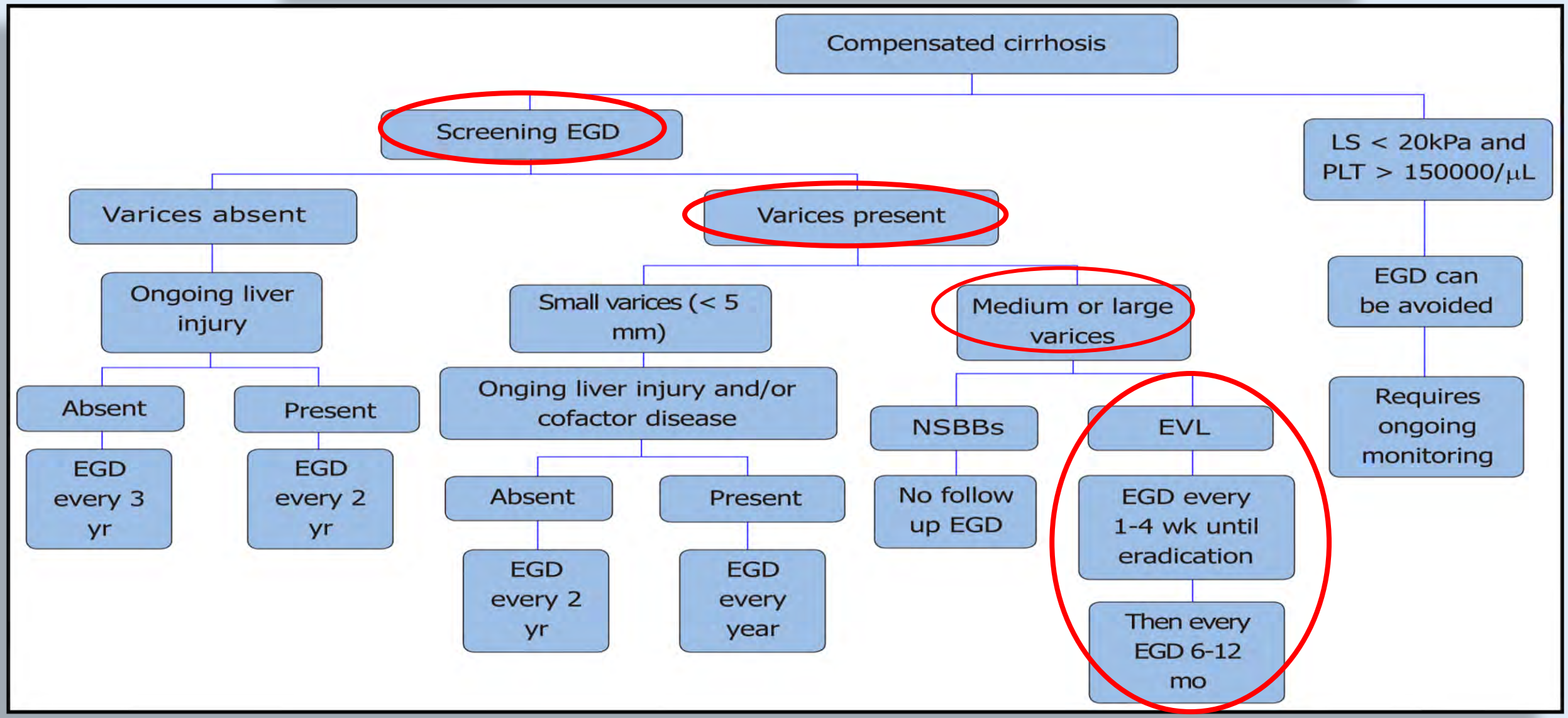
NSBB

NSBB	Frequency	Starting Dose (mg)		Therapy Goal		Maximum Dose (mg)	
		No Ascites	With Ascites	With or Without Ascites		No Ascites	With Ascites
Propranolol	Twice a day	20-40	10-20	HR: 55-60	Maintain SBP > 90	320	160
Nadolol	Daily	10-20	10-20			160	80
Carvedilol	Daily	6.25-12.5	NA	No HR goal		12.5-25*	NA

- **PREDESCI trial: Pts with compensated cirrhosis and CSPH treated as above had an increased decompensation-free survival.**

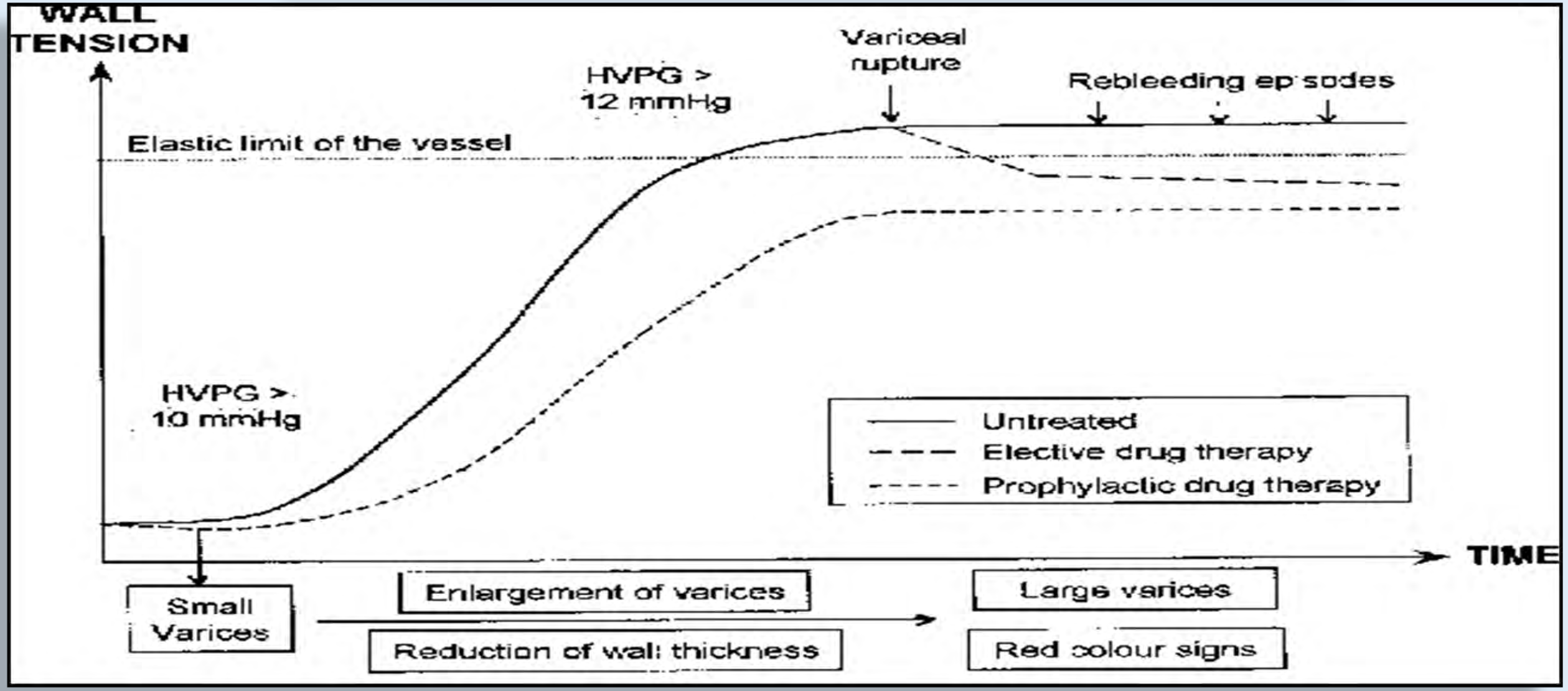
AASLD: Non-selective Beta- Blockers in Portal Hypertension: 2021. Lancet 2019; 393: 1597.

ESOPHAGEAL VARICEAL HAEMORRHAGE



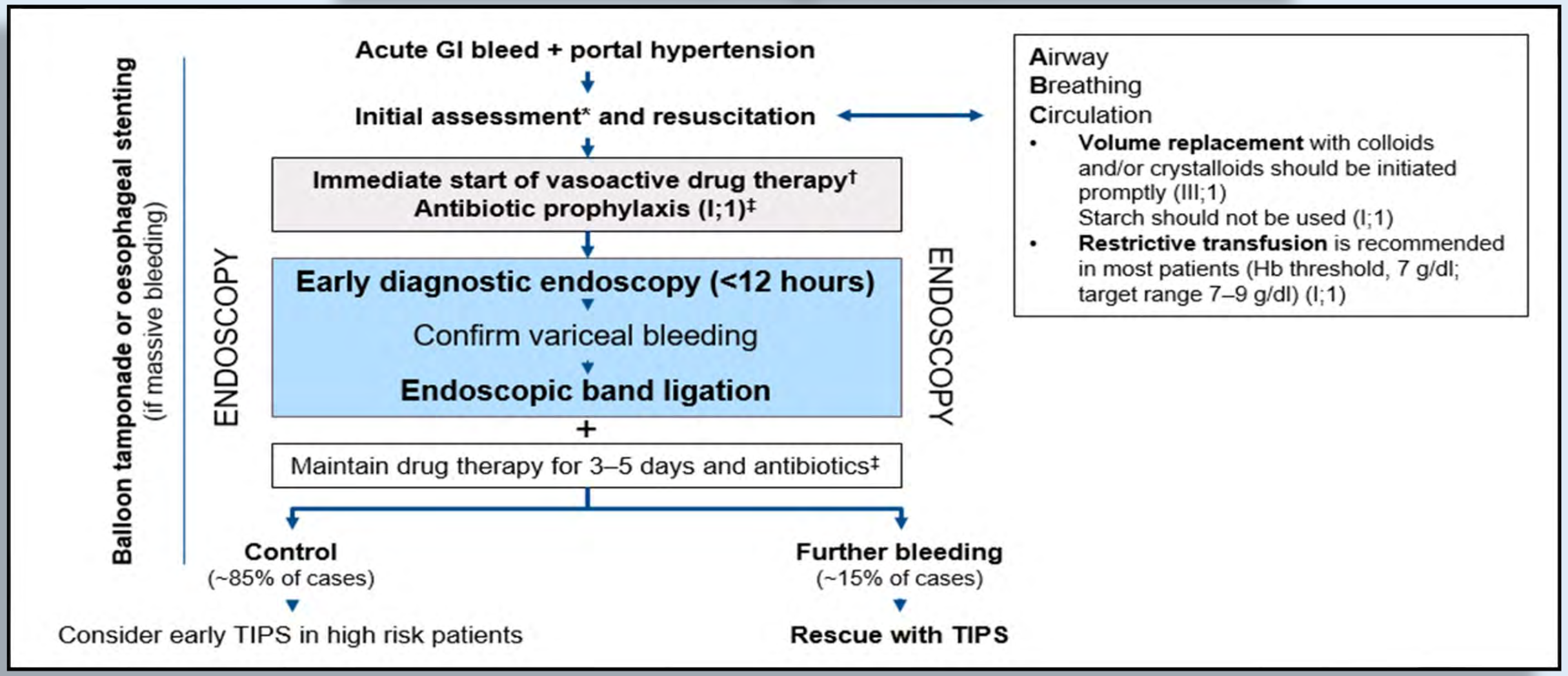
World J Gastrointest Pharmacol Ther. Jan 21, 2019; 10

ESOPHAGEAL VARICEAL HAEMORRHAGE



Pathophysiology of variceal bleeding in cirrhotics A. Berzigotti, À. Escorsell, J. Bosch

ACUTE VARICEAL HAEMORRHAGE Management



EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

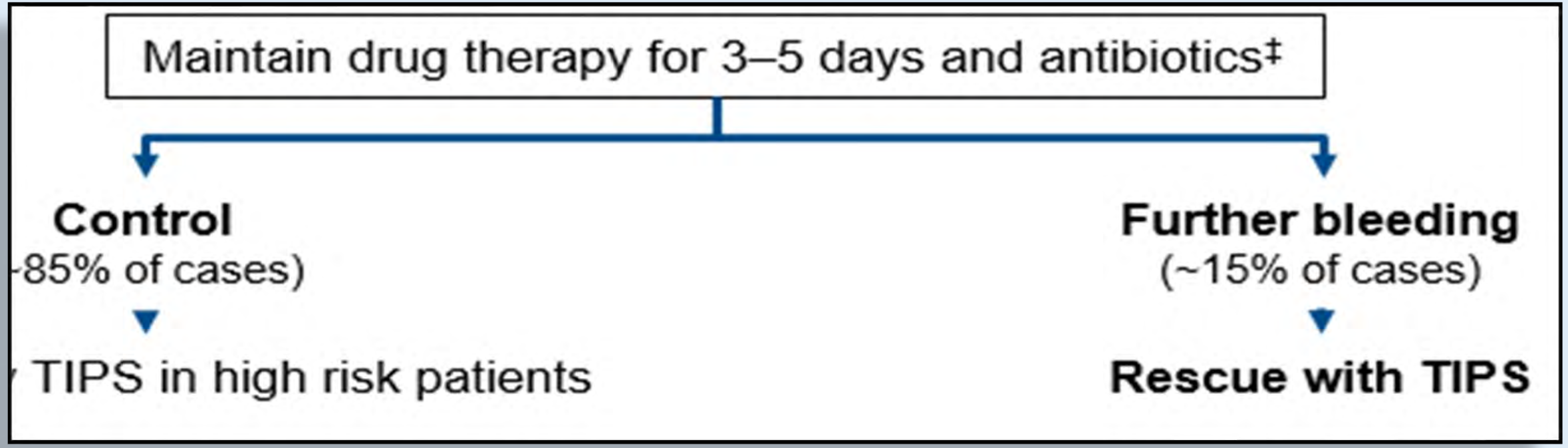
ACUTE VARICEAL HAEMORRHAGE
Management: Pre-Endoscopy

- Initial assessment and resuscitation.
  - ✓Airway.
  - ✓Breathing.
  - ✓Circulation: Volume replacement, Restrictive transfusion.

- Immediate start of Vasoactive drug therapy and antibiotics prophylaxis.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

ACUTE VARICEAL HAEMORRHAGE
Management: Post Endoscopy



EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

ACUTE VARICEAL HAEMORRHAGE
Management: Endoscopy

Early diagnostic endoscopy (<12 hours)

▼

Confirm variceal bleeding

▼

Endoscopic band ligation

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

Project ECHO
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GASTRIC VARICES

- Gastric varices are present in about 20% of patients with cirrhosis.
- **The Sarin classification** is used for risk stratification and management of gastric varices.

Type	Definition	Relative frequency	Overall bleeding risk without treatment
Gastro-oesophageal varices (GOV)			
GOV type 1	OV extending below cardia into lesser curvature	70%	28%
GOV type 2	OV extending below cardia into fundus	21%	55%
Isolated gastric varices (IGV)			
IGV type 1	Isolated varices in the fundus	7%	78%
IGV type 2	Isolated varices else in the stomach	2%	9%

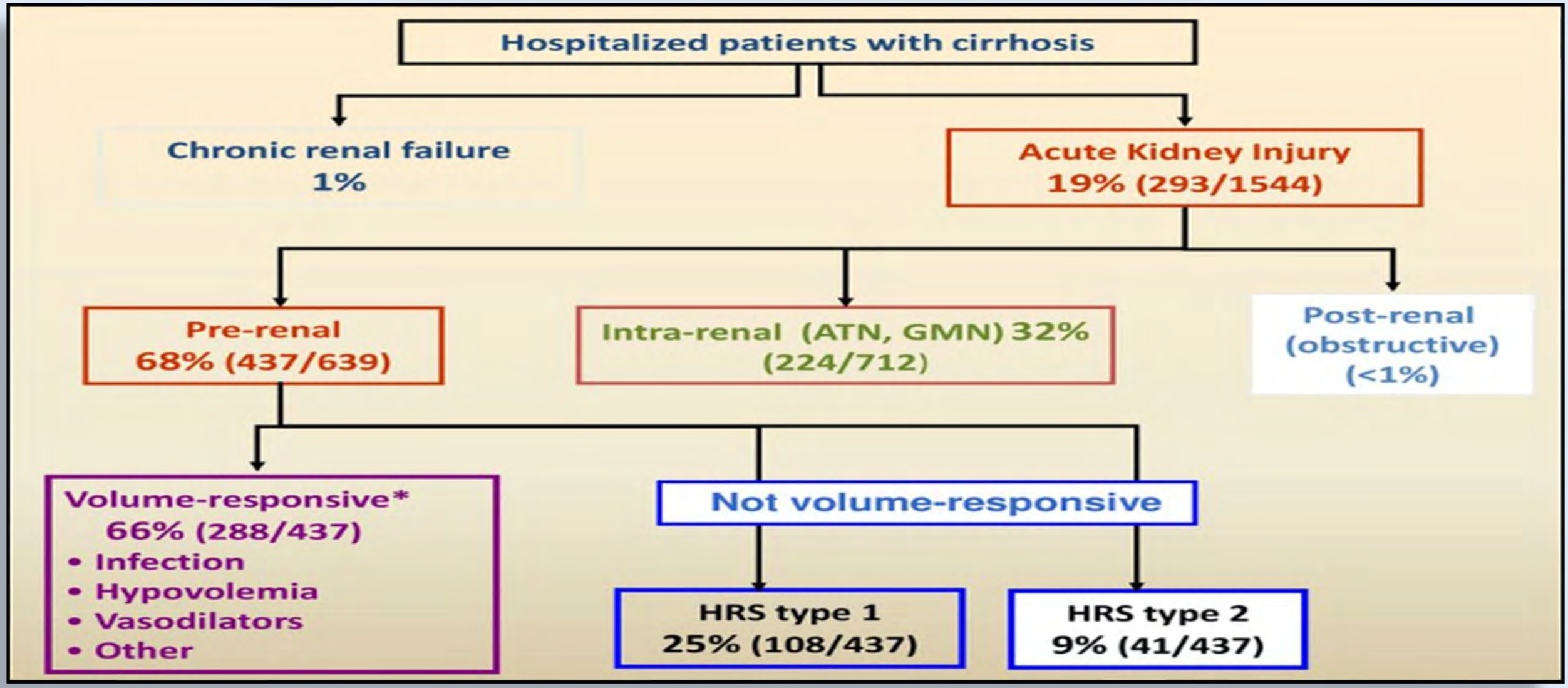
EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

GASTRIC VARICES Management

- NSBBs: Primary prophylaxis of VH from GOV type 2 or IGV type 1.
- Primary prophylaxis for GOV type 1 follows as oesophageal varices.
- Cyanoacrylate: Cardiofundal varices (GOV type 2 or IGV type 1).
- TIPS with potential embolization.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

HEPATORENAL SYNDROME



Garcia-Tsao G et al. Hepatology 2008

HEPATORENAL SYNDROME

- **Type 1 HRS** now corresponds to **HRS-AKI.**

- **Type 2 HRS** includes renal impairment that fulfills the criteria of HRS but not of AKI (**non-AKI-HRS or NAKI**).

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

AKI IN CIRRHOSIS: ICA DEFINITIONS

Subject	Definition		
Baseline sCr	• sCr obtained within 3 months prior to admission • If >1 value within the previous 3 months, the value closest to the admission • If no previous sCr, the sCr on admission should be used		
Definition of AKI	• Increase in sCr ≥0.3 mg/dl (≥26.5 µmol/L) within 48 hours or • Increase sCr ≥50% within the prior 7 days		
Staging of AKI	• **Stage 1**: increase in sCr ≥0.3 mg/dl (≥26.5 µmol/L) or an increase in sCr ≥1.5-fold to 2-fold from baseline • **Stage 2**: increase in sCr >2-fold to 3-fold from baseline • **Stage 3**: increase of sCr >3-fold from baseline or sCr ≥4.0 mg/dl (353.6 µmol/L) with acute increase ≥0.3 mg/dl (≥26.5 µmol/L) or initiation of renal replacement therapy		
Progression of AKI	**Progression** Progression of AKI to a higher stage and/or need for RRT	**Regression** Regression of AKI to a lower stage	
Response to treatment	**No response** No regression of AKI	**Partial response** Regression of AKI stage with a reduction of sCr to ≥0.3 mg/dl (≥26.5 µmol/L) above baseline	**Full response** Return of sCr to a value within 0.3 mg/dl (≥26.5 µmol/L) of baseline

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

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HRS ICA DIAGNOSTIC CRITERIA

- Cirrhosis and ascites.
- Diagnosis of AKI according to ICA-AKI criteria.
- No response to diuretic withdrawal and plasma volume expansion with albumin(48 hours).
- Absence of shock.
- No current or recent use of nephrotoxic drugs.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

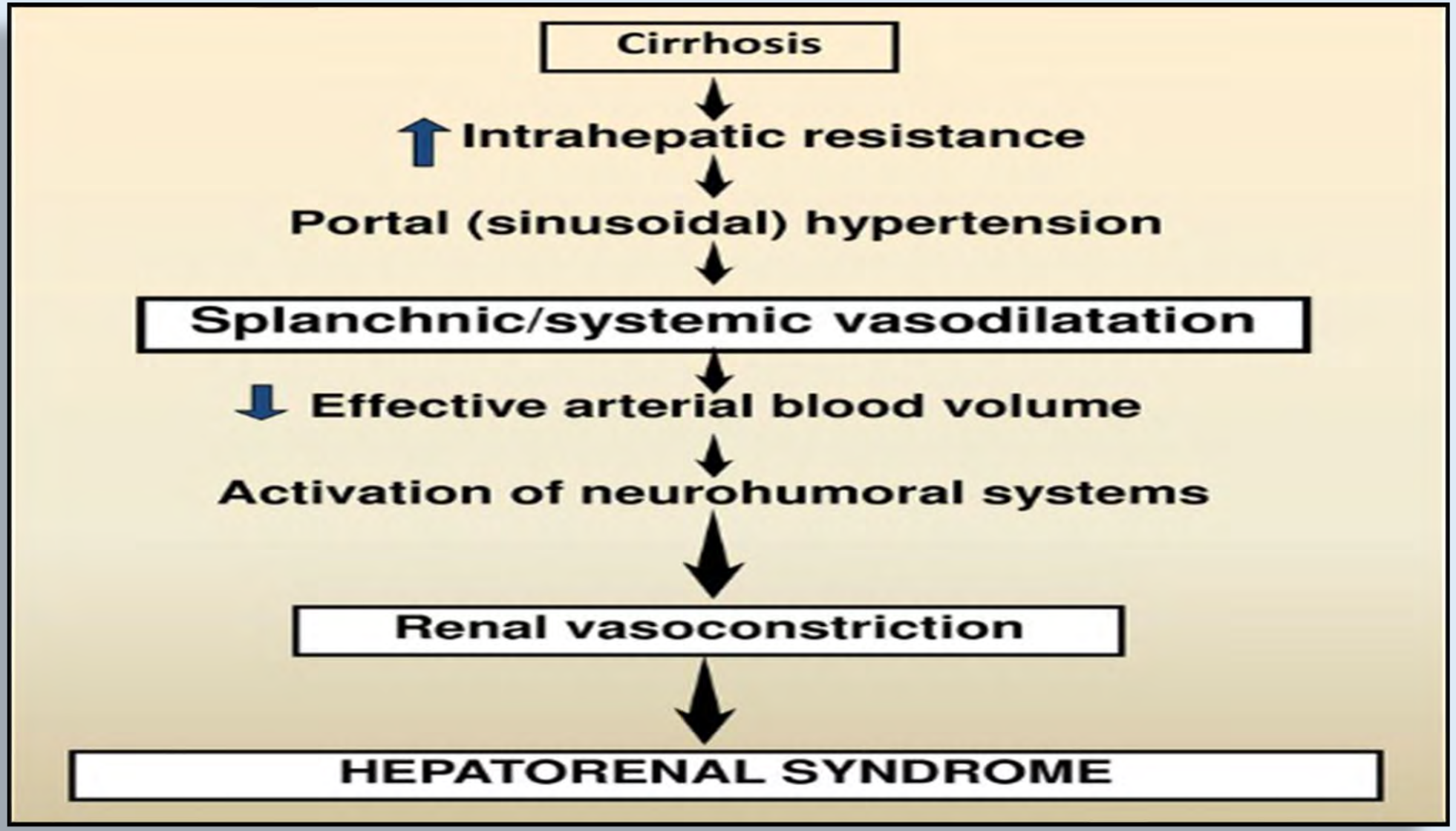
HRS ICA DIAGNOSTIC CRITERIA

No macroscopic signs of structural kidney injury, defined as:

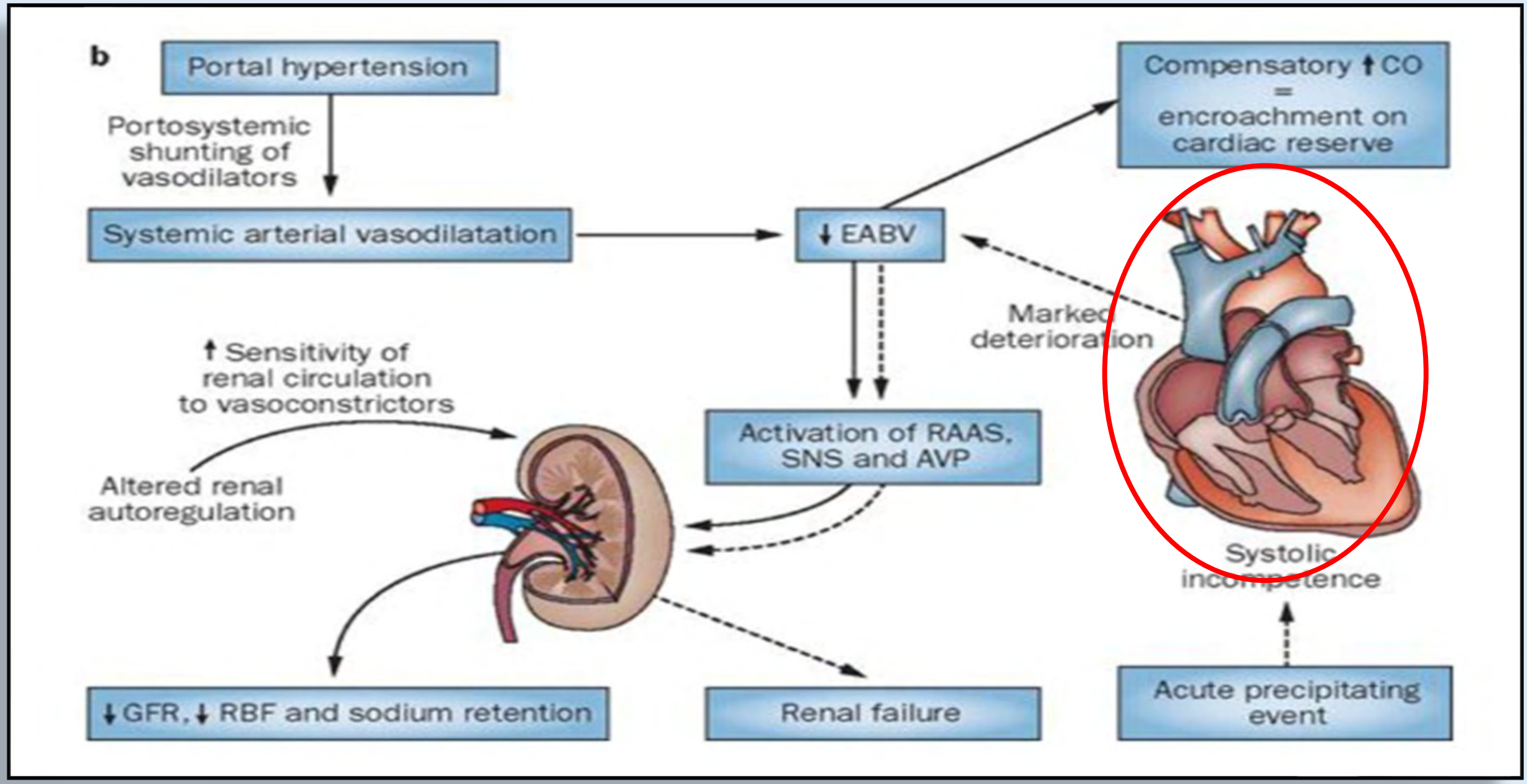
- Absence of proteinuria (>500 mg/day).
- Absence of microhaematuria (>50 RBCs per high power field).
- Normal findings on renal ultrasonography.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

PATHOPHYSIOLOGY



Garcia-Tsao G et al. Hepatology 2008



Wong F. Nat Rev. Gastroenterology 2012

HRS AKI: TREATMENT

- First-line therapy is terlipressin plus albumin.
- Patients should be monitored for AEs and treatment response.
- HRS-AKI TIPS is contraindicated because of severe degree of liver failure.
- LT is the best therapeutic option.

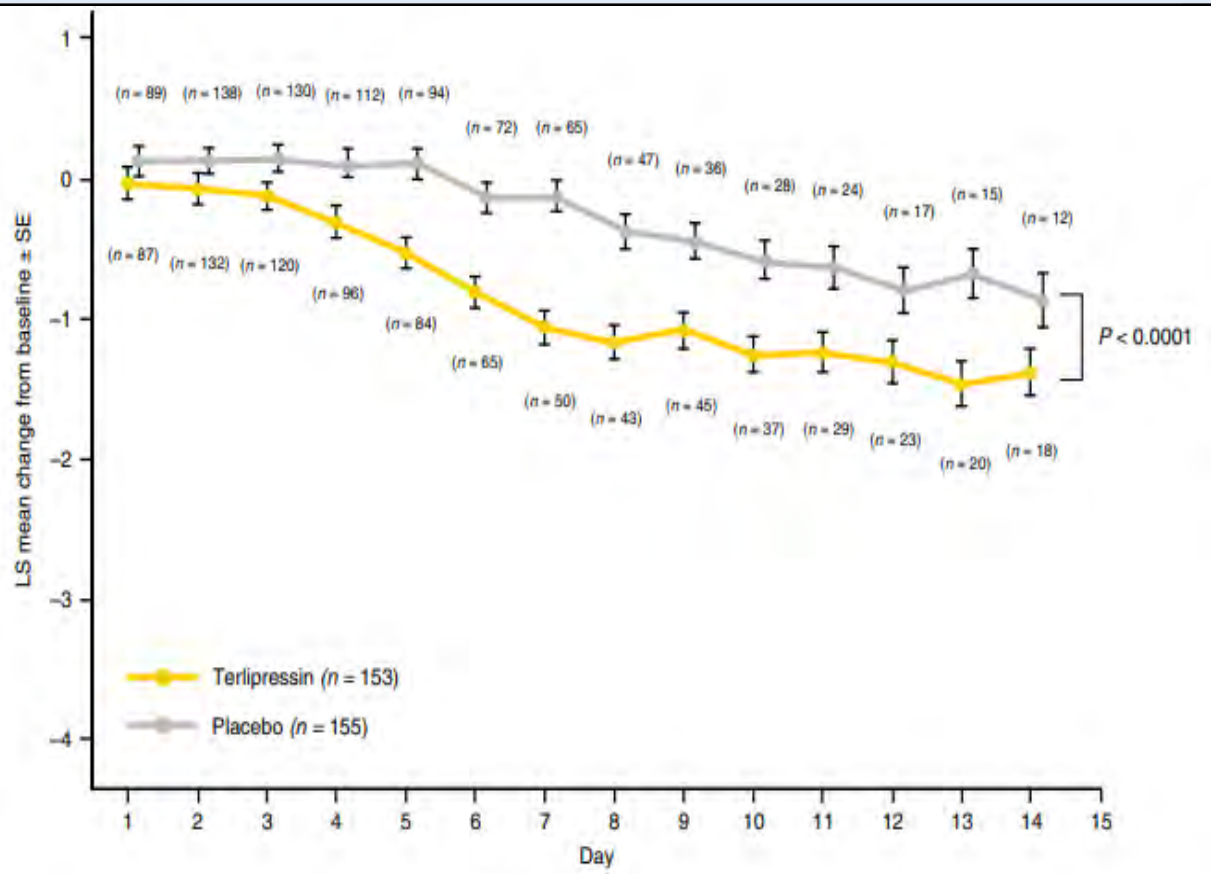
EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

HRS AKI: TREATMENT

AP&T Alimentary Pharmacology and Therapeutics

Reversal of hepatorenal syndrome type 1 with terlipressin plus albumin vs. placebo plus albumin in a pooled analysis of the OT-0401 and REVERSE randomised clinical studies

A. J. Sanyal*, T. D. Boyer†, R. T. Frederick‡, F. Wong§, L. Rossaro¶, V. Araya**, H. E. Vargas††, K. R. Reddy‡‡, S. C. Pappas§§, P. Teuber§§, S. Escalante¶¶ & K. Jamil¶¶



Conclusions

Terlipressin plus albumin resulted in a significantly higher rate of HRS reversal vs. albumin alone in patients with HRS-1. Terlipressin treatment is

HRS AKI: TREATMENT

- RRT decision should be based on the individual severity of illness.
- The indication for liver-kidney transplantation remains controversial.
- Prevention: Albumin in patients who develop SBP and SBP prevention.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

HEPATIC HYDROTHORAX

- Accumulation of transudate in the pleural space in the absence of cardiac, pulmonary or pleural disease.
- Ascites moves through small diaphragmatic defects. Negative intrathoracic pressure induced by inspiration.
- Can be complicated by spontaneous bacterial infections (empyema).
- Associated with poor prognosis.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

HEPATIC HYDROTHORAX
Diagnosis and treatment

- Diagnostic thoracentesis is required to rule out bacterial infection.
- First-line management relies on treatment of ascites with diuretics and/or LVP.
- Refractory hepatic hydrothorax.
- Therapeutic thoracentesis is required to relieve dyspnea.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

HEPATIC HYDROTHORAX
Diagnosis and treatment

- Patients with hydrothorax should be evaluated for LT.
- TIPS.
- Pleurodesis.
- Mesh repair of diaphragmatic defects

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.02

RELATIVE ADRENAL INSUFFICIENCY

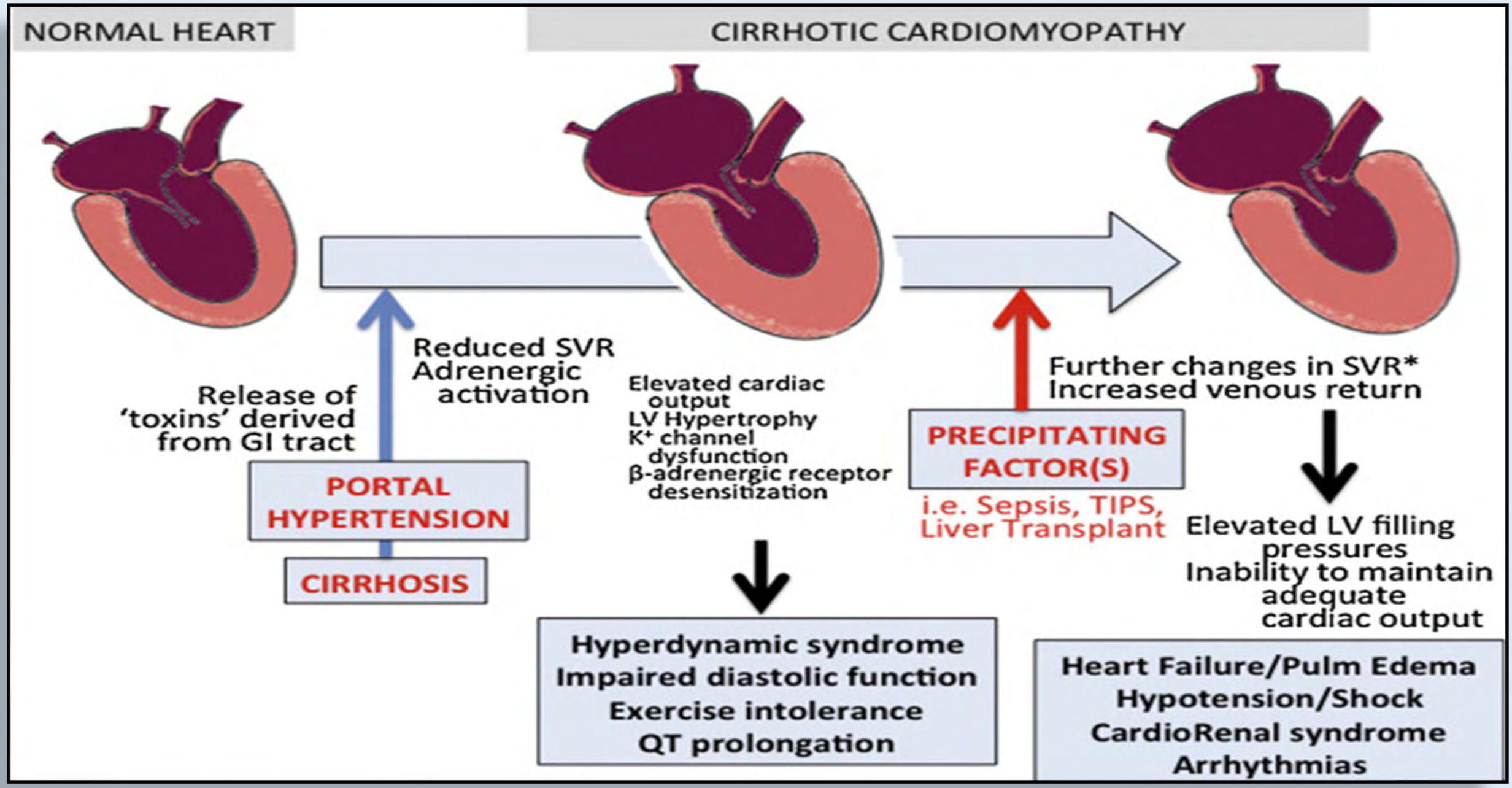
- Inadequate cortisol response to stress in the setting of critical illness.
- Pathophysiology in cirrhosis is not well defined.
- Diagnosis is influenced by the method used to measure cortisol.
- It is not known whether cortisol supplementation in clinically stable cirrhosis with RAI is of any value

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

CIRRHOTIC CARDIOMYOPATHY

- CCM occurs in patients with established cirrhosis characterized by:
  - ✓Blunted contractile response to stress (pharmacological/surgery or inflammatory).
  - ✓Altered diastolic left ventricular relaxation or/and increased left atrial volume.
  - ✓Electrophysiological abnormalities e.g. prolonged QTc.
  - ✓Cardiac output tending to decrease with decompensation.
  - ✓Systolic dysfunction: LVEF <55%.
- CCM is largely subclinical but its presence influences prognosis in advanced disease.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.



https://ars.els-cdn.com/content/image.

CIRRHOTIC CARDIOMYOPATHY
Treatment

- Liver transplantation may revert cardia dysfunction.
- Surgery and TIPS insertion may aggravate cardiac dysfunction.
- Treatment is non specific and directed towards left ventricular failure.

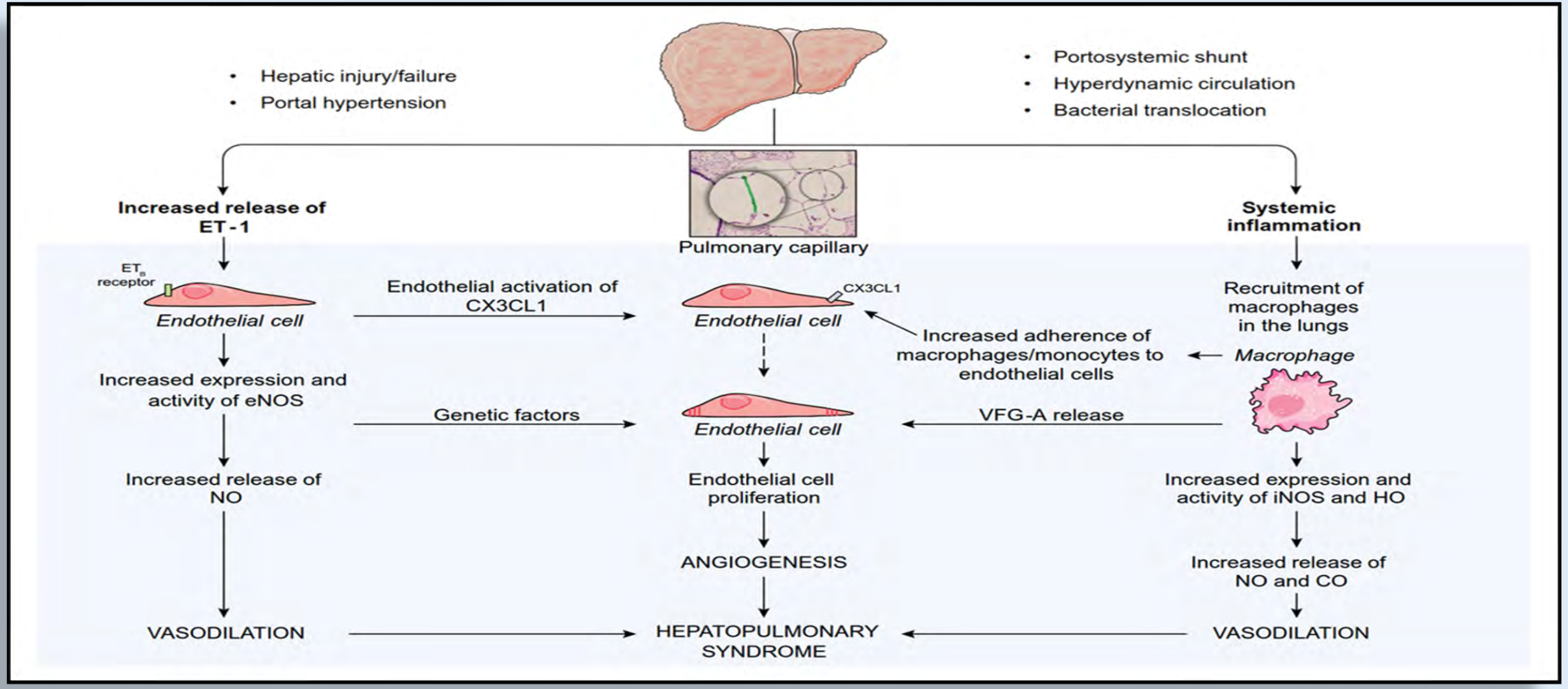
EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

HEPATOPULMONARY SYNDROME

- HPS is defined as a disorder in pulmonary oxygenation, caused by intrapulmonary vasodilatation.
- Pleural and pulmonary arteriovenous communications less commonly cause HPS.
- Clinical manifestations: Dyspnoea and platypnoea.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

HPS PATHOGENESIS



EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

HPS DIAGNOSTIC CRITERIA

- Hypoxia with **PaO2** <80 mmHg/**A-a gradient** ≥15 mmHg in ambient air.

- Pulmonary vascular defect.
  - ✓ +ve findings on contrast-enhanced echocardiography/abnormal uptake in the brain (>6%) with radioactive lung-perfusion scanning.

- Hepatic portal hypertension with underlying cirrhosis.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

HPS MANAGEMENT

- There is no established medical therapy currently available for HPS, the only successful treatment for HPS is LT.
- Long-term oxygen therapy is recommended in patients with HPS .
- Severe hypoxaemia (PaO_2 <45–50 mmHg) is associated with increased post-LT mortality.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

PORTOPULMONERY HYPERTENSION

- PPHT occurs in patients with portal hypertension in the absence of other causes of arterial or venous hypertension.
- Incidence between 3–10% cirrhosis patients.
- Women are at 3x greater risk and it is more common in autoimmune liver disease.
- There is no clear association between the severity of liver disease or PHT and the development of severe PPHT.

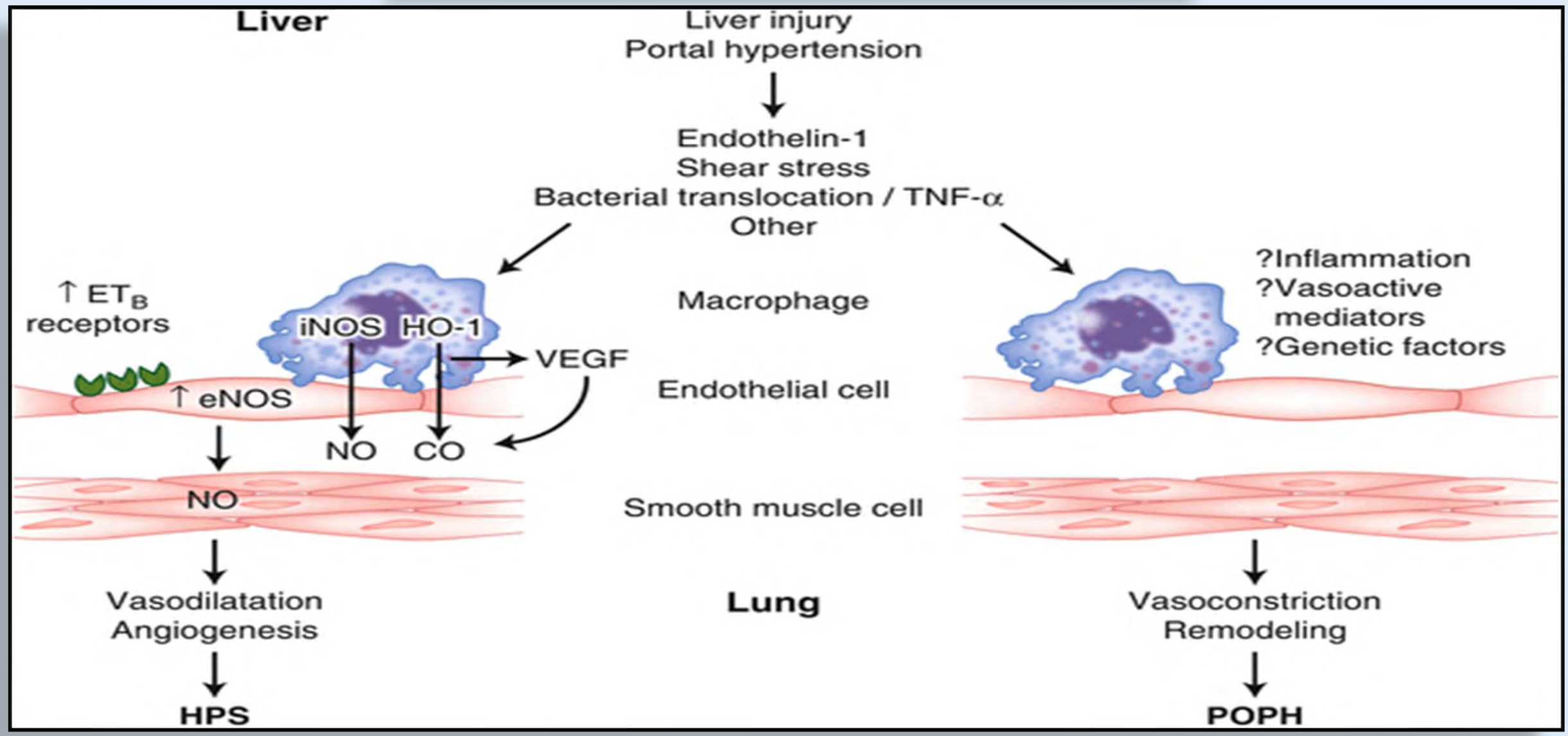
EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

PORTOPULMONERY HYPERTENSION

- Classification is based on mean pulmonary arterial pressure (mPAP):
  - ✓Mild: mPAP ≥25 and <35 mmHg.
  - ✓Moderate: mPAP ≥35 and <45 mmHg.
  - ✓Severe: mPAP ≥45 mmHg.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

PPHT PATHOPHYSIOLOGY



Eur Respir Rev. 2012 Sep 1;21(125):223-33.

PORTOPULMONERY HYPERTENSION Management

- The evidence base for pharmacological therapies in PPHT is limited.
- Endothelin antagonists should be used with caution(hepatic impairment).
- TIPS should not be used in patients with PPHT.
- If mPAP <35 mmHg and right ventricular function is preserved, LT should be considered.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

HYPONATREMIA

- Common in patients with advanced cirrhosis.
- Arbitrarily defined as serum sodium concentration <130 mmol/L.
- Hypo- and hypervolaemic hyponatraemia.
- Increased mortality and morbidity, particularly neurological complications.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024

HYPONATREMIA Treatment

- Evaluation for LT.
- Removal of the identified cause.
- **Hypovolaemic hyponatraemia**: Administration of normal saline.
- **Hypervolemic hyponatremia**: Fluid restriction to 1L/day.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

TRIGGERS ON LIVER TRANSPLANT REFERRAL

- Recurrent variceal bleed.
- Intractable ascites.
- Spontaneous Bacterial peritonitis.
- Refractory encephalopathy.
- Hepatorenal syndrome.
- Decompensation.

EASL CPG decompensated cirrhosis. J Hepatol 2018;doi: 10.1016/j.jhep.2018.03.024.

CONCLUSION

- **Although effective therapy is available for most of cirrhosis complications, liver transplantation is the only treatment modality.**