



Diseases affecting small intrahepatic vessels

Pierre-Emmanuel RAUTOU

Inserm U1149, Centre de recherche sur l'inflammation, Paris

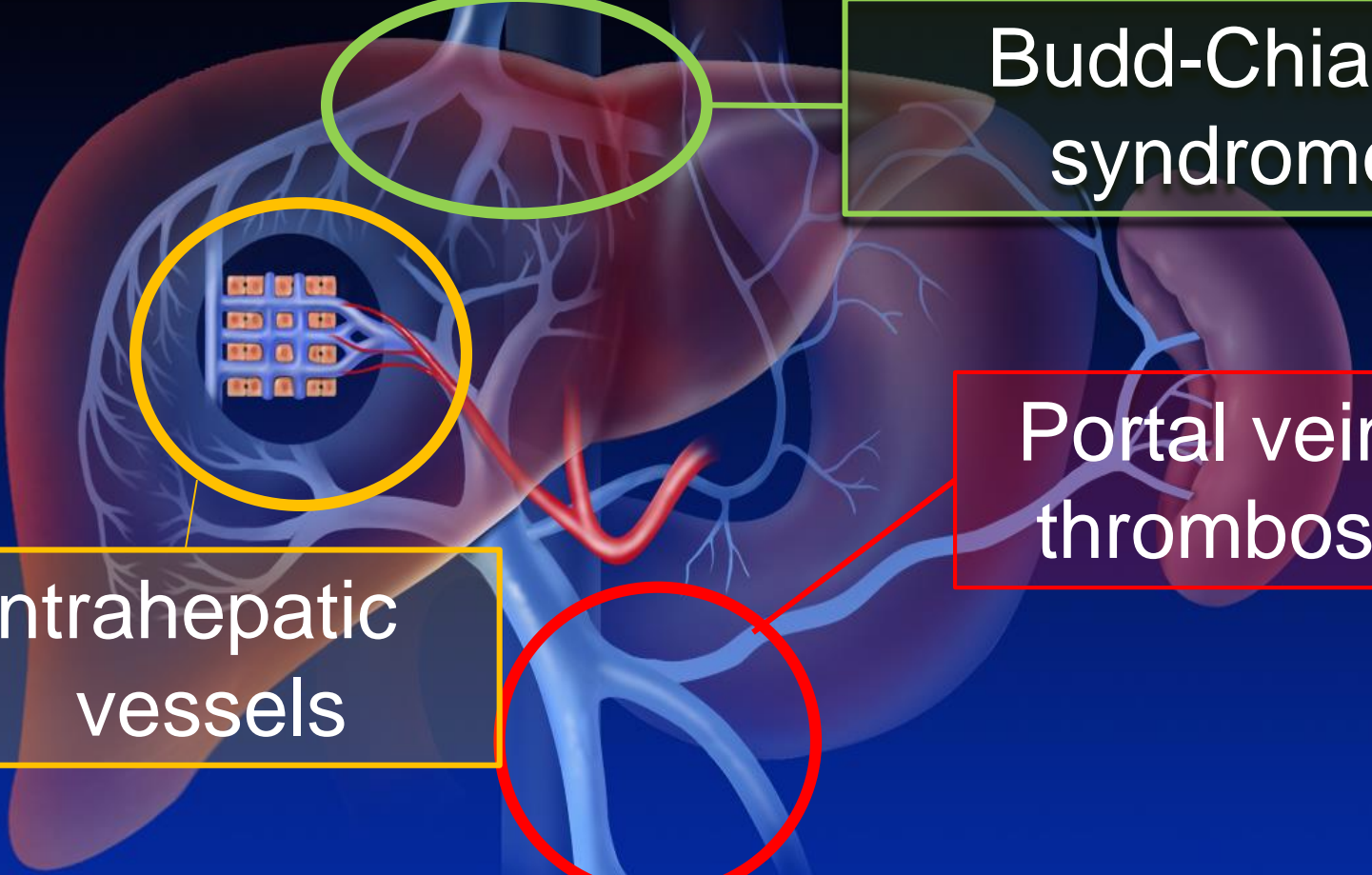
Service d'hépatologie, Hôpital Beaujon, Clichy, France

pierre-emmanuel.rautou@inserm.fr

Conflict of interest

None related to the presentation

Vascular liver diseases



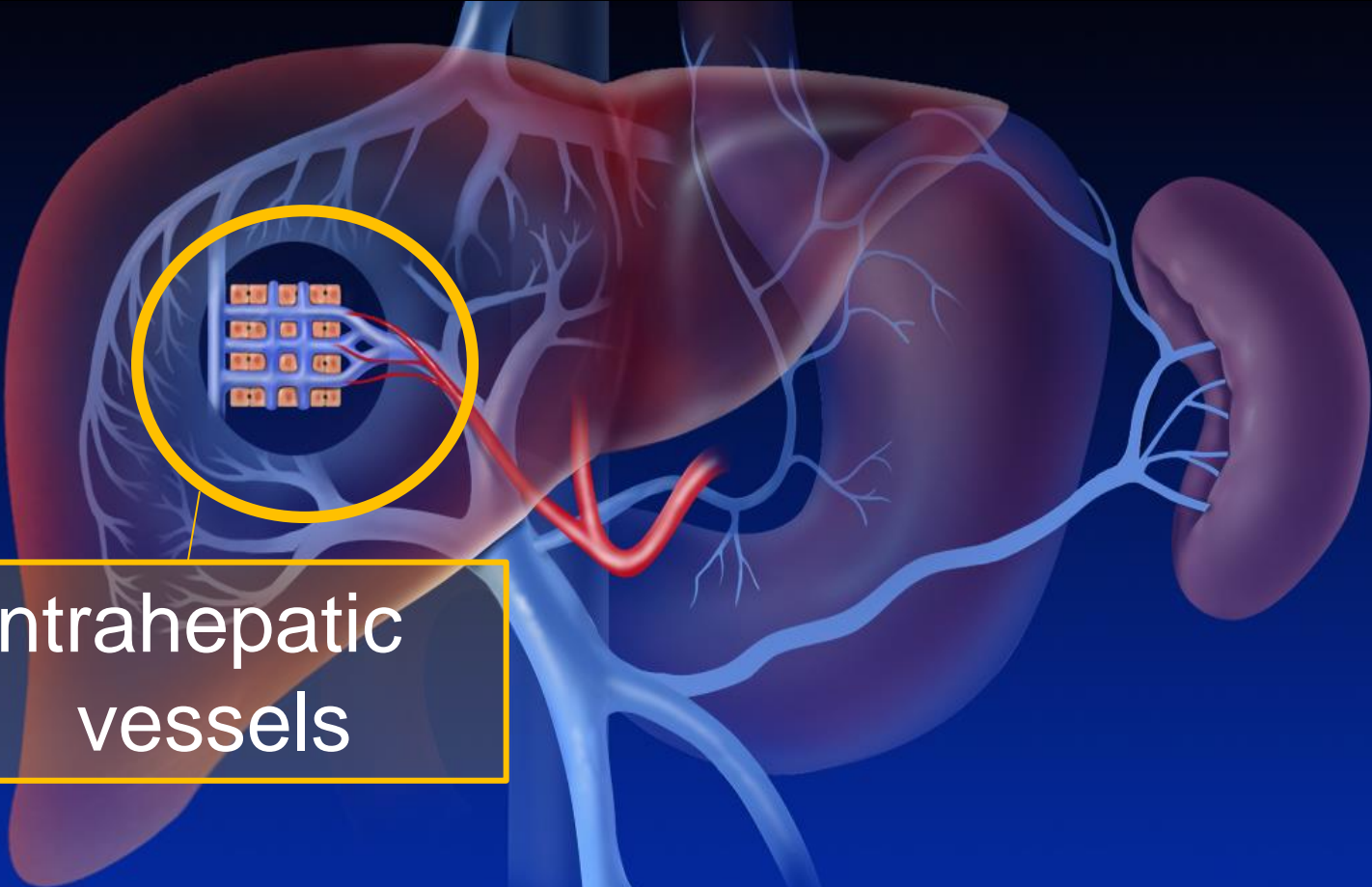
Budd-Chiari syndrome

The diagram illustrates the liver and its associated blood vessels. The liver is shown in a reddish-brown color, with its branching network of blood vessels. The hepatic veins, which drain the liver into the inferior vena cava, are highlighted with a green circle. The portal vein, which carries blood from the gastrointestinal tract to the liver, is highlighted with a red circle. The intrahepatic vessels, which are the smaller vessels within the liver, are highlighted with a yellow circle. The background is a dark blue gradient.

Portal vein thrombosis

Intrahepatic vessels

Vascular liver diseases



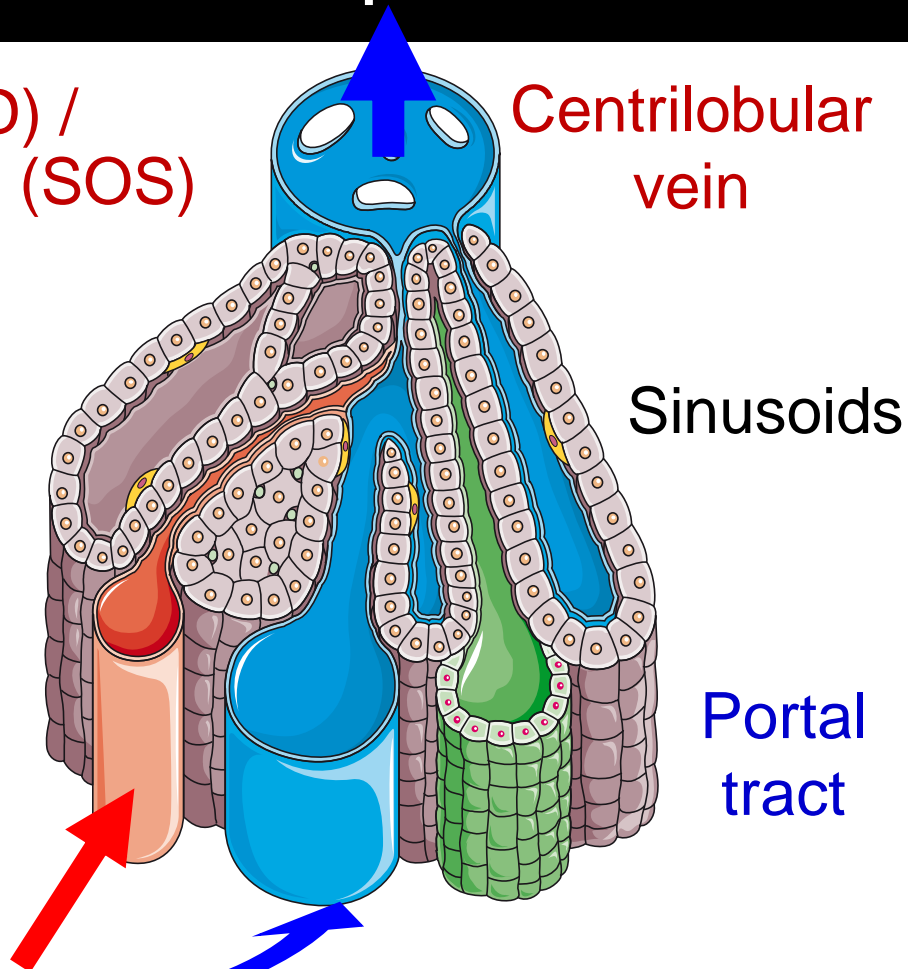
Intrahepatic
vessels

Diseases affecting small intrahepatic vessels

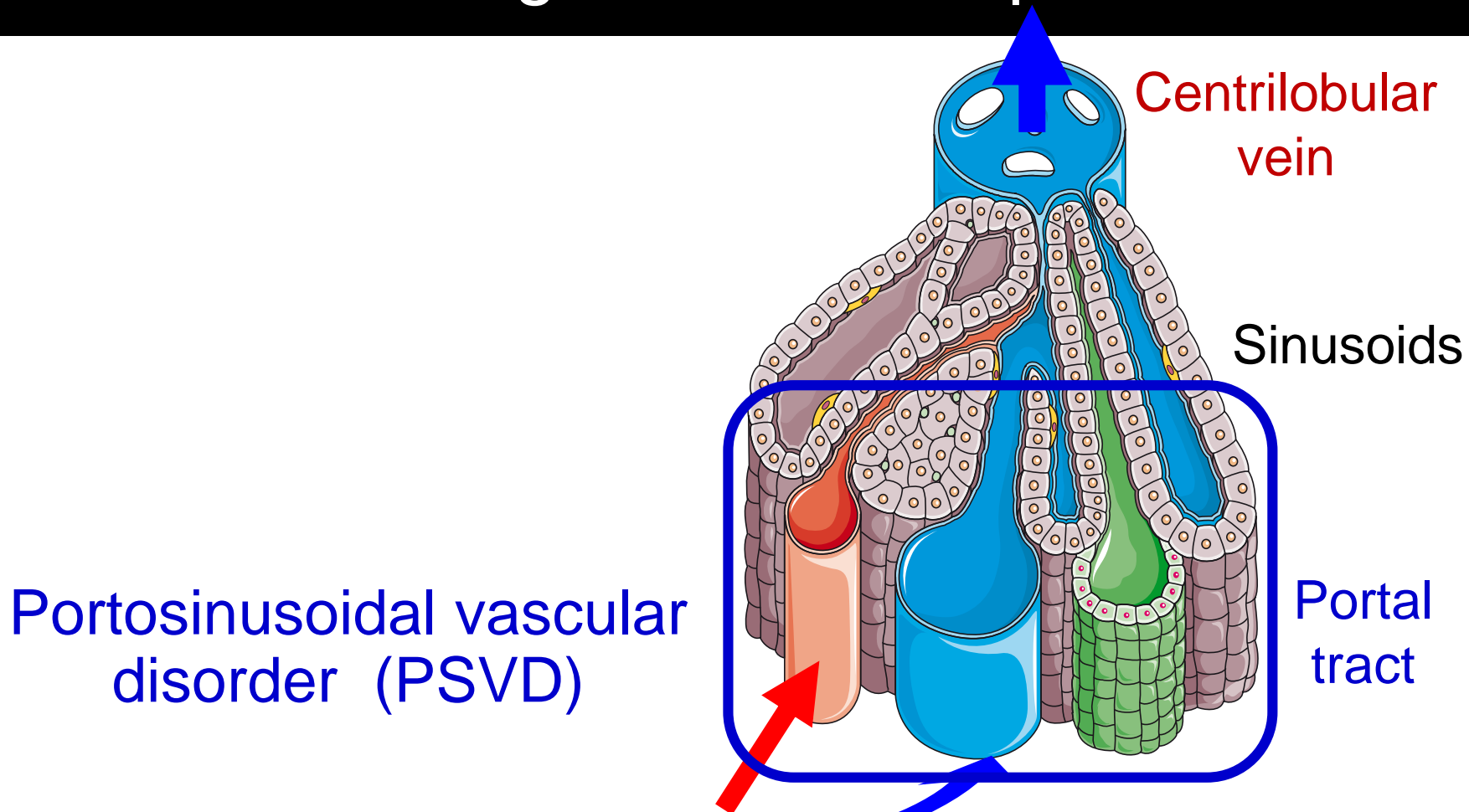
Veno-occlusive disease (VOD) /
sinusoidal obstruction syndrome (SOS)

Sinusoidal dilation /
Peliosis

Portosinusoidal vascular
disorder (PSVD)

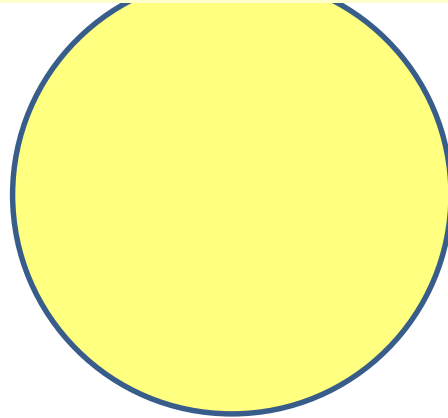


Diseases affecting small intrahepatic vessels



HISTOLOGY

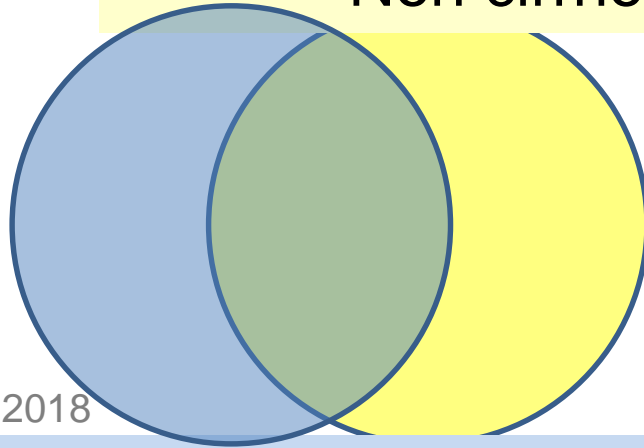
- Obliterative portal venopathy
- Nodular regenerative hyperplasia
 - Hepatoportal sclerosis
- Non cirrhotic portal fibrosis



Verheij J, Histopathology. 2013
Guido M, Histopathology. 2019
Kmeid M, Diagn Pathol. 2020

HISTOLOGY

- Obliterative portal venopathy
- Nodular regenerative hyperplasia
 - Hepatoportal sclerosis
 - Non cirrhotic portal fibrosis



Schouten JN, APT 2012
Schouten JN, Hepatology. 2011
Hernández-Gea V, Hepatology. 2018

Idiopathic portal hypertension
Intrahepatic non cirrhotic portal hypertension

CLINIC

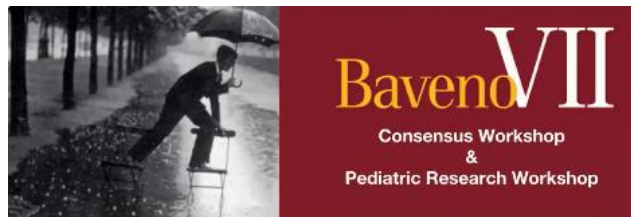
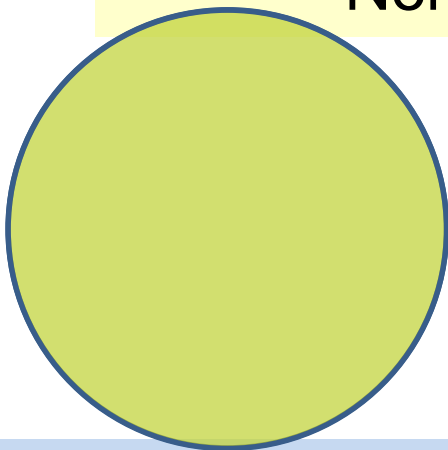
“Porto-sinusoidal vascular disorder” (PSVD)

HISTOLOGY

- Obliterative portal venopathy
- Nodular regenerative hyperplasia
 - Hepatoportal sclerosis
 - Non cirrhotic portal fibrosis



De Gottardi et al,
Lancet Gastro Hepatol 2019



De Franchis et al, J Hepatol 2022

Idiopathic portal hypertension
Intrahepatic non cirrhotic portal hypertension

CLINIC

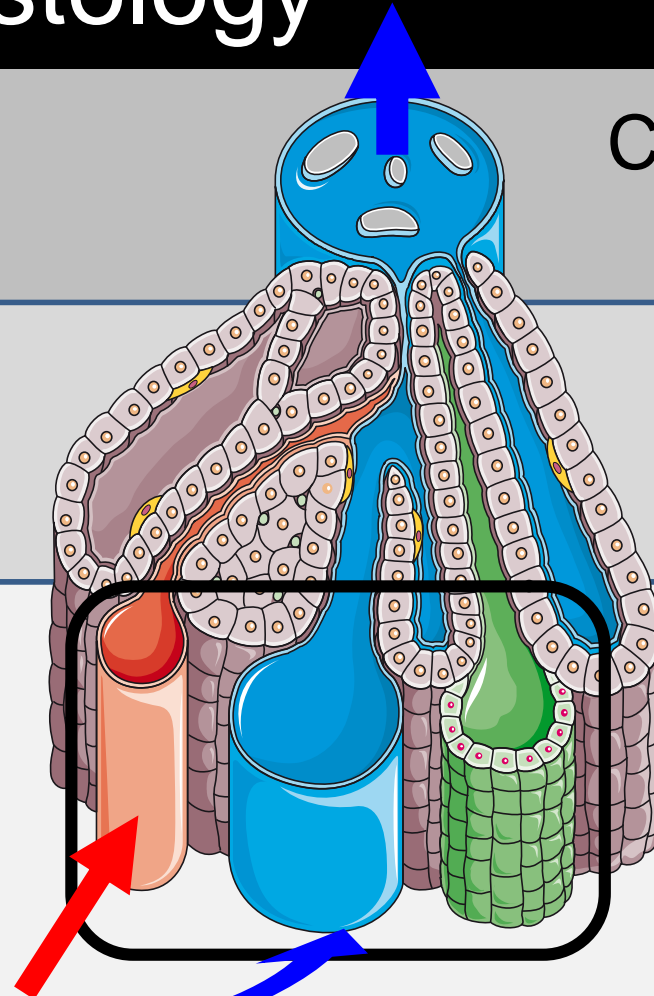
Liver histology

Central vein

Sinusoids

Portal tract

Porto-sinusoidal
vascular
disorder



“Porto-sinusoidal vascular disorder” (PSVD)



Porto-sinusoidal vascular disorder

- When to suspect?
- Definition
- Associated conditions
- Outcome

PSVD among cirrhosis

PSVD
0.4%

Cirrhosis
99.6%



➔ Screening tools needed

PSVD: when to suspect?

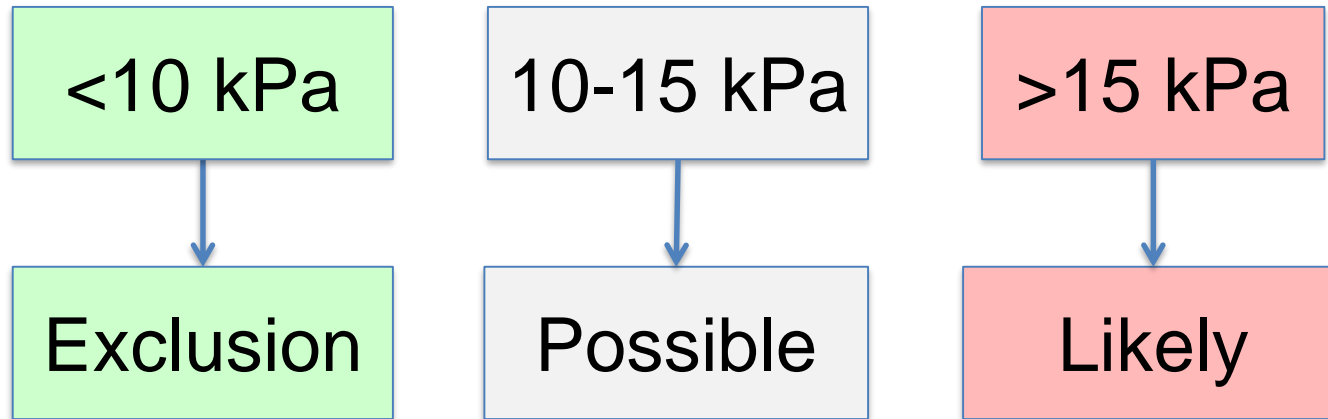
Median age (yrs)	40 - 50
Abnormal liver blood tests	90 %
Signs of portal hypertension / complication	70%/50%
Portal vein thrombosis	30 - 50%
Fatigue	?
Prothrombin index < 50%	15%
Low liver stiffness measurement	70%
Normal or ↑ segment IV & smooth liver surface	65%
Low HVPG & hepatic veno-venous communications	60%/30%

PSVD: when to suspect?

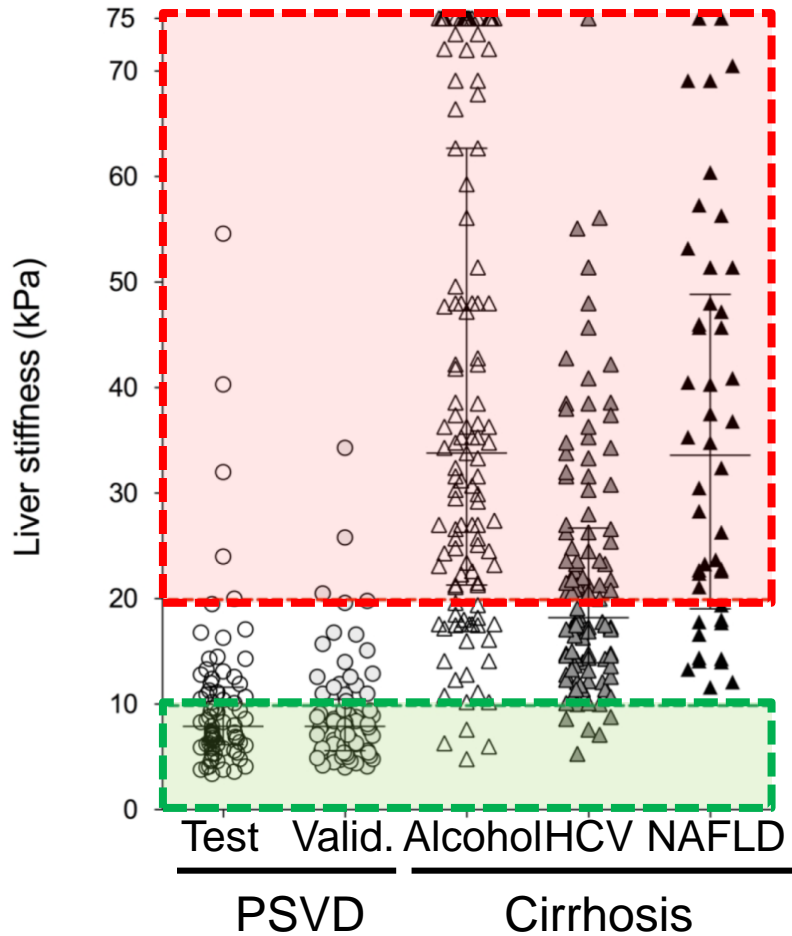
Median age (yrs)	40 - 50
Abnormal liver blood tests	90 %
Signs of portal hypertension / complication	70%/50%
Portal vein thrombosis	30 - 50%
Fatigue	?
Prothrombin index < 50%	15%
Low liver stiffness measurement	70%
Normal or ↑ segment IV & smooth liver surface	65%
Low HVPG & hepatic veno-venous communications	60%/30%

Liver stiffness measurement (LSM-TE) for cirrhosis

2 liver stiffness measurement (Fibroscan®)



PSVD: liver stiffness measurement (TE)

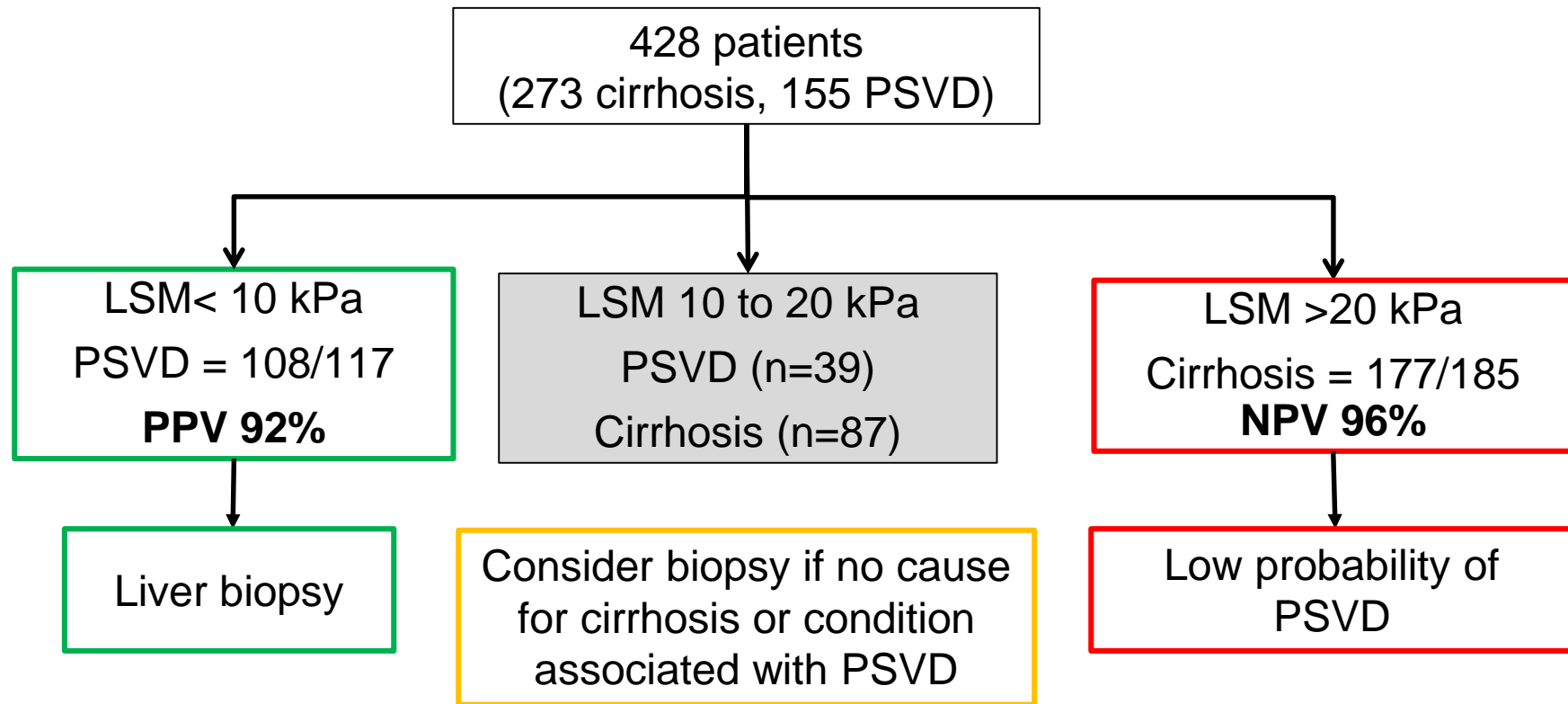


Patients with signs of portal hypertension
155 PSVD, 273 cirrhosis

Elkrief, Lazareth, *et al.*, *Hepatology* 2021
Similar results in:

- Laharie *Eur J Gastroenterol Hepatol* 2010
- Seijo *Dig Liver Dis* 2012
- Sharma *J Clin Exp Hepatol* 2017
- Ferreira-Silva *J, Dig Liver Dis.* 2022

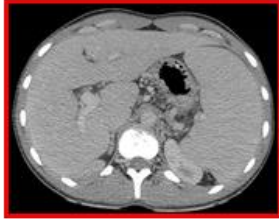
PSVD: liver stiffness measurement (TE)



PSVD: when to suspect?

Median age (yrs)	40 - 50
Abnormal liver blood tests	90 %
Signs of portal hypertension / complication	70%/50%
Portal vein thrombosis	30 - 50%
Fatigue	?
Prothrombin index < 50%	15%
Low liver stiffness measurement	70%
Normal or ↑ segment IV & smooth liver surface	65%
Low HVPG & hepatic veno-venous communications	60%/30%

PSVD: CT-scan



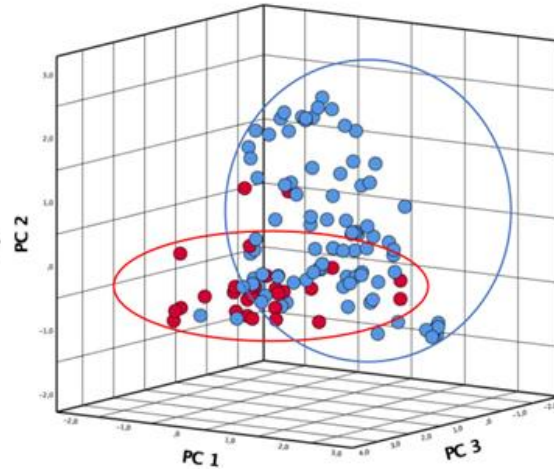
50 patients
with PSVD

*Matched on
ascites*

100 patients
with cirrhosis



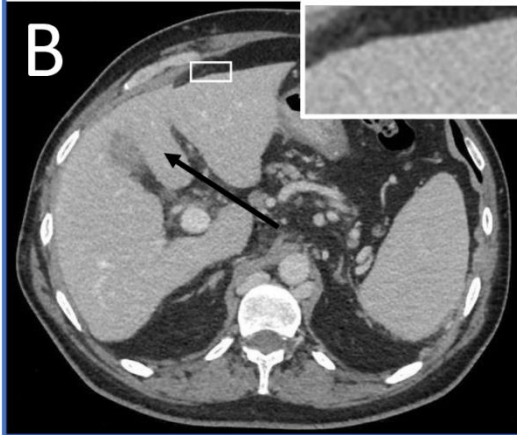
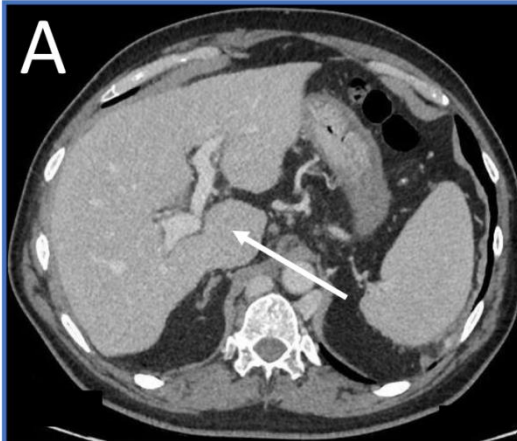
Different imaging
pattern at CT scan



PSVD Cirrhosis



PSVD: CT-scan



Smooth liver surface

PSVD

No segment IV atrophy

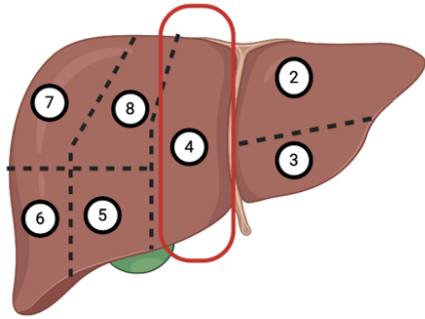
Cirrhosis

PSVD: CT-scan

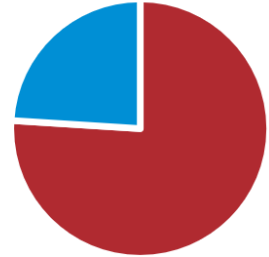
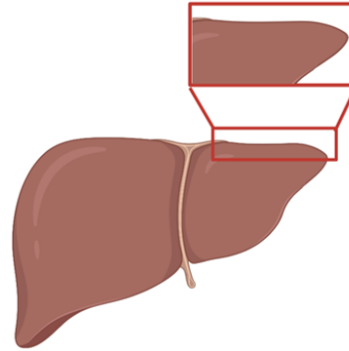
CT features for PSVD diagnosis

No atrophy of segment
IV

LSN < 2.5



+



With the features

PSVD Cirrhosis

Spe > 90% for the diagnosis of PSVD
in patients with signs of portal hypertension

Valainathan *et al.* Hepatology 2022; Similar results in: Lampichler K *et al.* , Eur Radiol. 2022;
Glatard *et al.* Radiology 2012; Kang, *et al.* Abdominal Radiology 2020

PSVD: when to suspect?

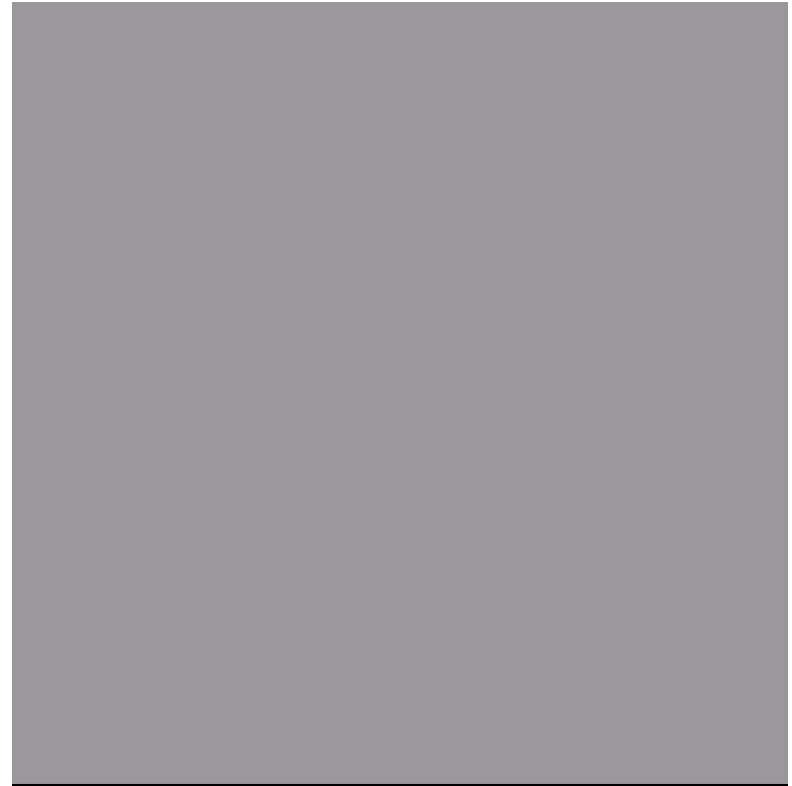
Median age (yrs)	40 - 50
Abnormal liver blood tests	90 %
Signs of portal hypertension / complication	70%/50%
Portal vein thrombosis	30 - 50%
Fatigue	?
Prothrombin index < 50%	15%
Low liver stiffness measurement	70%
Normal or ↑ segment IV & smooth liver surface	65%
Low HVPG & hepatic veno-venous communications	60%/30%

Hepatic veno-venous communications

Cirrhosis: 3%



PSVD: 30 to 50%

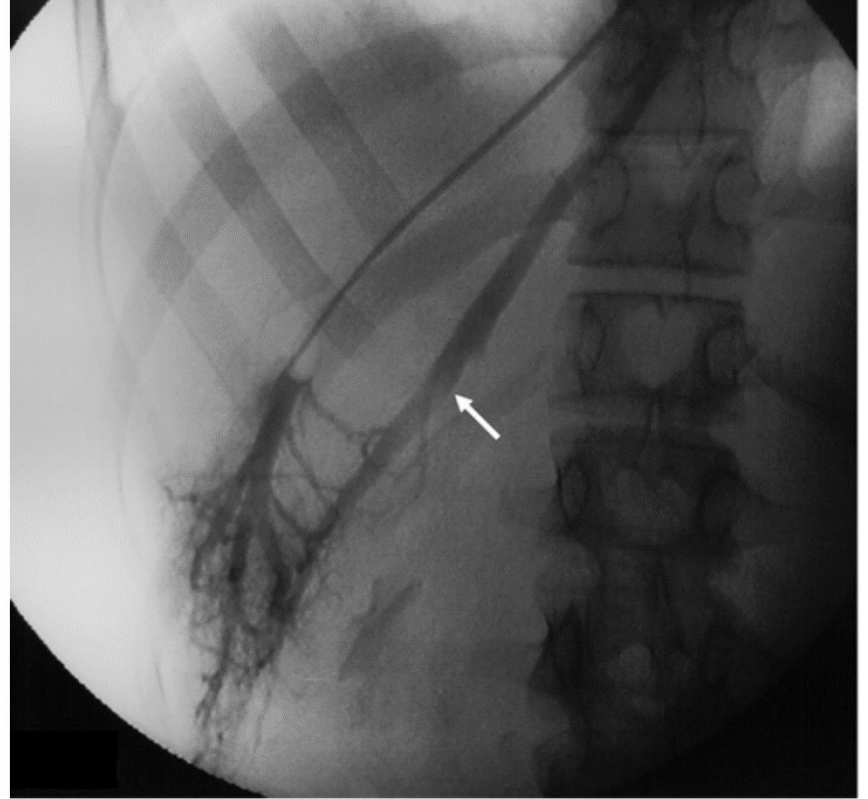


Hepatic veno-venous communications

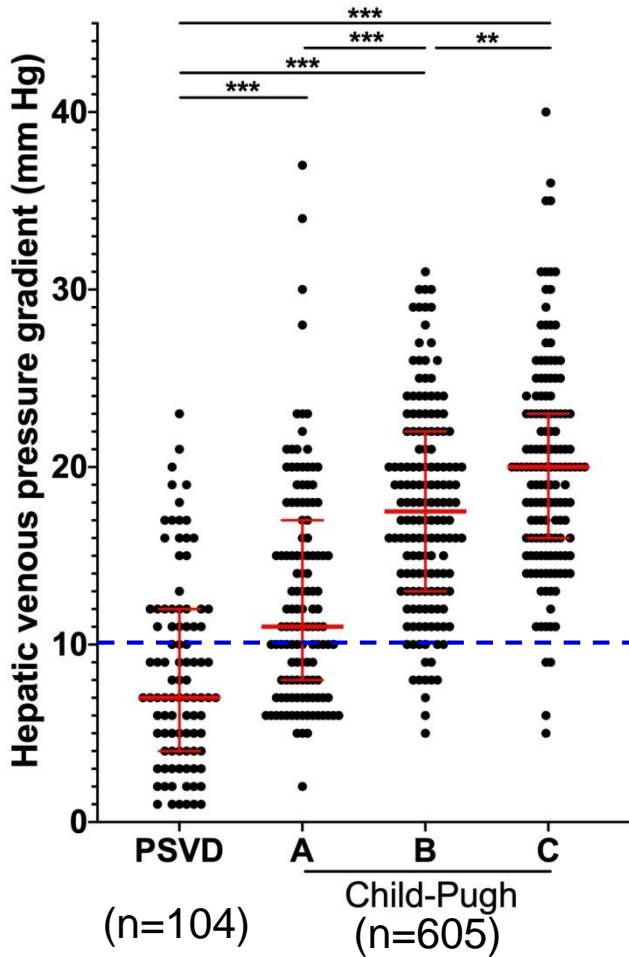
Cirrhosis: 3%



PSVD: 30 to 50%

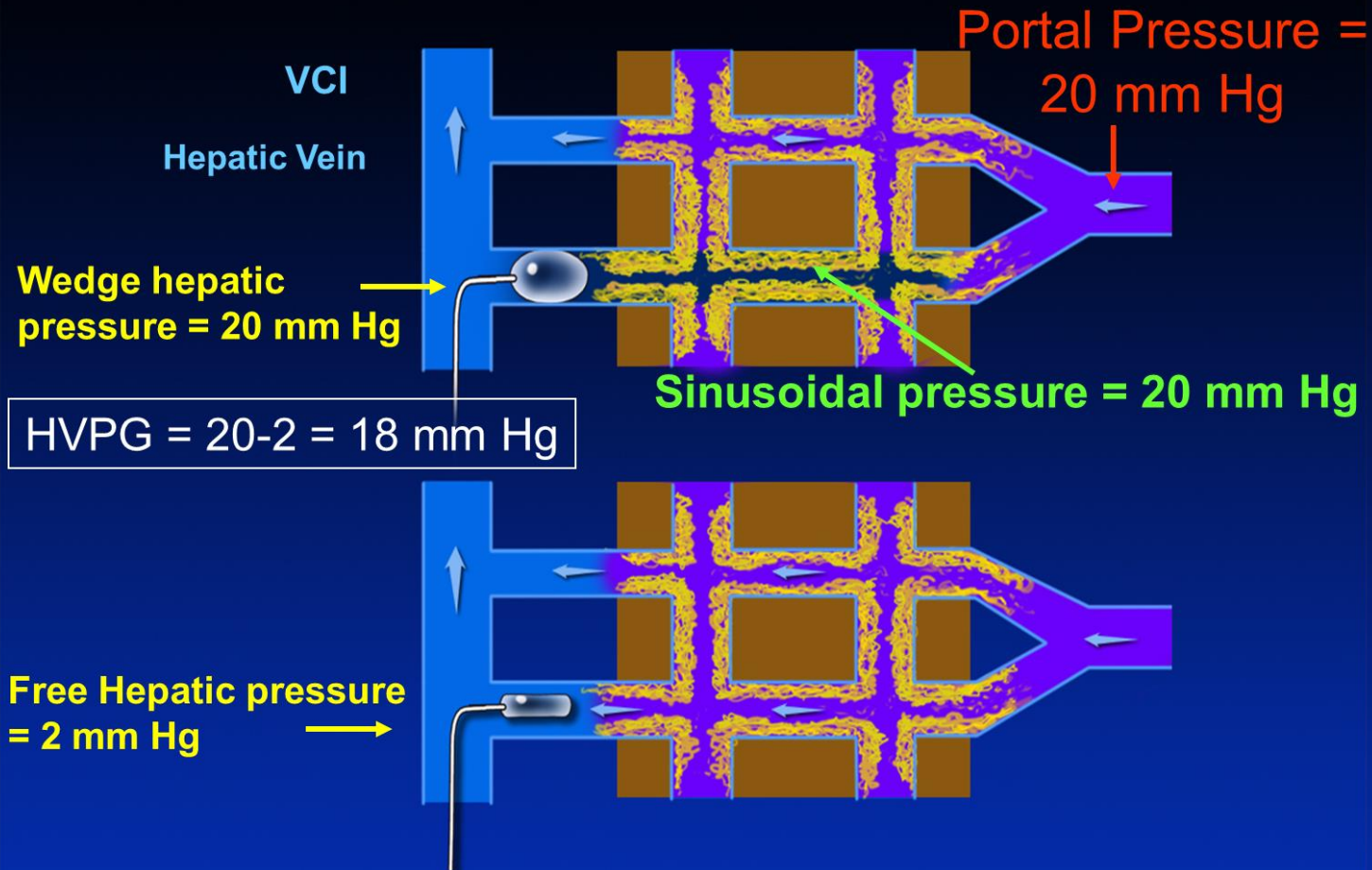


HVPG: PSVD vs. cirrhosis

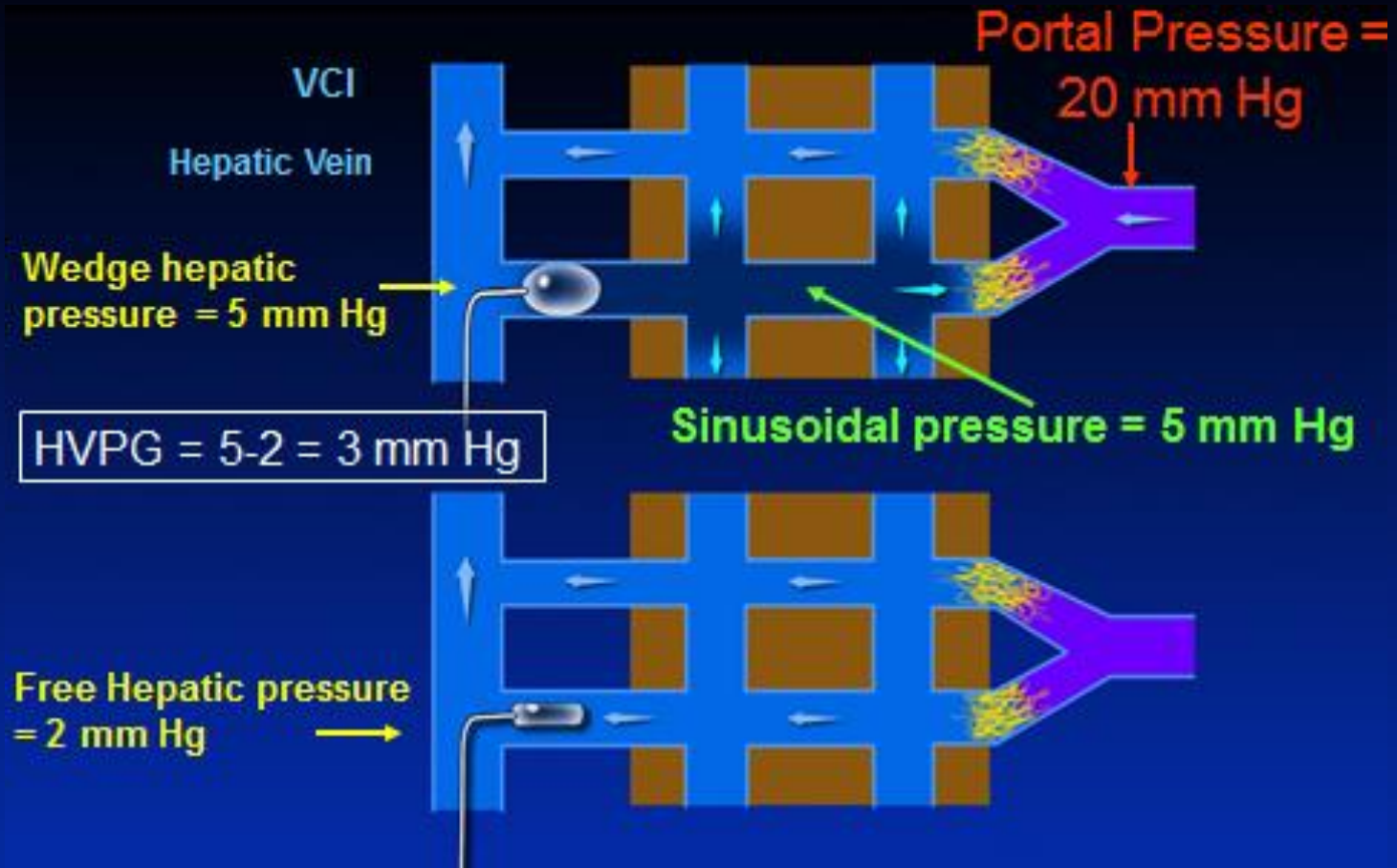


Patients with signs of portal hypertension

Hepatic hemodynamics: cirrhosis



Hepatic hemodynamics: PSVD

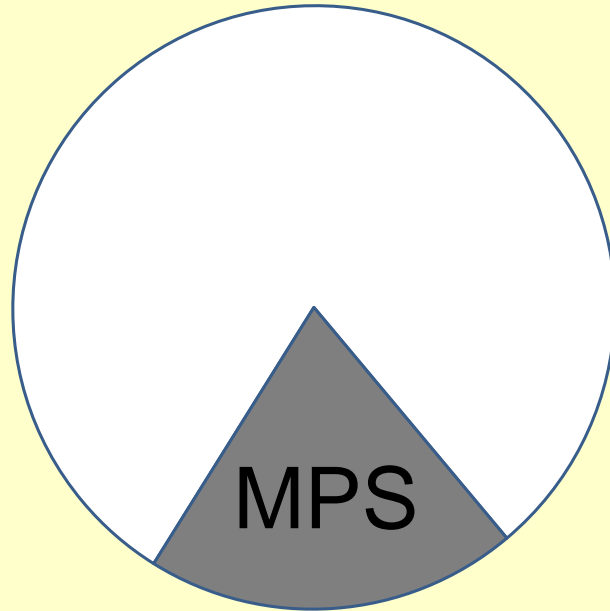


PSVD: when to suspect?

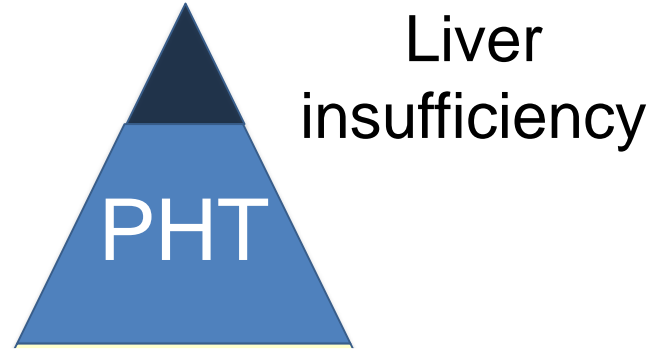
Median age (yrs)	40 - 50
Abnormal liver blood tests	90 %
Signs of portal hypertension / complication	70%/50%
Portal vein thrombosis	30 - 50%
Fatigue	?
Prothrombin index < 50%	15%
Low liver stiffness measurement	70%
Normal or ↑ segment IV & smooth liver surface	65%
Low HVPG & hepatic veno-venous communications	60%/30%

PSVD: manifestations

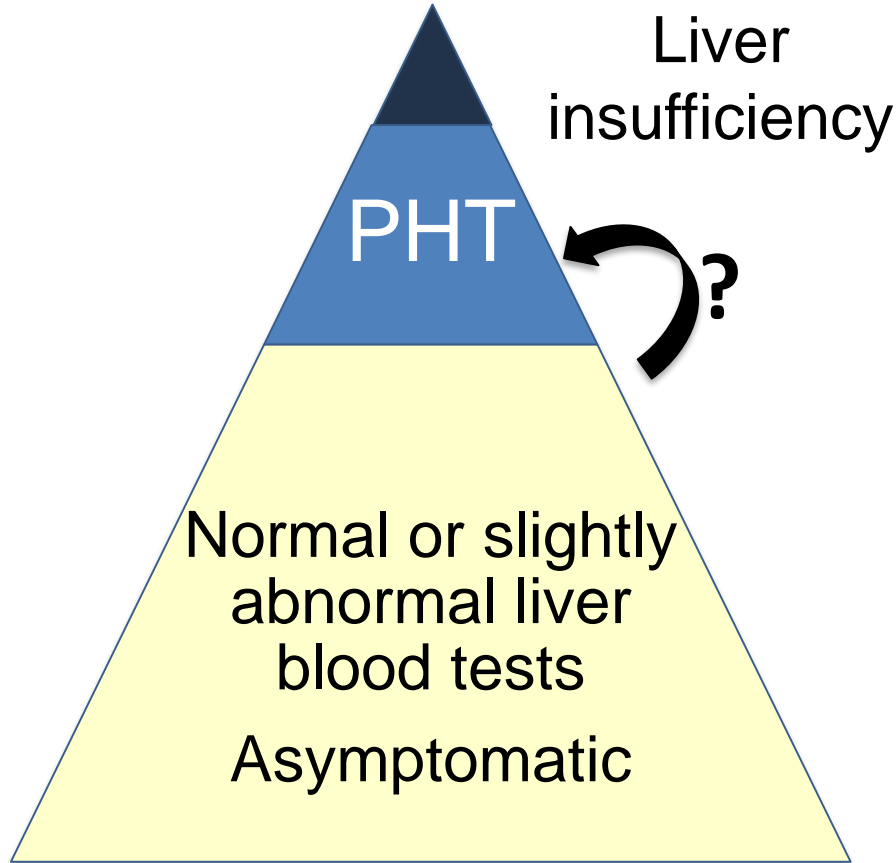
Abnormal liver blood tests (n=1271)



PSVD: manifestations



PSVD: manifestations



Porto-sinusoidal vascular disorder

- Presentation
- Definition
- Associated conditions
- Outcome

Porto-sinusoidal vascular disorder: definition

Biopsy
> 20 mm
without cirrhosis



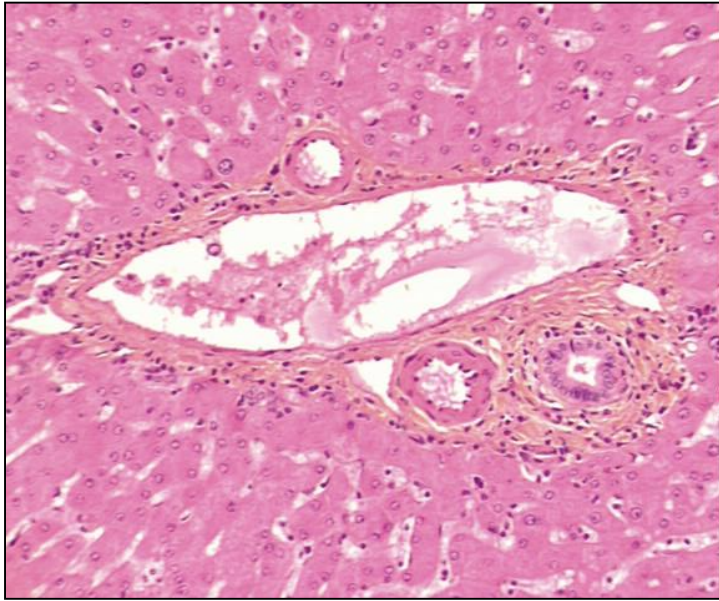
1 specific
sign

Signs specific for portal hypertension

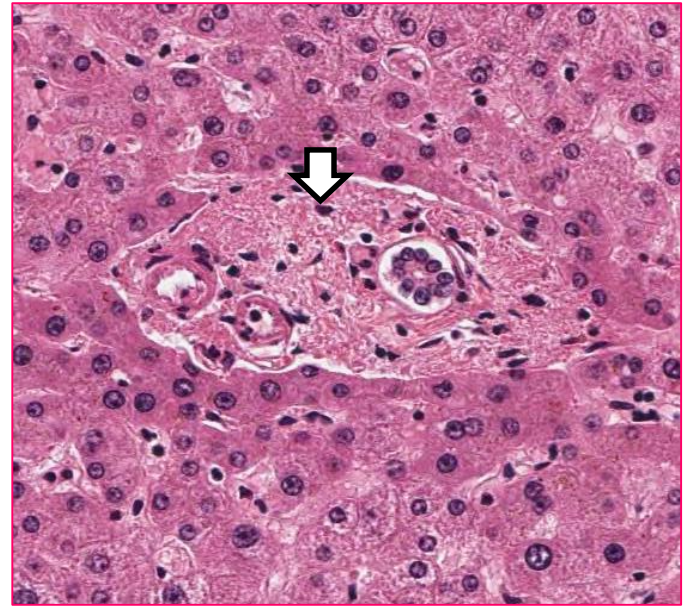
- ✓ Esophageal, gastric or ectopic varices
- ✓ Portal hypertension related bleeding
- ✓ Porto-systemic collaterals at imaging

Histological lesions specific for PSVD

- Obliterative portal venopathy



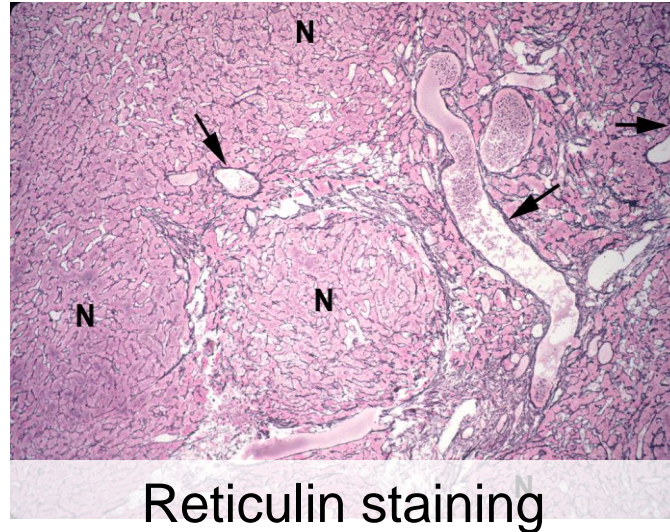
Normal portal tract



Obliterative portal venopathy

Histological lesions specific for PSVD

- Obliterative portal venopathy
- Nodular regenerative hyperplasia



Histological lesions specific for PSVD

- Obliterative portal venopathy
- Nodular regenerative hyperplasia
- Incomplete septal fibrosis/cirrhosis

Porto-sinusoidal vascular disorder: definition

Biopsy
> 20 mm
without cirrhosis



1 specific
sign

Biopsy
> 20 mm
w/o cirrhosis



1 non specific sign of PHT and
1 non specific histological lesion

Non specific signs of portal hypertension

- Ascites
- Platelet count $< 150'000/\text{mm}^3$
- Spleen height $> 13 \text{ cm}$

Histological lesions non specific for PSVD

- Portal tract abnormalities
- Architectural changes
- Sinusoidal dilatation
- Peri-sinusoidal fibrosis

Porto-sinusoidal vascular disorder

- Presentation
- Definition
- Associated conditions
- Outcome

PSVD: associated conditions

Prothrombotic conditions	++
Systemic or blood diseases	++
Infections (HIV, schistosomiasis)	++
Toxic / Drugs	+
Congenital/genetic diseases	+
Liver hyperarterialization	+
Aging	2%
No cause	+++

Porto-sinusoidal vascular disorder

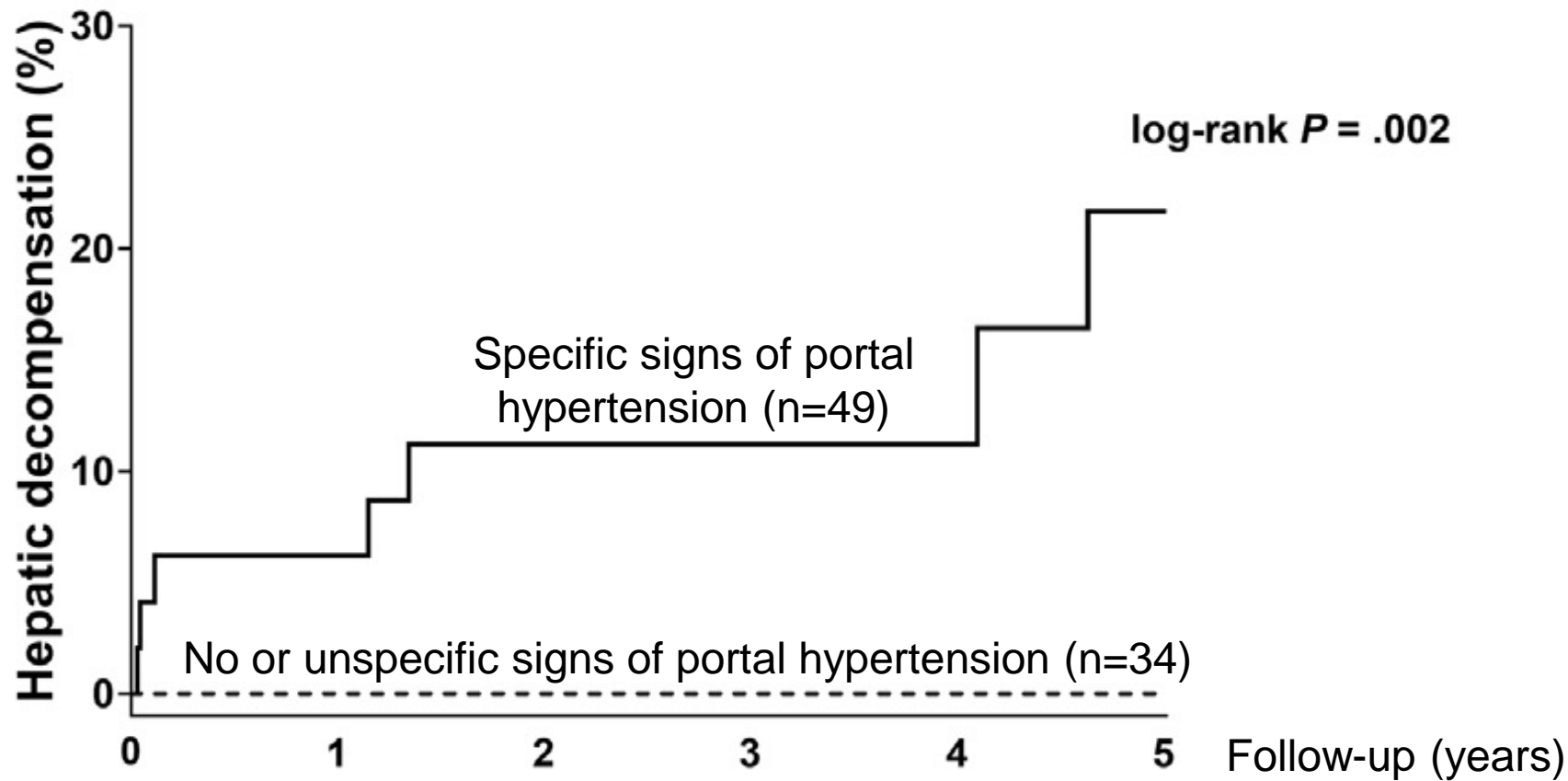
- Presentation
- Definition
- Associated conditions
- Outcome

PSVD: outcome and complications

Gastro-intestinal bleeding	23% at 5 yrs (despite prophylaxis)
Portal vein thrombosis	33% at 5 yrs
Ascites	26% (at the time of GI bleeding; easily controlled)
Hepatic encephalopathy	7%
Hepatocellular carcinoma	0%

69 patients followed for 7 yrs

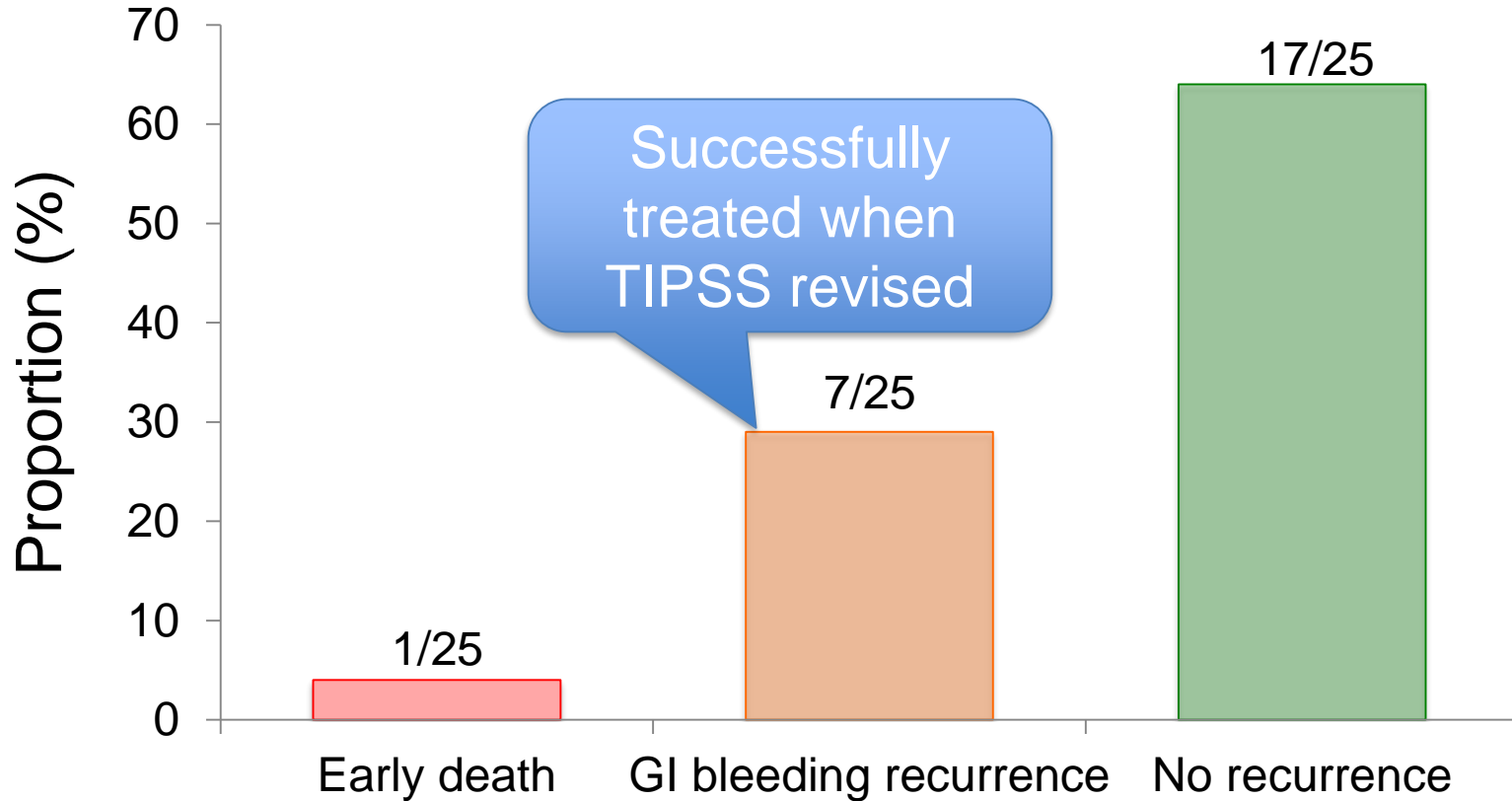
Outcome of PSVD: portal hypertension



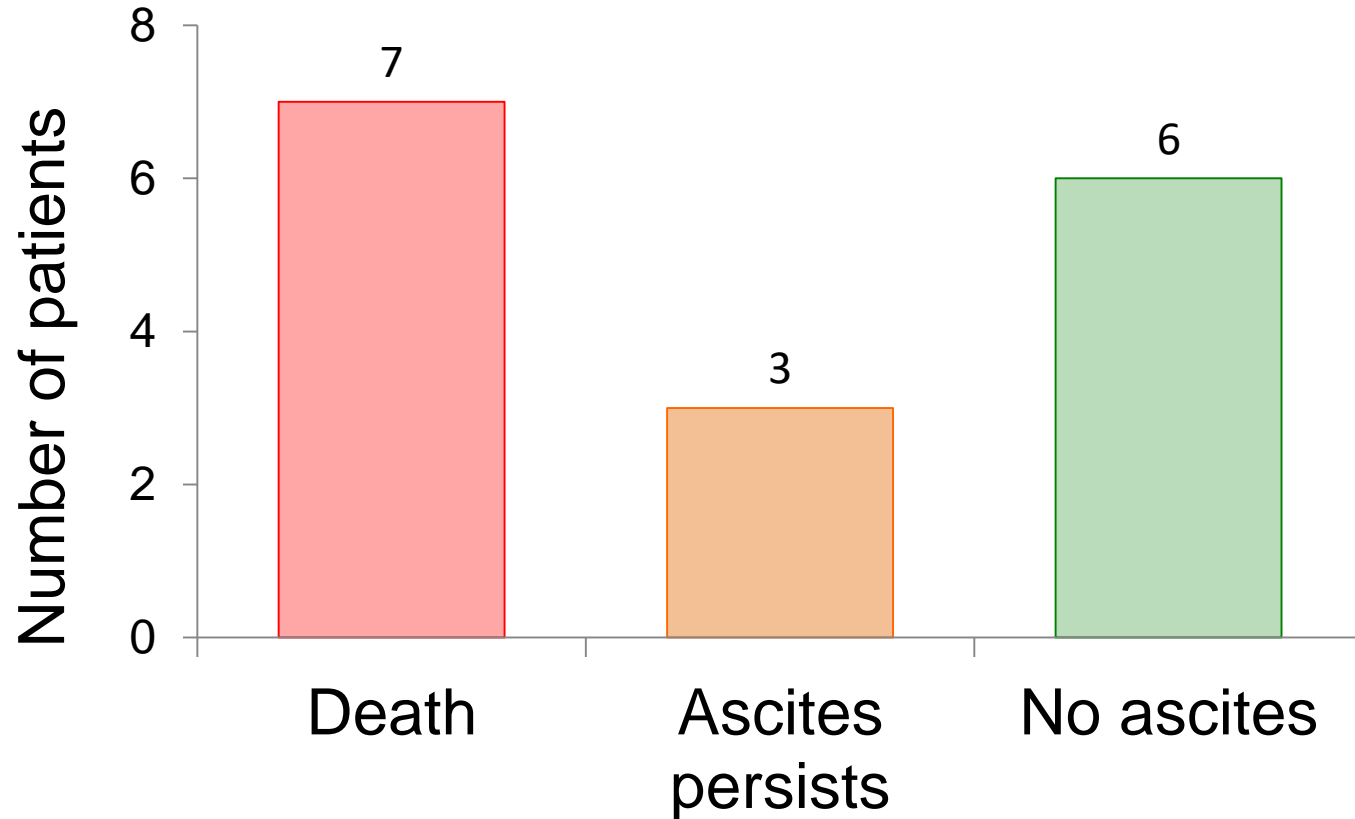
PSVD: treatment

- Prophylaxis for variceal bleeding \approx like in cirrhosis
(Baveno VI)
- Anticoagulation?
- Diuretics if ascites
- Rarely: TIPSS or liver transplantation

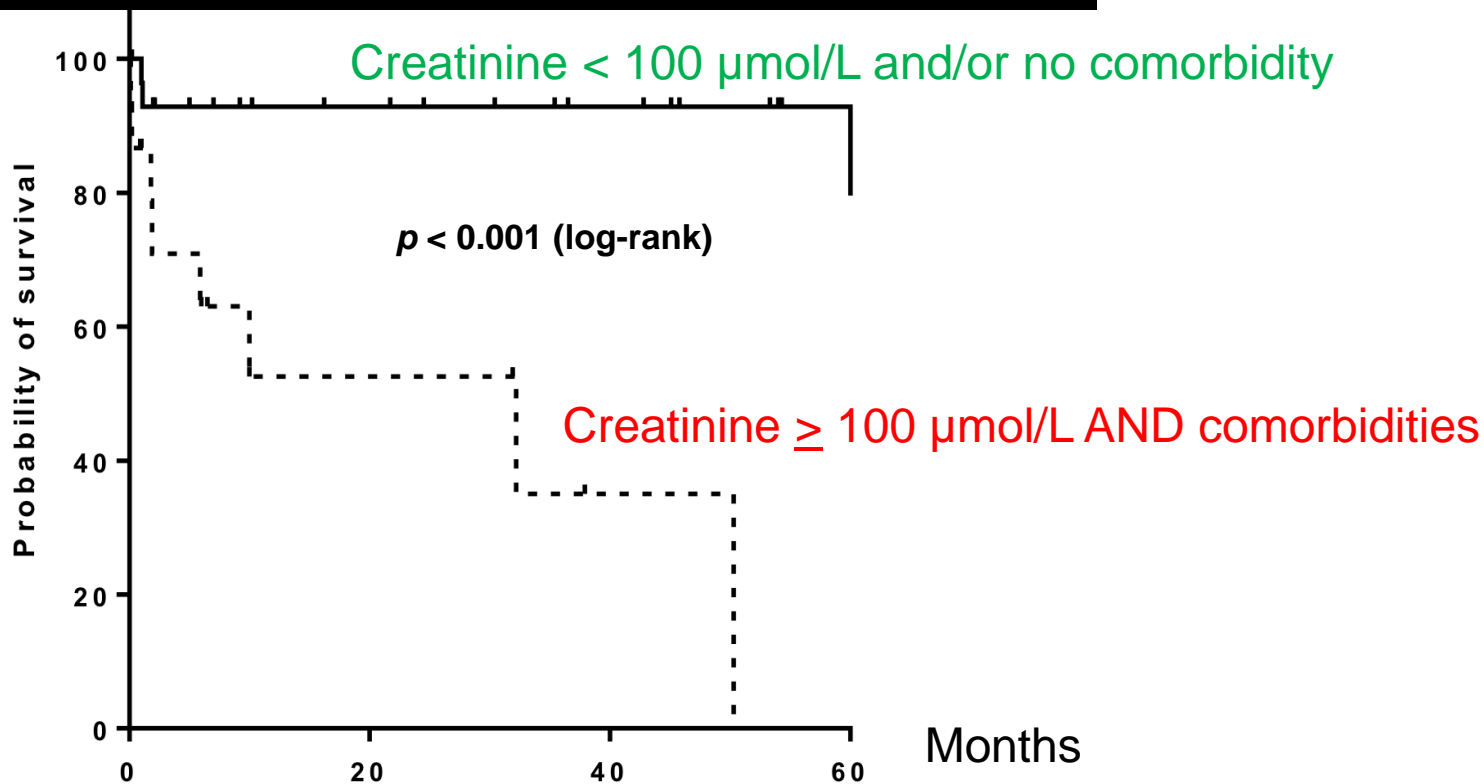
TIPSS for GI bleeding



TIPSS for refractory ascites



Survival after TIPSS

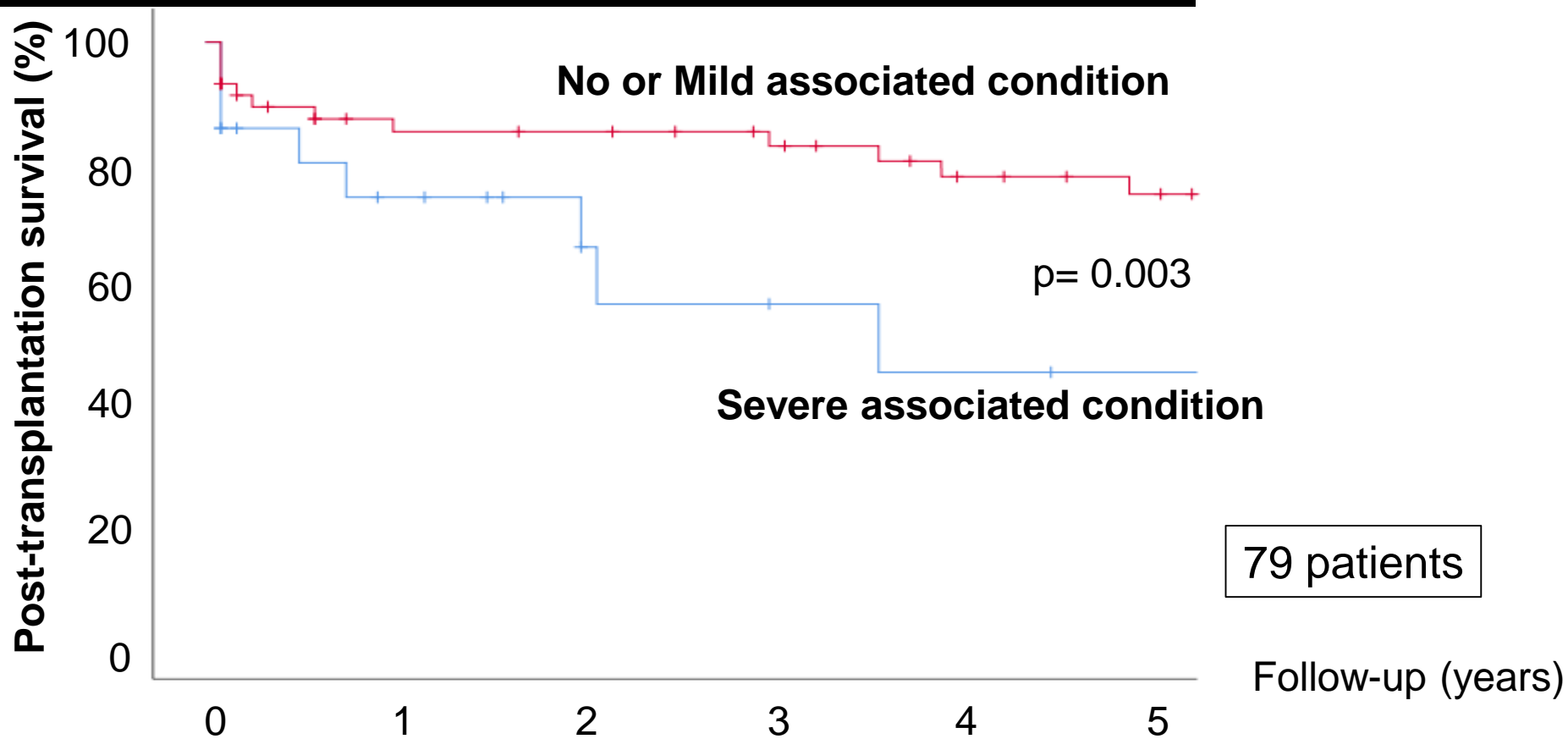


Creatinine $\geq 100 \mu\text{mol/L}$
AND comorbidities

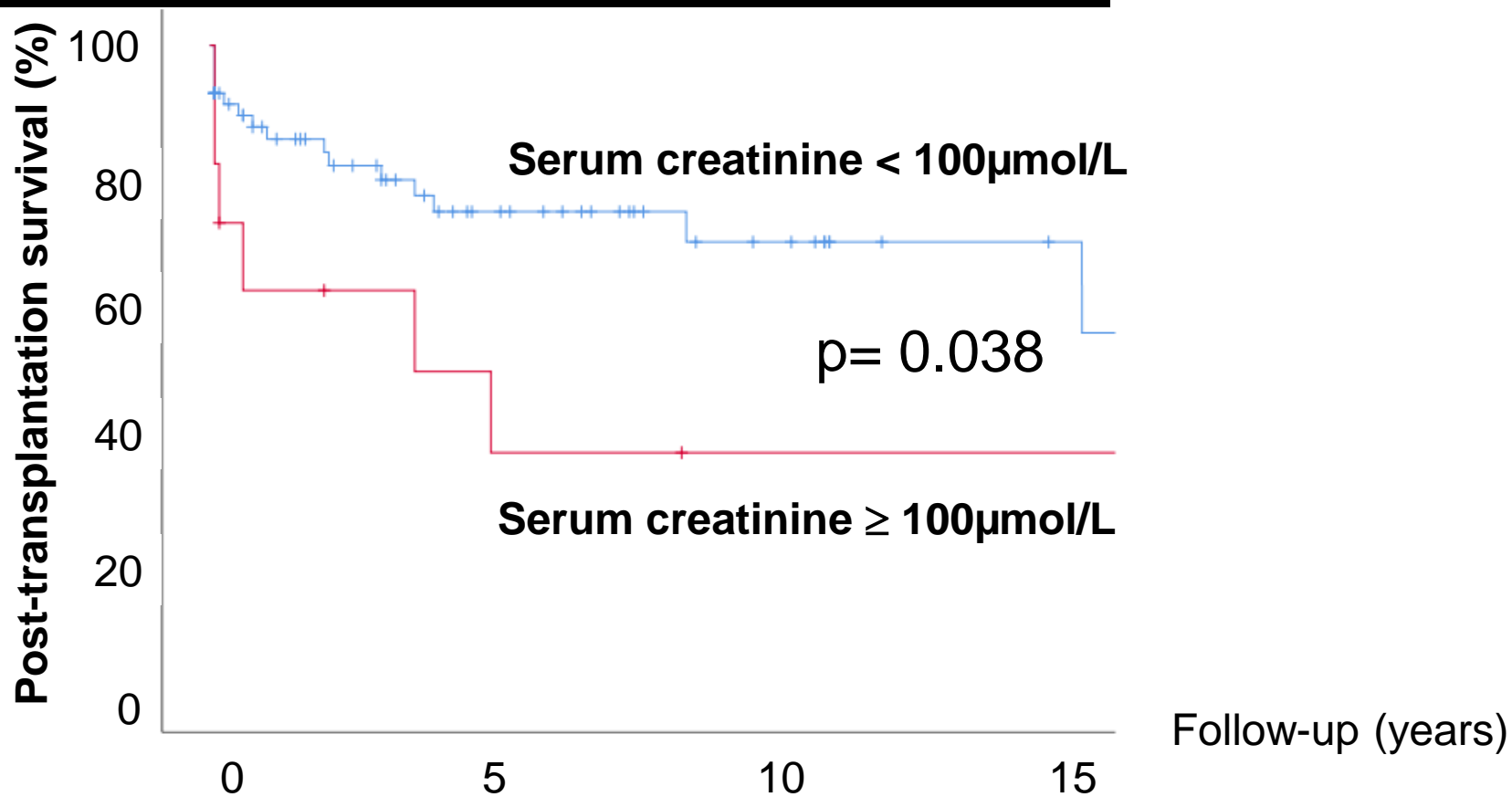
Others

7	2	1	0
34	18	12	7

Liver transplantation PSVD

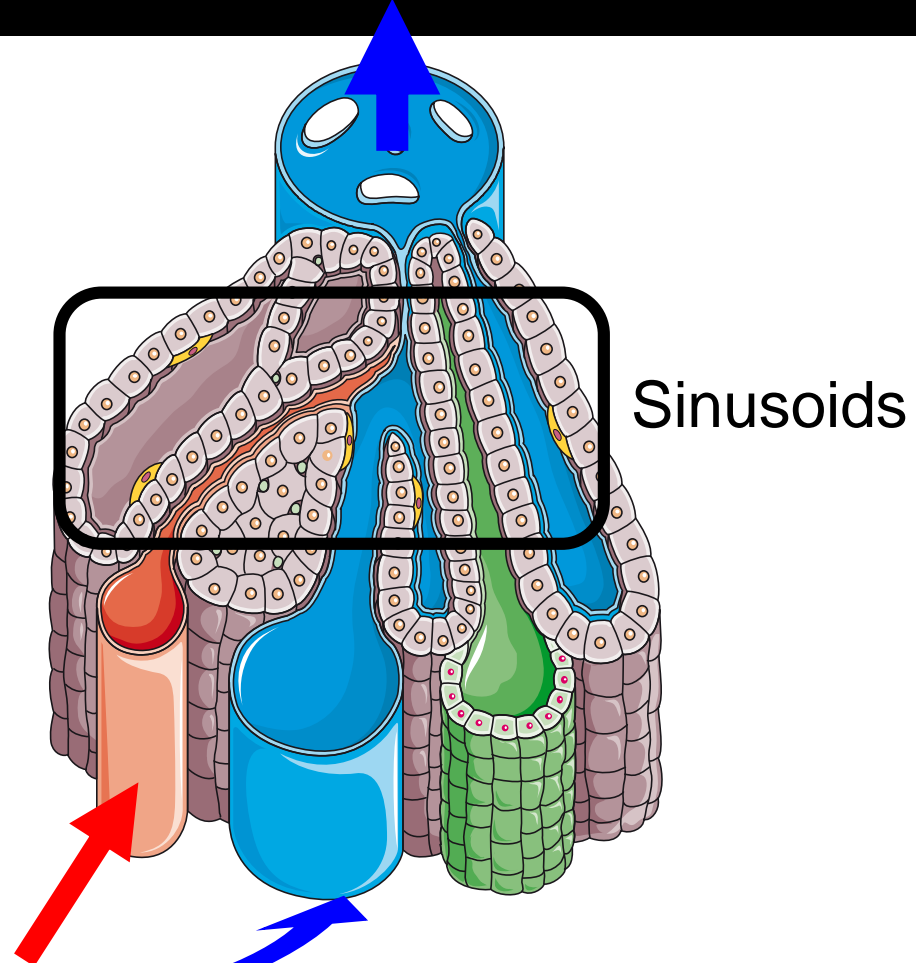


Liver transplantation PSVD



Diseases affecting small intrahepatic vessels

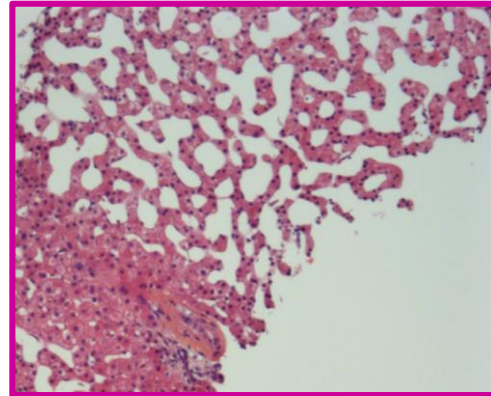
Sinusoidal dilation /
Peliosis



Sinusoidal dilation and peliosis: definitions

Sinusoidal dilation

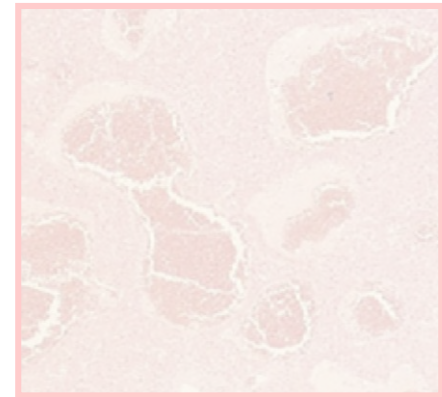
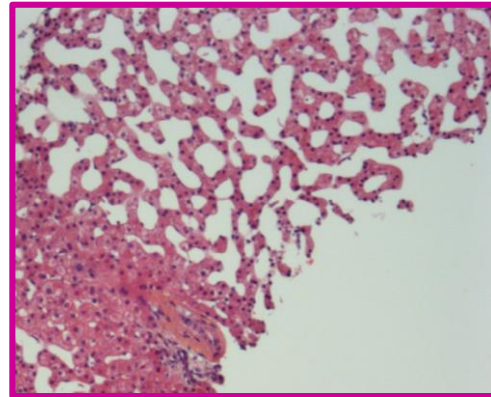
- > 1 hepatocyte plate
- Several lobules



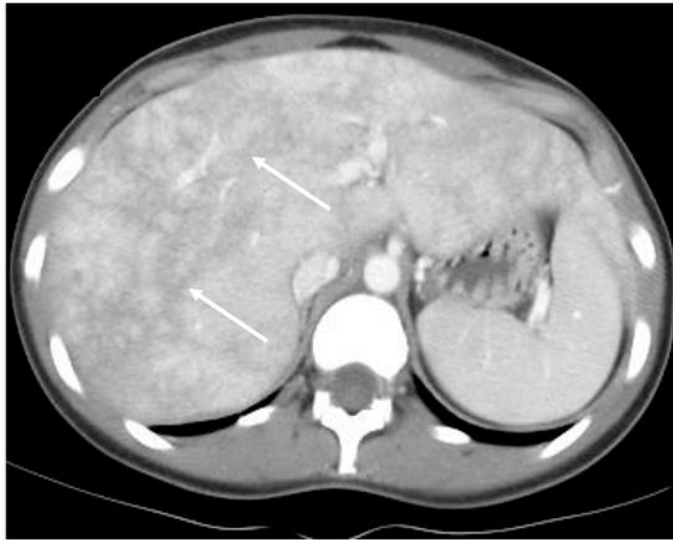
Sinusoidal dilation and peliosis: definitions

	Sinusoidal dilation	Peliosis
Hepatocytes atrophy	Yes	Yes
Endothelial rupture	No	Yes
Hemorrhagic cavities	No	Yes

- > 1 travée hépatocyttaire
- dans plusieurs lobules



Sinusoidal dilation and peliosis: definitions



Mosaic pattern at the arterial
and/or portal phase

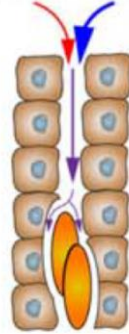
Proof
= biopsy

Sinusoidal dilation: causes

- **Obstructive** sinusoidal dilation:

Hemodynamic changes

Unchanged
arterial and
portal inflow



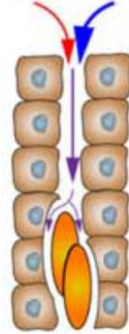
Obstructed
sinusoids

Sinusoidal dilation: causes

- **Obstructive** sinusoidal dilation:

Hemodynamic changes

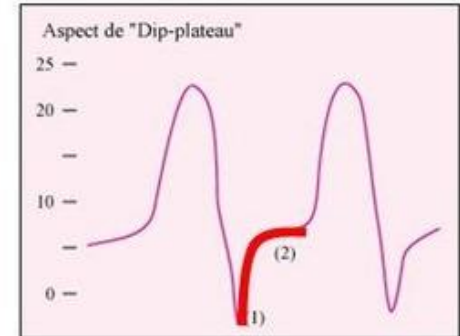
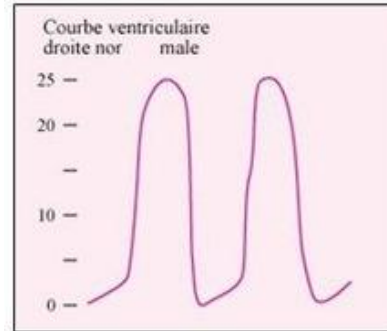
Unchanged
arterial and
portal inflow



Obstructed
sinusoids

Sinusoidal dilation: causes

- **Obstructive** sinusoidal dilation:
 - ✓ Budd-Chiari
 - ✓ Right heart failure
 - ✓ Constrictive pericarditis :
 - ➔ cardiac MRI
 - ➔ right heart catheterization: DIP-plateau



Sinusoidal dilation: causes

- **Non-obstructive** sinusoidal dilation :

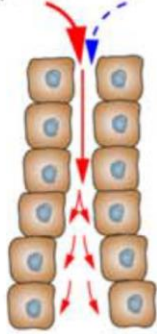
Hemodynamic changes

Unchanged
arterial and
portal inflow



Obstructed
sinusoids

Increased arterial
inflow/reduced
portal inflow



Sinusoidal
remodeling

Sinusoidal dilation

- Portal vein obstruction
- PSVD
- Porto-systemic congenital shunts

Sinusoidal dilation: causes

- **Non-obstructive sinusoidal dilation :**

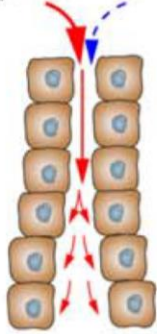
Hemodynamic changes

Unchanged arterial and portal inflow



Obstructed sinusoids

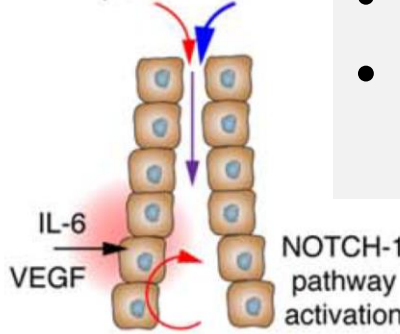
Increased arterial inflow/reduced portal inflow



Sinusoidal remodeling

Soluble factors

Unchanged arterial and portal inflow



- Neoplasia with SIRS
- Inflammatory diseases (including infections)

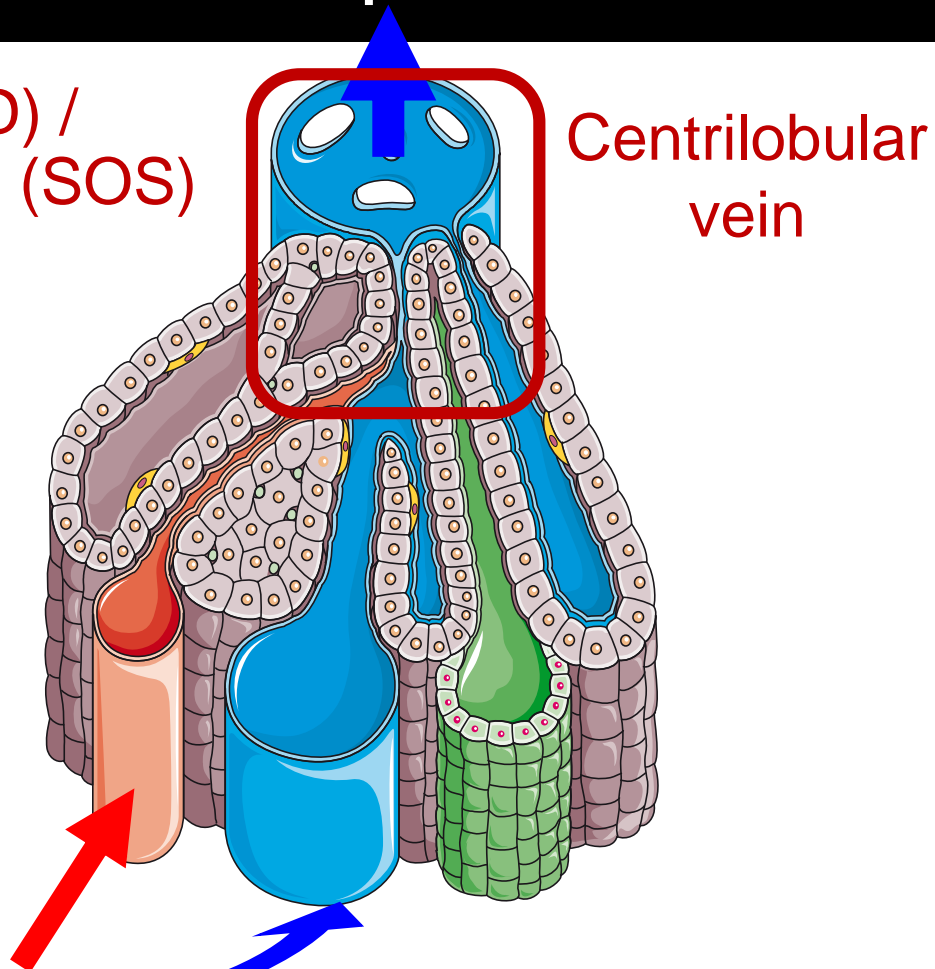
Sinusoidal dilation

Sinusoidal dilation: outcome

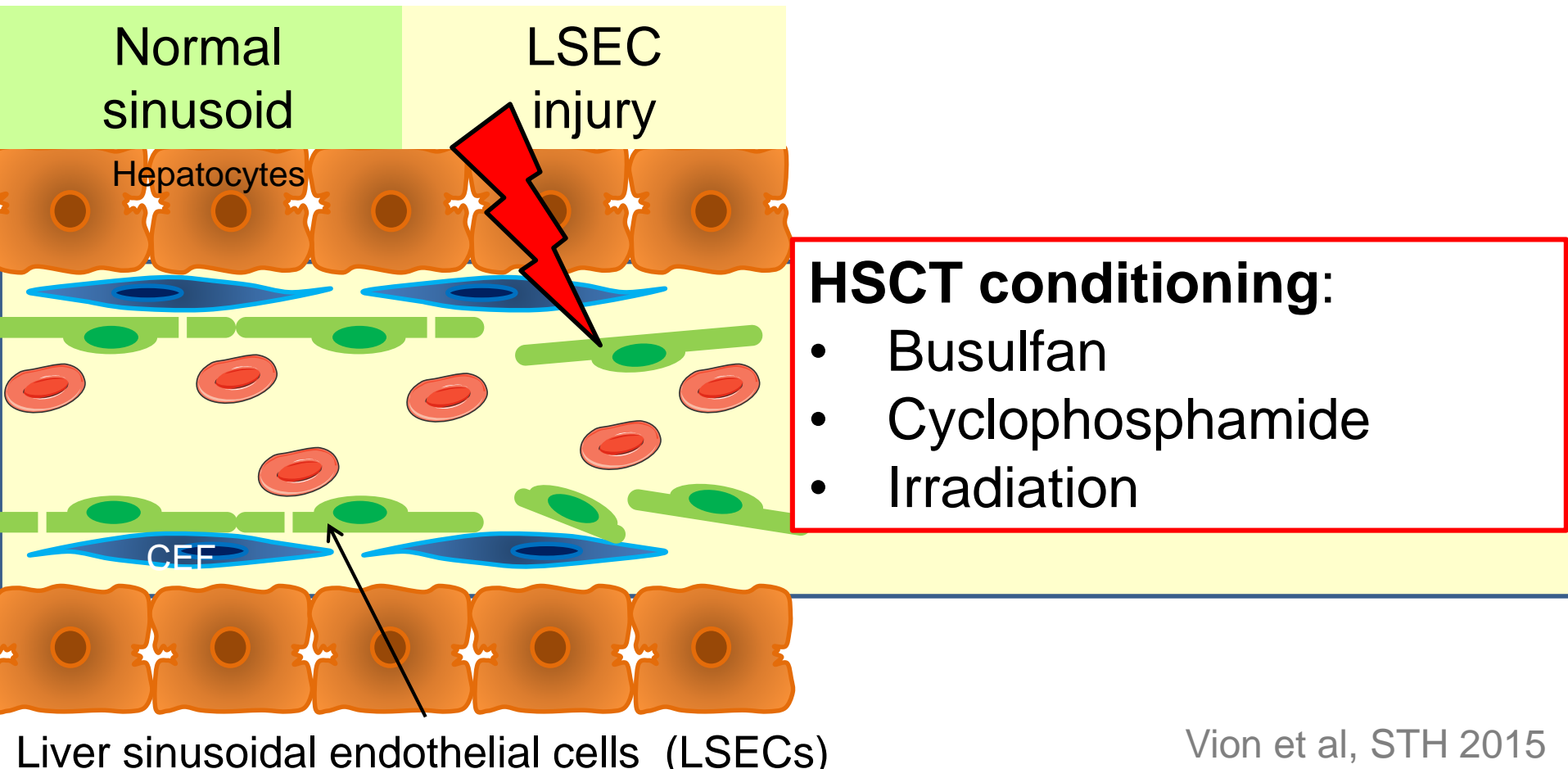
- Regression possible if acute triggering factor
- Lead to PSVD?

Diseases affecting small intrahepatic vessels

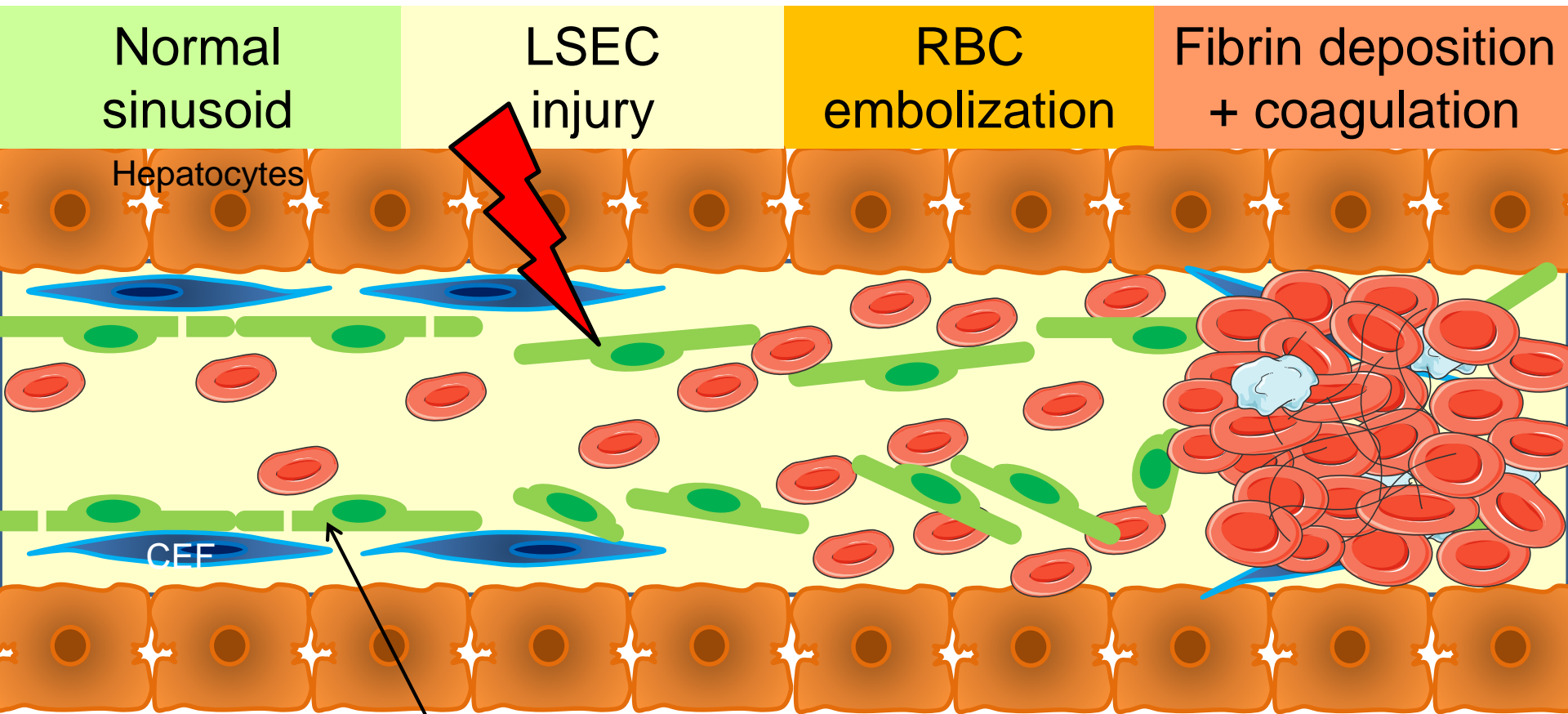
Veno-occlusive disease (VOD) /
sinusoidal obstruction syndrome (SOS)



SOS / VOD post HSCT: mechanisms



SOS / VOD post HSCT: mechanisms



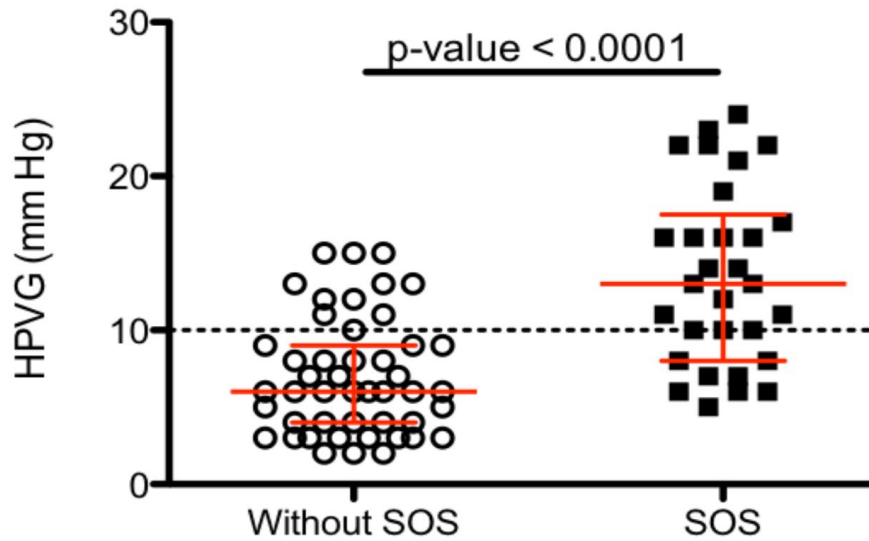
Liver sinusoidal endothelial cells (LSECs)

SOS / VOD following HSCT

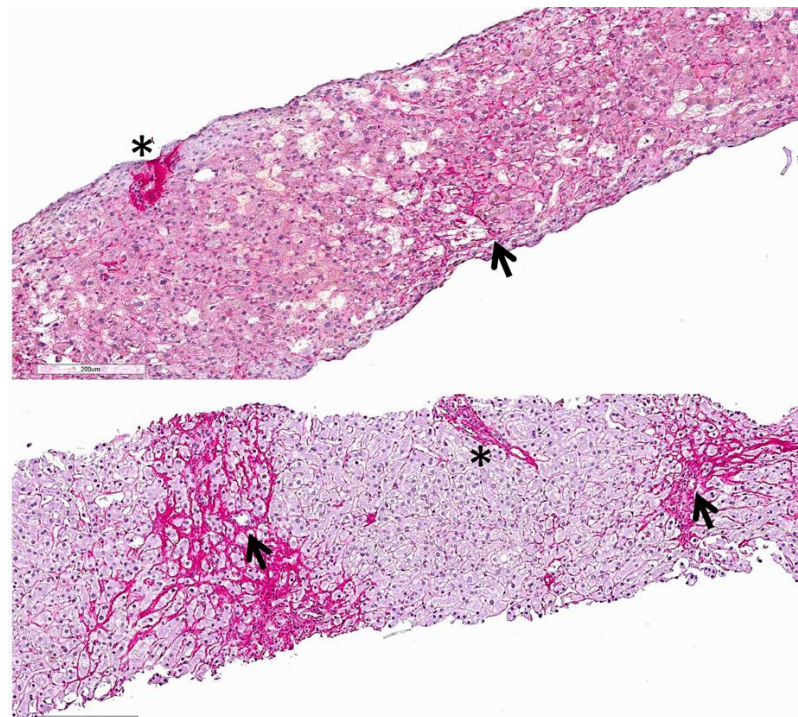
- In the weeks after HSCT
 - ✓ Jaundice
 - ✓ Hepatomegaly or right upper quadrant pain
 - ✓ Weight gain

SOS / VOD following HSCT: diagnosis

HPVG > 10 mm Hg suggests



Proof: biopsy



PSVD: conclusion

✓ **Suspect PSVD:**

- Unexplained liver blood test abnormalities
- No liver insufficiency
- Low liver stiffness measurement
- Low HVPG, hepatic collaterals
- Normal or ↑ segment IV + smooth surface

} ≠ **signs of portal hypertension**

✓ **Outcome:**

- Portal vein thrombosis
- Variceal bleeding

Sinusoidal dilation: into practice

- CT-scan or MRI: mosaic pattern
- Diagnosis: biopsy
- Cause :
 - ✓ Rule out hepatic venous outflow obstruction
 - ✓ Acute or chronic inflammation
 - ✓ Same work-up as PSVD

SOS/VOD post-HSCT: into practice

- In the weeks following HSCT
- Favored myeloablative conditioning
- HVPG suggest, biopsy proves
- Severe forms :
 - ✓ ICU
 - ✓ Defibrotide

Networks for vascular liver diseases



European
Reference
Network

Hepatological Diseases
(ERN RARE-LIVER)



VALDIG

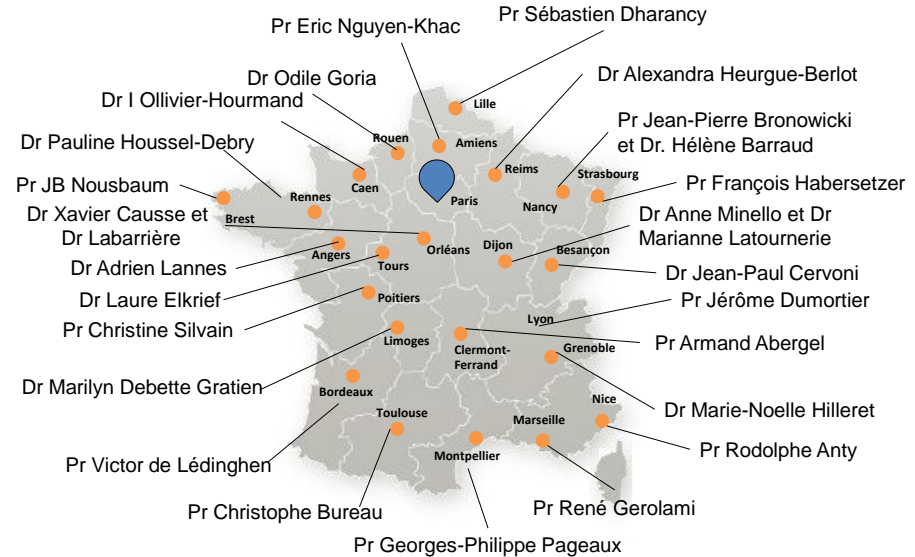
VASCULAR LIVER DISEASE GROUP



French network for vascular liver diseases



CENTRE DE RÉFÉRENCE
MALADIES VASCULAIRES
DU FOIE





Instituts
thématiques

Inserm
Institut national
de la santé et de la recherche médicale

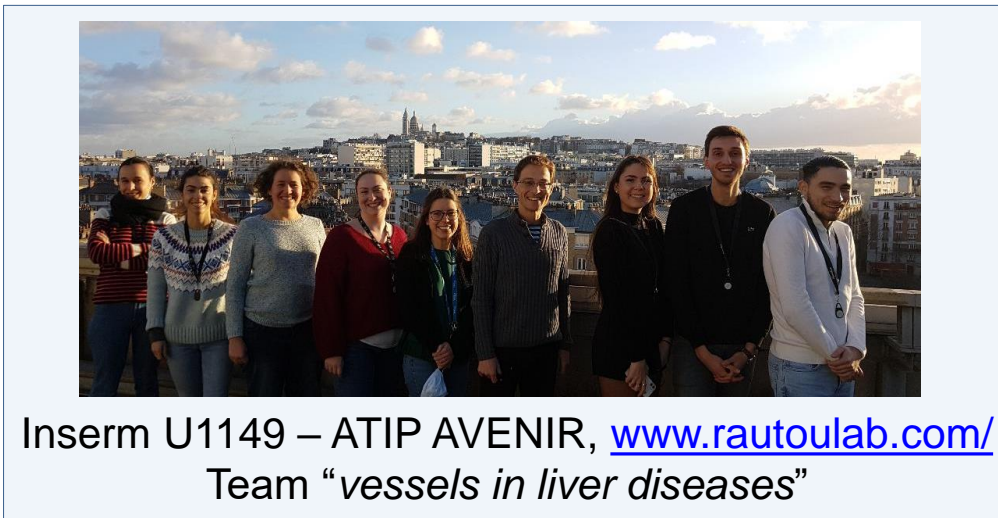


Université
de Paris

CRi
CENTRE de RECHERCHE
sur l'INFLAMMATION



Hepatology unit, Beaujon Hospital
Reference center for vascular liver diseases



Inserm U1149 – ATIP AVENIR, www.rautoulab.com/
Team “vessels in liver diseases”



Get these slides there:



Les Programmes Hospitaliers
de Recherche Clinique
(PHRC)



Question 1

Porto-sinusoidal vascular disorder diagnosis strictly requires:

- A. a liver biopsy
- B. signs of portal hypertension
- C. no of cause of cirrhosis
- D. a patent portal vein
- E. no ascites

Question 2

The 2 most common complications of porto-sinusoidal vascular disorder are:

- A. ascites
- B. hepatocellular carcinoma
- C. portal vein thrombosis
- D. variceal bleeding
- E. hepatic encephalopathy