PVT Risk Factors: What's New

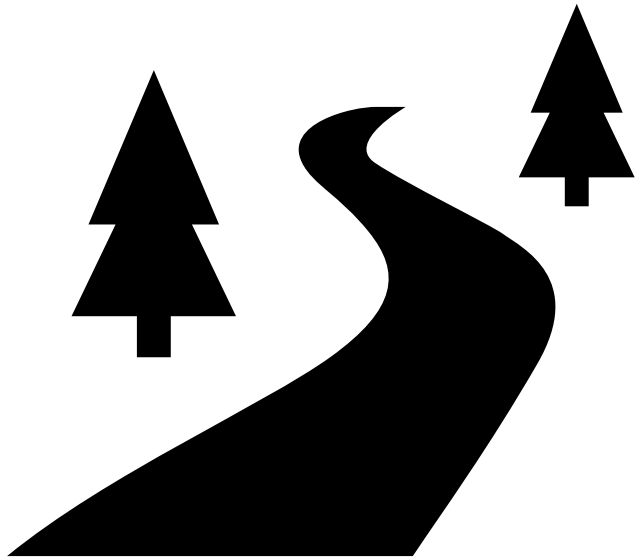
Jessica P.E. Davis, MD, MSCR

Director of Liver Transplant, DC VA Medical Center

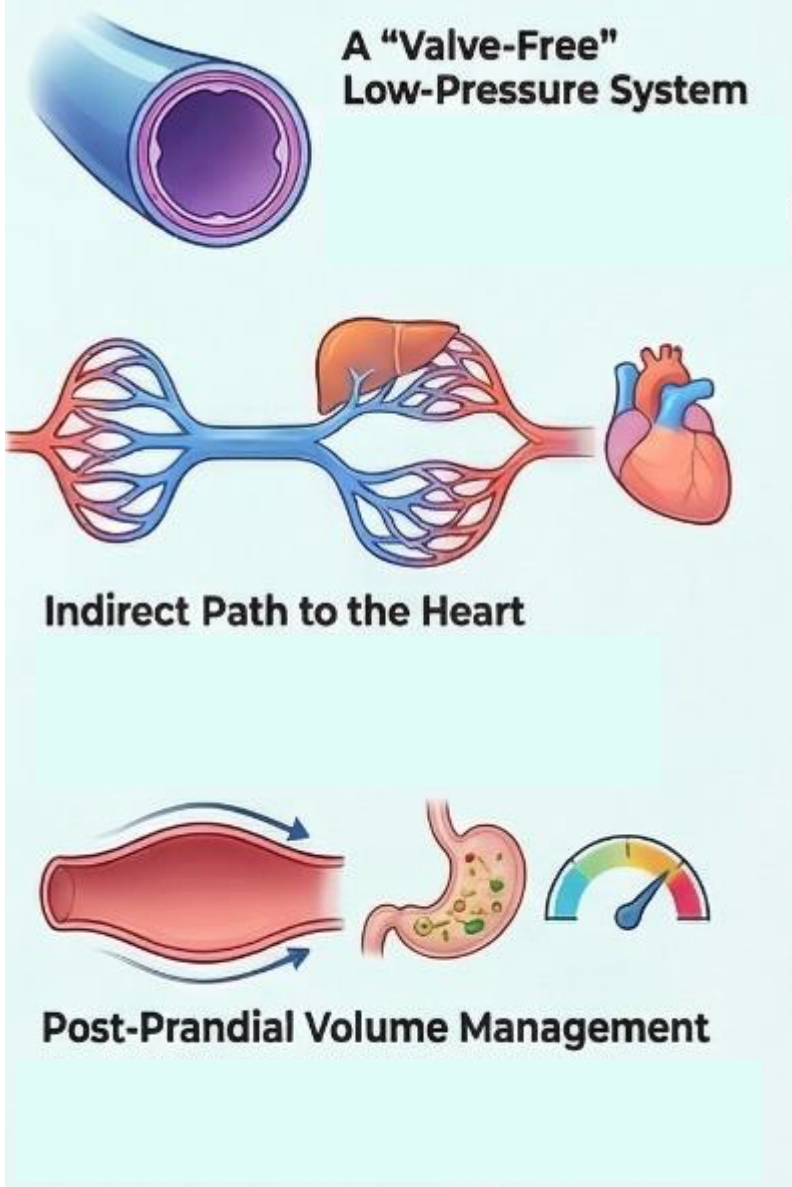
Associate Professor of Medicine, Georgetown University

Outline

- Portal vein physiology
- Non-cirrhotic PVT
- PVT in cirrhosis

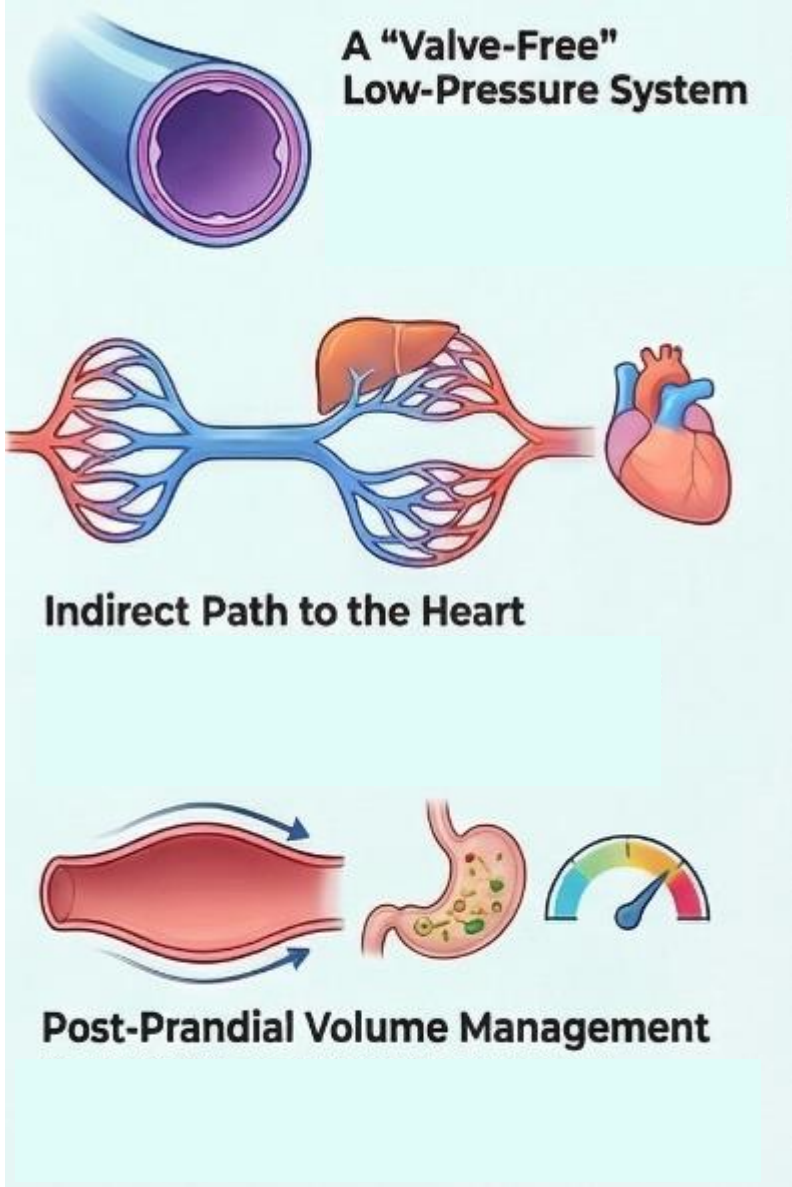


Portal vasculature is unique



Schematics created with Notebook LM using Elkrief Lancet Gastro Hep 2024

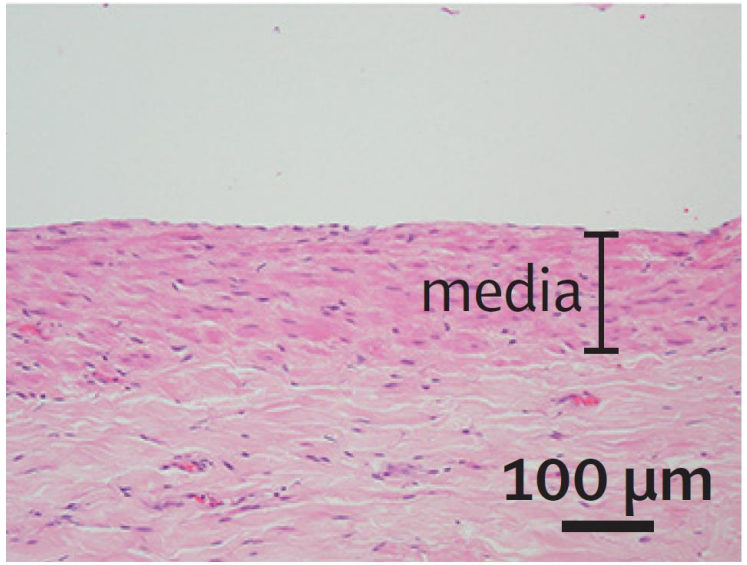
Portal vasculature is unique



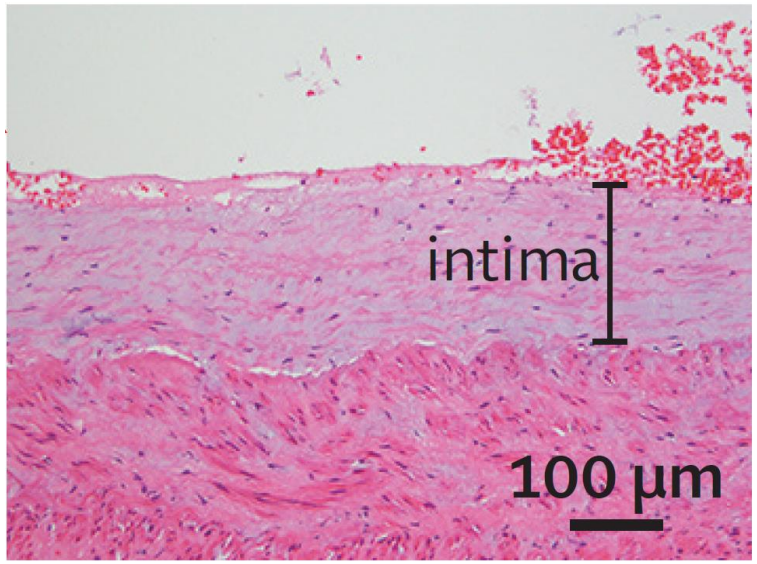
cPVT	ncPVT
• Dynamic pHTN • Portosystemic collaterals • Intimal hypertrophy	• No dynamic component • Porto-portal collaterals

Schematics created with Notebook LM using Elkrief Lancet Gastro Hep 2024

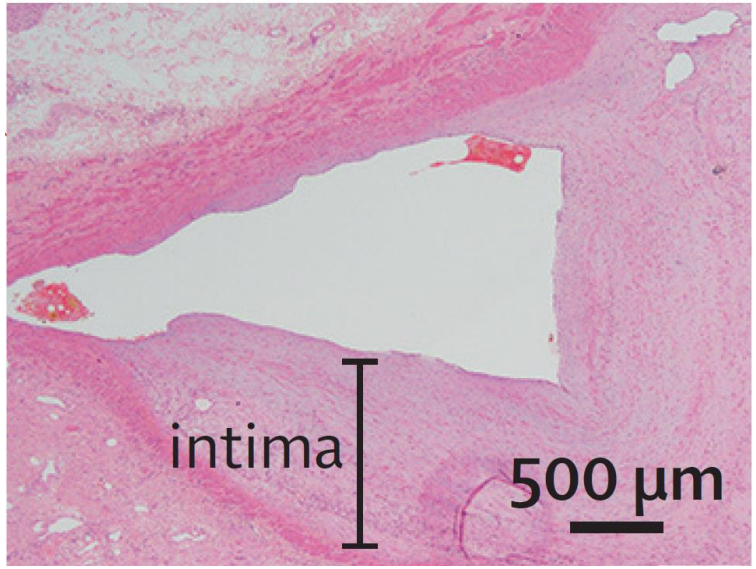
Intimal hypertrophy may drive PVT in cirrhosis



normal



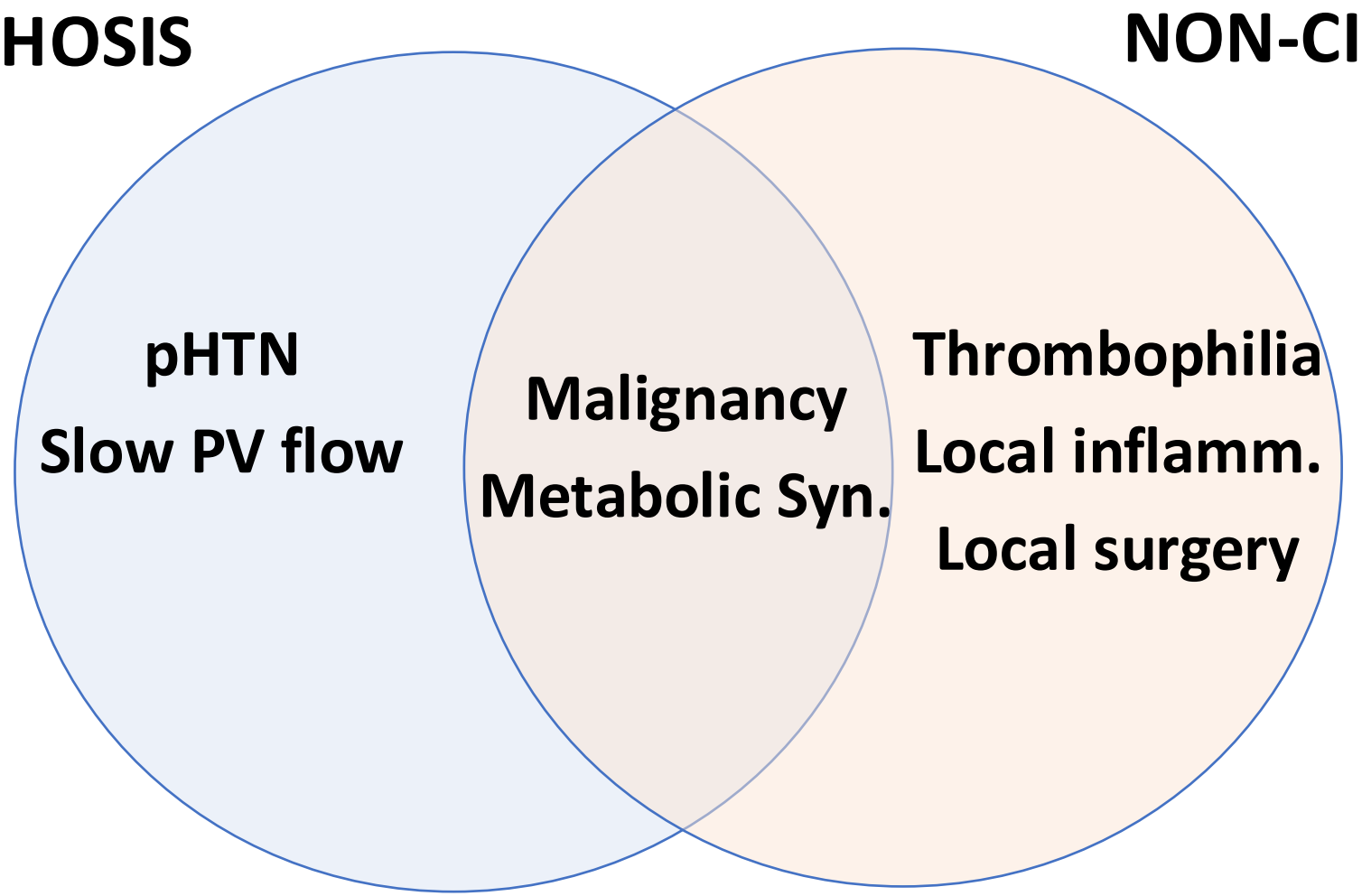
cirrhosis



cirrhosis with PVT

Driever EG Hepatology 2022; Elkrief 2024.

Risk factors differ in cirrhotic & non-cirrhotic PVT



Turon F J Hep 2021

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Local inflammation & thrombophilic states are important risk factors for non-cirrhotic PVT

LOCAL

- Inflammation
  - *Abscess*
  - *IBD*
  - *Pancreatitis*
  - *Cholecystitis*
- Trauma/surgery
  - *GI/GB surgery*
  - *Abd. trauma*

THROMBOPHILIA

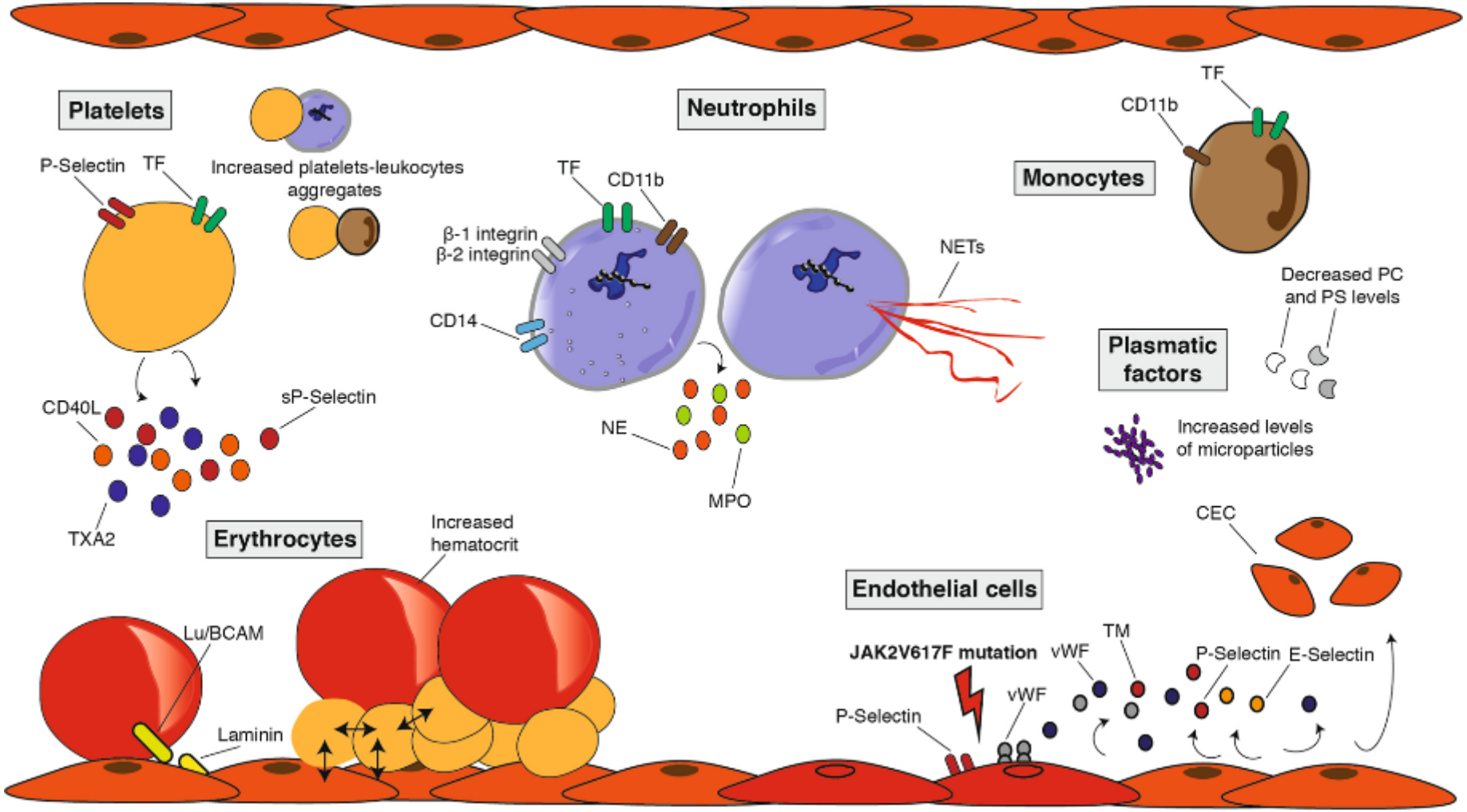
- Inherited
  - *FVL*
  - *Antithrombin def.*
  - *Protein C/S def.*
- Acquired
  - *MPN (**JAK2**)*
  - *OCP, pregnancy*
  - *Abd. malignancy*
  - ***obesity***

SYSTEMIC

- Viral
  - ***CMV***
  - ***SARS-CoV-2***
  - *HIV*
- Autoimmune
  - *Behcet's*
  - *Sarcoid*
  - *Celiac*

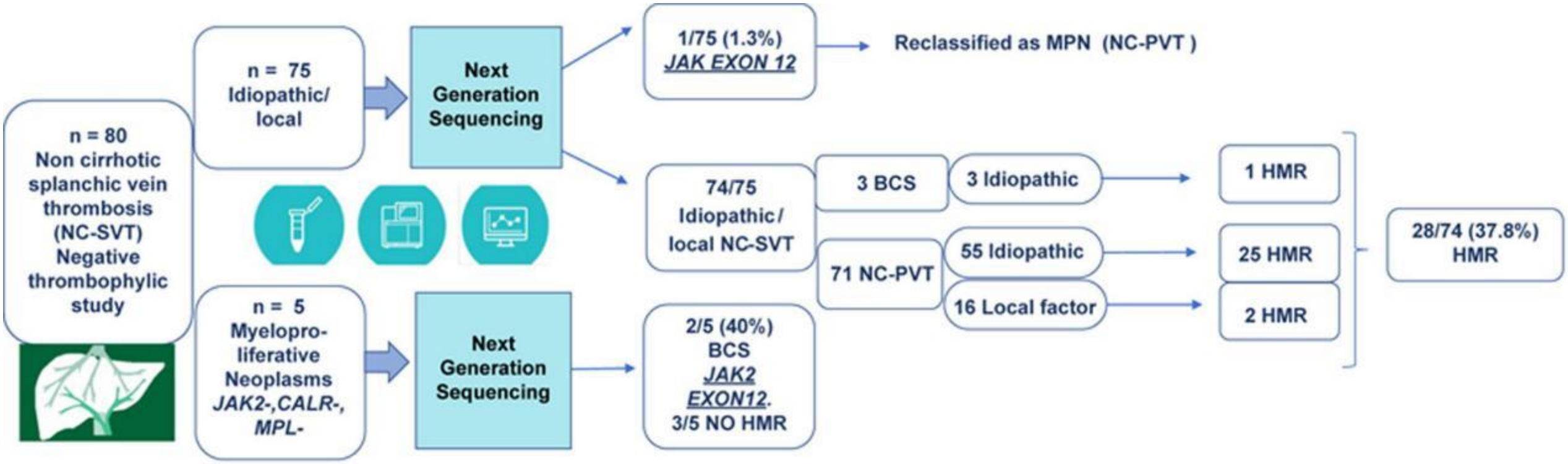
Hernández-Gea V J Hep 2019

JAK2 mutations in endothelial cells increase P-selectin & VWF expression



Guy Leukemia 2021

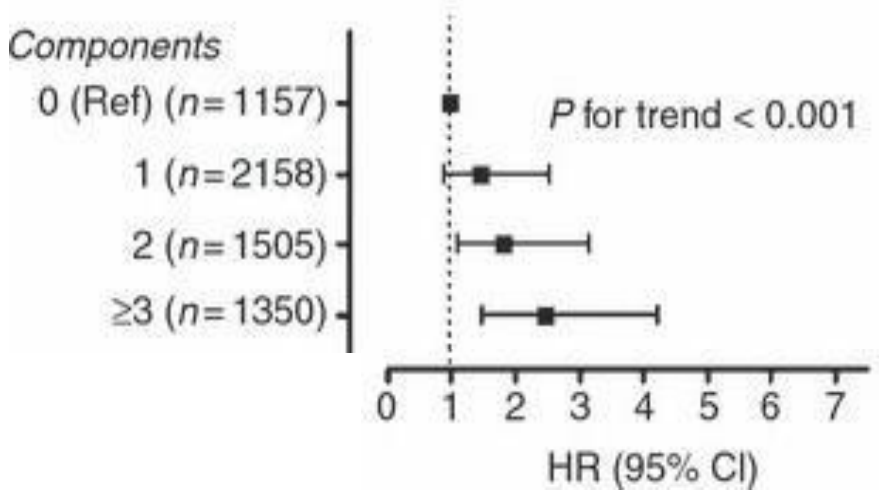
Next Gen Sequencing should be performed in idiopathic ncPVT to look for CHIP



Magaz J Hep 2021

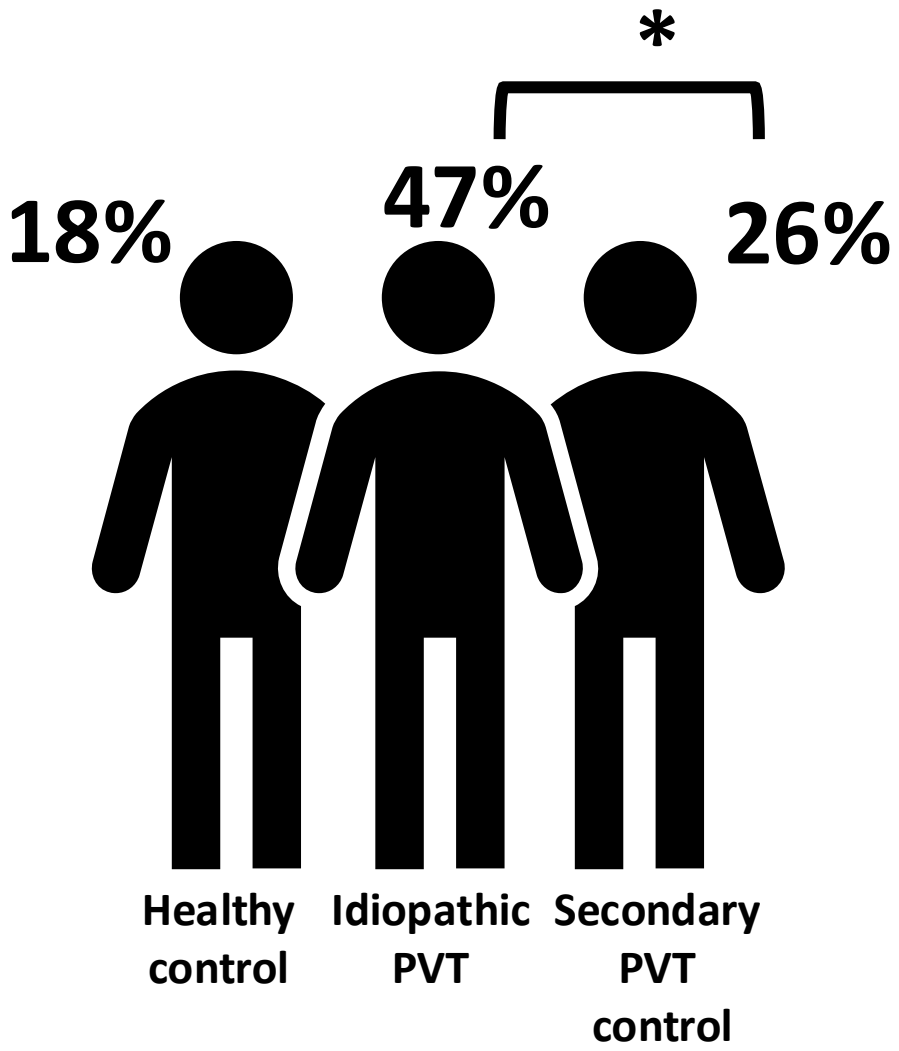
Metabolic syndrome associated with increased rates of thrombosis

	Unadjusted HR (95 % CI)	Age and gender adjusted HR (95 % CI)	Multivariable* HR (95 % CI)
Metabolic syndrome	1.86 (1.38–2.51)	1.65 (1.22–2.23)	–
Abdominal obesity	2.37 (1.79–3.13)	2.12 (1.59–2.83)	2.03 (1.49–2.75)
Hypertriglyceridemia	1.31 (0.98–1.75)	1.26 (0.95–1.69)	1.08 (0.79–1.49)
Low HDL cholesterol	1.01 (0.72–1.43)	1.07 (0.76–1.52)	0.87 (0.60–1.27)
Hypertension	1.87 (1.33–2.63)	1.39 (0.98–1.97)	1.19 (0.83–1.70)
Impaired glucose metabolism	1.86 (1.21–2.88)	1.51 (0.98–2.35)	1.26 (0.80–1.96)



Borch J Thromb Haemost 2009

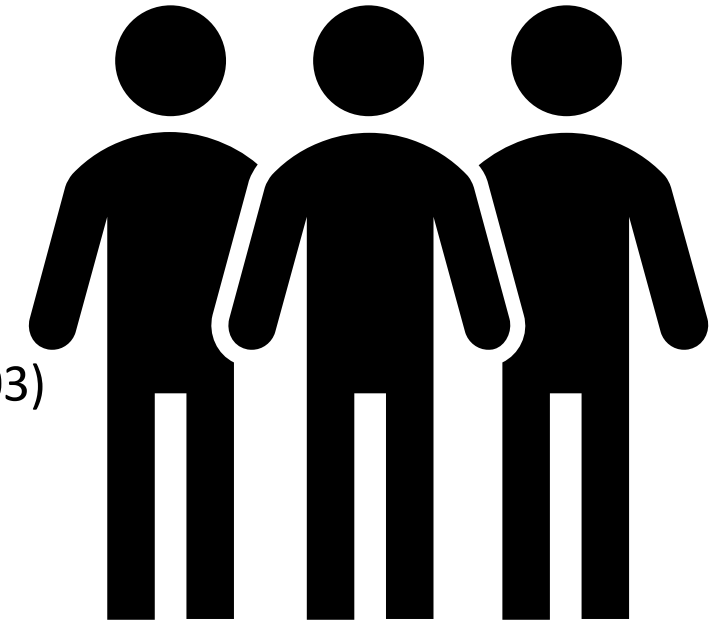
Metabolic syndrome is more prevalent among those with idiopathic PVT vs HC or PVT w/known risk factor



Bureau J Hep 2016

Abdominal circumference had strongest association with PVT on multivariate analysis

- ↑ weight (86.8 vs. 75.2 kg, p = 0.003)
- ↑ BMI (29.4 vs. 25.8 kg/m 2, p = 0.003)
- ↑ waist circumference (104.6 cm vs. 92.2 cm, p = 0.004)

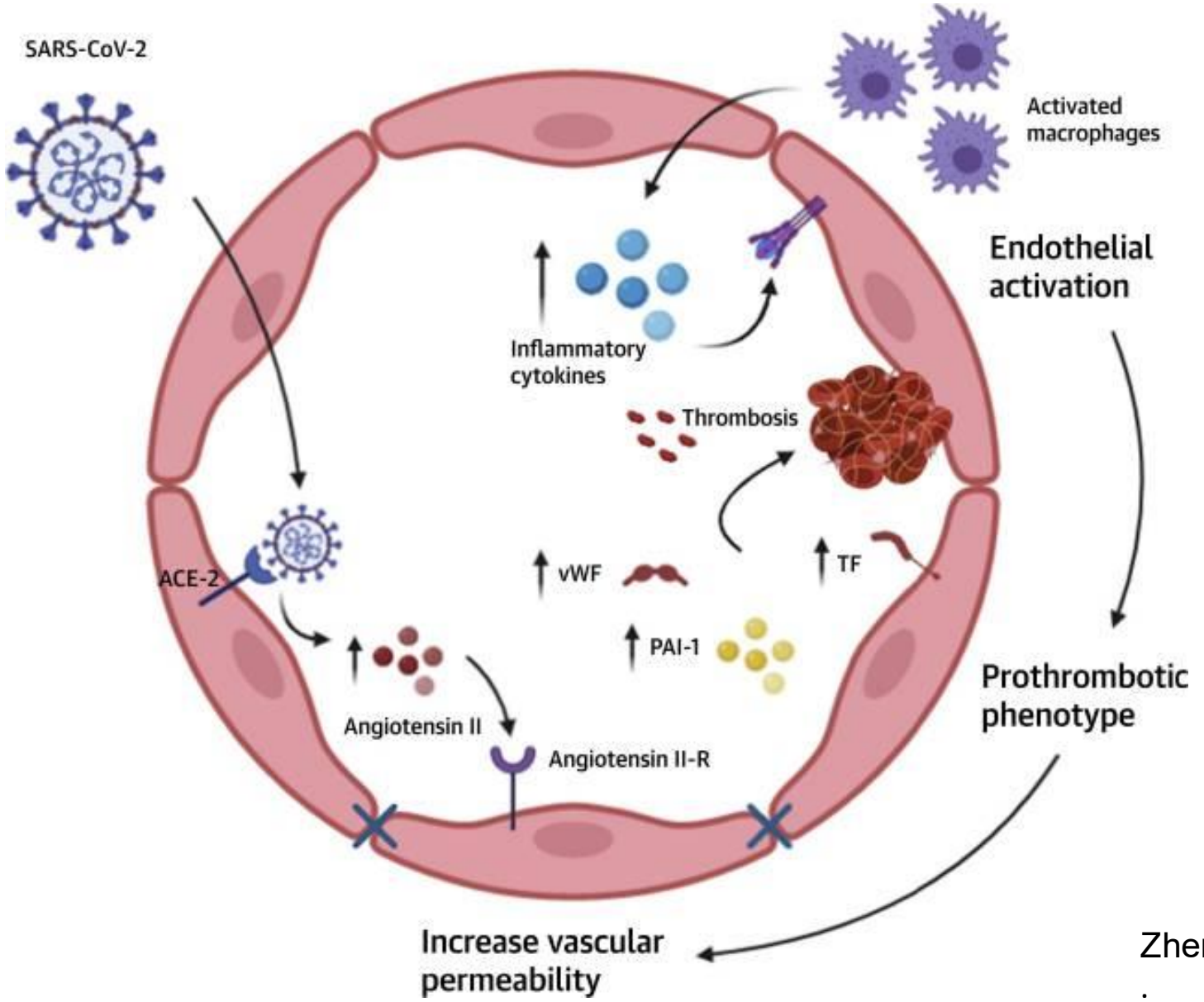


Healthy control **Idiopathic PVT** **Secondary PVT control**

- ↑ weight (86.8 vs. 73.1 kg, p <0.001)
- ↑ BMI (29.4 vs. 25.0 kg/m 2, p = 0.004)
- ↑ waist circumference (104.6 cm vs. 93.2 cm, p = 0.004)
- ↑ Visceral fat (18.2 vs 12.6 (p=0.02)

Bureau J Hep 2016

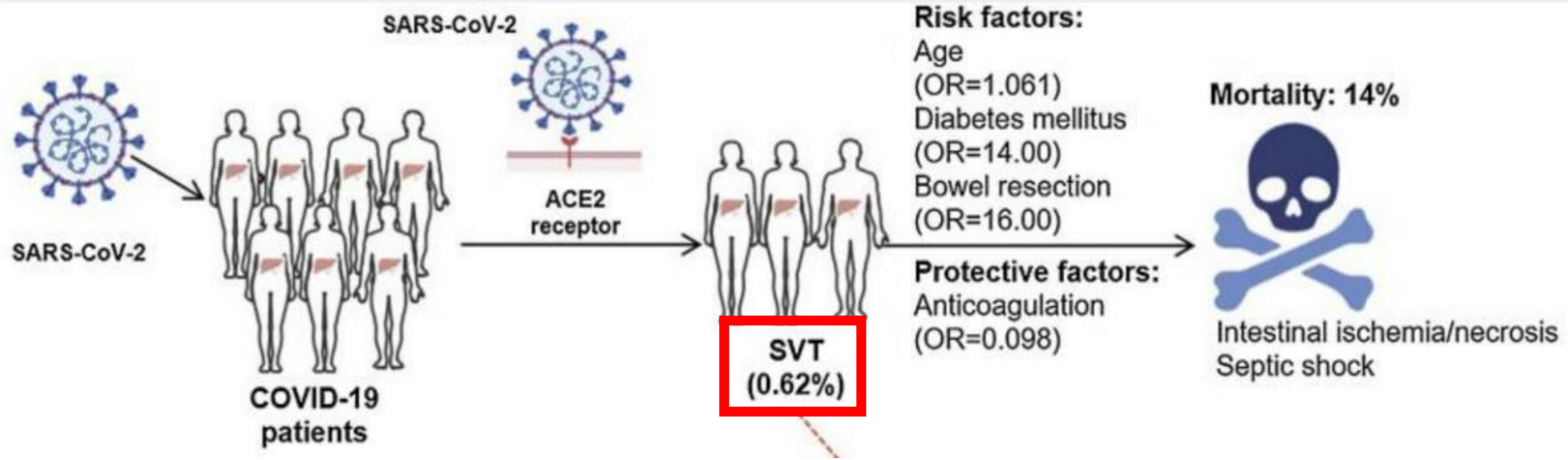
SARS-CoV-2 increases risk of VTE



Zheng J Thromb Thrombolysis 2022

· Giustino J Am Coll Cardiol 2020

Splanchnic thrombus incidence 150x higher in SARS-CoV-2 vs gen pop.

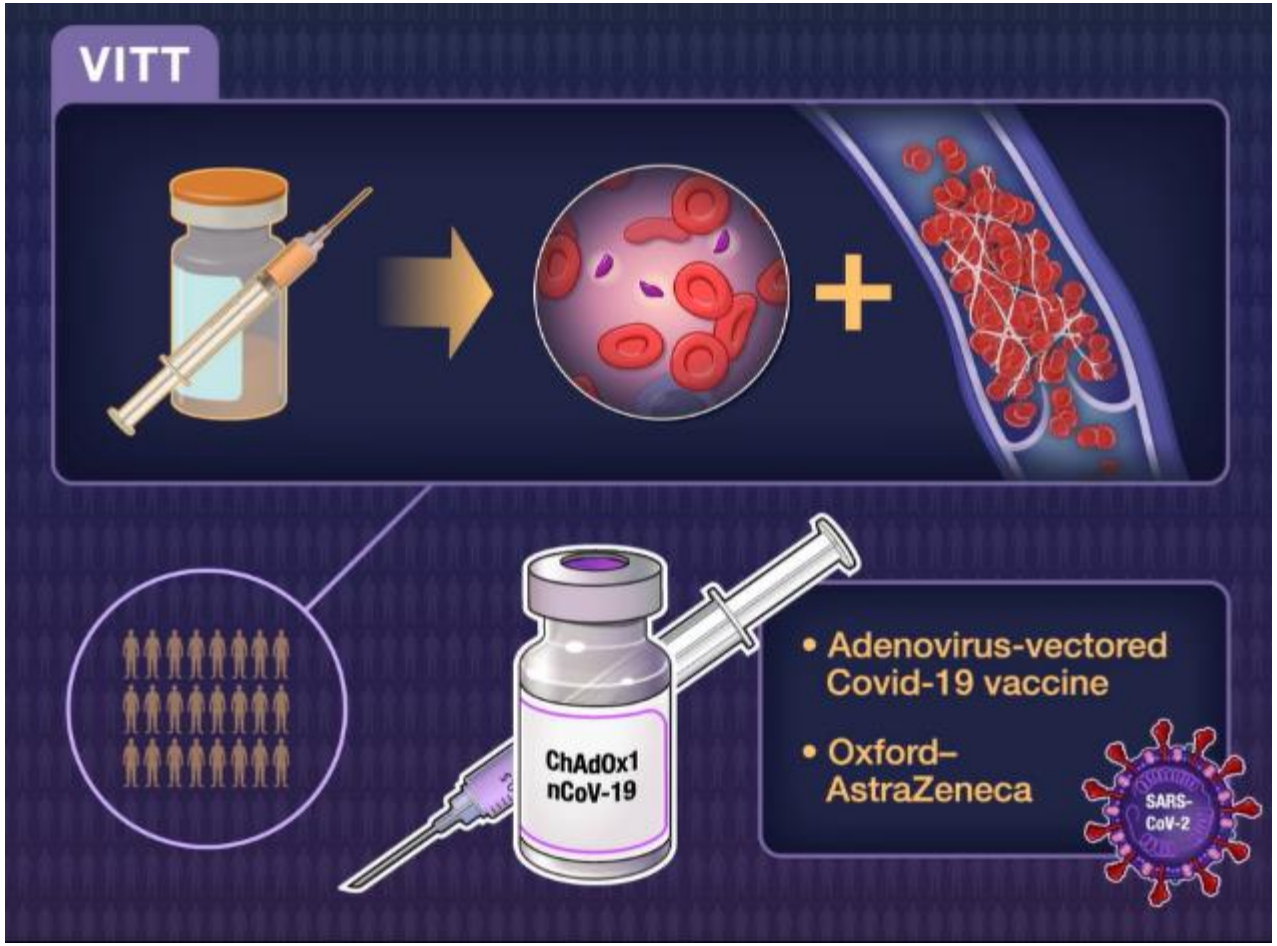


Zheng J Thromb Thrombolysis 2022

Splanchnic vein thromboses can occur rarely after SARS-CoV-2 vaccination

Definite VITT:

- Within 5-42 days vaccination
- VTE present
- Thrombocytopenia
- D-dimer >4000 FEU
- + anti-PF4 antibodies



Pavord NEJM 2021

SARS-CoV-2 vaccine-related splanchnic thromboses are extensive with high morbidity & mortality

VALDIG cohort

- ↑ bowel resection (17% vs 3%, $p < 0.001$)
- 69% had multi-vessel
- 14% extra-abdominal thromboses
- ↑ 1-year mortality (3% vs 0.2%, $p = 0.01$)

Mann Hepatology 2024

Prothrombin G20210 gene variant is more common in those w/CMV-associated ncPVT

Recent portal venous system thrombosis (PVT) associated with cytomegalovirus disease

A multicentric controlled cohort study of the French Network for the vascular liver diseases

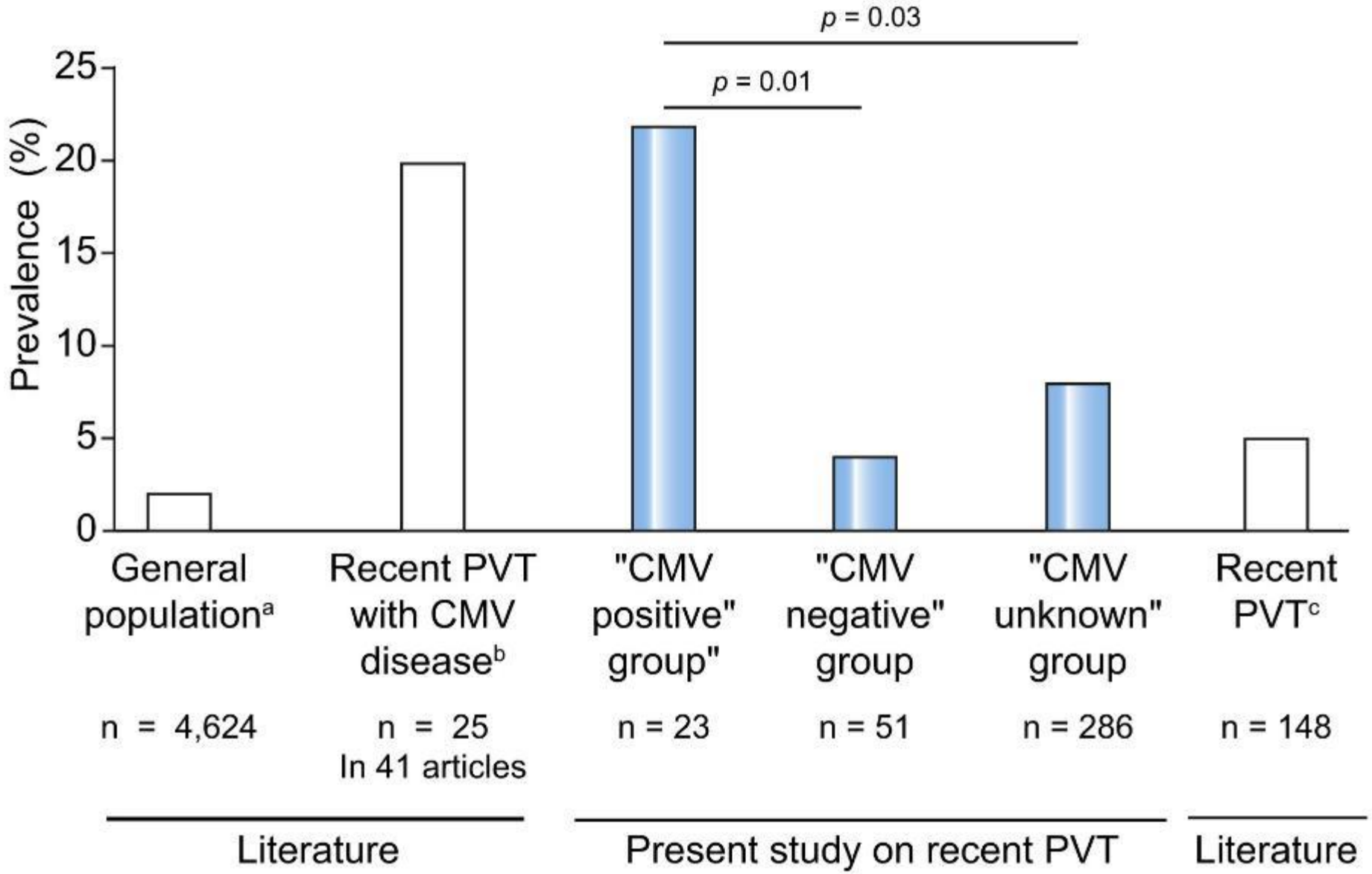
Recent PVT

	Cytomegalovirus disease	No cytomegalovirus disease	Unavailable cytomegalovirus status
	n = 23	n = 53	n = 297
	• Younger • More signs of viral infection • >50% patients had another risk factor for thrombosis		
Prothrombin G20210A gene variant	22%	4%	8%

No difference regarding localization, extension or recanalization of PVT

De Broucker J Hep 2021

Prothrombin G20210 gene variant is more common in those w/CMV-associated ncPVT



De Broucker J Hep 2021

Portal hypertension is the most established risk factor for PVT in cirrhosis

Associated with cPVT:

-High-risk varices

-Variceal bleeding

-Ascites

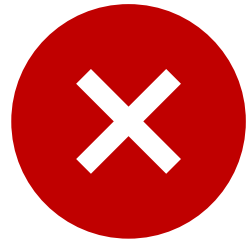
-Thrombocytopenia

Debated:

-Inflammation

-NSBB

-Met. syndrome



Not associated with cPVT:

-Thrombophilias

Elkrief 2024

Portal hypertension is the most established risk factor for PVT in cirrhosis

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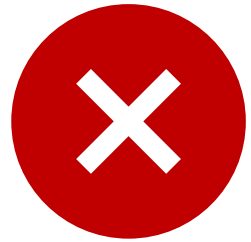


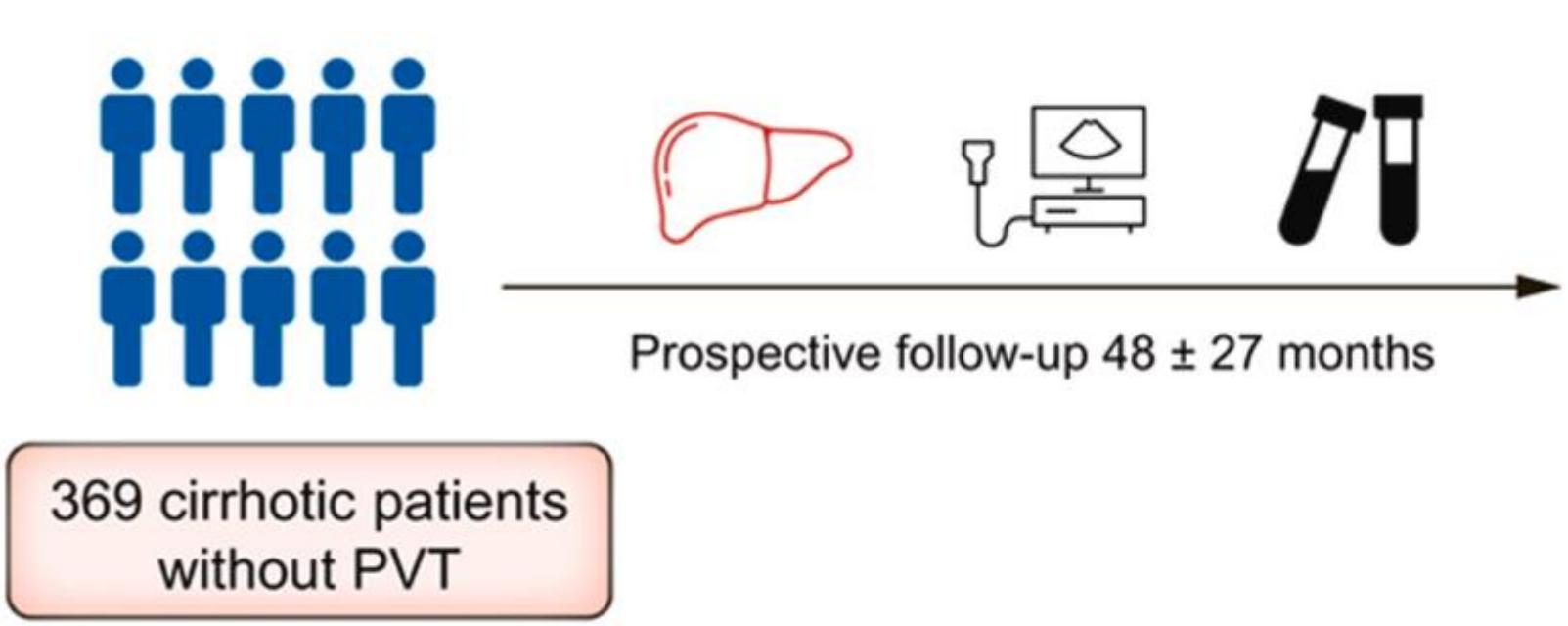
Not associated with cPVT:

-Thrombophilias

-NSBB

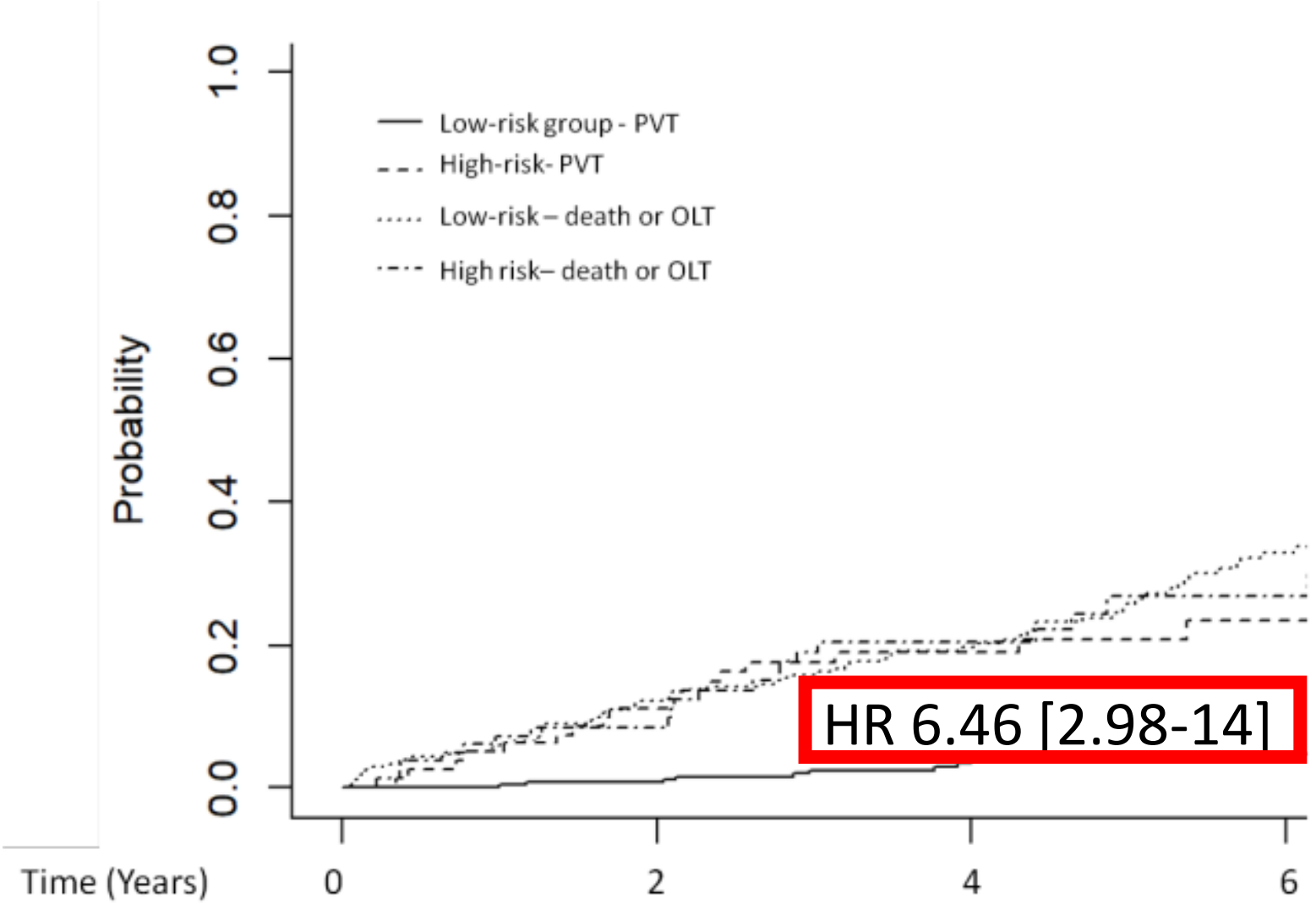
Elkrief 2024

Platelets, flow velocity & EVB predictive of PVT



Turon 2021

2+ Risk Factors Increases Risk of PVT in cirrhosis 6.5x

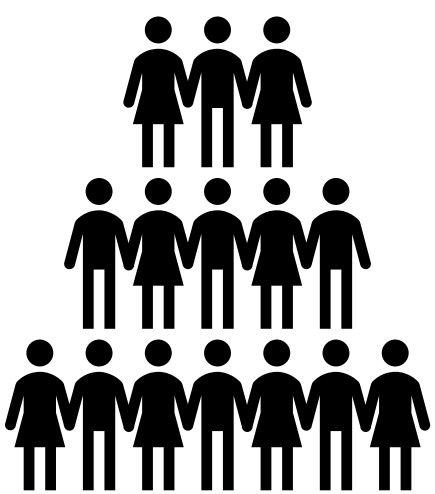


Risk Factors
• Platelet <100k • PBFV <15 cm/s • h/o variceal bleeding
0-1 risk factor: low risk
2+ risk factors: high risk

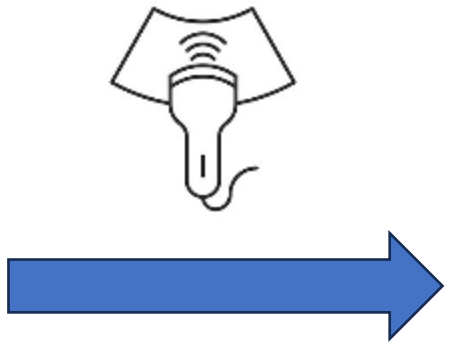
Turon 2021

Large varices also predictive in second large prospective study

Large EV (HR 1.78 [1.2-2.8])



1243
CTP A/B



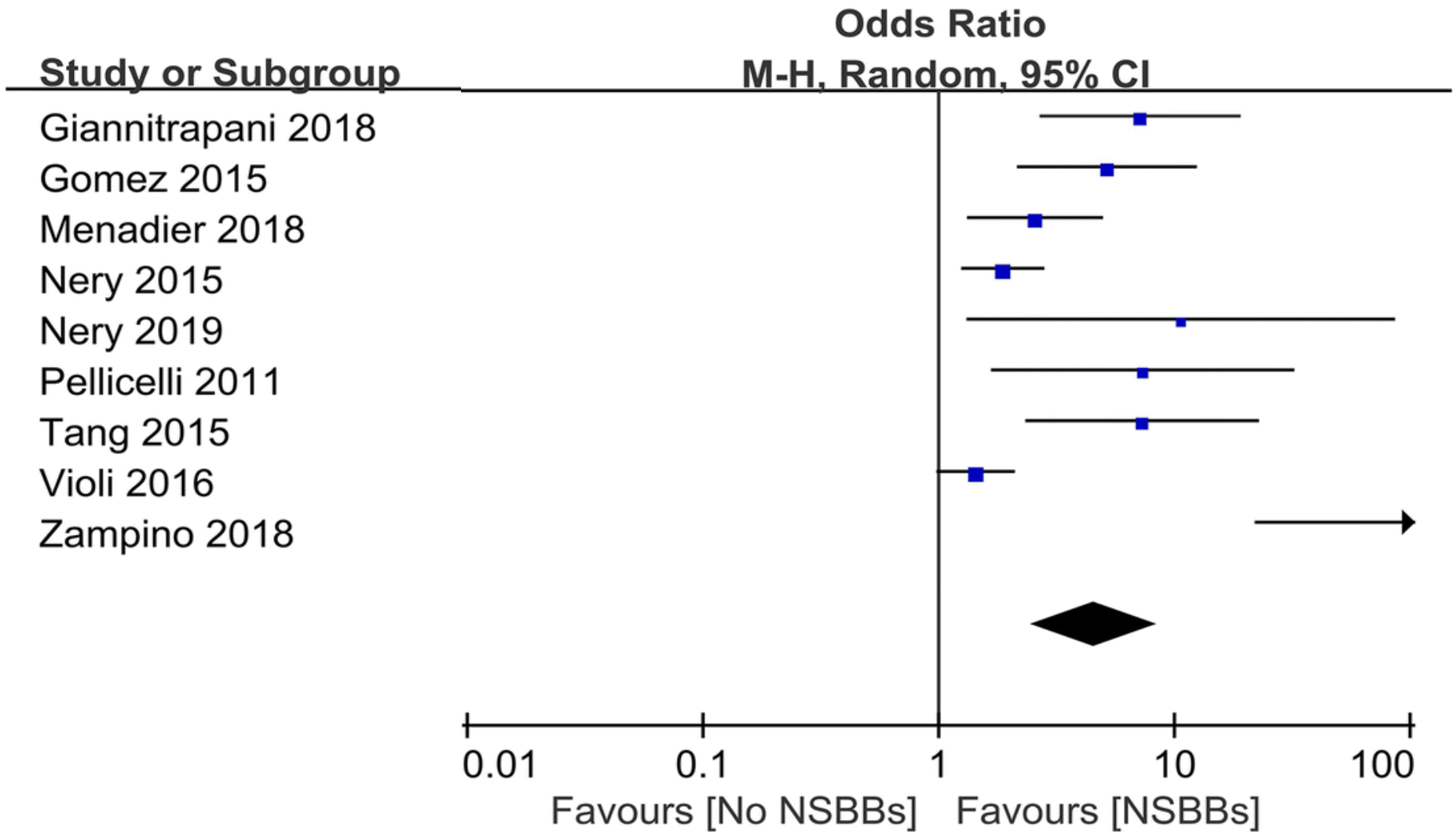
q3-q6 mos.

118 PVT

1125 no PVT

Nery 2015

Could NSBB slow PV flow & increase PVT risk?



Xu X Hepatol Int 2019

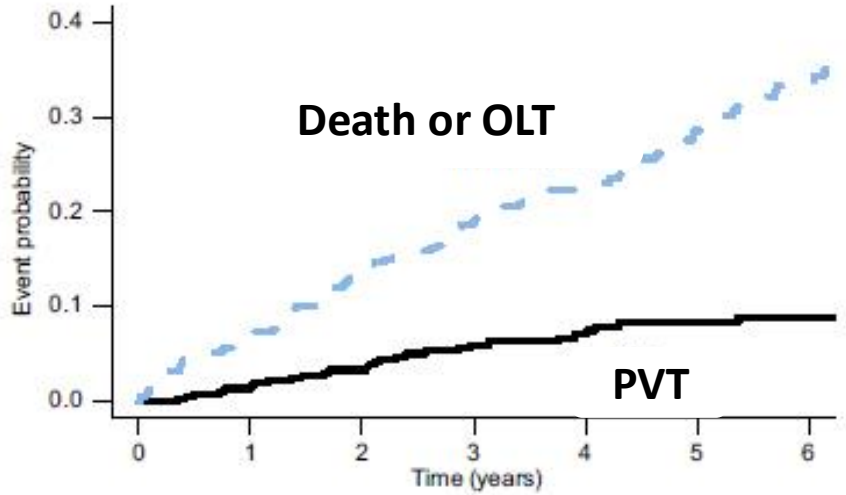
…NSBB & PVT are NOT associated if control for pHTN

369 cirrhotic patients without PVT

Prospective follow-up 48 ± 27 months

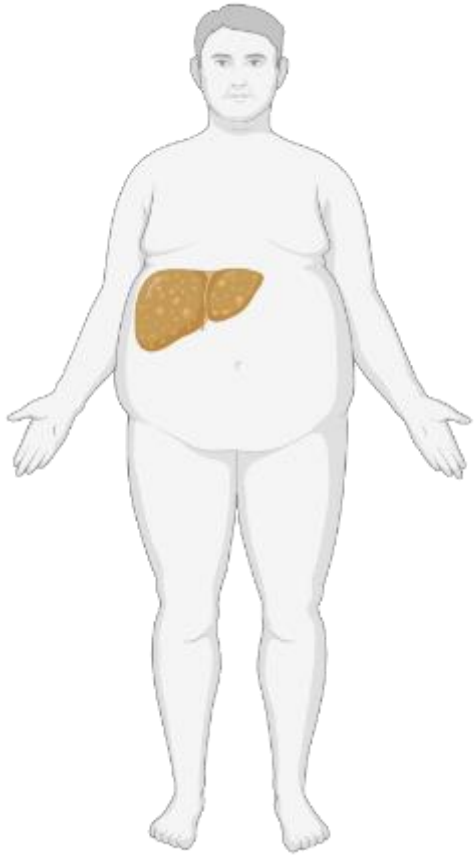
NSBB use *not* assoc. w/PVT (HR = 0.745, 95% CI 0.154-3.60)

29 patients developed PVT

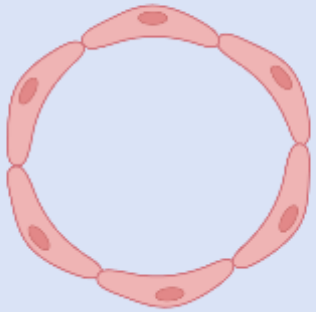


Turon F J Hep 2021; Violi F Intern Emerg Med 2016

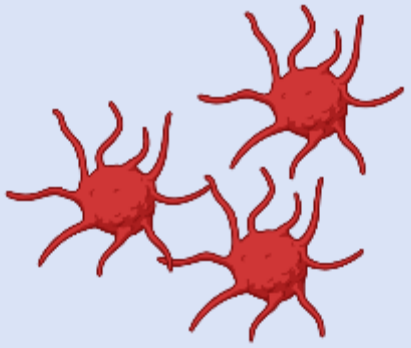
MASLD increases thrombosis risk through multiple avenues



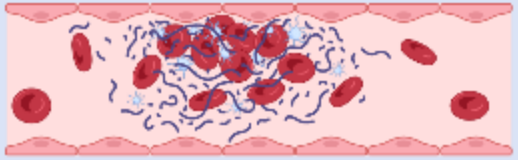
Endothelial dysfunction

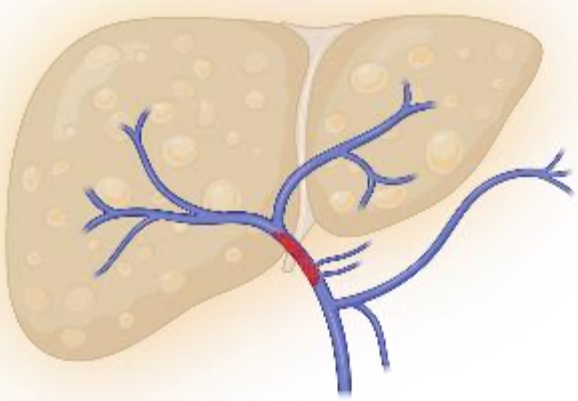


Platelet activation



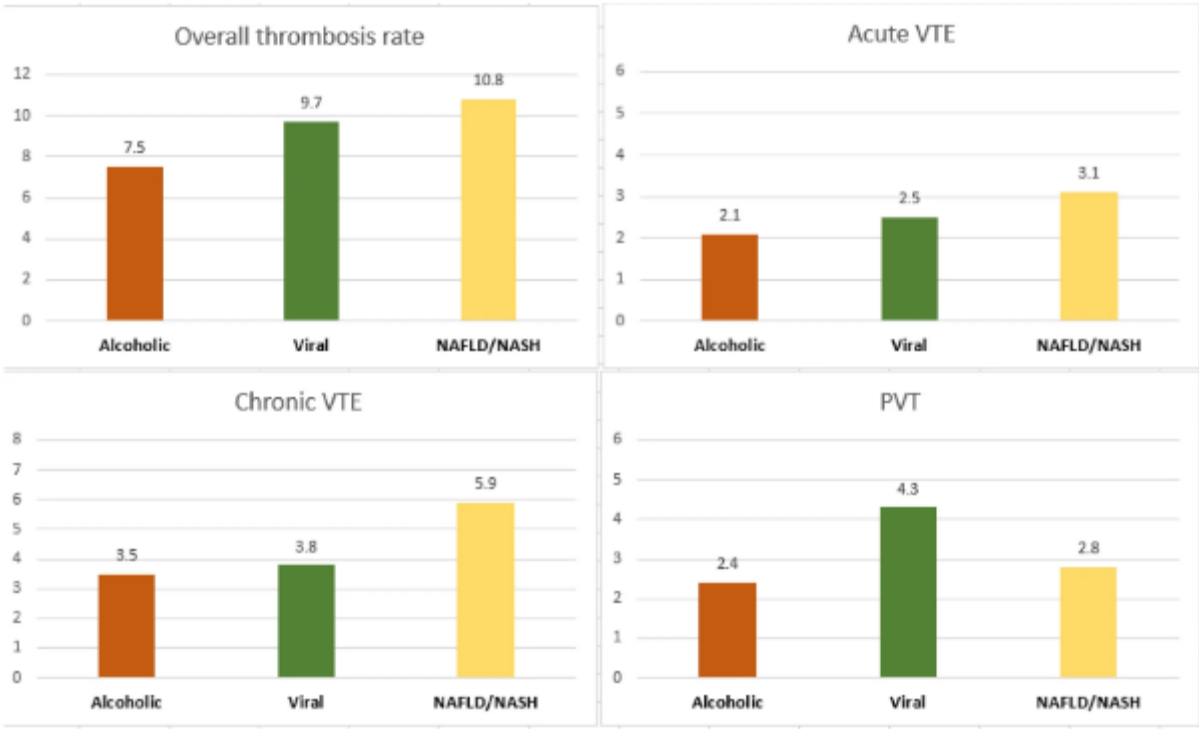
Decreased fibrinolysis





created with Biorender Davis JPE 2024

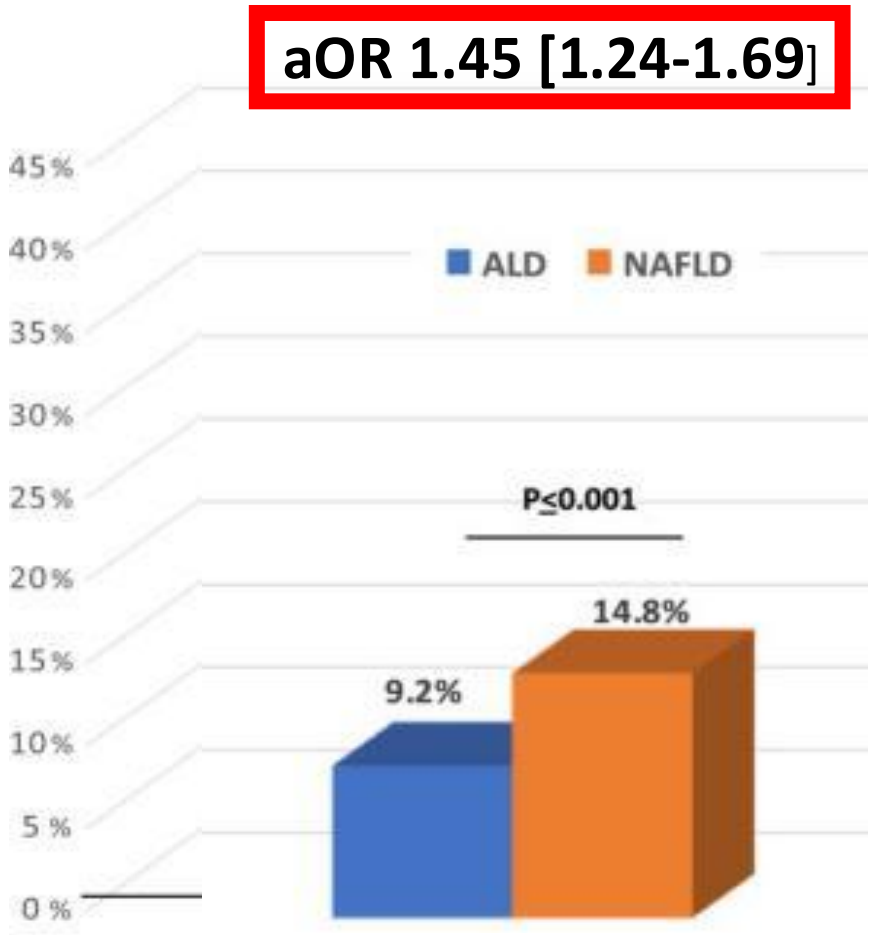
MASH cirrhosis confers higher thrombotic risk than other etiologies of cirrhosis



Outcome	Alcoholic cirrhosis	Viral cirrhosis	NAFLD/NASH cirrhosis
Overall thrombosis rate	Reference category	1.22 (1.17–1.29)	1.48 (1.42 – 1.54)
Acute VTE	Reference category	1.08 (0.99–1.17)	1.37 (1.27–1.47)
Chronic VTE	Reference category	1.01 (0.94–1.09)	1.58 (1.49–1.67)
PVT	Reference category	1.61 (1.50–1.72)	1.41 (1.31–1.52)

Pemmasani Dig Dis Sci 2024

PVT more prevalent in MASLD vs ALD transplant recipients

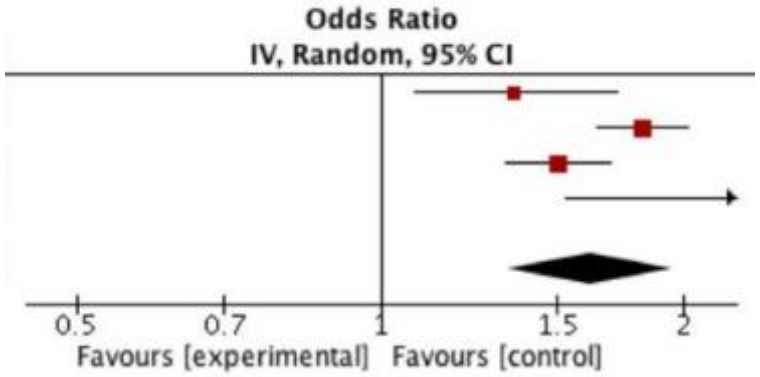


Risk factor	Portal vein thrombosis		
	Adjusted OR	95% CI	*P*-value
NAFLD	1.45	1.24–1.69	**<0.001**
Male gender	1.31	1.12–1.54	**<0.001**
Age	1.02	1.01–1.03	**<0.001**
Race			
Caucasian	Reference	–	
Hispanic	1.35	1.12–1.62	**0.001**
BMI	1.01	1.00–1.02	0.012
Diabetes	1.36	1.18–1.57	**<0.001**
Spontaneous bacterial peritonitis	1.62	1.32–2.00	**<0.001**
Abdominal surgeries	1.15	0.99–1.32	0.057
MELD	0.99	0.98–0.99	**0.016**

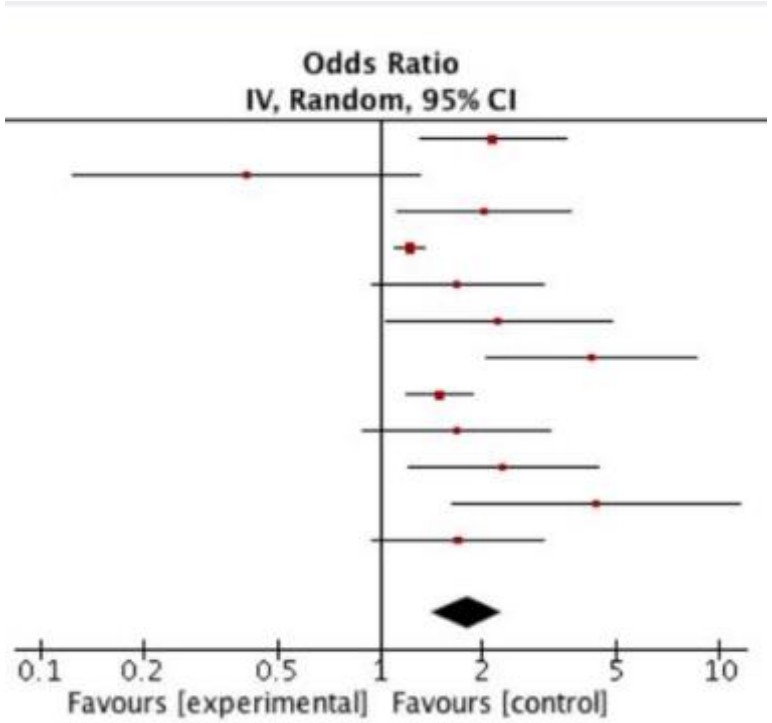
Molinari 2021

Multiple features of metabolic syndrome are associated with PVT

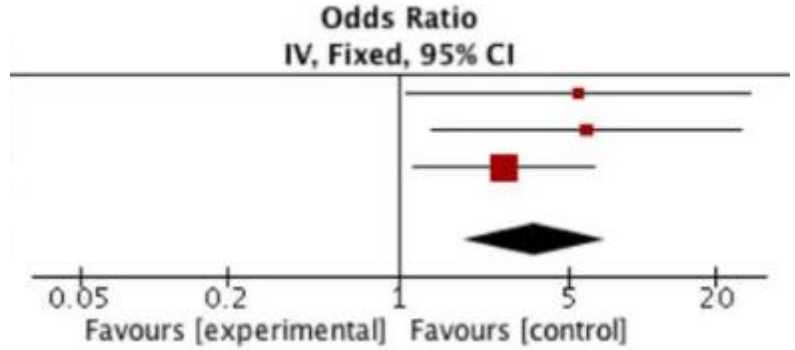
NAFLD & risk of PVT
OR 1.61 [1.34, 1.95]



DM & risk of PVT
OR 1.80 [1.42, 2.28]

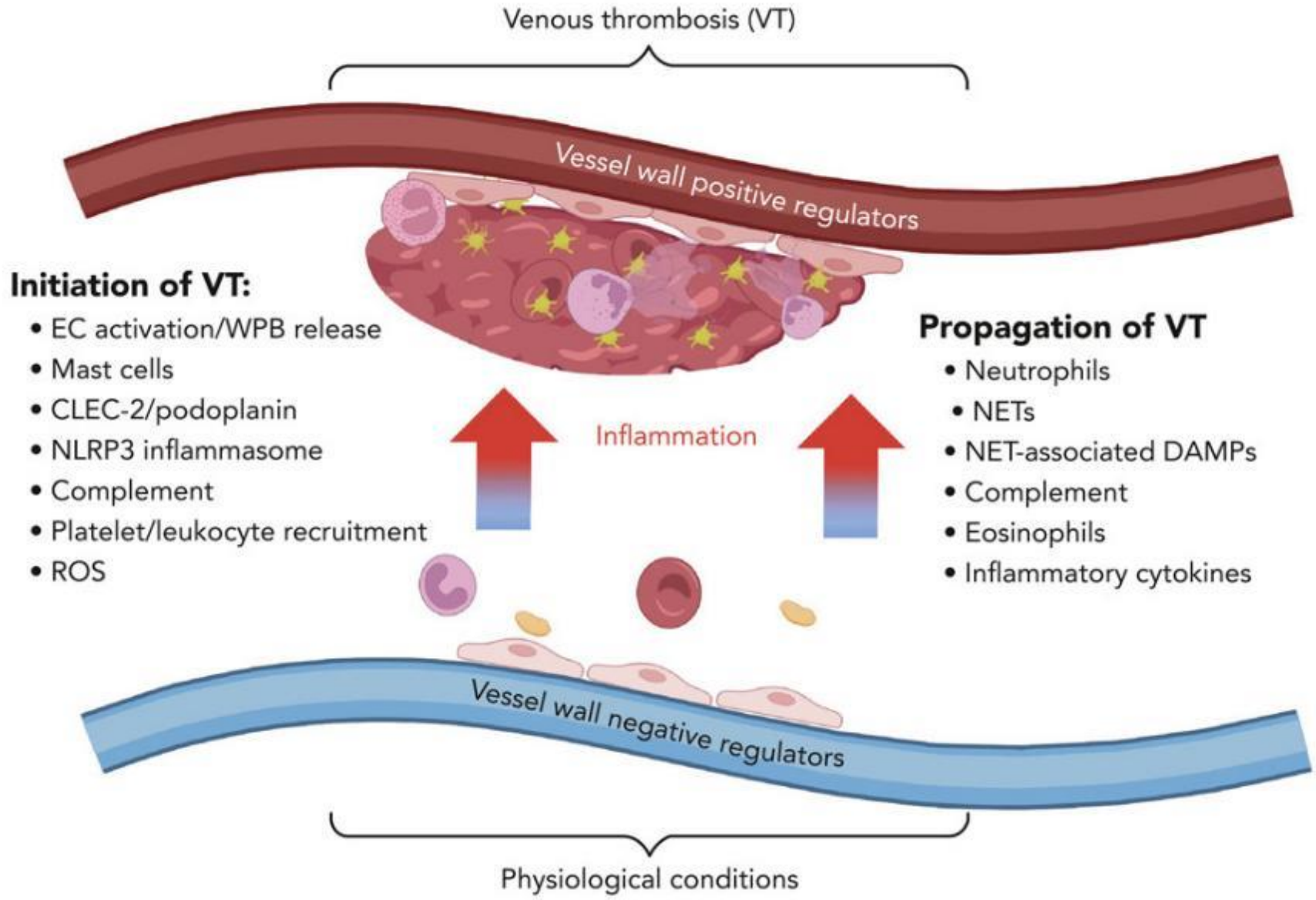


HLD & risk of PVT
OR 3.59 [1.83, 7.03]



Li Turk J Gastro 2022

Inflammation plays a role in VTE



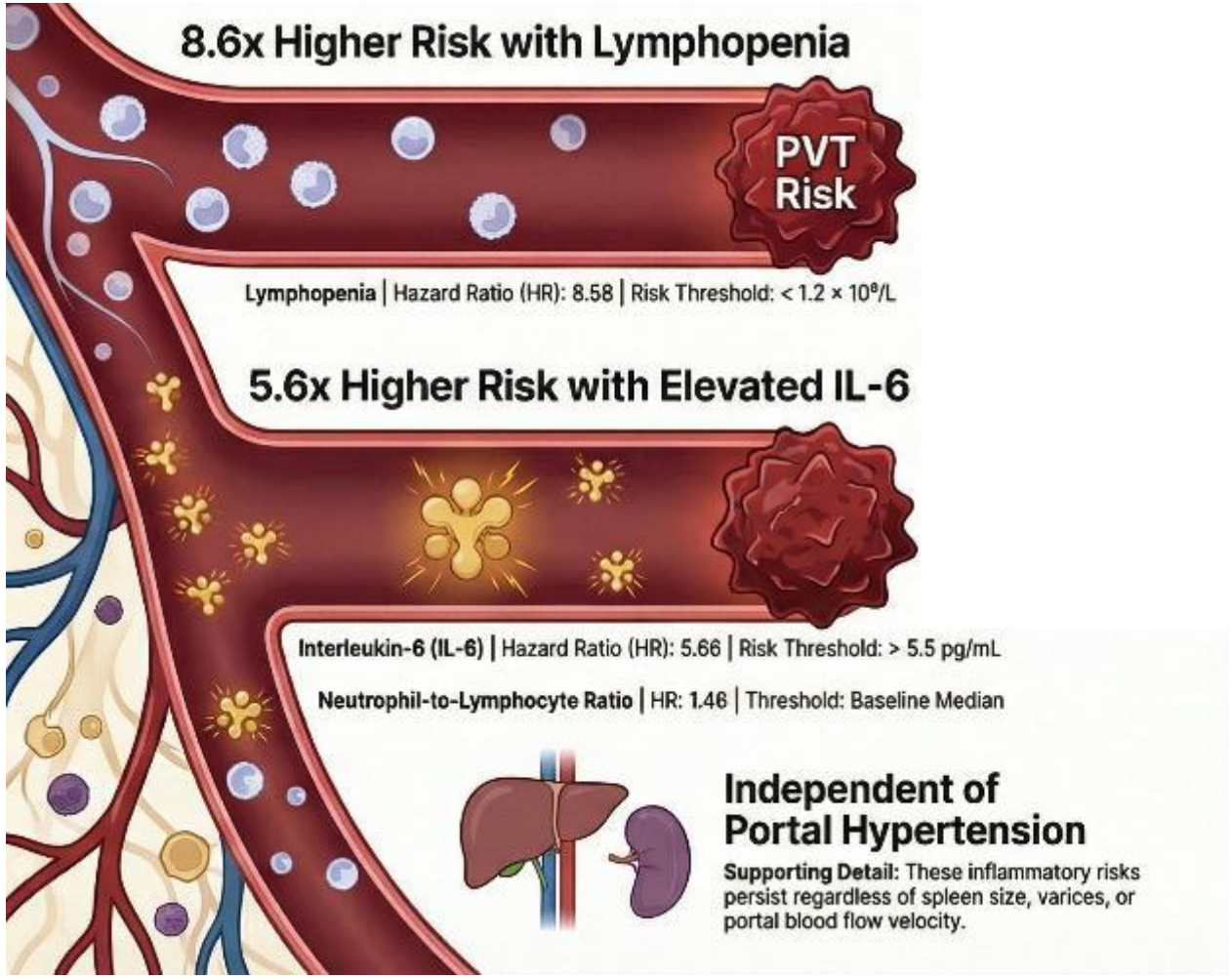
Rayes Blood 2024

Baseline inflammatory markers not associated with PVT in large prospective cohort study

	PVT (n = 23)	No PVT (n = 287)	sHR (95% CI)	*p* value
Inflammatory markers				
Cell-free DNA, ug/ml	0.89 ± 0.16	0.89 ± 0.22	0.97 (0.22–4.27)	0.97
MPO-DNA (AU)	0.21 ± 0.29	0.29 ± 0.46	0.68 (0.28–1.67)	0.40
IL-6, pg/ml	7.7 ± 7.9	8.4 ± 12.5	0.99 (0.97–1.02)	0.70
TNF-α,pg/ml	12.4 ± 5.1	11.6 ± 10.5	0.01 (0.99–1.03)	0.32
CRP, ng/ml	5315 ± 8044	3584 ± 6631	1 (1–1)	0.24

Turon J Hep 2021

IL-6 & lymphopenia were associated with PVT when controlling for pHTN

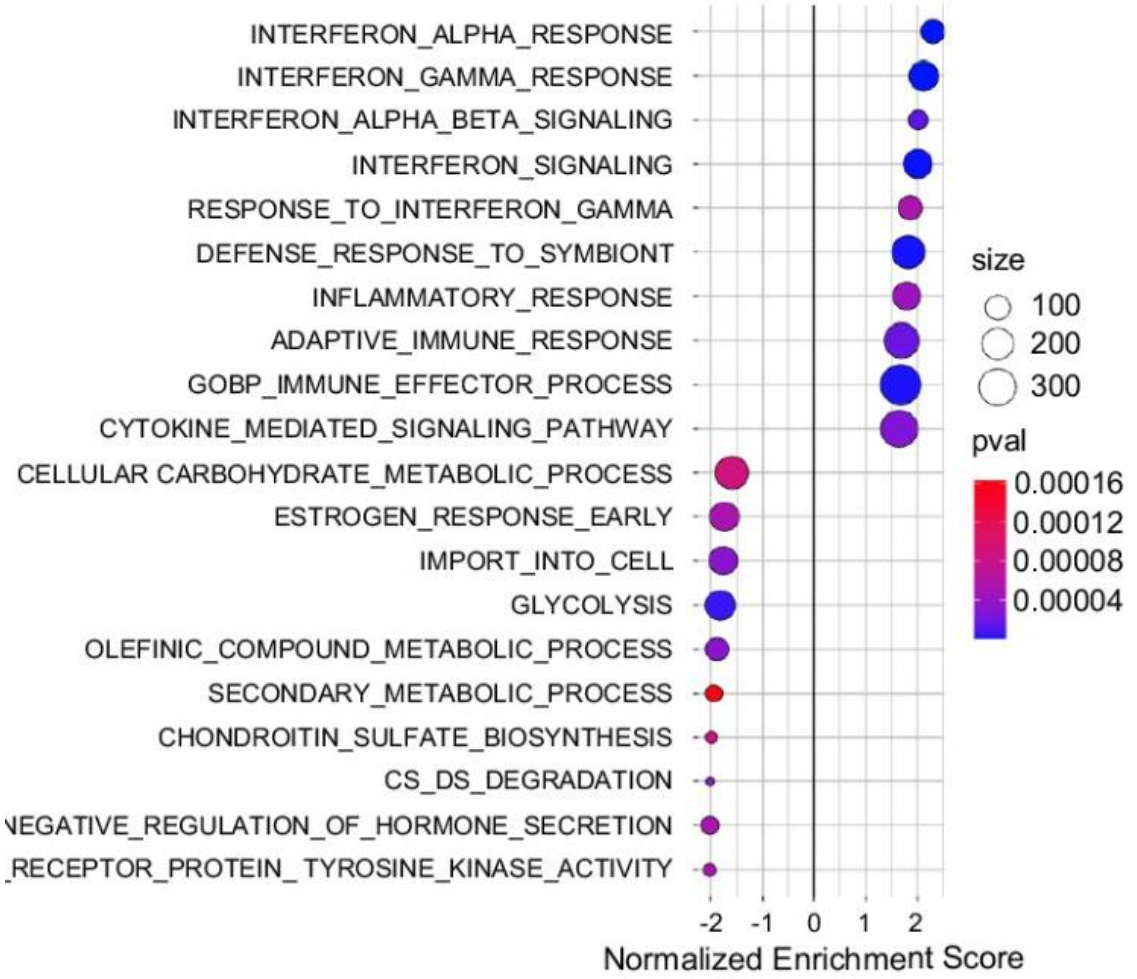


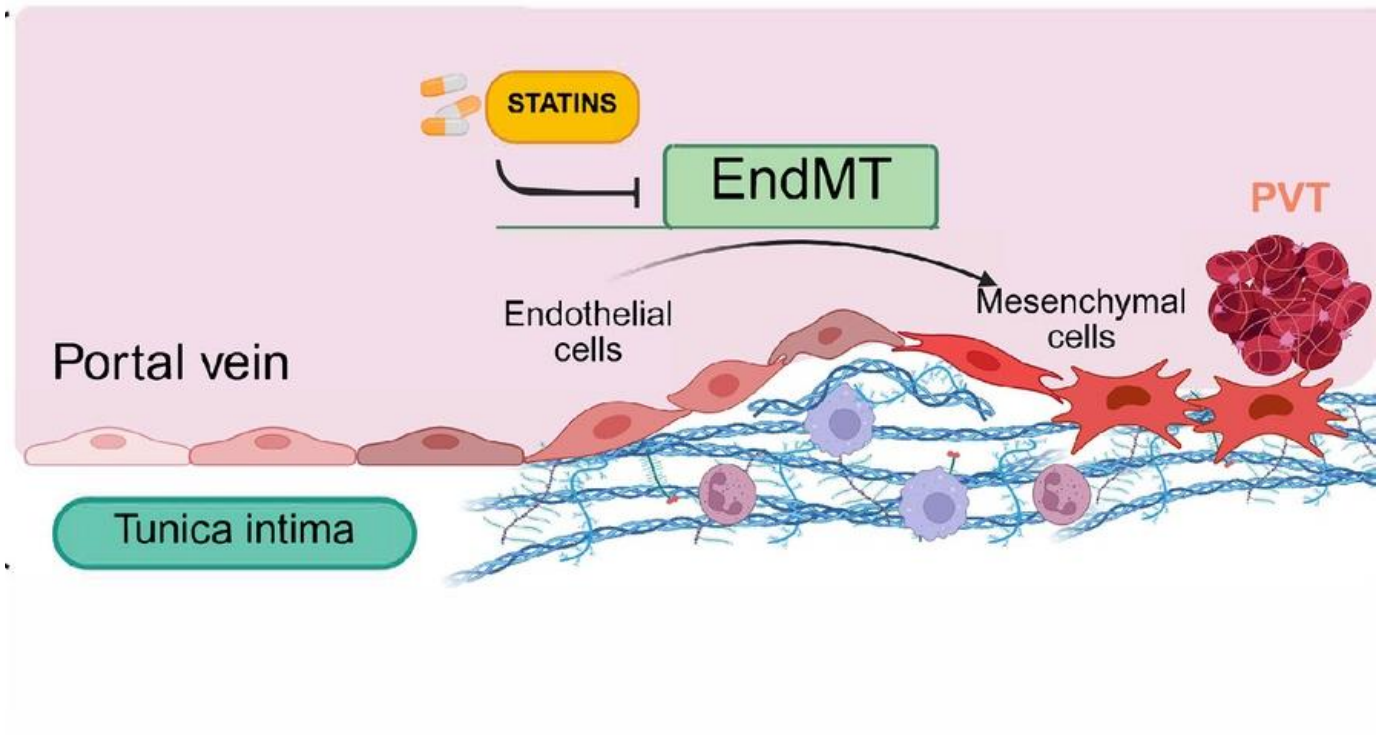
Schematic created with Notebook LM using Nery 2024

Adjusted for: varices/collaterals, ascites, spleen size, NSBB, alcohol etiology, MELD ≥ 13

Nery 2024

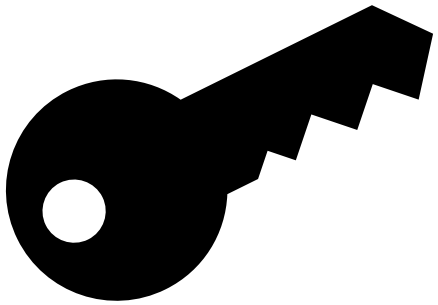
Inflammatory cytokines are upregulated in portal endothelial cells





Anton Hepatology 2025

Key Points



- NSBB don’t cause PVT (pHTN does)
- Idiopathic = underdiagnosed
- MetSyn is a prothrombotic state
- Practice update: NGS in idiopathic ncPVT

Lingering questions

- Is it unhelpful to group together PVT vs other VTE? cPVT & ncPVT?
- Does anticoagulation work via hemostatic or anti-inflammatory mechanism?
- Does resolution of metabolic syndrome reduce risk of PVT?
- Are JAK-2 mutations present at extra-splanchnic endothelial cells? How should dx. of CHIP change management?