International Congress on Coagulopathy in Liver Disease
Hemostasis and Thrombosis in Liver Disease
from Bench to Bedside

# Debate
# PVT – Cause or Consequence of Decompensation?


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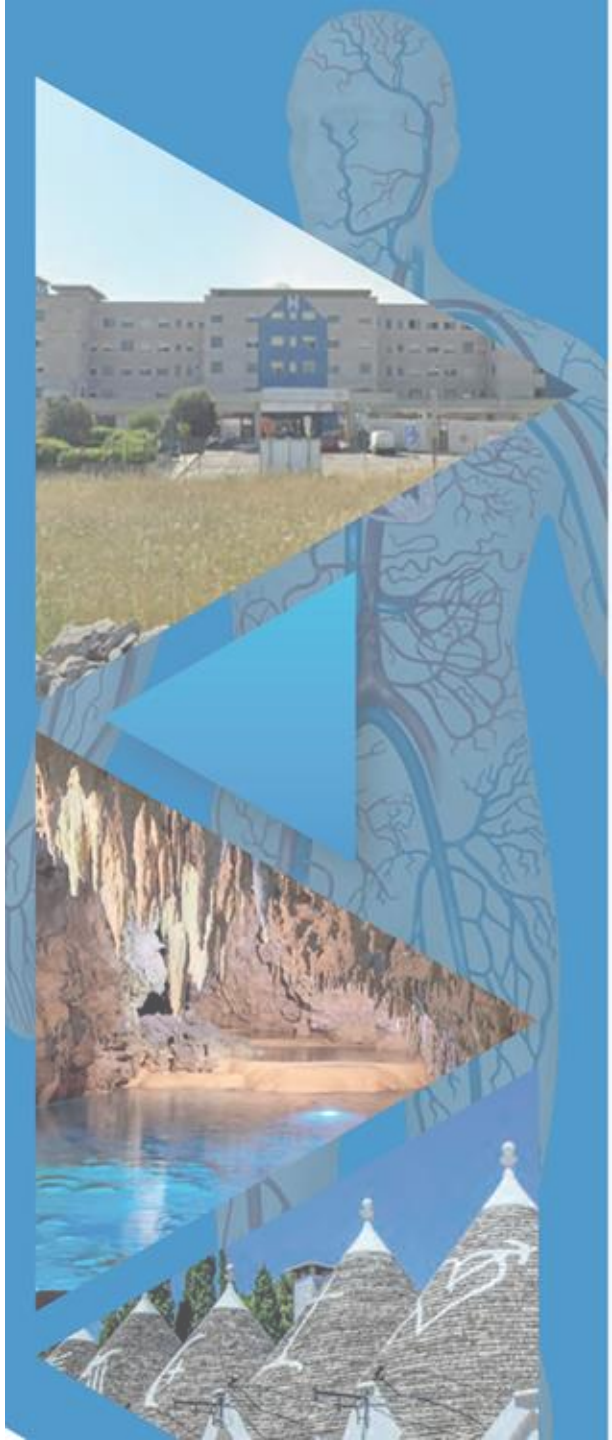


# PVT is an innocent bystander ?

# PREVALENCE CORRELATED WITH SEVERITY OF LIVER DISEASE/PH

| | | | |
|---|---|---|---|
| **Pan et al., 2022** | Systematic review and meta-analysis | Pooled cross-sectional and cohort evidence | Cross-sectional data linked PVT with **Child-Pugh B/C** and **ascites**; cohort data also linked incident PVT with **Child-Pugh B/C**, **higher MELD**, and **ascites**. The authors conclude that progression of cirrhosis and portal hypertension parallels PVT risk. |
| **Zhang et al., 2020** | Retrospective multicenter analysis, **2,826** patients with cirrhosis, with and without acute decompensation (AD) | **Direct comparison: AD vs no AD** | PVT prevalence was **9.36% in AD** vs **5.24% without AD** (**P=.04**). Among AD patients, PVT was also linked with a higher proportion of variceal bleeding (**47.33% vs 19.63%**, **P<.001**). |
| **Noronha Ferreira et al., 2019** | Prospective study | Prior decompensation history as severity marker | The study concluded that **previous decompensations of cirrhosis** and thrombocytopenia predicted PVT development, supporting a role for **more severe portal hypertension** in PVT occurrence. |
| **Turon et al., 2021** | Prospective study of clinical, ultrasonographic, and hemostatic factors | Severity of portal hypertension | Authors conclude that factors predictive of PVT development were **mainly those related to the severity of portal hypertension**; lay summary states that patients with cirrhosis and **more severe portal hypertension** are at higher risk of non-tumoral PVT. |
| **Zocco et al., 2009** | Prospective study | **MELD-based severity** | The study title and abstract identify a **correlation with MELD score and PVT development**, indicating that worsening liver disease severity tracks with PVT risk. |
| **Nadinskaia et al., 2019** | Case-control study from database of **1,512** cirrhotics | Direct severity markers: Child-Pugh, ascites, portal hypertension | Overall PVT prevalence was **6.2%**. Compared with controls, PVT cases had **Child-Pugh B/C 90.4% vs 54.6% (P<0.00001)**, higher MELD (**12.8 vs 11.1, P=0.005**), more grade 3 ascites (**35.1% vs 11.7%, P<0.00001**), and more ascites as first portal-hypertension presentation (**57.4% vs 42.9%, P=0.013**). In multivariable modeling, **Child-Pugh B/C** and **ascites** remained independent predictors. |
| **Koumar et al., 2023** | Observational prevalence study | Cirrhosis severity + ascitic fluid infection | Reported PVT prevalence **17.2%**; **ascitic fluid infection**, longer disease duration, and **increased cirrhosis severity** were significantly associated with PVT development. |
| **Arabpour et al., 2024** | Retrospective single-center study | Clinical decompensation markers | PVT was more likely in cirrhotic patients with **ascites**, **SBP**, splenomegaly, hypoalbuminemia, elevated INR, advanced age, HBV, and HCC. |
| **Cangemi et al., 2024** | Risk study | **Hypoalbuminemia** as severity marker | Patients with serum albumin **≤35 g/L** had a higher risk of PVT than those with albumin **>35 g/L**. |
| **Lankarani et al., 2015** | Cross-sectional/case-control in transplant candidates | Severe portal hypertension surrogate | In transplant candidates, PVT prevalence ranged up to high levels in this advanced population; within the study, **previous variceal bleeding/endoscopic treatment** was more common in the PVT group (**OR 2.526; 95% CI 1.200–5.317; P=0.013**). |

# PVT AND VARICEAL BLEEDING AS DECOMPENSATION

- Higher proportion history of AVB

  (Doumit 2009, Schassman 1993, Francoz 2005)

- Higher risk of UGIB (AVB and other sources)

  (Amitrano 2012, Dell'Era 2014, Nery 2015)

- Higher risk of overall re-bleeding; lower rate variceal obliteration

  (Attili 2012, Doumit 2012)

- Greater risk of 5-days failure, also in ACLF (OR 3)

  (Amitrano 2012, D'Amico 2003, Trebicka 2020)

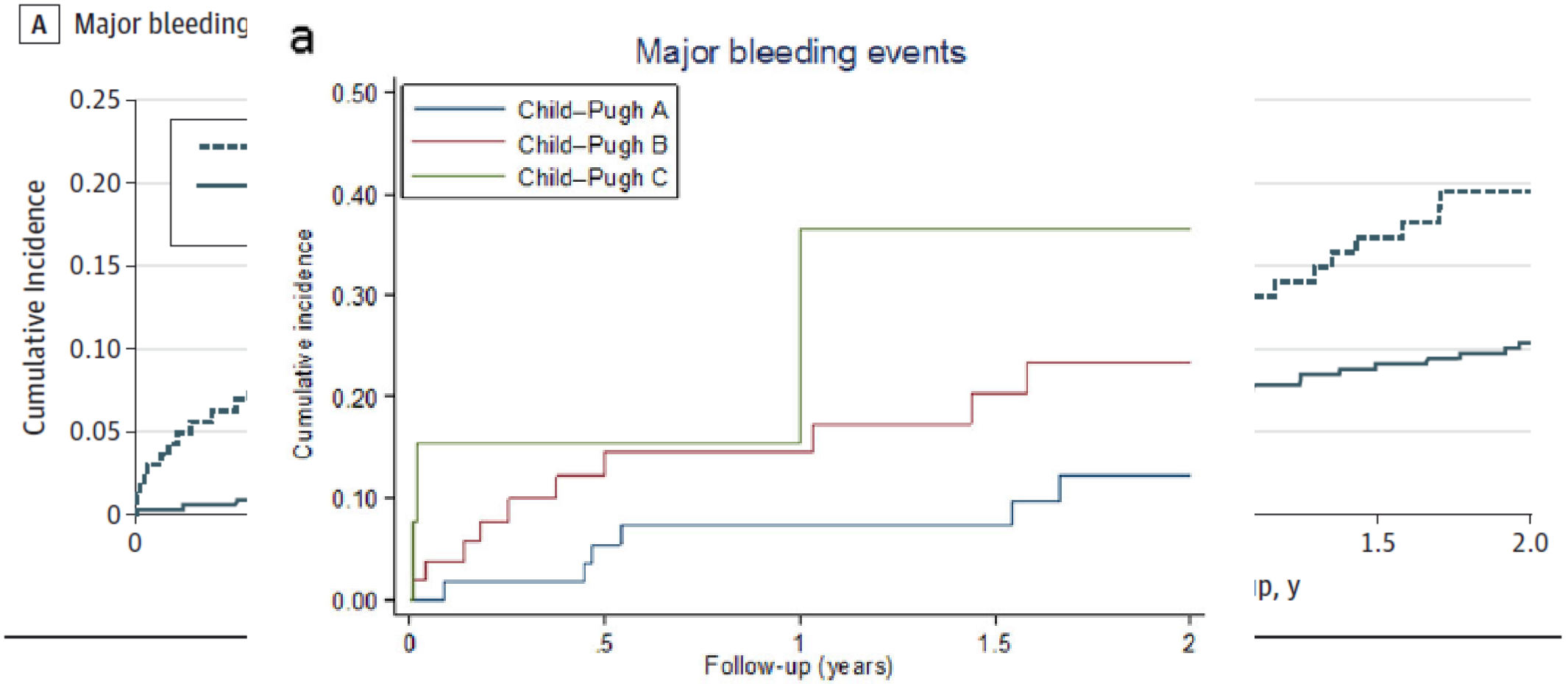
- Higher 14 days and 6 weeks rebleeding

  (Chen 2012, Lee 2009)

- More severe varices during follow-up after AVB

  (Chen 2023)

# PVT AND VARICEAL BLEEDING AS DECOMPENSATION



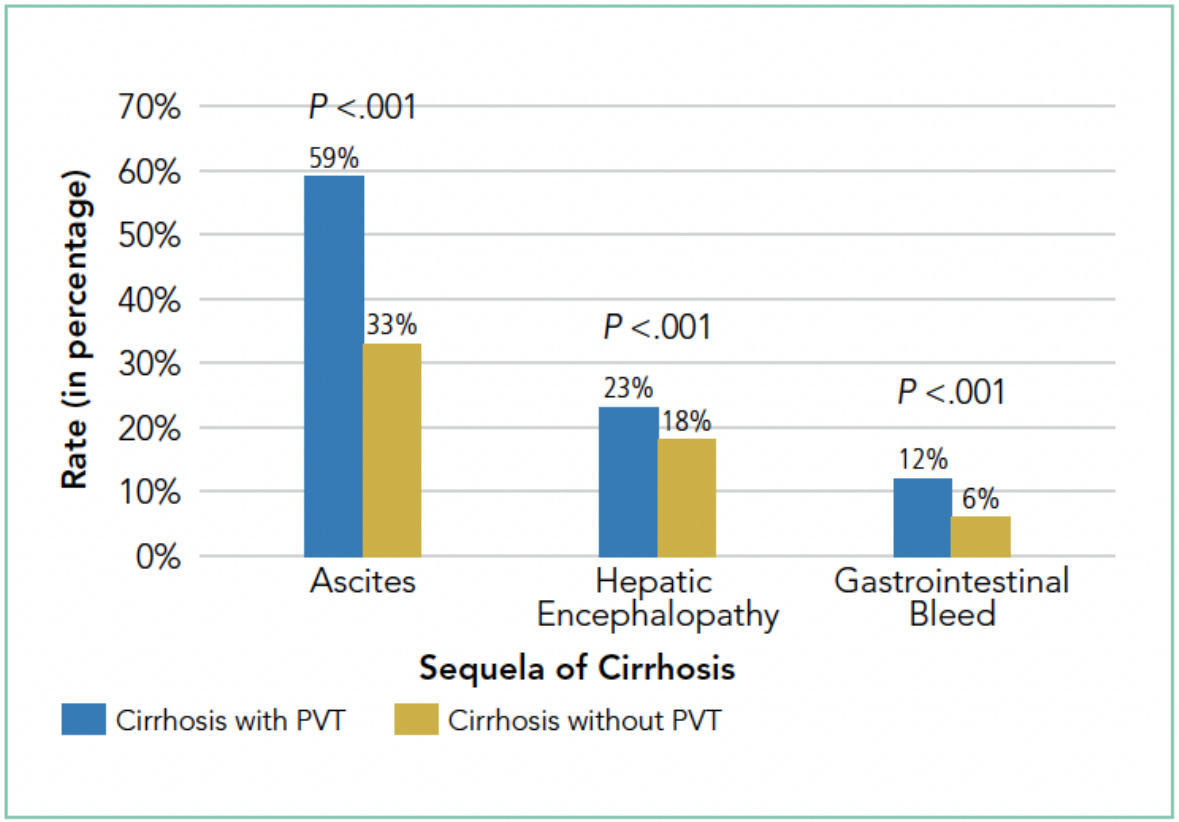

| | |
|---|---|
| On-treatment (n=11) | 11.3 (6.3-20.5) per 100 pt-y |
| Off-treatment - after discontinuation | 2.8 (0.4-19.9) per 100 pt-y |
| - never treated | 11.3 (5.6-22.6) per 100 pt-y |

Ageno, JAMA 2015; Senzolo, CTG 2018

# PVT IN HOSPITALIZED PATIENTS WITH CIRRHOSIS: A NATIONWIDE ANALYSIS FROM THE NATIONAL INPATIENT SAMPLE

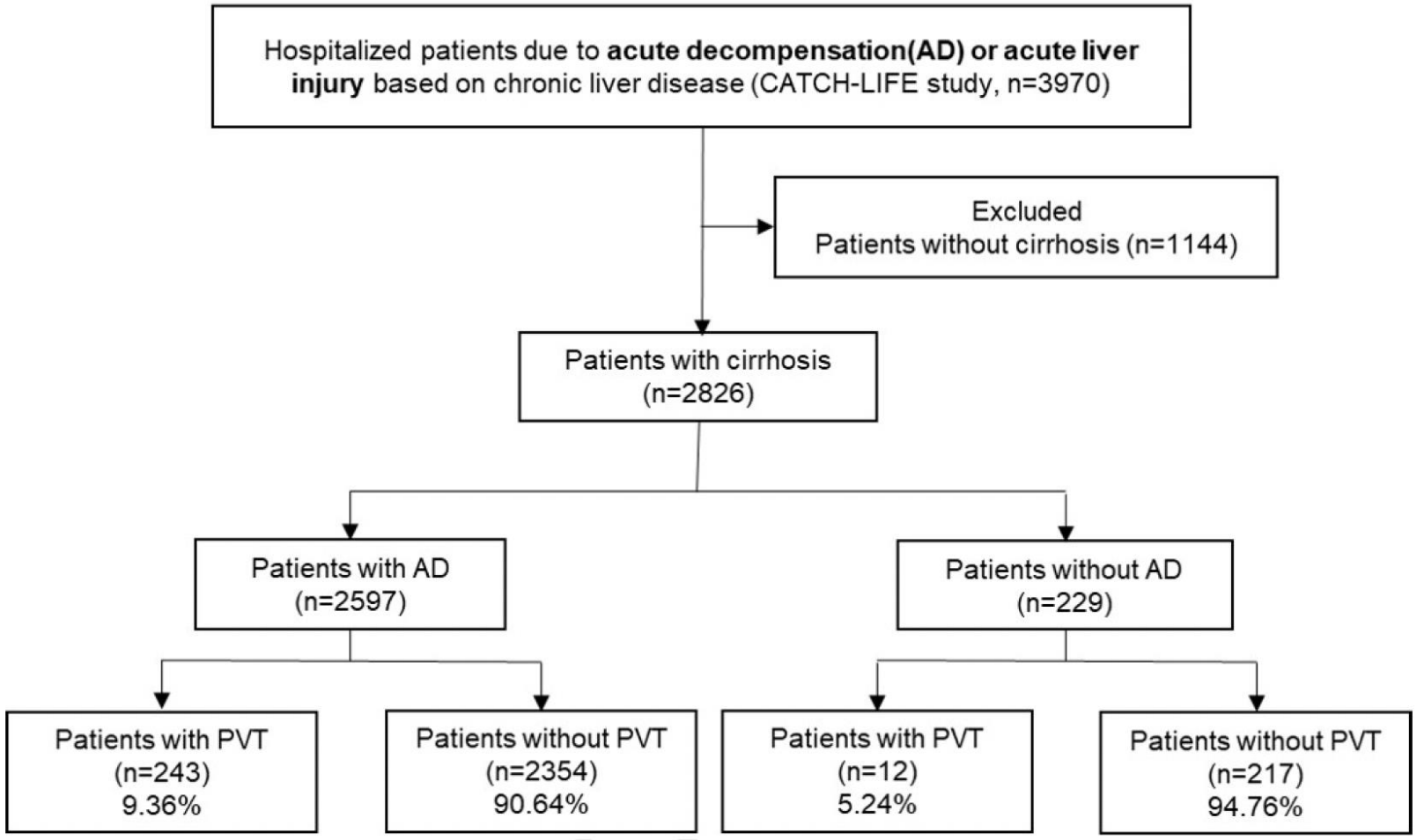
The prevalence of PVT among all inpatient admissions was 0.07% (n = 5046) and 1.8% (n = 2046) in patients with cirrhosis (P < .001)

PVT (7.7 vs 5.9 days, respectively; P < .05) and in-hospital mortality (9.5 vs 6%, respectively; P < .05).




Shah, J Hospital Medicine 2018

# AC AND PH BLEEDINGS




*Variceal bleeding (47.33% vs 19.63%; p<0.001) was significantly more commonly observed in patients with PVT*

Zhang, Clinical Gastroenterol Hepatol 2020

# PORTAL VEIN THROMBOSIS AND DECOMPENSATION

A total of 3 045 098 discharges were included, of which 1.5% had PVT. PVT prevalence increased from 0.7% to 2.4%, annual percent change of 9%.

**Table 4** Logistic regression for risk of renal complications in patients with decompensated cirrhosis

| | Acute kidney injury | | Hepatorenal syndrome | |
|---|---|---|---|---|
| | Adjusted OR | *P* value | Adjusted OR | *P* value |
| Portal vein thrombosis | 1.75 (1.67–1.83) | < 0.001 | 1.62 (1.52–1.72) | < 0.001 |
| Age | | | | |
| Female | | | | |
| Encephalopathy | | | | |
| Esophageal variceal bleed | | | | |
| Spontaneous bacterial peritonitis | | | | |

Parentheses indicate 95% confidence in

**Table 2** Logistic regression for risk of mortality in patients with decompensated cirrhosis

| | Unadjusted OR | *P* value | Adjusted OR† | *P* value |
|---|---|---|---|---|
| PVT | 1.17 (1.09–1.26) | < 0.001 | 1.12 (1.04–1.20) | < 0.001 |
| Age | 1.01 (1.01–1.01) | < 0.001 | 1.01 (1.01–1.01) | < 0.001 |
| Female | 0.95 (0.93–0.96) | < 0.001 | 0.92 (0.90–0.94) | < 0.001 |
| Ascites | 1.08 (1.06–1.10) | < 0.001 | 1.29 (1.26–1.32) | < 0.001 |
| Encephalopathy | 1.94 (1.91–1.98) | < 0.001 | 2.06 (2.02–2.10) | < 0.001 |
| Variceal bleed | 1.10 (1.04–1.18) | 0.02 | 1.40 (1.31–1.50) | < 0.001 |
| Spontaneous bacterial peritonitis | 2.70 (2.60–2.80) | < 0.001 | 2.73 (2.62–2.84) | < 0.001 |
| Socioeconomic quartile‡ | | | | |
| 2nd quartile | 1.05 (1.02–1.08) | < 0.001 | 1.03 (1.01–1.06) | 0.01 |
| 3rd quartile | 1.07 (1.04–1.10) | < 0.001 | 1.04 (1.02–1.07) | 0.001 |
| 4th quartile | 1.16 (1.13–1.19) | <0.001 | 1.11 (1.08–1.14) | < 0.001 |

†Adjusted for all variables included above, including socioeconomic quartiles.
‡The 1st socioeconomic quartile was the reference value.
Parentheses indicate 95% confidence intervals. OR, odds ratio; PVT, portal vein thrombosis.

Cool, EJG 2019

# METANALYSIS OLD STUDIES

| Study or subgroup | PVT Events | PVT Total | No PVT Events | No PVT Total | Weight | Odds ratio M-H, random, 95%CI |
|---|---|---|---|---|---|---|
| Englesbe *et al* | 81 | 148 | 1171 | 3147 | 54.8% | 2.04 (1.46, 2.84) |
| John *et al* | 24 | 70 | 64 | 220 | 29.7% | 1.27 (0.72, 2.26) |
| Maruyama *et al* | 9 | 42 | 21 | 108 | 15.4% | 1.13 (0.47, 2.72) |
| Total (95%CI) | | 260 | | 3475 | 100.0% | 1.62 (1.11, 2.36) |
| Total events | 114 | | 1256 | | | |

Heterogeneity: $Tau^2 = 0.04$; $\chi^2 = 2.96$, df = 2 ($P = 0.23$); $I^2 = 32\%$

Test for overall effect: $Z = 2.50$ ($P = 0.01$)

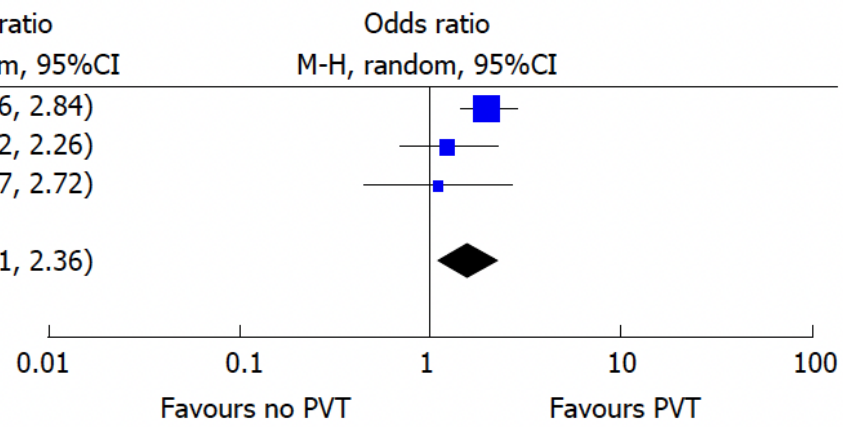



**Figure 3 Portal vein thrombosis and mortality.** PVT is associated with an increased pooled risk of death in the absence of significant heterogeneity. PVT: Portal vein thrombosis.

| Study or subgroup | PVT Events | PVT Total | No PVT Events | No PVT Total | Weight | Odds ratio M-H, fixed, 95%CI |
|---|---|---|---|---|---|---|
| John *et al* 2013 | 31 | 70 | 76 | 220 | 83.0% | 1.51 (0.87, 2.60) |
| Maruyama *et al* 2013 | 27 | 42 | 21 | 108 | 17.0% | 7.46 (3.38, 16.45) |
| Total (95%CI) | | 112 | | 328 | 100.0% | 2.52 (1.63, 3.89) |
| Total events | 58 | | 97 | | | |

Heterogeneity: $\chi^2 = 10.63$, df = 1 ($P = 0.001$); $I^2 = 91\%$

Test for overall effect: $Z = 4.17$ ($P < 0.0001$)

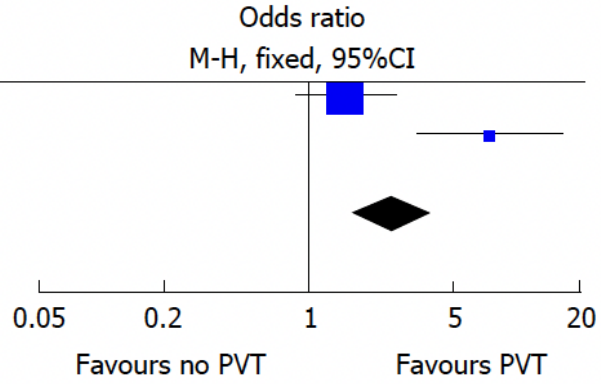
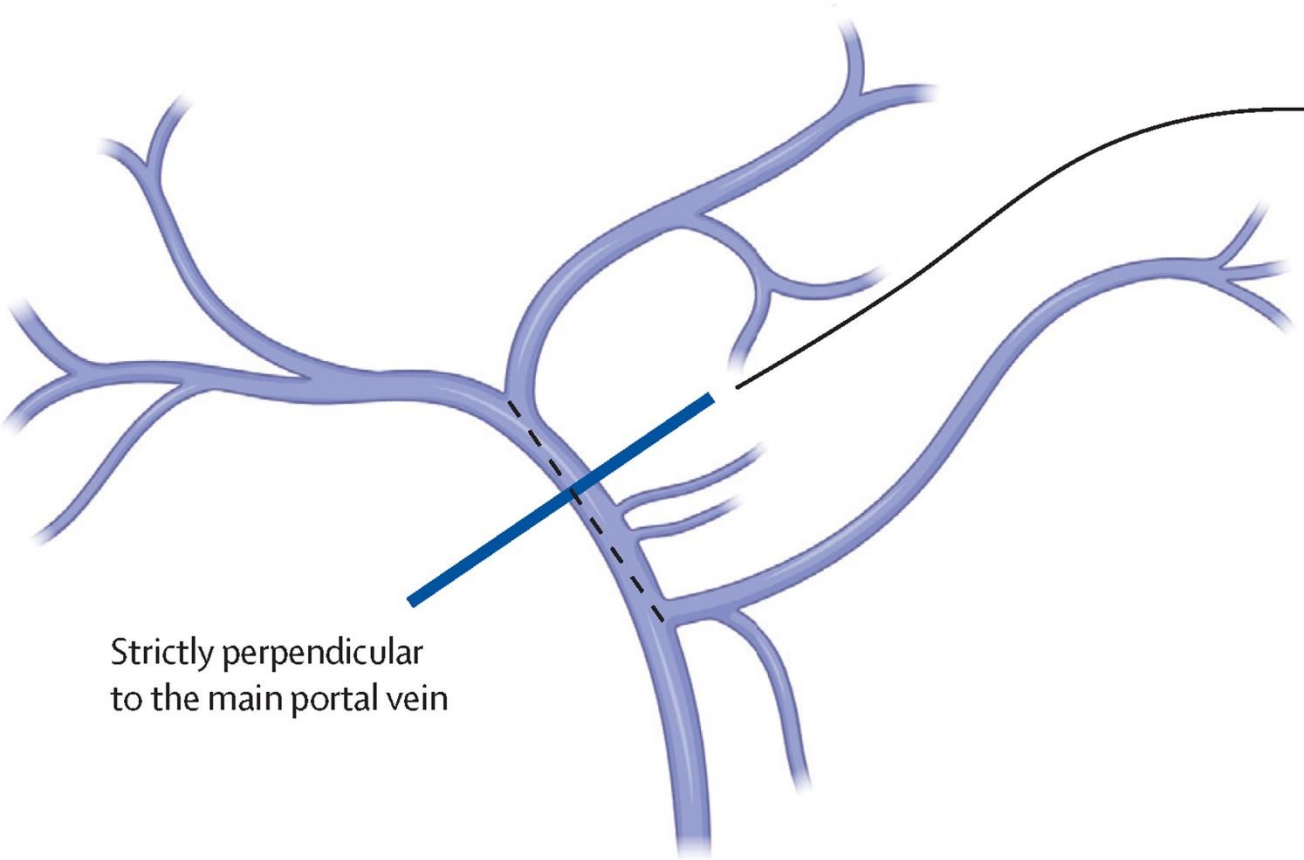
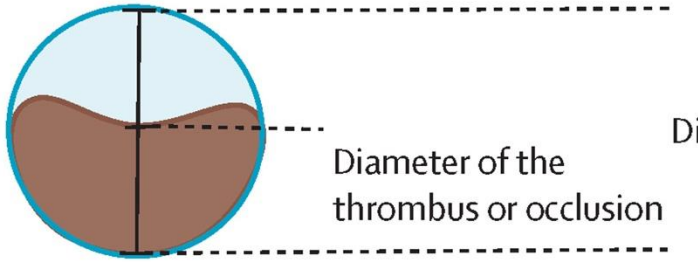


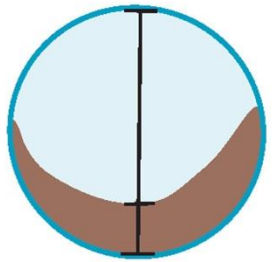

**Figure 4 Portal vein thrombosis and ascites.** PVT is associated with an increased pooled risk of hepatic decompensation manifested as ascites. This conclusion may be limited by heterogeneity in the included studies. PVT: Portal vein thrombosis.

# SIZE OF OCCLUSION MATTERS....

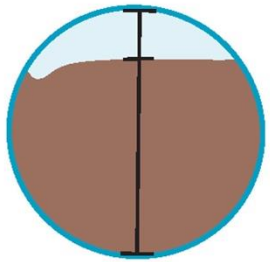


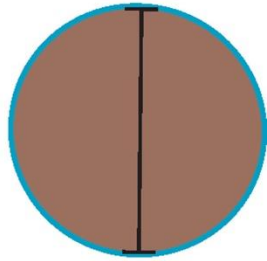

$$\%\ \text{of remnant lumen (\%RL)} = \frac{(\text{Main portal vein} - \text{thrombus})}{\text{Main portal vein}}$$



Minimal
%RL ≥50%



Partial
%RL <50



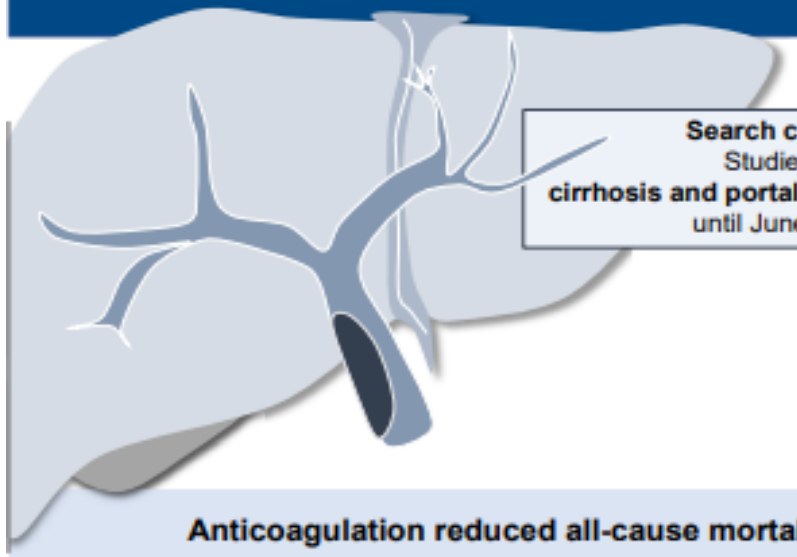
Complete
%RL=0%

Intrahepatic portal branches, the superior mesenteric vein, and splenic vein are assessed separately and semi-quantitatively (no occlusion, partial occlusion, or complete occlusion)

Elkief, Lancet Gastroenterol Hepatol 2023

# SIZE OF OCCLUSION MATTERS...

## The IMPORTAL competing-risk individual patient data meta-analysis



**Search criteria:**
Studies of
**cirrhosis and portal vein thrombosis**
until June 2020

**Selection**
✓ 5 studies
✓ 500 patients

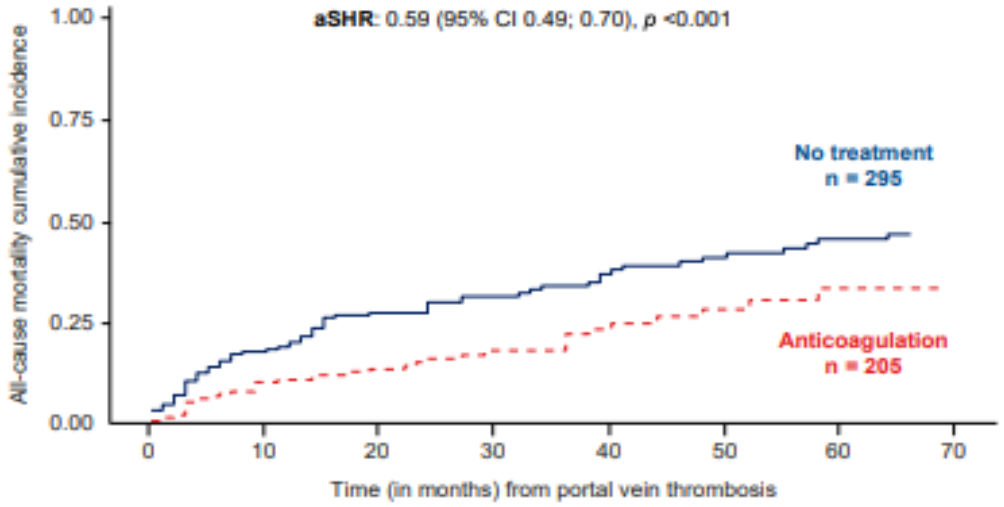
**Primary outcome:**
All-cause mortality

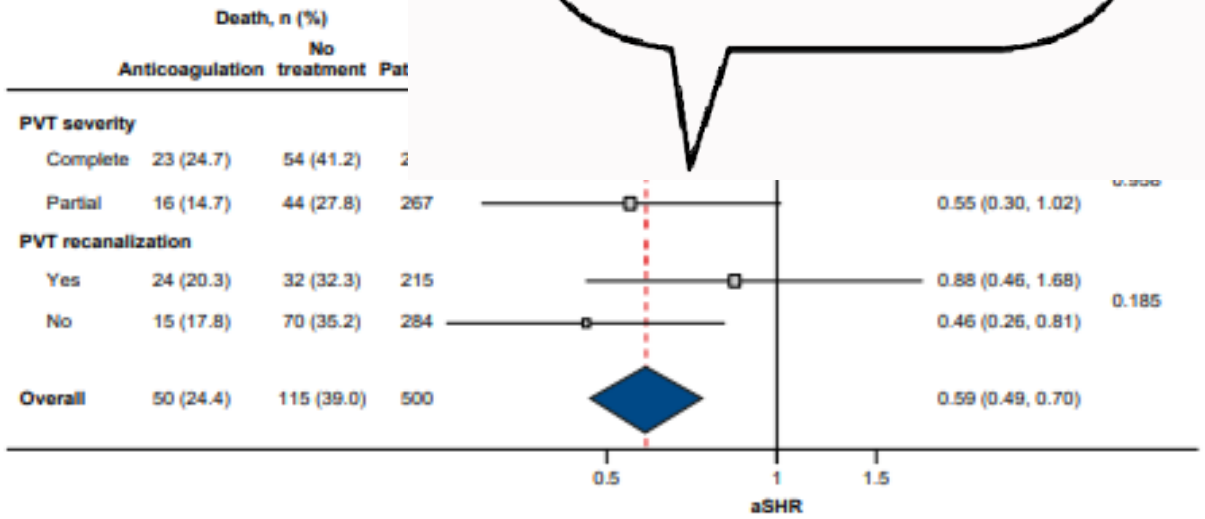
**Method:**
One-step meta-analysis
Competing-risk model with liver transplantation

**Anticoagulation** *vs.* **No treatment**



**Anticoagulation reduced all-cause mortality...** ...independentl




Yeah, but...

Guerrero et al. Journal of Hepatology 2023

# ROLE OF PVT VERSUS AC

**Table S9. Adjusted sub-hazard ratios (aSHR) of the final multivariable competing risk model analyzing the effect of anticoagulation on all-cause mortality**

| | aSHR | (95% confidence interval) | p-value |
|---|---|---|---|
| **Antithrombotic treatment** | 0.59 | (0.49; 0.70) | <0.001 |
| **Age at diagnosis** | 1.04 | (1.03; 1.05) | <0.001 |
| **MELD score** | 1.08 | (1.02; 1.15) | 0.010 |
| **Etiology of cirrhosis**, viral (*reference*) | | | |
| Alcohol | 0.78 | (0.43; 1.40) | 0.400 |
| Others | 0.82 | (0.60; 1.12) | 0.212 |
| **Use of beta-blockers** | 0.74 | (0.55; 0.99) | 0.048 |
| **Portal vein thrombosis location,** trunk of the portal vein (*reference*) | | | |
| Isolated intrahepatic branches | 0.74 | (0.37; 1.51) | 0.419 |
| Isolated mesenteric vein | 1.32 | (1.12; 1.57) | 0.001 |
| **Complete portal vein thrombosis** | 1.91 | (1.62; 2.25) | <0.001 |

Guerrero et al. Journal of Hepatology 2023

# EVOLUTION OF PVT AND DECOMPENSATION

**Table 2: Correlation between the natural course of partial portal vein thrombosis and clinical evolution**

| Parameter | Stable/improved (*n*=16) (%) | Worsened (*n*=6) (%) | *P* value |
|---|---|---|---|
| Esophageal varices (size) | | | |
| Small | 2 (12.5) | 1 (16.6) | 0.230 |
| Medium | 8 (50.0) | 1 (16.6) | <0.0001 |
| Large | 6 (37.5) | 4 (66.6) | <0.0001 |
| Variceal bleeding | 5 (31.2) | 5 (83.3) | <0.0001 |
| Refractory ascites | 6 (37.5) | 4 (66.6) | <0.0001 |

Girleanu, 2014

# EVOLUTION OF PVT AND DECOMPENSATION/MORTALITY

*Characteristics of 42 Patients with Cirrhosis and Nonmalignant, Partial PVT*

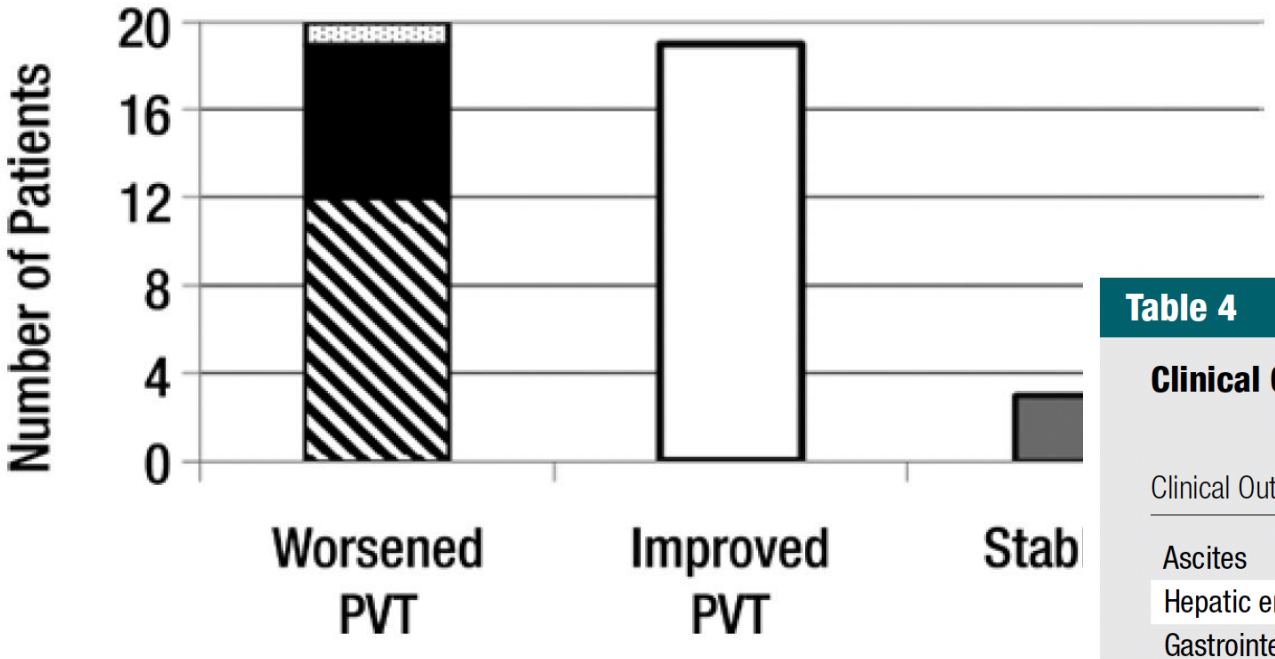



**Table 4**

**Clinical Outcome in Relation to Evolution of Partial PVT**

| Clinical Outcome | Improved PVT ($n = 19$)* | Increased or Stable PVT ($n = 23$)* | *P* Value |
|---|---|---|---|
| Ascites | 14 | 12 | .213 |
| Hepatic encephalopathy | 6 | 9 | .751 |
| Gastrointestinal variceal bleeding | 4 | 4 | .99 |
| Spontaneous bacterial peritonitis | 1 | 3 | .612 |
| Hepatocellular carcinoma | 6 | 2 | .111 |
| Hepatic decompensation | 13 | 14 | .756 |
| Admission for hepatic decompensation | 12 | 11 | .374 |
| Liver transplantation | 5 | 3 | .435 |
| Off transplant waiting list | 10 | 13 | .99 |
| Added to transplant waiting list | 4 | 5 | .99 |
| Death | | | .176 |

15% versus 39%

* Data are number of patients.

Luca et al,

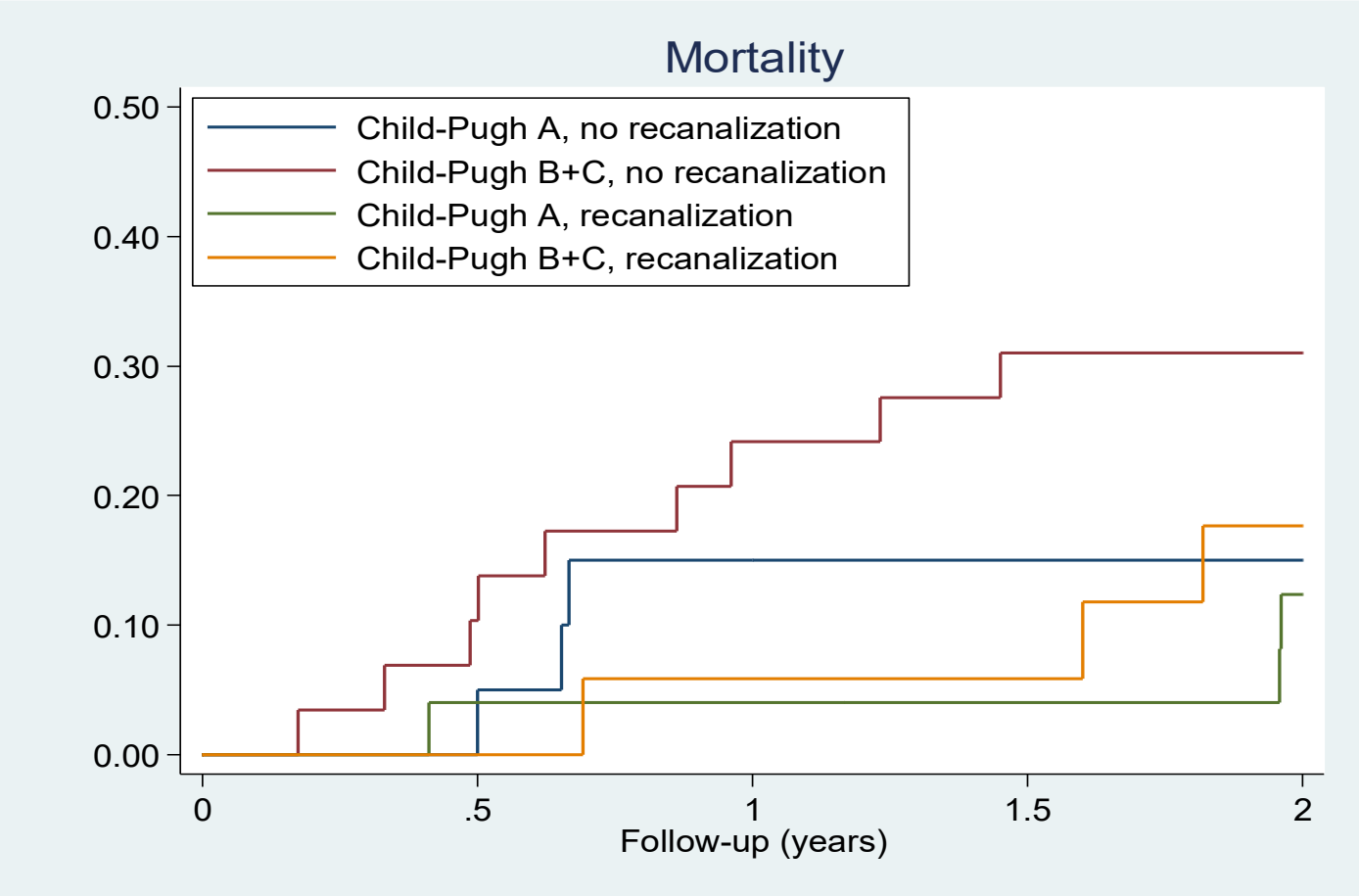
# EVOLUTION OF PVT AND MORTALITY

- 16 cohort studies
- Cirrhosis presenting with PVT have a lower 1-year survival rate than patients without PVT (odds ratio (OR), 0.32; 95% confidence interval (CI), 0.14–0.75; P=.008).
- PVT was associated with a higher mortality rate in patients with Child-Pugh class >B disease.
- A significantly increased risk of death was observed in patients with complete PVT.
- Patients with both PVT and cirrhosis had a higher rate of decompensation than patients without PVT.

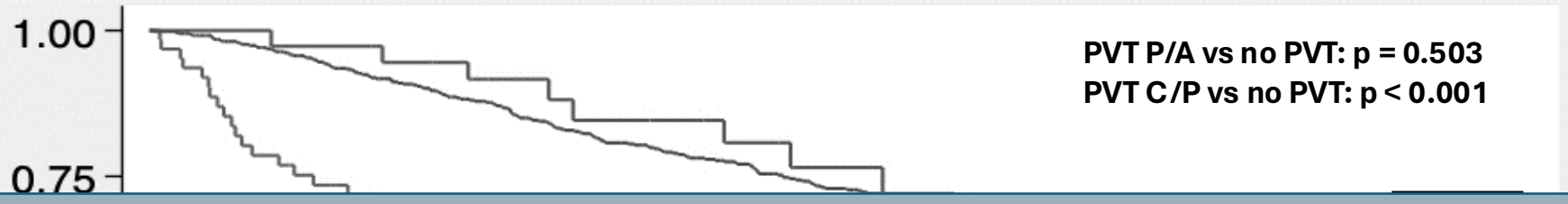
# EVOLUTION OF PVT AND MORTALITY

98 patients had available imaging that evaluated the abdominal vessels during follow-up,

61 (out of 98, 62.2%) had more than one imaging test



# EVOLUTION OF PVT AND MORTALITY




## Multivariate analysis

**Complete/progressive PVT vs no PVT** (HR 3.41, 95%CI 2.46-4.71, p= <.0001)

Child-Pugh score B/C vs A (HR 1.89, 95%CI 1.47-2.43, p= <.0001)

AFP (HR 1.24, 95%CI 1.1-1.39, p= <.0001)

TTV at PVT diagnosis (HR 1.14, 95%CI 1.09-1.2, p= <.0001)

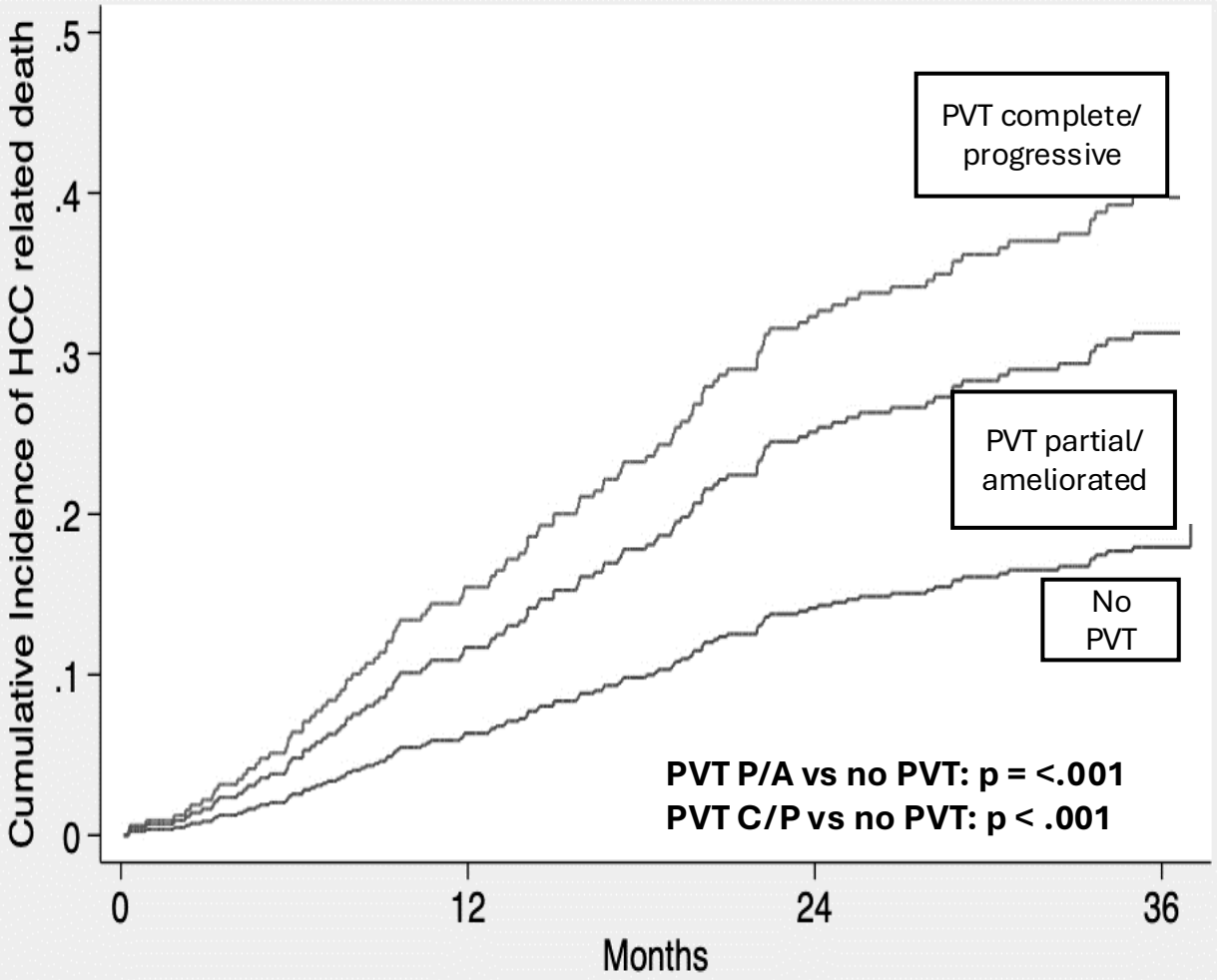
Number of nodules at PVT diagnosis (HR 1.23, 95%CI 1.1-1.39, p= <.0001)

| Number at risk | | | | |
|---|---|---|---|---|
| **No PVT:** | | | | |
| **PVT Partial/Ameliorated:** | 65 | 26 | 13 | 2 |
| **PVT Complete/Progressive:** | 37 | 24 | 13 | 4 |

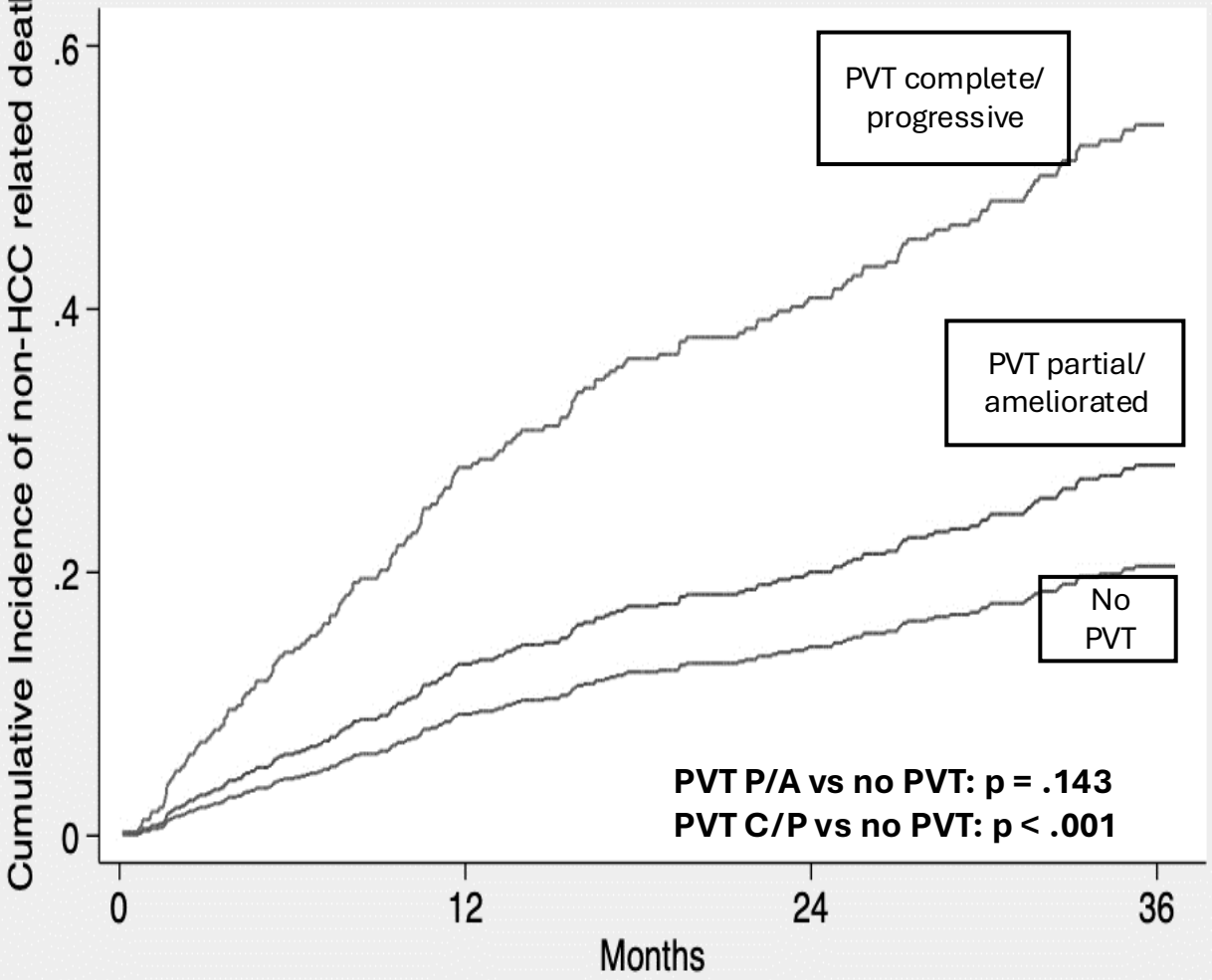
Senzolo et al. Hepatology 2024

# EVOLUTION OF PVT AND MORTALITY

A)




B)



# STILL AN OPEN QUESTION

- Bleeding seems to be the most common decompensating event
- Degree of occlusion matters
- Analysis of evolution is important
- Interaction with severity of liver disease and PH
- Standardized protocol of follow-up
- Interaction with effect of AC per se