VALDIG
VASCULAR LIVER DISEASE GROUP

AFEF
SOCIETÉ FRANÇAISE D'HÉPATOLOGIE

Paris Portal Vein Thrombosis Meeting

Wednesday Novembre 30 2022

Session 6: Consensus discussion : endpoints for studies in portal vein thrombosis

Classification of portal vein thrombus extension

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Question

Why bother classify ?

Define / describe the structure and relationship of groups of similar objects

Given two patients, determine if they are equivalent

Practical goals: manipulate and make sense

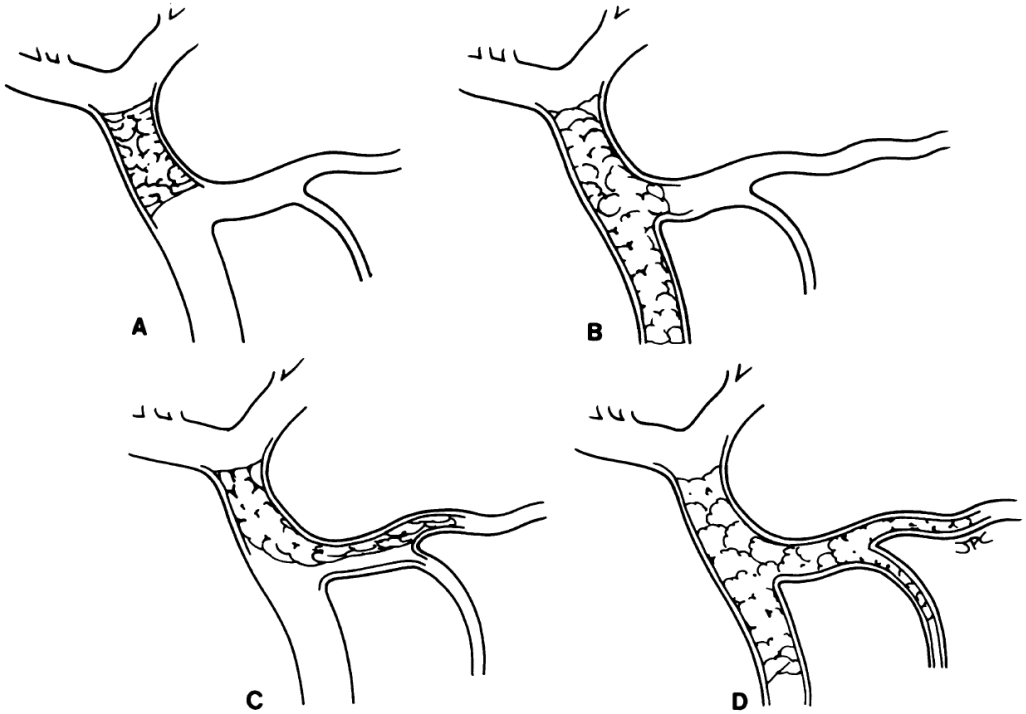
Standardization and **comparability**: reporting and trials

Generation of **scientific hypotheses**: improve scientific knowledge

Sokal Science 1974

How should we classify ?

34 patients undergoing OLT



According to the site of PVT

Typology based on anatomy

OLT patients

Context of use

Endpoint: post-OLT survival

Choice of endpoint

Stieber Ann Surg 1991

How should we classify ?

885 patients undergoing OLT
Severity of PHT

Grade 1 = Intrahepatic (segmental) PV branches
partial (>50% in diameter) or total

Grade 2 = Right or left PV branch or near the bifurcation of the main PV
partial (>50% in diameter) or total

Grade 3 = partial (>50% in diameter) occlusion of the main PV

Grade 4 = complete / near complete (> 90%) occlusion of the main PV + SMV/SV

Degree of occlusion

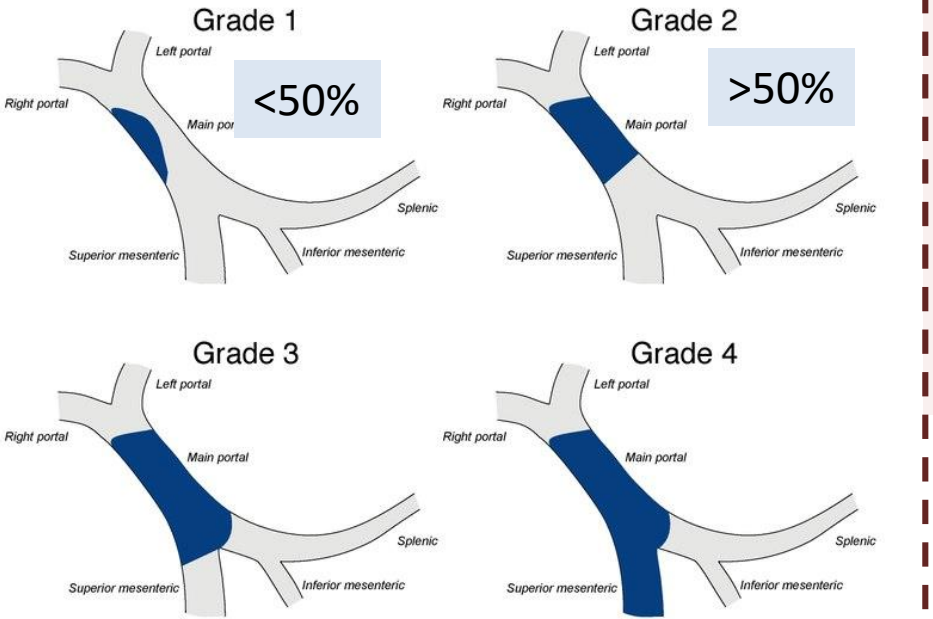
Scales and labels

Nonami Hepatology 1992

How should we classify ?

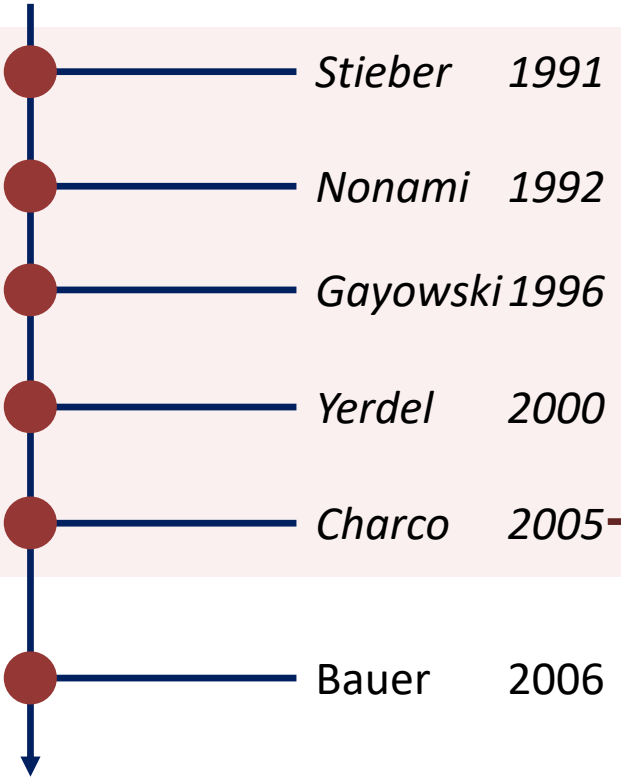
- *Stieber* *1991*
- *Nonami* *1992*
- *Gayowski* *1996*
- *Yerdel* *2000*
- *Charco* *2005*

Patients presenting for OLT



Yerdel Transplantation 2000

How should we classify ?



Patients presenting for OLT

1) confined to the PV (partial or complete)
2) extending to the proximal SMV
3) diffuse thrombosis of the splanchnic system + **dilated collateral veins**
4) diffuse thrombosis with presence of **fine collateral veins**

Cavernoma

Charco Transplant Proc 2005

How should we classify ?

First series dedicated to patients not necessarily undergoing LT

9 patients undergoing TIPS before OLT
Transplantation, dropout or death

- <25% occlusion of PV
- 26%-50% occlusion
- 51%-75% occlusion
- 76%-100% occlusion

Stratified by location of clot
and presence of cavernous transformation

TABLE 2. Pre-TIPS Degree of Thrombosis in the Main Portal Vein, SMV, and Splenic Vein

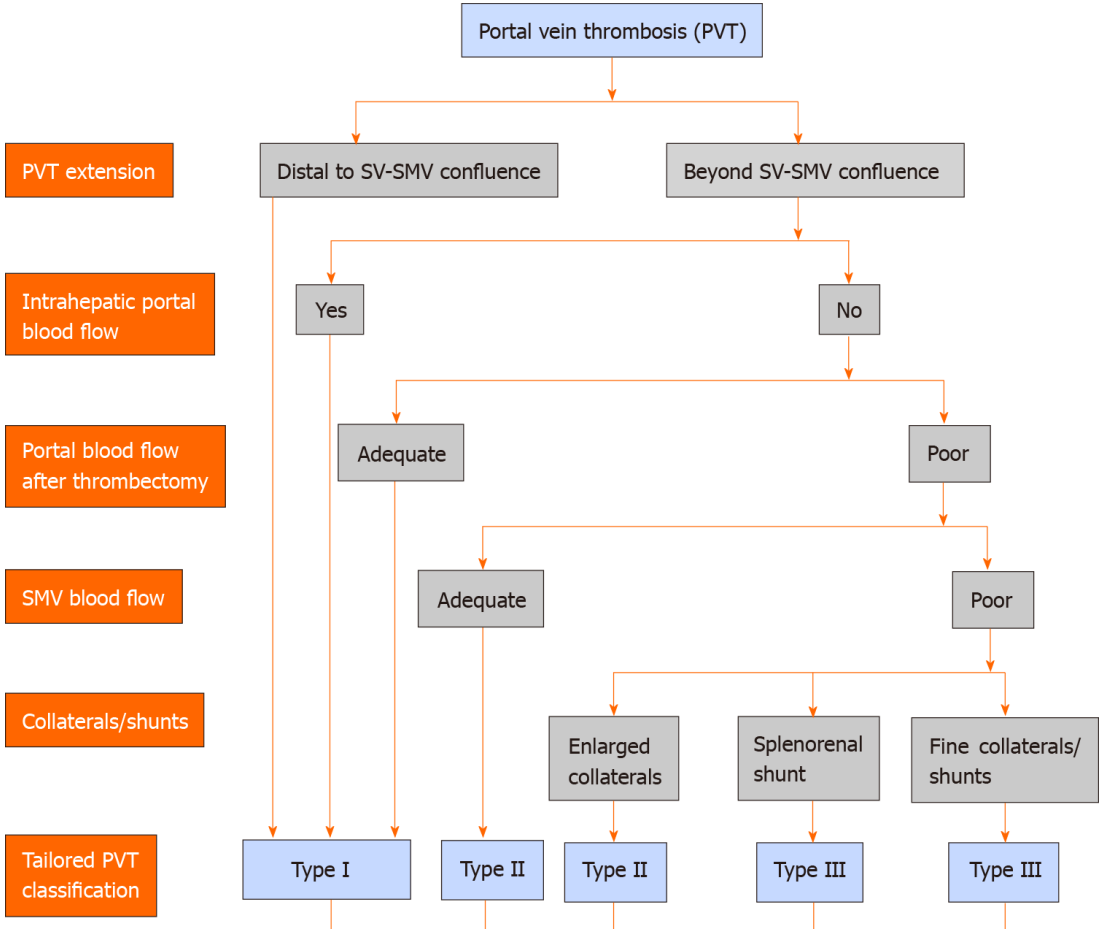
PT	MPV	SMV	SV	Cavernous Transformation
1	Grade IV	Grade II	Patent	Yes
2	Grade II	Grade IV	Patent	No
3	Grade IV	Grade IV	Grade II	Yes
4	Grade III	Grade III	Patent	No
5	Grade IV	Patent	Grade II	No
6	Grade II	Grade II	Patent	Yes
7	Grade IV	Grade III	Patent	Yes
8	Grade IV	Grade IV	Grade IV	No
9	Grade IV	Patent	Grade IV	No

Abbreviations: PT, patient; MPV, main portal vein; SMV, super mesenteric vein; SV, splenic vein.

Bauer Liver Transplantation 2006

How should we classify ?

Taxonomy



Teng WJ Gastro 2022

Other context, other classification

15 non-cirrhotic patients
Feasibility of PV recanalization

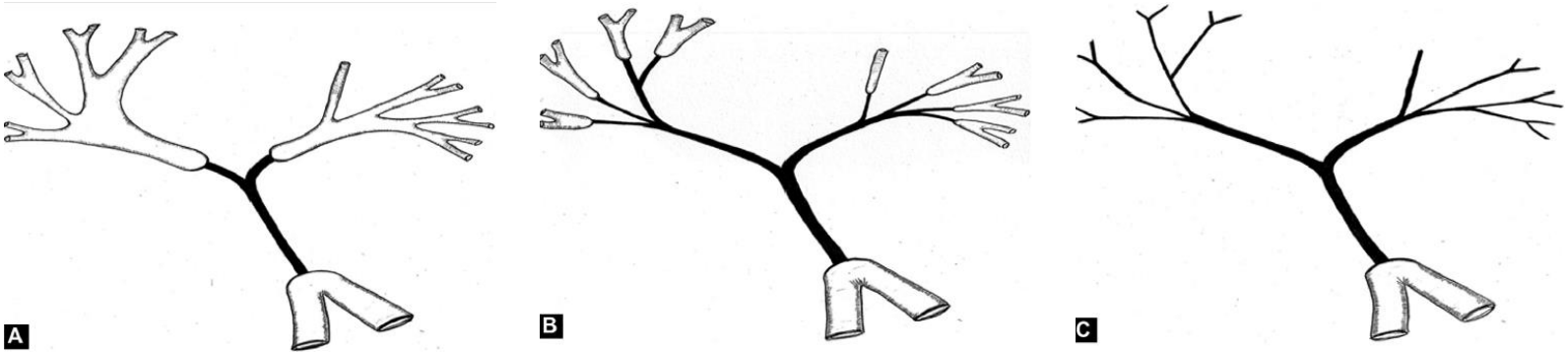


Table 3 Success and thrombosis rates following portal vein recanalization for portal vein occlusion in 15 non-cirrhotic patients.

Classification of PVO[a]	Feasibility of PVR (*n* feasible/*n* total; %)	Early (≤ 24 hours) stent thrombosis (*n* thrombosi/*n* performed; %)	Stent thrombosis at 2 years (*n* thrombosis/n performed; %)
Type 1	6/6 (100)	0/6 (0)	0/6 (0)
Type 2	6/7 (86)	0/6 (0)	2/6 (33)
Type 3	1/2 (50)	1/1 (100)	—

Marot Diag Interv Imaging 2018

Why focus on the anatomy ?

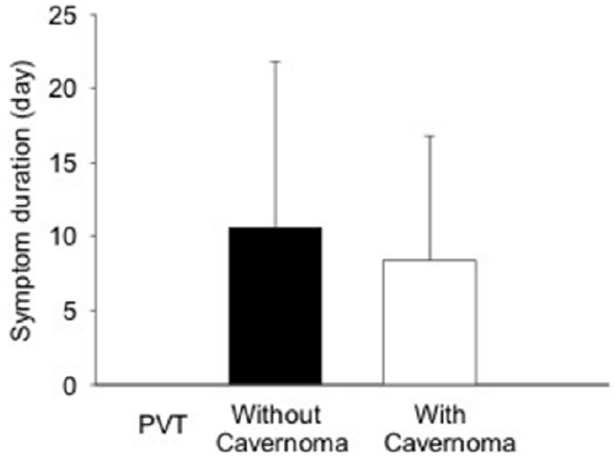
First series questioning the value of anatomical PVT classifications

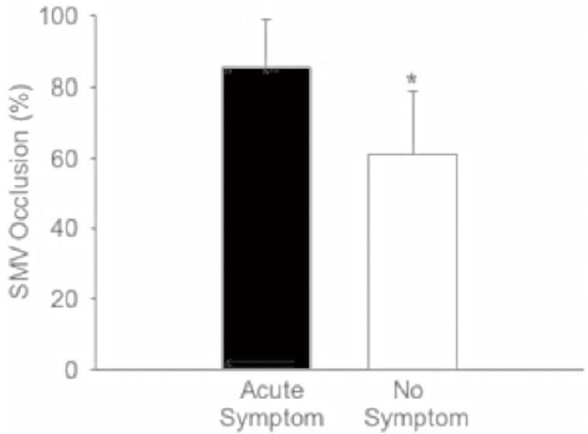
60 patients

Non-transplant cohort

Clinical classification

- Duration of clot
- Presence of symptoms
- Degree of portal hypertension





Ma PLoS One 2014

Question

Why focus on anatomy?

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Non-transplant cohort

Table 4. Relationship of complications of portal hypertension with PVT, cavernoma and cirrhosis.

	Complications	No complications	P
	n = 27	n = 33	
PVT			
Partial	18 (66.7)	20 (60.6)	0.789
Complete	9 (33.3)	13 (39.4)	
Cavernoma			
No	11 (40.7)	18 (54.5)	0.312
Yes	16 (59.3)	15 (45.5)	
Cirrhosis			
No	8 (29.6)	27 (81.8)	<0.001
Yes	19 (70.4)	6 (18.2)	

Ma PLoS One 2014

Question

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Table 4. Relationship of complications of portal hypertension with PVT, cavernoma and cirrhosis.

		No comp	
		n = 33	
PVT			
Partial		20 (60.6)	
Complete		13 (39.4)	
Cavernoma			
No		18 (54.5)	
Yes		15 (45.5)	
Cirrhosis			
No		27 (81.8)	1
Yes	19 (70.4)	6 (18.2)	

Simple classification

Partial wo cavernoma

Partial with cavernoma

Complete wo cavernoma

Complete with cavenoma

What endpoint ?

PV burden decrease

PV recanalization

Symptoms

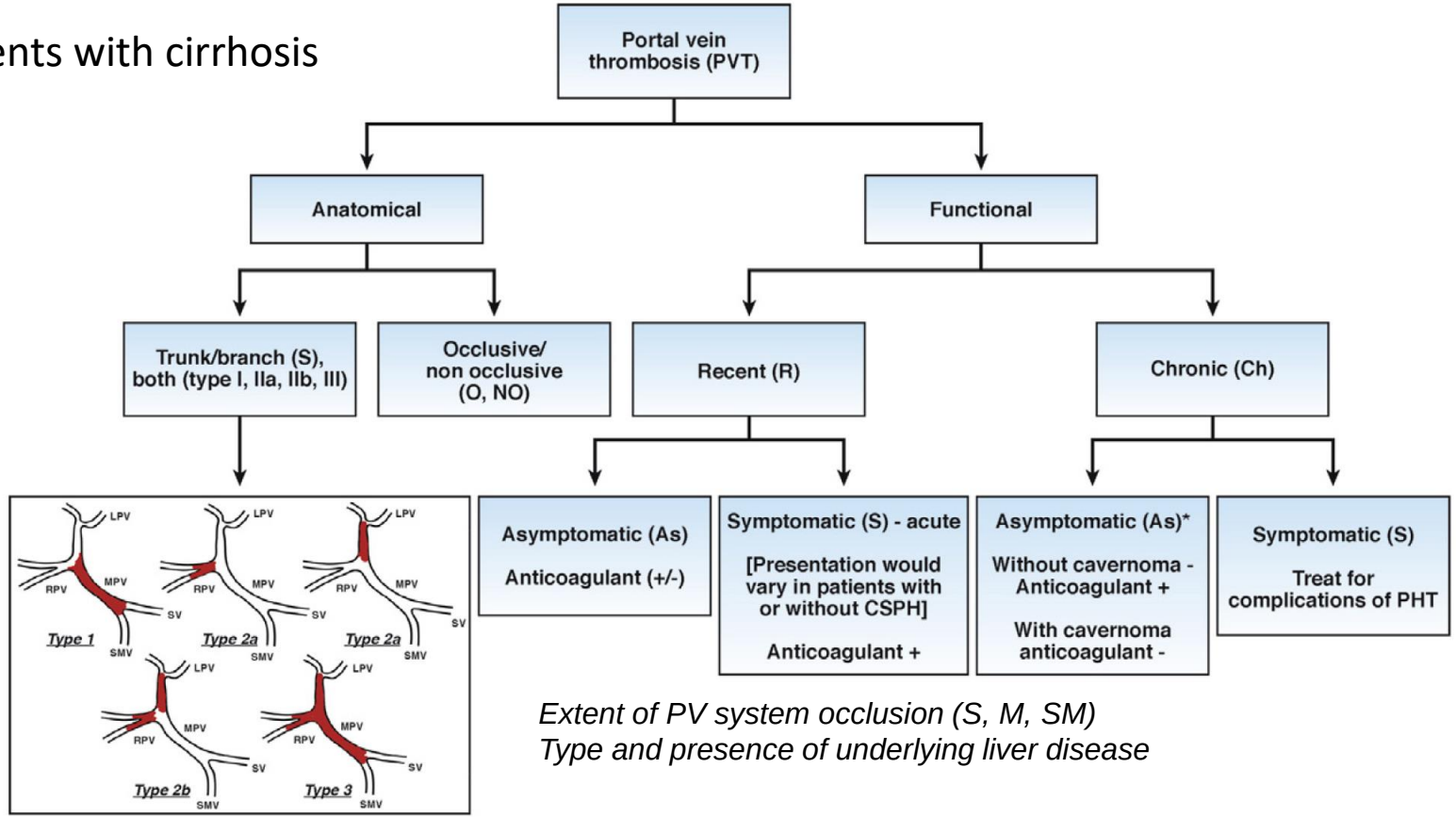
PHT

Other?

Ma PLoS One 2014

Complete (complex?) classification

Patients with cirrhosis

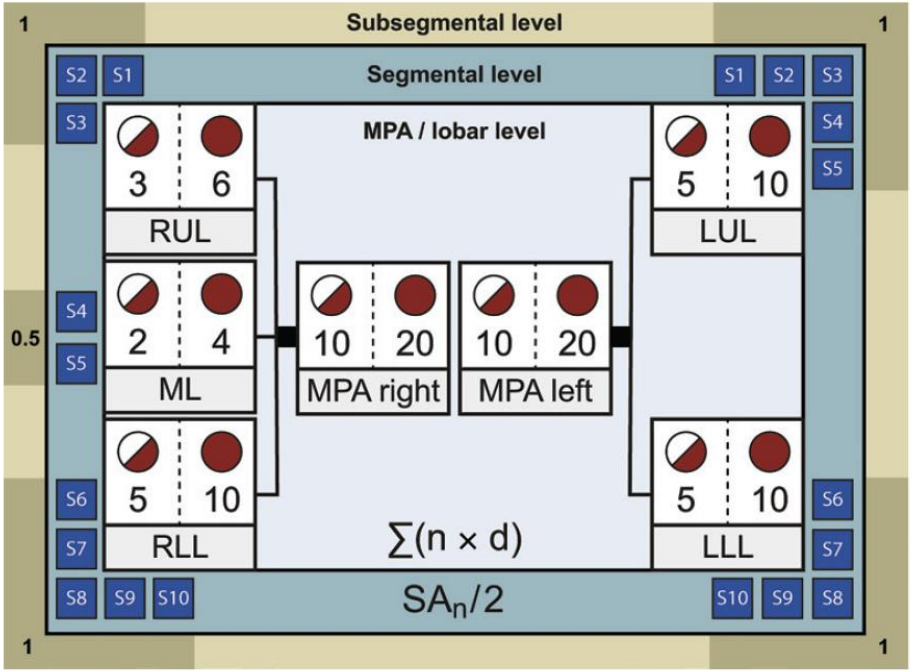


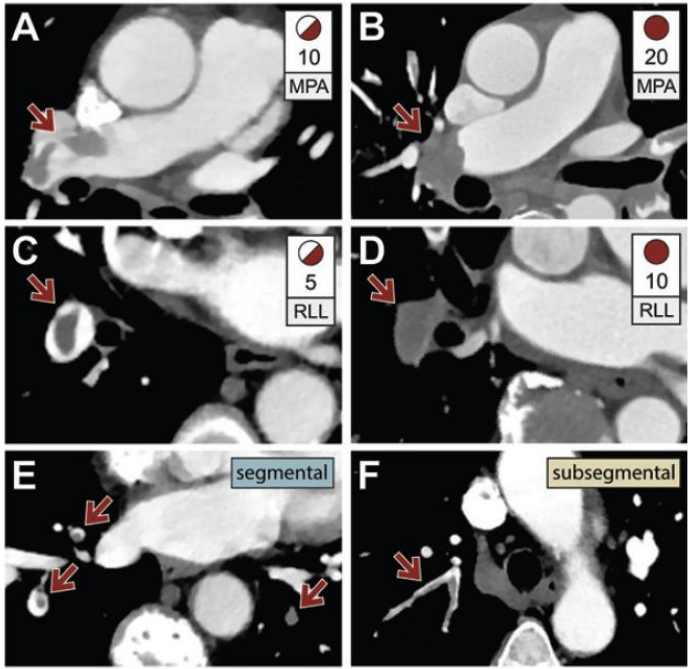
Extent of PV system occlusion (S, M, SM)
Type and presence of underlying liver disease

Sarin Gastroenterology 2016

Clot Burden Score

Semi-quantification or quantification of the clot burden
Associated with prognosis and outcomes

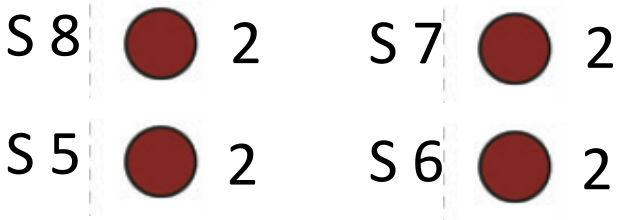


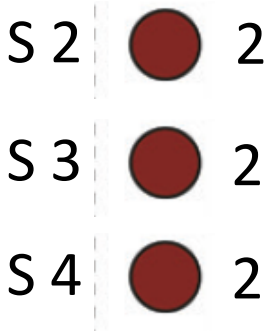


Tan AJNR 2008, Fink Radiology 2022

Opening

Clot Burden Score





Right Portal Branch

Left Portal Branch

Main Portal Vein

Clot Burden Quantification

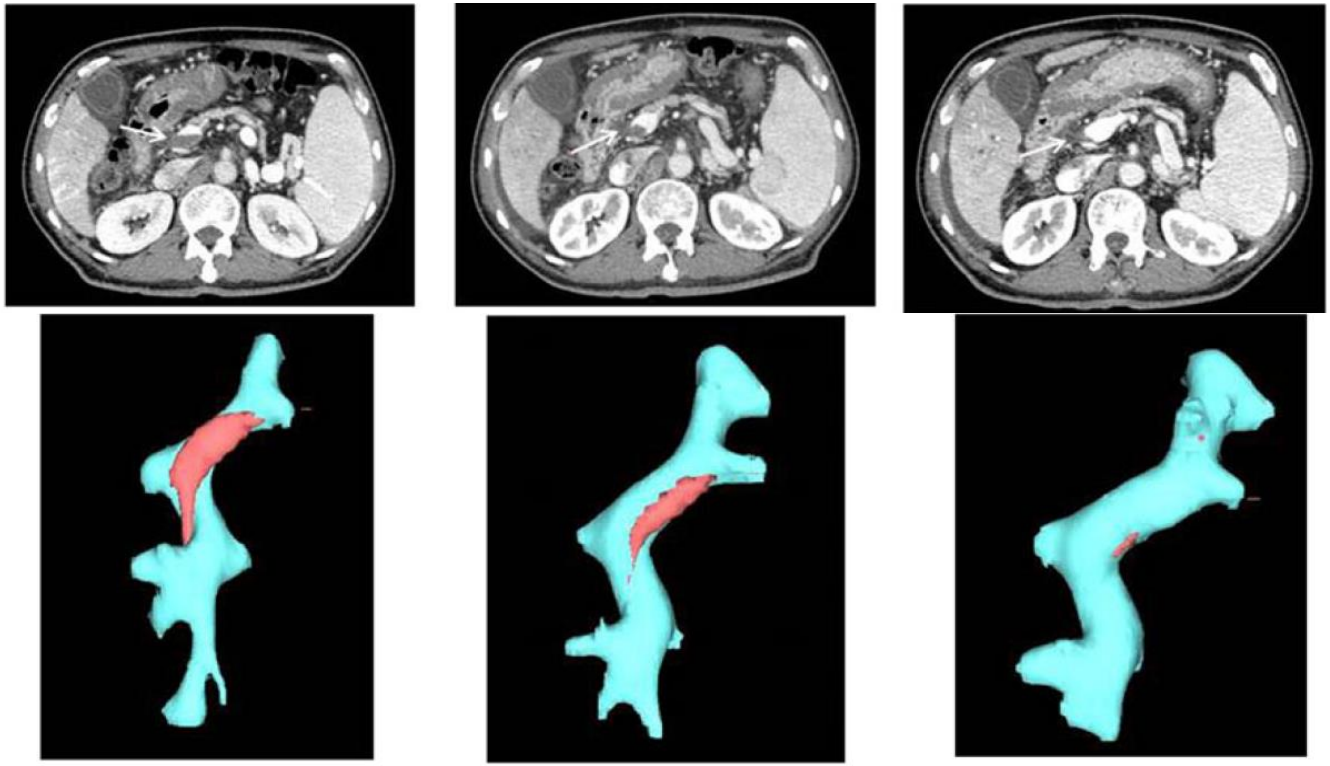
RCT 36 vs. 37 patients with PVT in patients with liver disease
AT III

PVT	Characteristic	AT-III ($n = 36$)	Placebo ($n = 36$)	P- value
Thrombosis location	Portal vein trunk	14 (38.9)	20 (55.6)	0.379
	Separate branch of the portal vein	16 (44.4)	11 (30.6)	
	Splenic vein	1 (2.8)	0 (0.0)	
	Superior mesenteric vein	5 (13.9)	5 (13.9)	
PVT occurrence at diagnosis	≤1 month	3 (8.3)	6 (16.7)	0.750
	≤3 months	15 (41.7)	12 (33.3)	
	≤6 months	18 (50.0)	18 (50.0)	
PVT measurements	Cross-sectional area, mm^2	113.71 (29.3–318.9)	135.38 (36.1–362.3)	.240
	Thrombus occupancy in the lumen, %	52.18 (19.0–100)	66.78 (17.3–100)	.047
	Volume, cm^3	2665.15 (302.4–22961.6)	3234.93 (218.5–20653.5)	.60
	Length, mm	52.70 (9.4–253.0)	72.10 (15.7–206.5)	.184

Hidaka Hepatology Research 2018

Clot Burden Quantification

Suitable endpoint for patients with PVT treated with medical treatments?

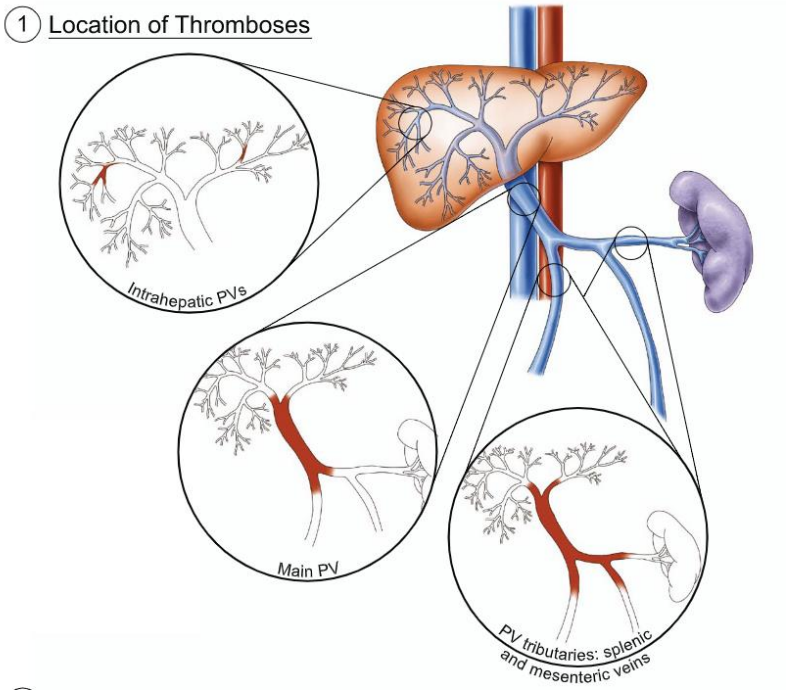


Hidaka Hepatology Research 2018

Guidelines

Surprizingly poor…

Descriptor	Definition
Time course	
Recent	PVT presumed to be present for <6 months
Chronic	PVT present or persistent for >6 months
Percent occlusion of main PV	
Completely occlusive	No persistent lumen
Partially occlusive	Clot obstructing >50% of original vessel lumen
Minimally occlusive	Clot obstructing <50% of original vessel lumen
Cavernous transformation	Gross portoportal collaterals without original PV seen
Response to treatment or interval change	
Progressive	Thrombus increases in size or progresses to more complete occlusion
Stable	No appreciable change in size or occlusion
Regressive	Thrombus decreases in size or degree of occlusion



De Franchis J Hepatol 2022, Northup Hepatology 2021

Debate

Proposition for the discussion

1. **Anatomical classifications make sense in surgical cohorts**
   Based on technical considerations
   Focus on the main PV and tributaries *Yerdel et al. 2000*

2. **Anatomical classifications make sense before PV recanalization**
   Based on technical considerations
   Focus on the intrahepatic PV branches
   Importance of inflow (SV-SMV) *Marot et al. 2018*

3. **Strictly anatomical classifications make little sense before med treatment**
   Poor correlation with symptoms and clinical outcomes

Ma et al. 2014

Proposition for the discussion

4. **Anatomical description valuable for population description**
   what level of granularity?
   Baveno/AASLD or Sarin et al. ?

5. **Clinically relevant (simpler) classifications for trials?**
   Complete vs. incomplete
   Cavernoma vs. no cavernoma
   Symptoms
   Age of thrombus *Ma et al. 2014*

6. **Future direction: Clot burden for trials?**

Future research
Location / extension / age
Vs. Symptoms
Vs. recanalization rate
Vs. PHT
VS. PHT complications

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