Portal vein thrombosis & liver transplantation
Evidence-based strategies for management

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Nothing to disclose

Portal vein thrombosis & liver transplantation

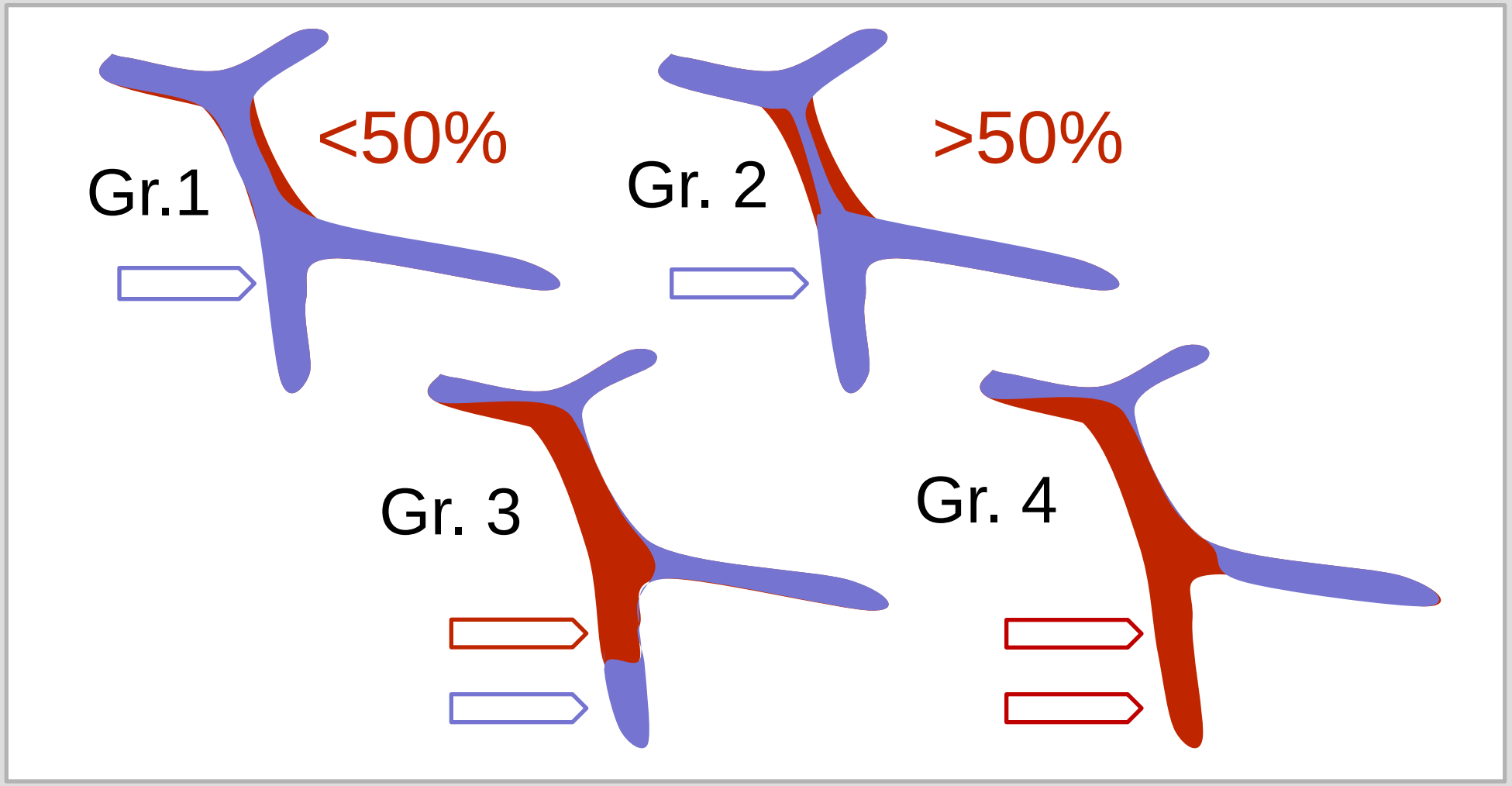
- Epidemiology
- Impact
- Treatment

Extrahepatic portal vein thrombosis in cirrhosis at liver transplantation

Prevalence	7.3% (2%-26%)
Incidence	7%-16% p.yr
% Partial/Occlusive	76%/24%
% Regressive	40% (31%-71%)
% Diagnosed at LTx	30%-50%

Ponziani, Transplant Rev 2014. Francoz, J Hepatol 2014. Harding, WJG 2015

Classification for portal vein thrombosis

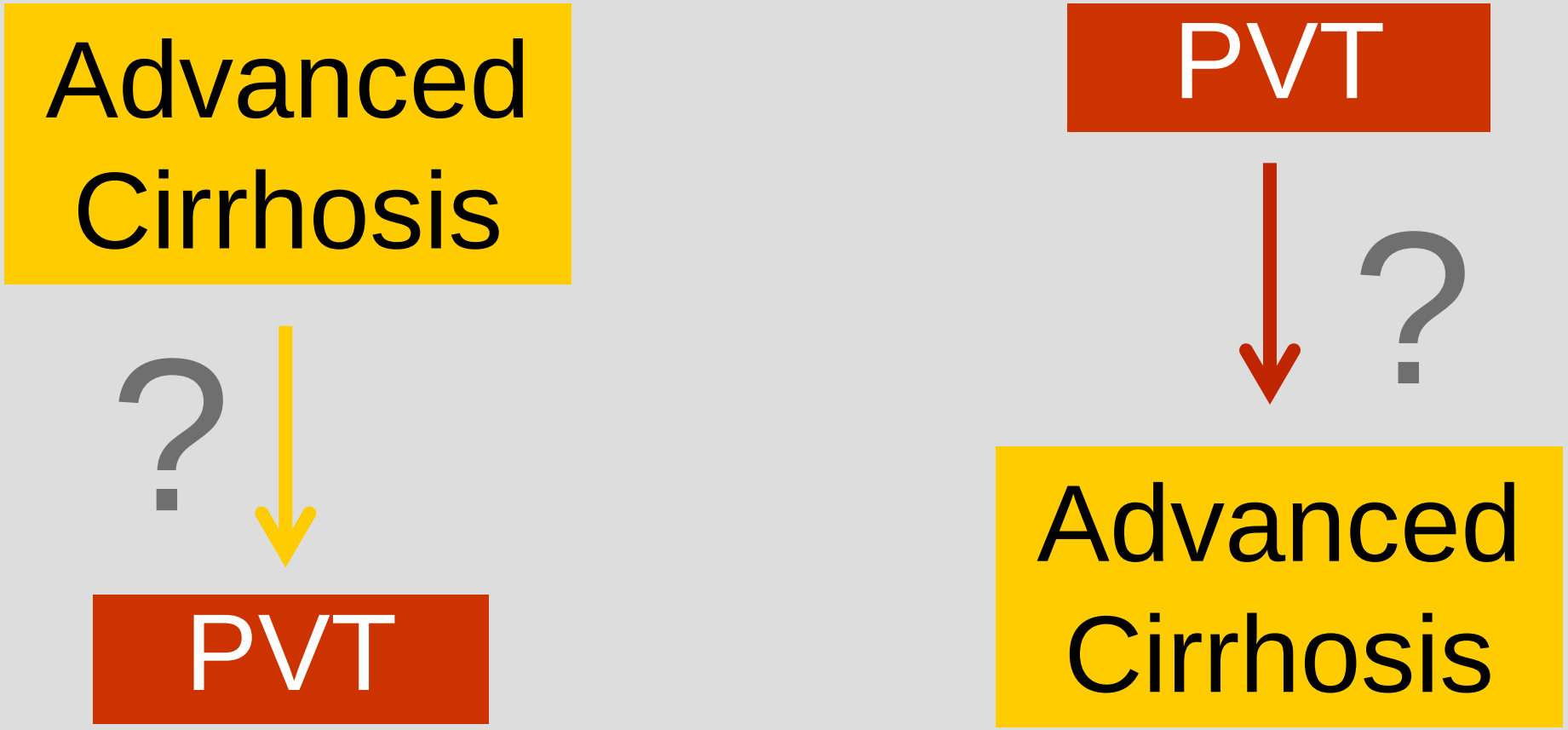


Adapted from Yerdel, Transplantation 2000

PVT is associated to cirrhosis severity in cross-sectional studies

- Small liver
- High Child-Pugh/MELD scores
- Severe portal hypertension
  size of varices, previous bleeding or treatment for bleeding, ascites, encephalopathy, low platelets
- Hepatocellular carcinoma
- Diabetes

Wanless, Hepatology 1995. Shimamatsu, Hepatology 1997.
Rodriguez-Castro, Transplantation 2012. Nery, Hepatology 2015


Advanced Cirrhosis
?
PVT
PVT
?
Advanced Cirrhosis

PVT and decompensation of cirrhosis

Multivariate, time-dependent analysis in THROMBOCIR

- Decompensation related to

Baseline esophageal varices & prothrombin

Not de novo PVT

- Portal vein thrombosis related to

Baseline esophageal varices & prothrombin

Not de novo ascites

Nery, Hepatology 2015

Relation of PVT with mortality is unclear in non-liver transplant patients

PVT not independently related with

- 5-day, 6-week and 1-year mortality
- overal mortality after surgical shunt or TIPS

PVT might be independently related with

- increased 3-yr mortality (abstract)
- Increased overall mortality (gastric VB, 2 studies)

Qi, Gastroenterol Res Pract 2015

PVT might be associated with decreased pretransplant mortality

UNOS + SSDMF registries (2002-2013)

Cirrhosis without HCC	66,506
PVT at listing	2207
Adjusted HR for death	0.88 *

* 95%CI, 0.81-0.96

Berry, Clin Gastroenterol Hepatol 2015

In a meta-analysis of 3 cohort studies (Stine, WJG 2015):
Unadjusted HR for death 1.62 [95% CI, 1.11-2.36]

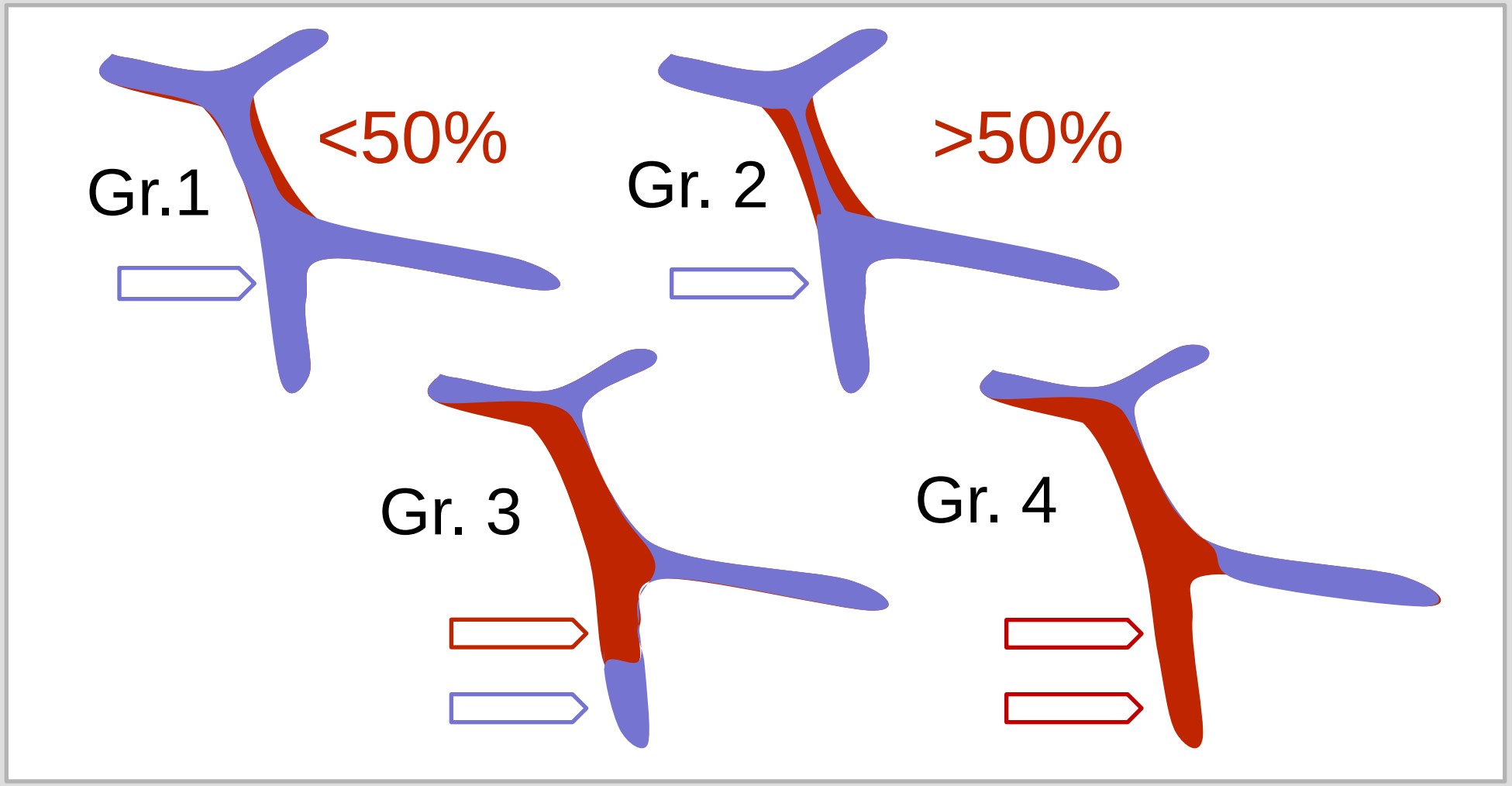
Extrahepatic portal vein thrombosis in cirrhosis without/before transplantation

Associated with severity in cross-sectional studies

PVT and decompensation share risk factors but are not directly related

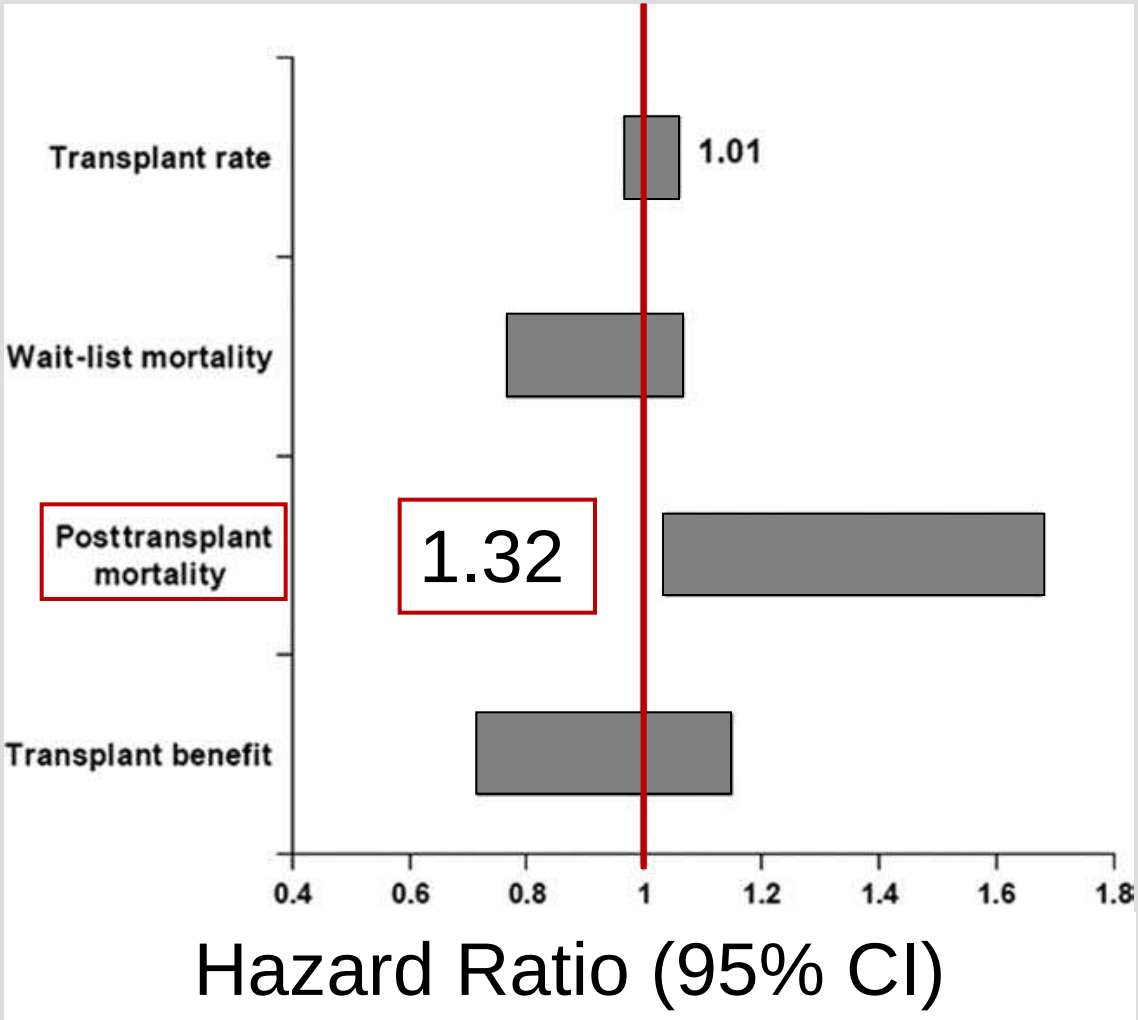
Independent impact on mortality inconsistent

Classification for portal vein thrombosis



Adapted from Yerdel, Transplantation 2000

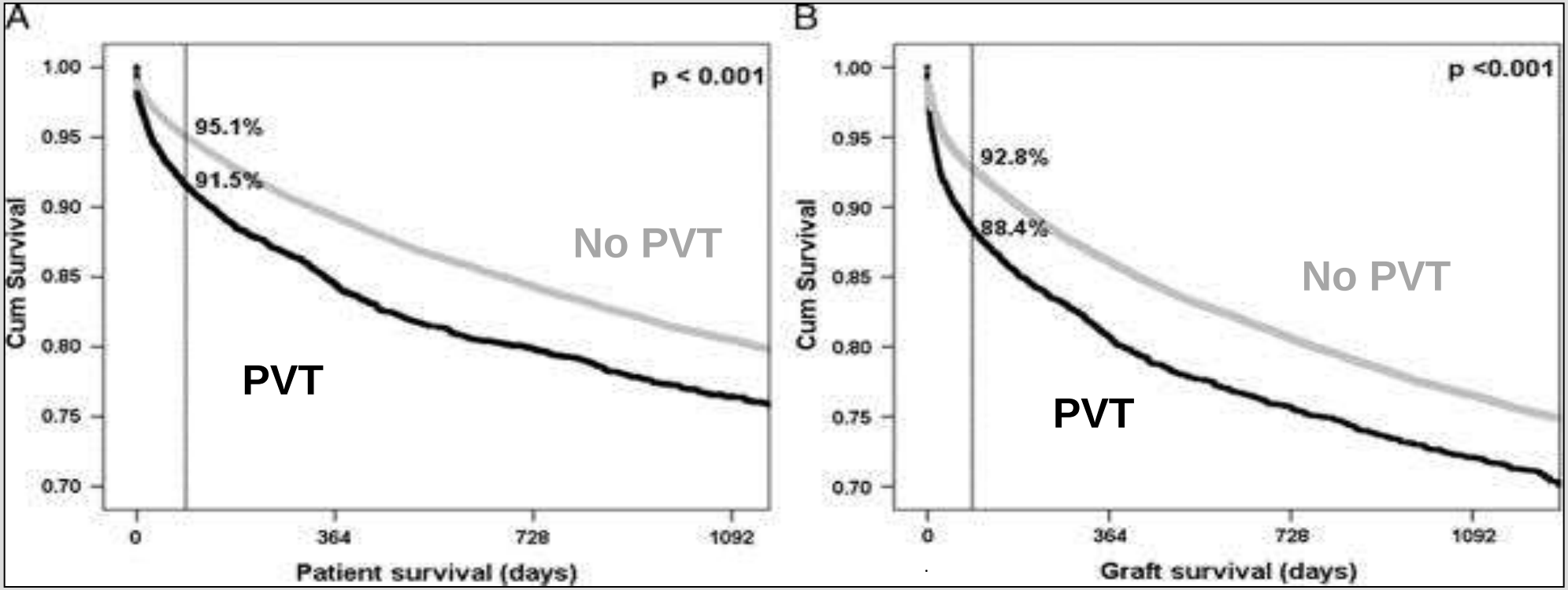
Impact of pretransplant PVT before and after LTx



Englesbe. Liver Transplant 2010. SRTR 22,291 listed candidates. Occlusive PVT 4.02%

Decreased early patient and graft survival in patients with PVT at listing

OPTN registries 2002-2013



Ghabril, Transplantation 2015

Extrahepatic portal vein thrombosis in cirrhosis and posttransplant outcome

Transplantability unaffected (preselected patients)

Pretransplant PVT impacts early posttransplant course

Portal vein thrombosis & liver transplantation

- Epidemiology
- Impact
- Treatment

Anticoagulation for PVT in cirrhosis: Systematic review & meta-analysis All studies until 2013

Recanalization	66%
Major AC related complication	3%
AC related death	0

OR for recanalization 4.16 (1.88-9.20)

Significant heterogenity

Qi, Eur J Intern Med 2014

Anticoagulation for PVT in cirrhosis:
Systematic review of 12 cohort studies

Outcome of the thrombus

	Anticoag.	Control
Progression	5%	38%

Chen, Eur J Gastroenterol Hepatol 2015. Median of reported rates

Anticoagulation for PVT in cirrhosis:

Predictors of outcome (multivariate analysis)

	Warfarin N = 30	Control N = 36
Recanalization	SMV > 50%	None

Predictor for recanalization, all group:
Anticoagulation *P* = 0.042, HR: 4.333; 95%CI: 1.052-17.842

Chen, Eur J Gastroenterol Hepatol 2015.

Anticoagulation for PVT in cirrhosis
Issues & unmet needs

- Degree and extent of initial occlusion
- Optimal regimen
- Monitoring efficacy and toxicity
- Impact of recanalization & anticoagulation
  - Pretransplant course
  - Transplantation
  - Posttransplant outcome

TIPS in cirrhosis with PVT
Review of cohort studies until 2016

Type of study	Studies	Patients
TIPS alone		
• Refractory complications	8	239
• Portal vein patency	3	67
PVT vs no PVT	1	34 vs 402
TIPS vs EBL/NSBB	3	86 vs 86
TIPS vs TIPS + Warfarin	1	33 vs 31

Harding, WJG 2015. Luo, Radiology 2015. Wang, Abdom Imaging 2015. Salem, Transplantation 2015. Lackhoo, Diag Intervent Imaging 2016. Chen, Eur Radiol 2014. Rosenquist, Acta Radiol 2015. Qi, Liver Int 2015. Wang, Radiology 2016

TIPS for reestablishing portal vein patency without anticoagulation therapy

Outcome	N
Number of patients	144
Complete recanalization	102
Stable or progressed	18

D’Avola, Transplant Proc 2012. Salem, Transplantation 2015.
Lackhoo, Diagn Interv; Imaging 2016. Chen, Eur radiol 2014. Luca, Gut 2011.

TIPS for reestablishing portal vein patency
Impact of anticoagulation therapy (ACT)

PVT status at 12 months	ACT	No ACT
Number of patients	31	32
Complete recanalization	26	23
Stable or progressed	4	7
No difference in bleeding, encephalopathy & mortality		

Wang, Radiology 2016

TIPS for reestablishing portal vein patency without anticoagulation therapy

Combining transjugular with transhepatic or transsplenic approach

- Preliminary experiences: ‘feasible and safe’
- Impact on transplantability ?

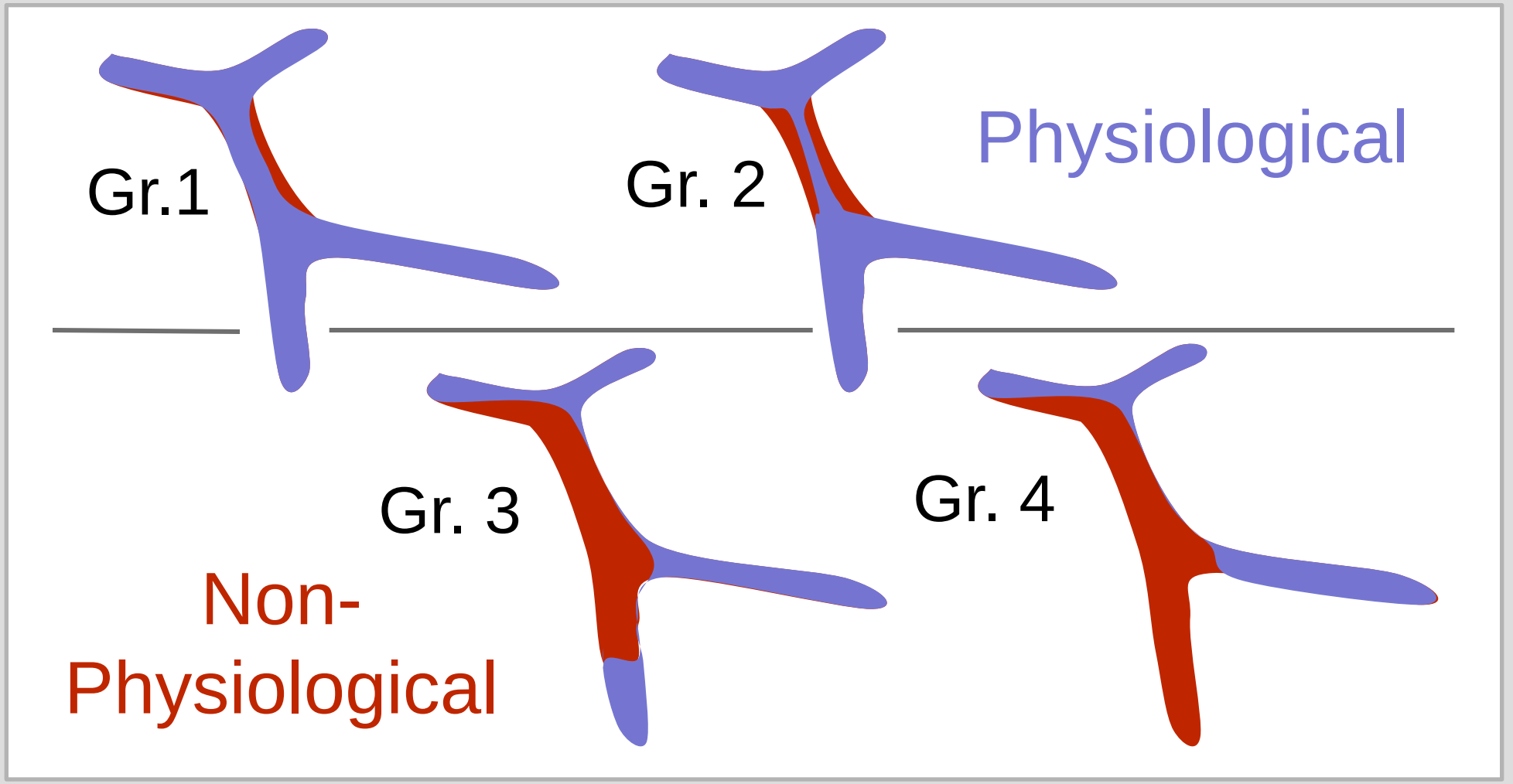
Han, J Hepatol 2011, Salem, Transplantation 2015. Habib, J Vasc Interv radiol 2015

TIPS in Cirrhosis with PVT

- Feasible when intrahepatic veins are visible.
- Effective recanalization of (partial) occlusion.
- No added benefit from anticoagulation therapy.
- TIPS dysfunction, encephalopathy & mortality were similar to TIPS patients without PVT.
- Impact on complications and mortality unclear.

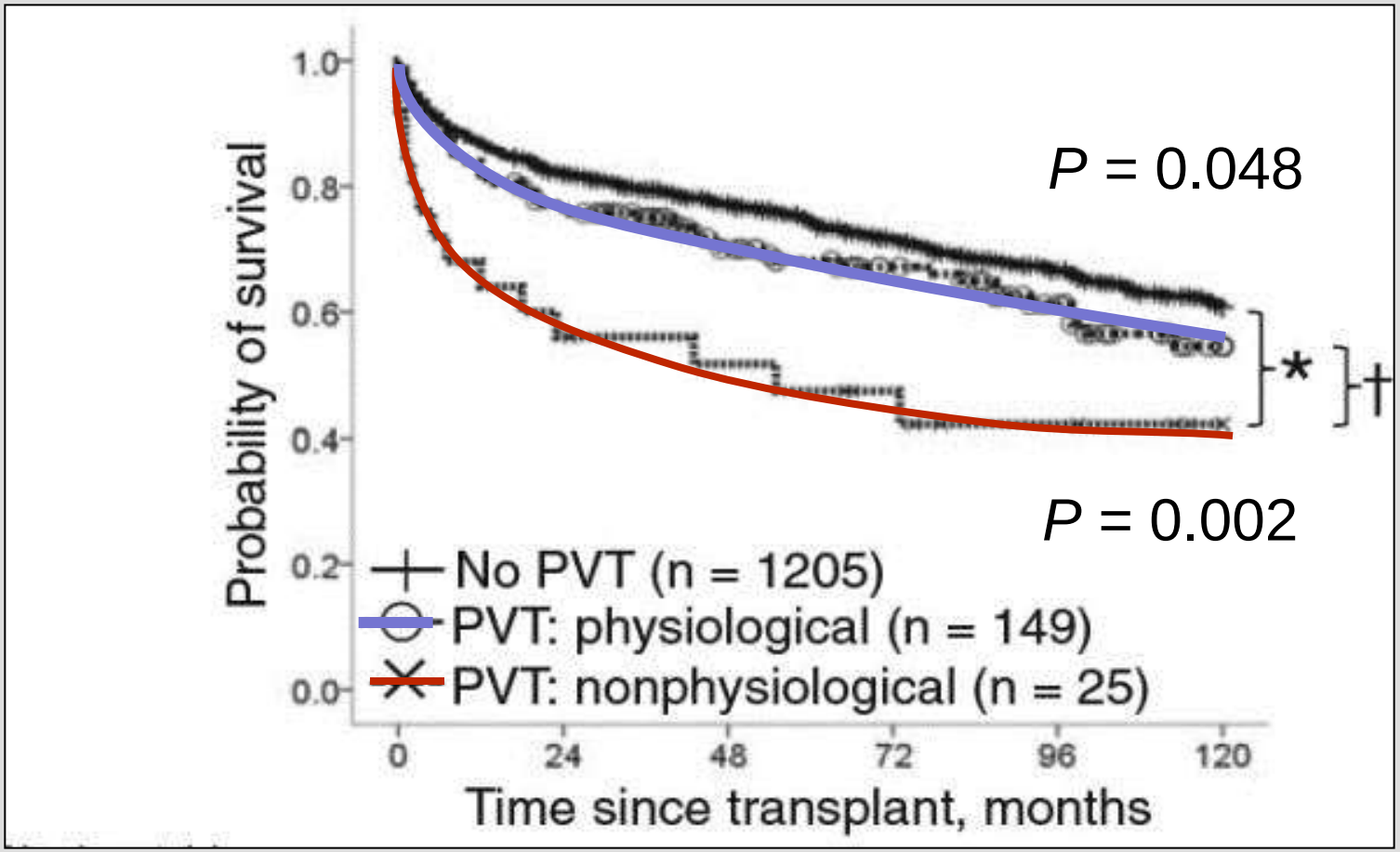
Senzolo, AP&T 2006. Van Ha, Cardiovasc Intervent Radiol 2006. Perarnaud, Eur J Gastro Hepato 2010. Han, J Hepatol 2010. Luca, Gut 2011. Senzolo, Liver Intern 2012

Reconstruction of portal inflow tract



Adapted from Yerdel, Transplantation 2000

Impact of the type of portal venous inflow reconstruction on patient survival



Hibi, Ann Surg 2014

Conclusion: PVT in cirrhosis and liver transplantation

- PVT common in candidates to liver transplantation
- PVT develops in patients with severe cirrhosis/portal hypertension
- PVT impact on natural history is uncertain or marginal.
- PVT negatively affects early posttransplant course.
- Anticoagulation or TIPS safe and efficient for recanalizing and preventing extension.
- Non physiological portal inflow reconstruction is not satisfactory.

Questions: PVT in cirrhosis and liver transplantation

- Predictors for spontaneous and treatment-induced recanalization (degree and extent of occlusion)
- Comparison of TIPS and anticoagulation on recanalization and on pre-, per- and post-transplant outcomes
- Safety and efficacy of endovascular procedures for restoring portal inflow (Yerdel 4 and 5)

Management

1. Screen/Diagnose — Doppler-US /3 months

2. Grade extension — Angio-CT/MR

- Yerdel 1 & 2
  - Physiological restoration
- Yerdel 3 & 4
  - Non-Physiological restoration

Management

Physiological restoration

Recanalize
Prevent extension

- Anticoagulation
- TIPS

Non-Physiological restoration

Reconstruct portal inflow

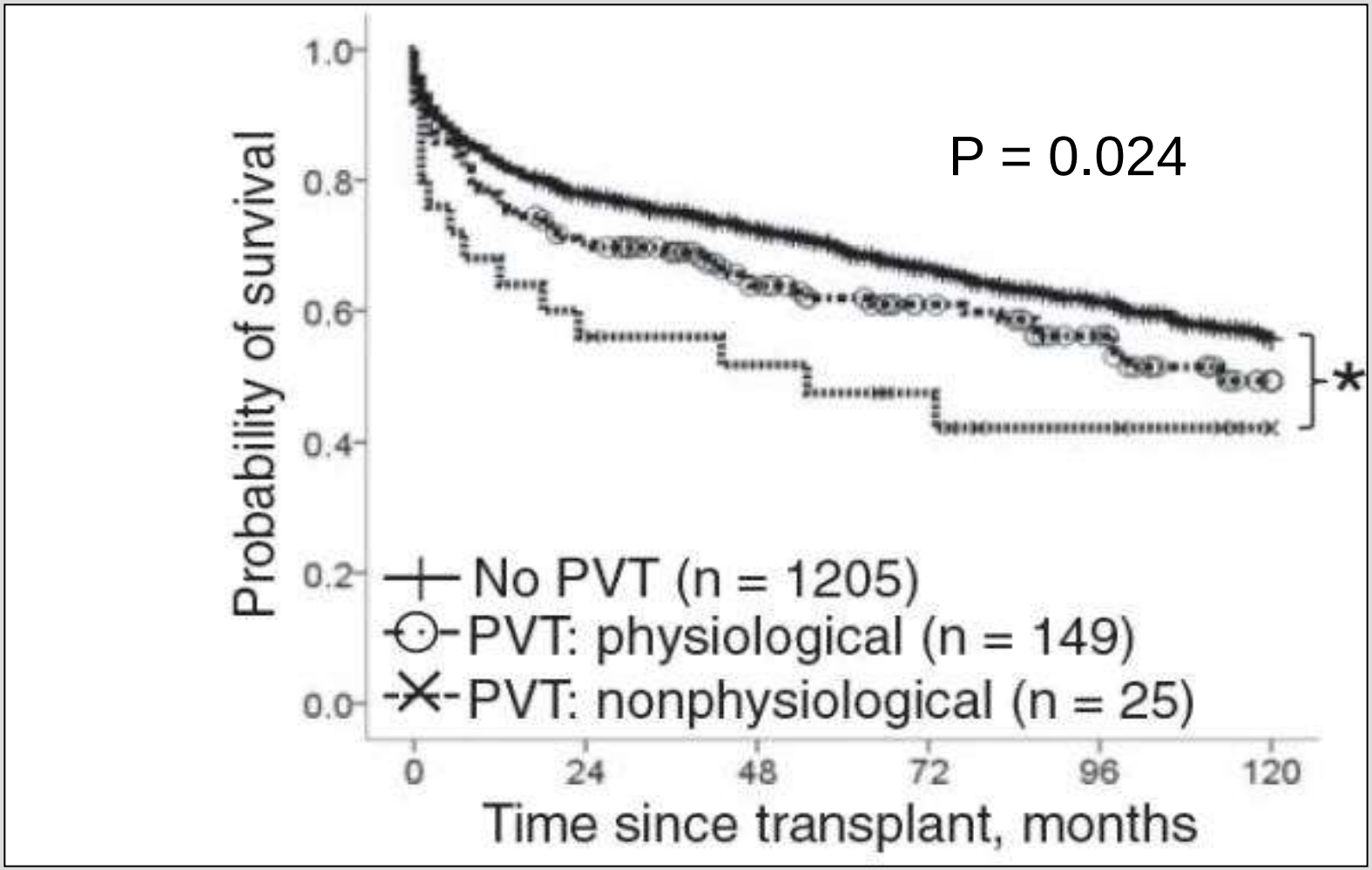
- Endovascular interventions ?
- Non physiological surgery?

TIPS for reestablishing portal vein patency without anticoagulation therapy

Outcome	N
Number of patients	144
Complete recanalization.	102
Partial recanalization	24
Stable or progressed	18

D'Avola, Transplant Proc 2012. Salem, Transplantation 2015. Lackhoo, Diagn Interv; Imaging 2016. Chen, Eur radiol 2014. Luca, Gut 2011.

Impact of the type of portal venous inflow reconstruction on graft survival



Hibi, Ann Surg 2014