



Management of invasive procedures in patients with cirrhosis

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Conflicts of interest

- I do not have a financial relationship relevant to that presentation
- I am not discussing off-label investigative use of a drug/device/product

Invasive procedures in patients with cirrhosis

- Coagulation changes in patients with cirrhosis
- Management of invasive procedures in cirrhosis
- Anticoagulants in cirrhosis

Coagulation in cirrhosis

Primary hemostasis:

platelet aggregation

Coagulation:

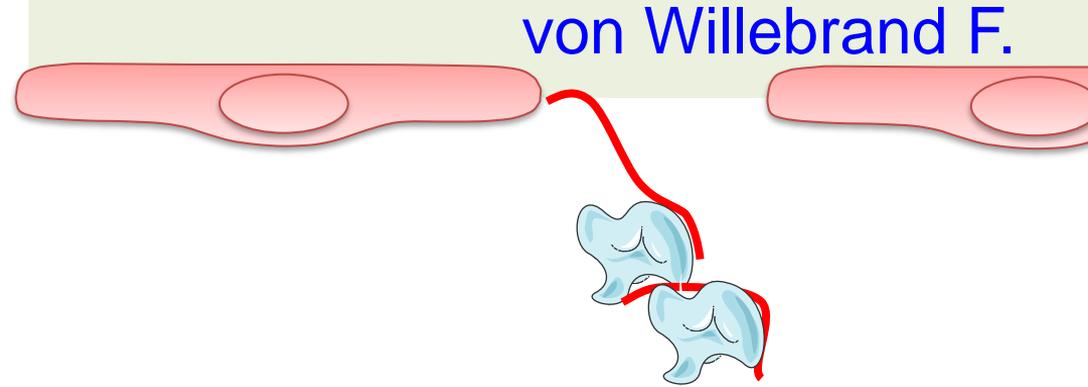
fibrin formation

Fibrinolysis:

fibrin lysis

Coagulation in cirrhosis

Primary hemostasis:
platelet aggregation



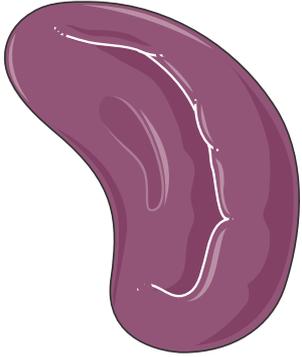
Thrombocytopenia

Favors bleeding

↑ von Willebrand F.
↑ Multimer size

Favors thrombosis

Thrombocytopenia and cirrhosis

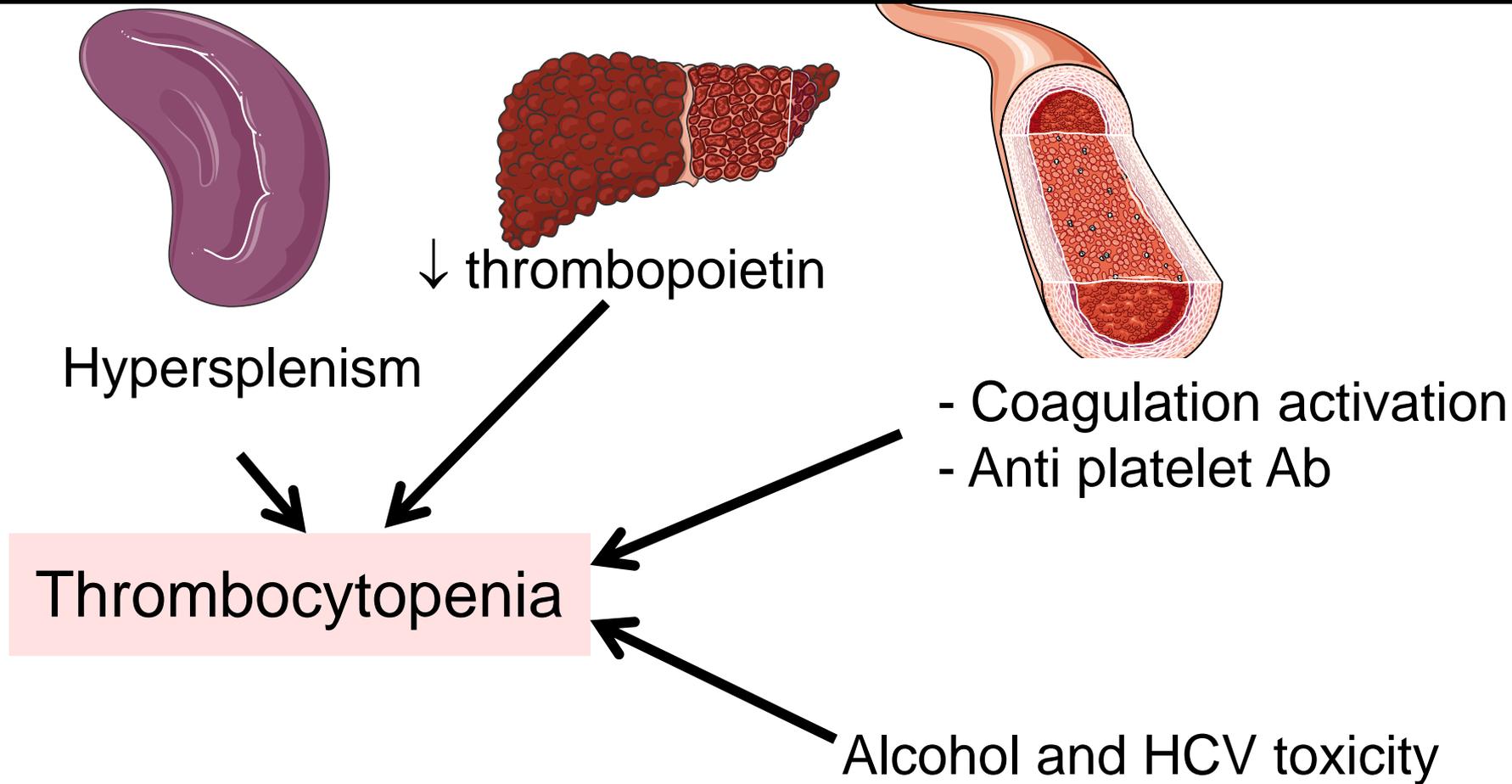


Hypersplenism



Thrombocytopenia

Thrombocytopenia and cirrhosis



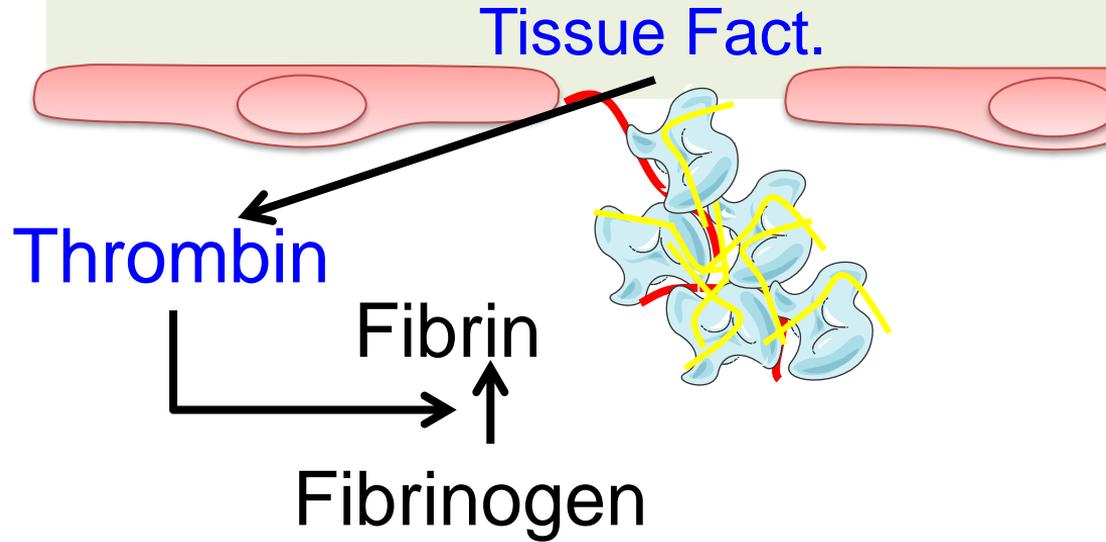
Coagulation in cirrhosis

Primary hemostasis:

platelet aggregation

Coagulation:

fibrin formation



↓ fact II, V, VII, IX,
X and Fg

Favors bleeding

↓ AT, prot C, S,
↓ ↑ factor VIII

Favors thrombosis

Coagulation in cirrhosis

Primary hemostasis:

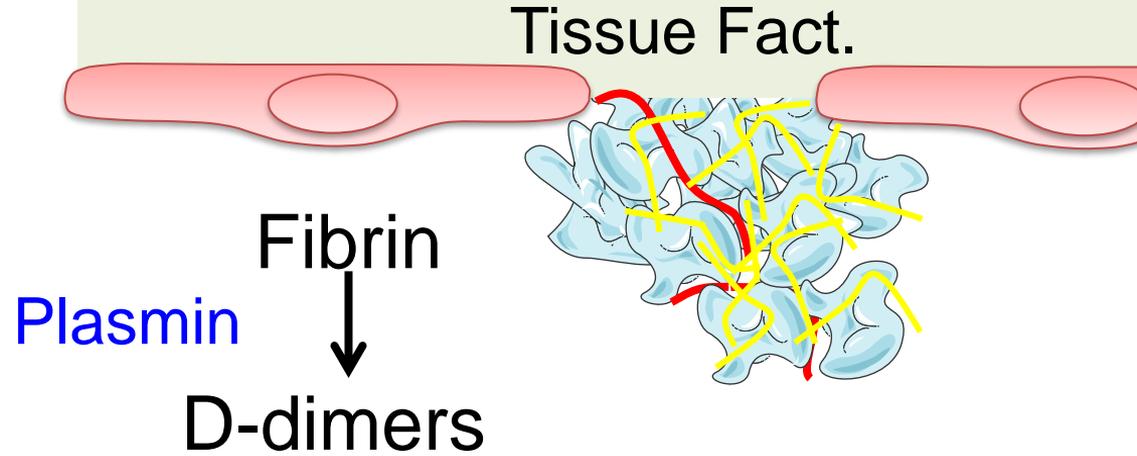
platelet aggregation

Coagulation:

fibrin formation

Fibrinolysis:

fibrin lysis



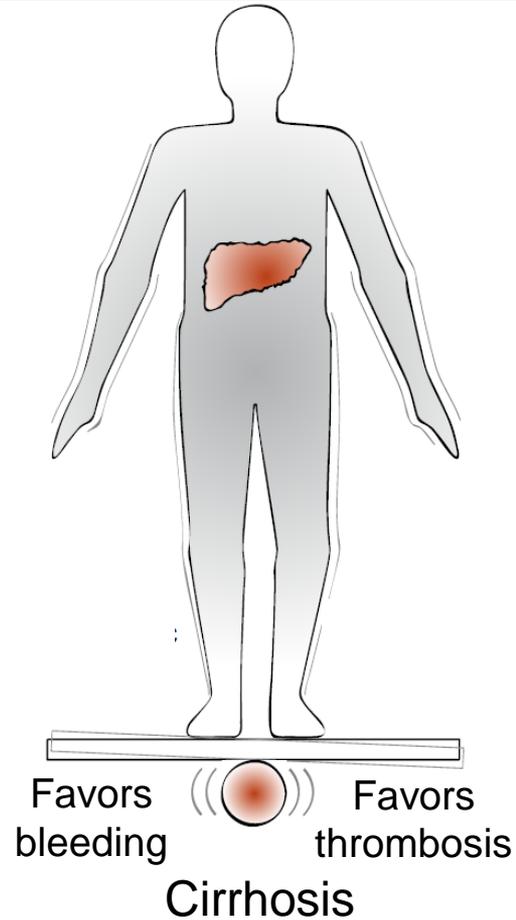
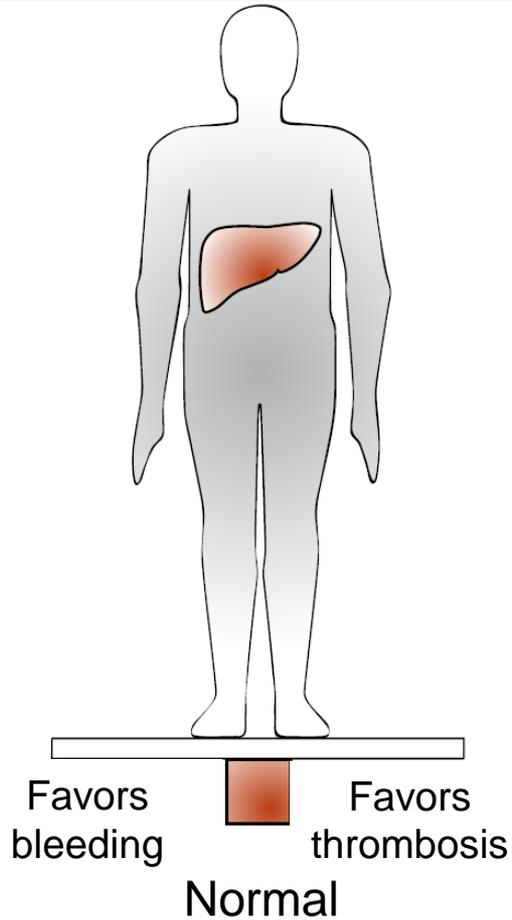
↑ tPA

↓ plasminogen, α_2
antiplasmin, ↑ PAI-1

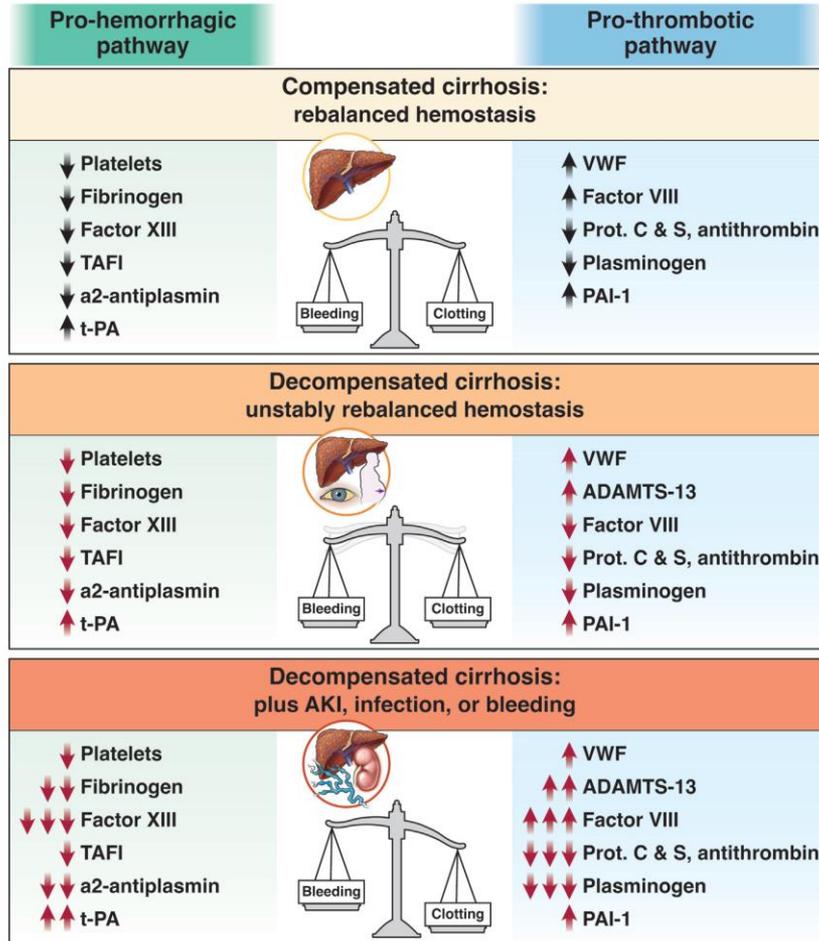
Favors bleeding

Favors thrombosis

Coagulation in cirrhosis



Coagulation changes with cirrhosis progression



Coagulation in cirrhosis



Invasive procedures in patients with cirrhosis

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Invasive procedures in patients with cirrhosis

- The patient
- The procedure
- The laboratory

Prediction: the patient

When the procedure is scheduled

- Personal or familial history of bleeding
- Anticoagulants / antiplatelet agents

No more VKA-LMWH bridging (for low thrombosis risk)

Randomized controlled study:
1884 patients with atrial fibrillation

	VKA-LMWH bridging n=934	VKA-placebo bridging n=950	P=
Arterial events	0.3%	0.4%	NS
Major bleeding	3.2%	1.3%	0.005

Prediction: the procedure

Guidelines	Percutaneous liver biopsy	Transjugular liver biopsy
EASL 2022	Low	Low
ISTH 2021	High	Low
AASLD 2021	High	High

Based on same definition: threshold > 1.5%



52 experts

80 invasive procedures



Consensus for 52 procedures

High risk:

- ✓ interventional endoscopy
- ✓ percutaneous biopsies
- ✓ central nervous system

Low risk:

“Can you put the finger?”

Prediction: the laboratory

	BSG 2020	ACG 2020	AASLD 2021	AGA 2021	ISTH 2021	EASL 2022
Platelet $\geq 50 \times 10^9/L$	Do not correct					
PT/INR	If INR > 1.4, transvenous	Do not correct				
aPTT	Not mentioned or do not evaluate					
Fibrinogen	No recommendation / Do not correct / Do not evaluate					
Viscoelastic tests	No specific recommendation / May be useful/ Do not use routinely					

➔ Do not correct most coagulation abnormalities

Prediction: the laboratory

	BSG 2020	ACG 2020	AASLD 2021	AGA 2021	ISTH 2021	EASL 2022
Platelet < 50× 10⁹/L	Trans-venous	Platelet infusions or TPO rec. agonists	No correction	severe thrombocytopenia and high-risk procedure	very high-risk surgery and <30-50 x 10 ⁹ /L: correct	< 50 × 10 ⁹ /L + local hemostasis not possible: correction possible

→ Platelet < 50× 10⁹/L should raise attention



52 experts

80 invasive procedures



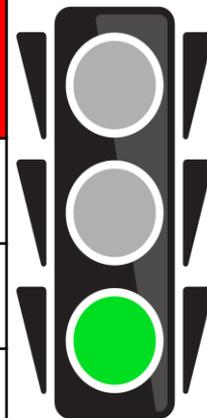
Consensus for 52 procedures

35 at low risk of bleeding

17 at high risk of bleeding

Suggested thresholds

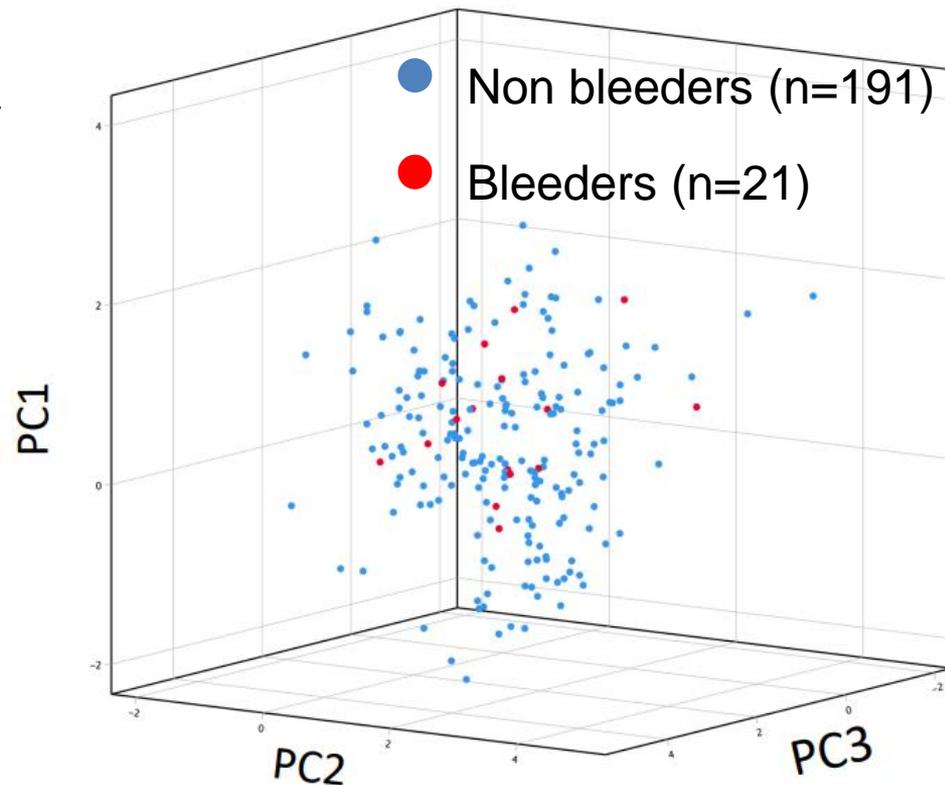
	Low-risk procedure	High-risk procedure or surgery
Platelet count	$> 30 \times 10^9/L$	$> 50 \times 10^9/L$
INR	Do not measure	$< 2^*$
aPTT	Do not measure	



A comprehensive work-up for hemostasis changes does not improve prediction of liver biopsy related bleeding

302 patients undergoing liver biopsy

- PT, aPTT, platelet
- Coag factors: II, V, VII, VIII
- PFA-100
- Thromboelastography (INTEM, FIBTEM)
- Thrombin generation assays
- Plasma clot lysis time



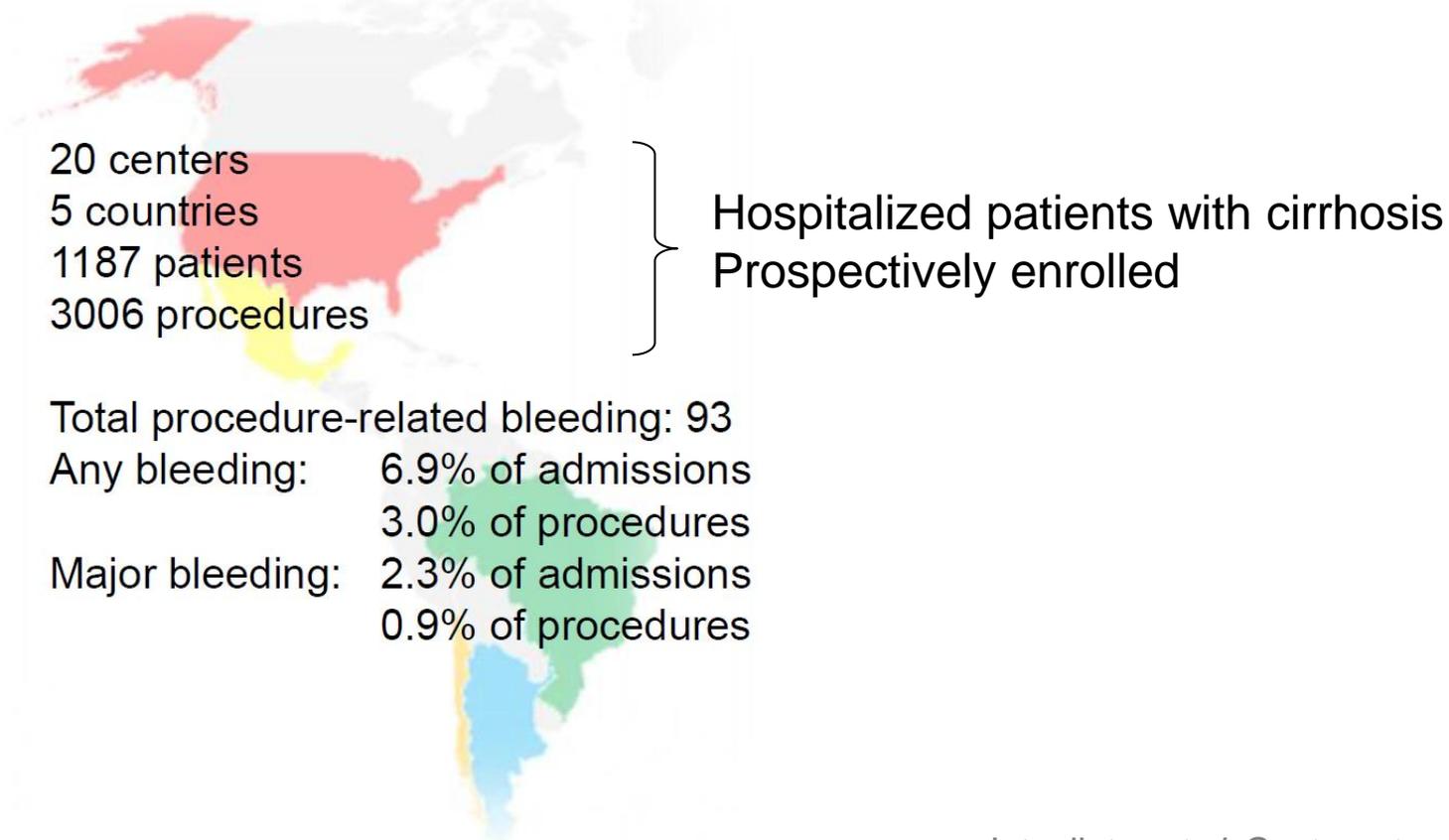
Going beyond the limits: interest of thromboelastography?

Cirrhosis; INR > 1.8 or PLT < 50'000 /mm³



	SOC (n=30)	TEG guided (n=30)
PLT transfusion	46%	17%
FFP transfusion	66%	10%
Bleeding	3%	0%
Allergic reaction	3%	0%

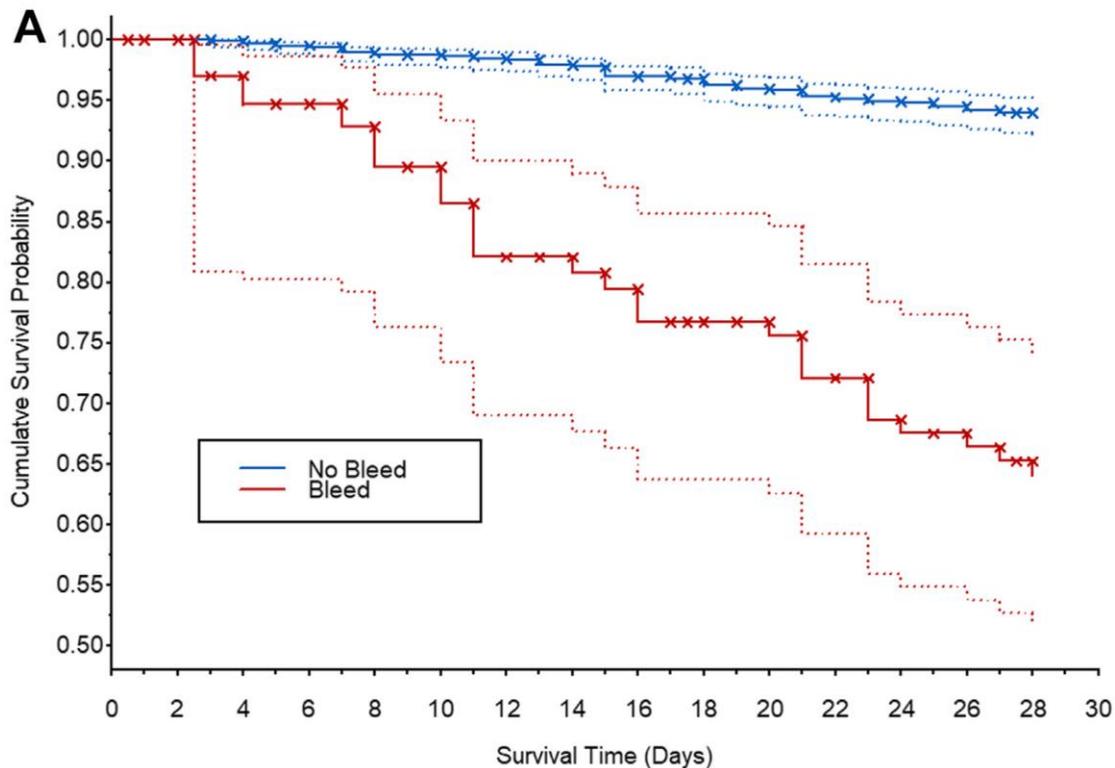
Predictors of bleeding in hospitalized patients with cirrhosis



Predictors of bleeding in hospitalized patients with cirrhosis

Independent predictors of procedure related bleeding	aOR	P value
Procedure risk	4.64	<.001
MELD score at admission	2.37	<.001
BMI	1.40	.007
Ascites	1.31	.062
Trainee	1.56	.177
AKI present at admission	0.72	.223
INR prior to procedure	1.22	.294
Infection at admission	1.26	.337
Antithrombotic prior to procedure	1.34	.394
Platelet level prior to procedure	0.93	.635
Number of prior procedures	1.02	.657
ACLF present at admission	1.04	.776
VTE prophylaxis at admission	1.01	.972

Bleeding in hospitalized patients with cirrhosis: a poorer survival



Treatment of post-procedure bleeding

Local treatment +++

Treatment	Indication
Platelet transfusion	Platelet < 50'000/mm ³ ; Thrombopathy Antiplatelet
TPO receptor agonists	Not for acute setting
Fibrinogen concentrates	If Fg < 100 or 120 mg/dL
Fresh frozen plasma	If hemorrhagic shock
Prothrombin complex conc.	If hemorrhagic shock
Tranexamic acid	If hyperfibrinolysis
Desmopressin	No
Recombinant FVIIa	No

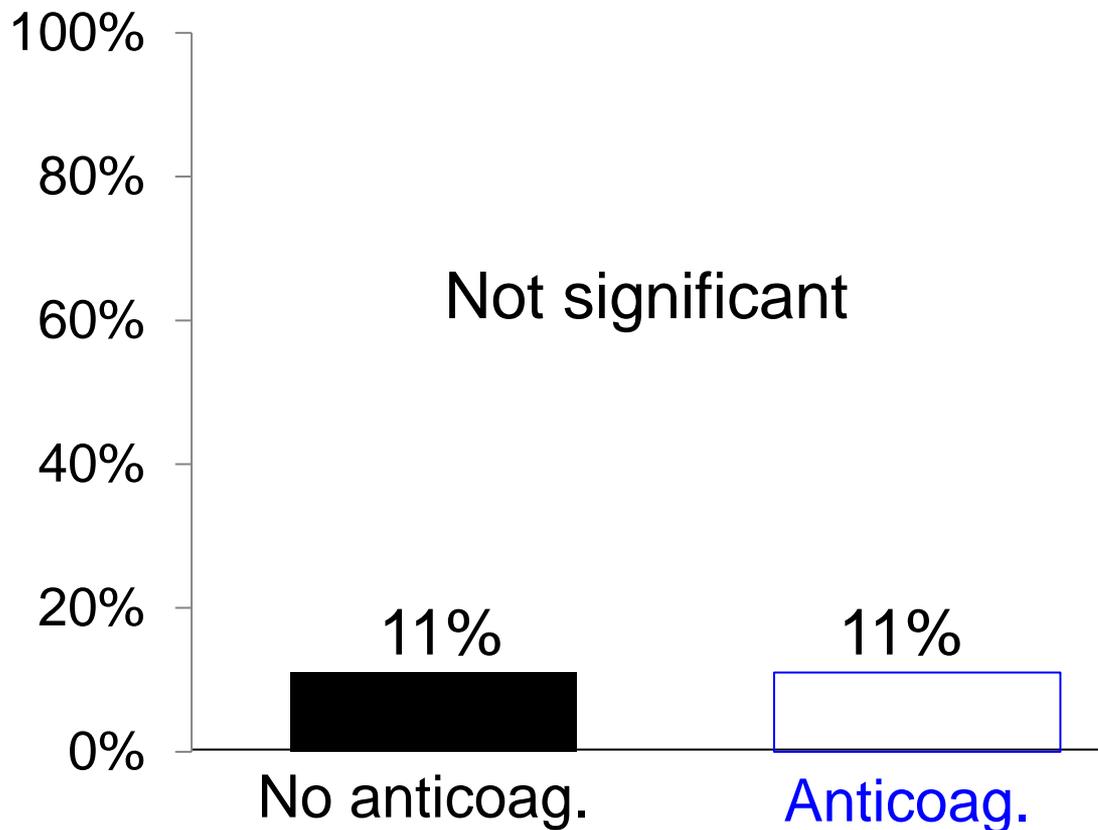
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Safety of anticoagulants in cirrhosis

	LMWH/VKA	No anticoagulant
Francoz, 2005	19	10
Garcovich, 2011	15	15
Senzolo, 2012	35	21
Cai, 2013	5	6
Chung, 2014	14	14
Risso, 2014	50	20
Chen, 2015	30	36
Wang, 2016	31	33
TOTAL	199	155

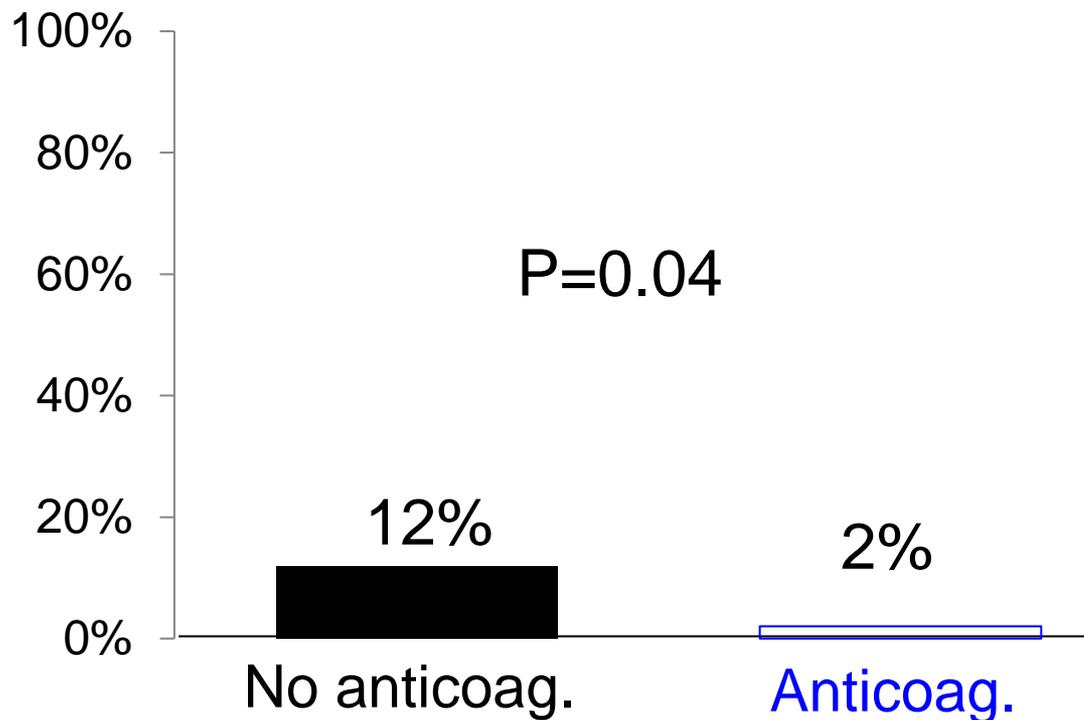
Major or minor bleedings



6 studies; 257 patients

Loffredo, Gastroenterology 2017

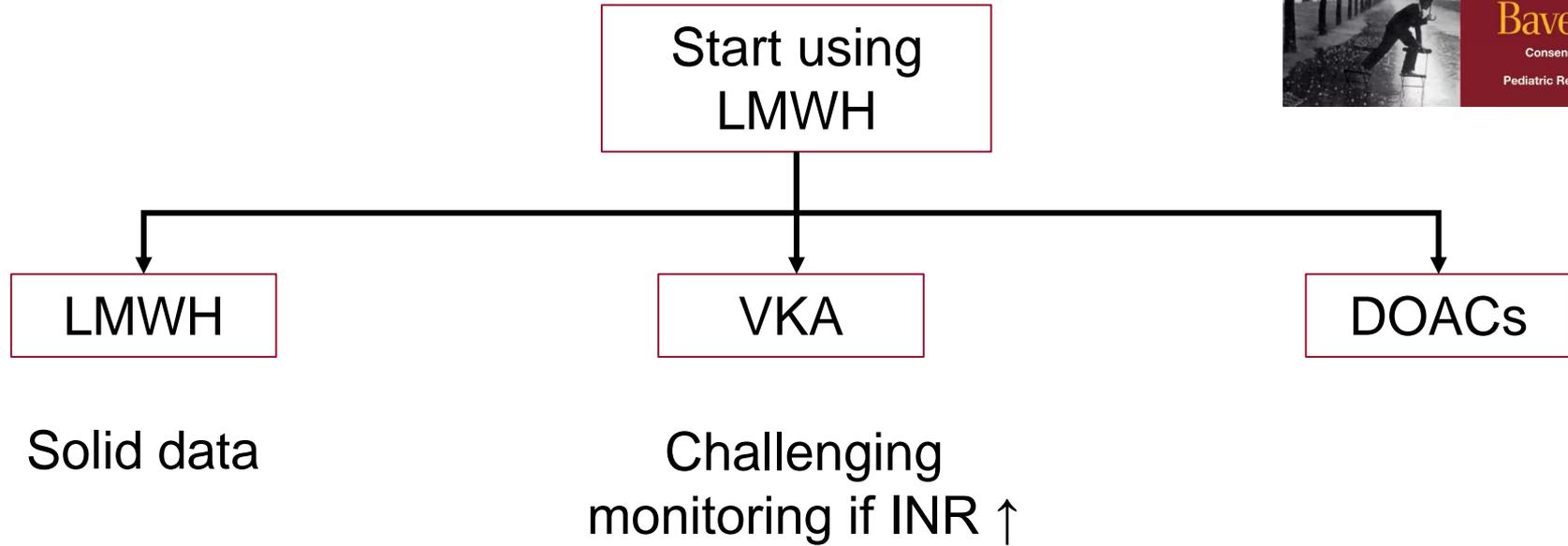
Portal hypertension related bleeding



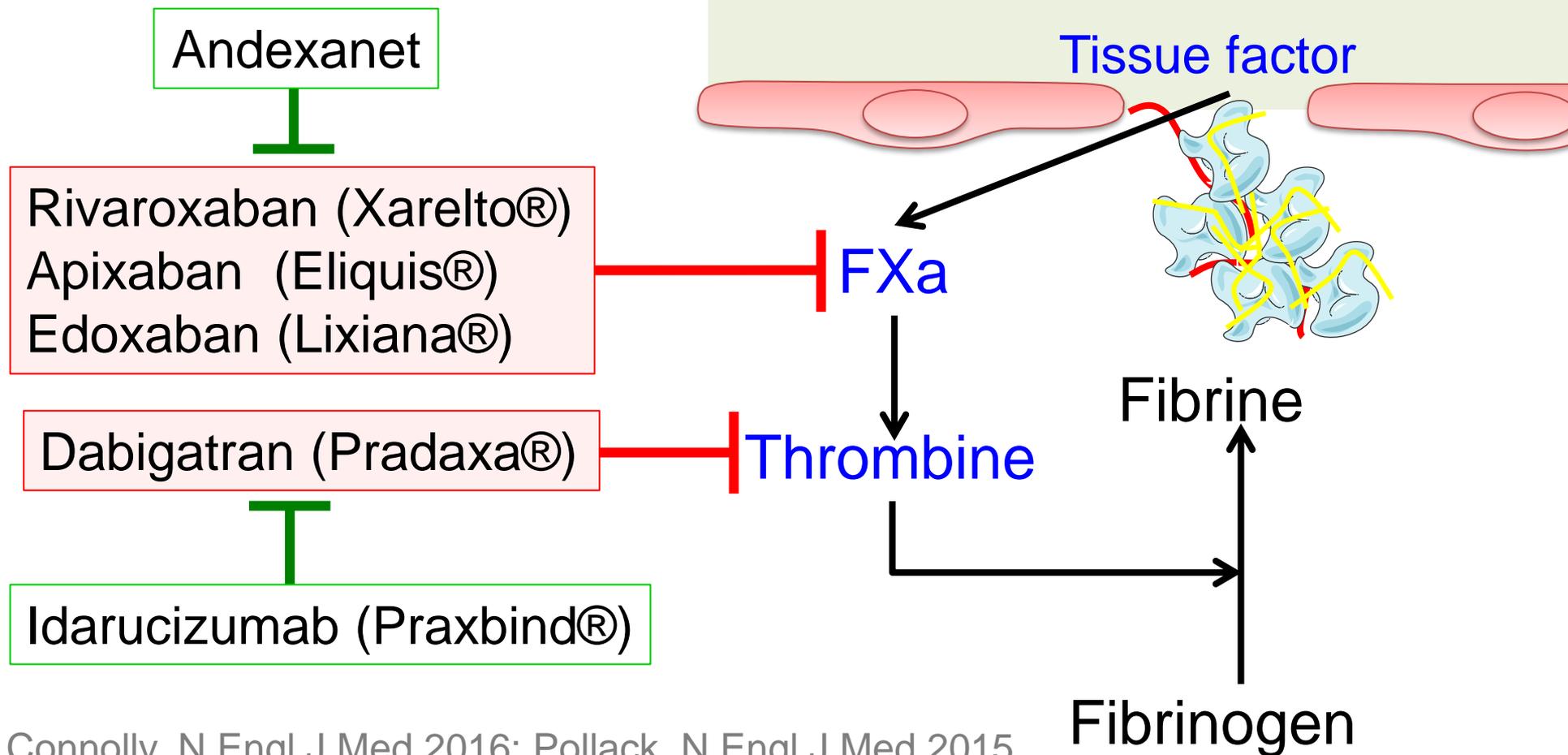
4 studies; 158 patients

Loffredo, Gastroenterology 2017

What kind of anticoagulants in cirrhosis?

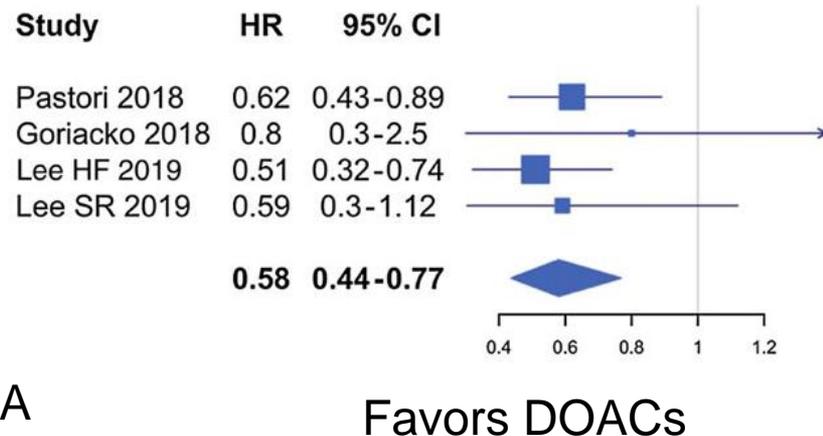
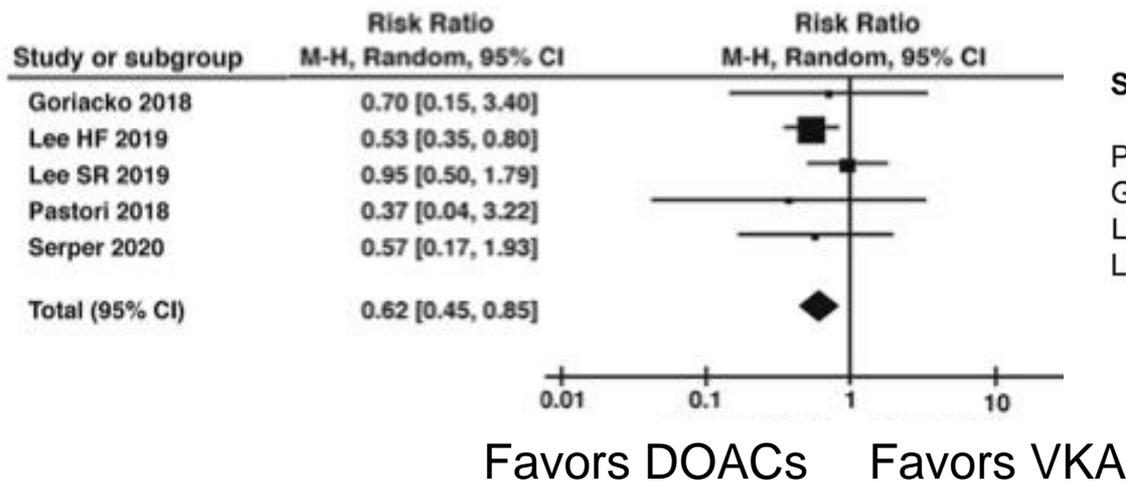


Direct oral anticoagulants (DOACs)



VKA vs. DOACs in patients with cirrhosis and atrial fibrillation

Major bleeding events



VKA vs DOACs in patients with cirrhosis and PVT

References	Number of patients	Bleeding risk
Koh <i>et al.</i> 2022	N=551	DOAC = VKA
Chen <i>et al.</i>	N= 3479	DOAC = VKA
Ng <i>et al.</i> Hepatology Int 2021	N=527	DOAC = VKA
Mohan <i>et al.</i> Ann Gastr 2020	N=648	DOAC = VKA
Valeriani <i>et al.</i> Thromb H. 2021	N=1475	

Safety of DOACs according to cirrhosis severity

- Child A: no concern
- Child B or creatinine clearance < 30 ml/min: used with caution
- Child C: do not use

De Franchis et al, J Hepatol 2022; EASL CPG guidelines 2022 on bleeding & coagulation

Child-Pugh category	Dabigatran	Apixaban	Edoxaban	Rivaroxaban
A (5–6 points)	No dose reduction	No dose reduction	No dose reduction	No dose reduction
B (7–9 points)	Use with caution	Use cautiously	Use cautiously	Do not use
C (10–15 points)	Do not use	Do not use	Do not use	Do not use

Conclusion #1

- **Cirrhosis:** fragile balance of haemostasis
- **Predict: be careful if**
 - ✓ platelets < 50'000/mm³
 - ✓ “we can not put the finger”

Conclusion #2

- DOAC have a good efficacy and can be:
 - ✓ used in Child-Pugh A
 - ✓ used with caution in Child-Pugh B
 - ✓ not used in Child-Pugh C



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