

# Prediction and prevention of post-procedural bleedings in patients with cirrhosis

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# Rebalanced hemostasis in cirrhosis

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## IMPAIR

Low platelet  
Platelet function defects  
↑ NO prostacyclin  
↓ II, V, VII, IX, X, XI  
Vit K deficiency  
Dysfibrinogenemia  
↓ a2 antilplasmin, FXIII, TAFI  
↑ TPA

## HAEMOSTATIC BALANCE



## PROMOTE

↑ vWF  
↓ ADAMTs-13  
↑ FVIII  
↓ protein C, S, ATIII,  
↓ a-Macroglob.,  
↓ heparin cofactor II  
↓ plasminogen

# INR is NOT correlated with procedural bleeding in cirrhosis

Study or Subgroup	Bleeding			No bleeding			Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
3.1.1 Mean INR among patients with and without a periorcedural bleeding event									
Sam et al 2001	3.8	4.81	4	2	1.66	25	0.0%	1.80 [-2.96, 6.56]	
Pandey et al 2017	3.13	1.33	11	2.2	0.89	79	1.0%	0.93 [0.12, 1.74]	
Heleniu-Hietala et al 2016	2	1.2	11	1.4	0.5	108	1.2%	0.60 [-0.12, 1.32]	
Rowley et al 2019	2	0.8	6	1.6	0.6	3110	1.5%	0.40 [-0.24, 1.04]	
Wadei et al 2019	1.64	0.22	16	1.36	0.22	112	11.4%	0.28 [0.16, 0.40]	
Medina et al 2018	1.67	0.46	12	1.53	0.3	160	5.9%	0.14 [-0.12, 0.40]	
Huang et al 2016	1.27	0.44	24	1.15	0.23	283	8.7%	0.12 [-0.06, 0.30]	
Cocero et al 2019	1.7	0.5	50	1.6	0.4	612	10.2%	0.10 [-0.04, 0.24]	
Blasi et al 2019	1.34	0.07	13	1.3	0.15	452	14.2%	0.00 [-0.17, 0.17]	
Kraja et al 2017	1.65	0.43	34	1.65	0.48	105	9.0%	-0.02 [-0.31, 0.27]	
Kim et al 2017	1.25	0.21	2	1.27	0.26	248	5.2%	-0.02 [-0.16, 0.12]	
Jacobs et al 2014	1.45	0.07	2	1.47	0.44	80	10.5%	-0.13 [-0.30, 0.04]	
Giannini et al 2010	1.36	0.21	210	1.49	0.27	22	9.0%	-0.14 [-0.31, 0.03]	
Jeon et al 2012	1.14	0.11	2	1.28	0.23	28	8.9%	-0.34 [-0.73, 0.05]	
Hung et al 2018	2.02	0.75	21	2.36	0.9	62	3.4%	-0.05 [-0.03, 0.13]	
Subtotal (95% CI)			218			5486	100.0%		

Heterogeneity:  $\text{Tau}^2 = 0.01$ ;  $\text{Chi}^2 = 39.63$ ,  $\text{df} = 14$  ( $P = 0.0003$ );  $I^2 = 65\%$

Test for overall effect:  $Z = 1.20$  ( $P = 0.23$ )

Total (95% CI)

Heterogeneity:  $\text{Tau}^2 = 0.01$ ;  $\text{Chi}^2 = 39.63$ ,  $\text{df} = 14$  ( $P = 0.0003$ );  $I^2 = 65\%$

Test for overall effect:  $Z = 1.20$  ( $P = 0.23$ )

Test for subgroup differences: Not applicable

Favors [no bleeding] Favors [bleeding]

# Platelet count does NOT predict bleeding in cirrhosis

Predictor variable	Ratio <sup>b</sup>	AOR (95% CI)	P value <sup>c</sup>
Procedure risk	High: Low	4.64 (2.44–8.84)	<.001
MELD score at admission	3rd quantile (25.9): 1st quantile (13.6)	2.37 (1.46–3.86)	<.001
BMI	3rd quantile (33.3): 1st quantile (24.1)	1.40 (1.10–1.80)	.007
Ascites present	Present: Absent	1.31 (0.99–1.75)	.062
Trainee performed	Yes: No	1.56 (0.81–2.99)	.177
AKI present at admission	Present: Absent	0.72 (0.42–1.22)	.223
INR prior to procedure	3rd quantile (2.0): 1st quantile (1.3)	1.22 (0.84–1.79)	.294
Infection at admission	Present: Absent	1.26 (0.76–2.08)	.337
Antithrombotic prior to procedure	Yes: No	1.34 (0.69–2.61)	.394
Platelet level prior to procedure	3rd quantile (137.0): 1st quantile (59.0)	0.93 (0.65–1.27)	.635
Number of prior procedures	$x + 1$ : $x$	1.02 (0.92–1.13)	.657
ACLF present at admission	Yes: No	1.04 (0.80–1.35)	.776
VTE prophylaxis at admission	Yes: No	1.01 (0.52–1.96)	.972

# EASL guidelines

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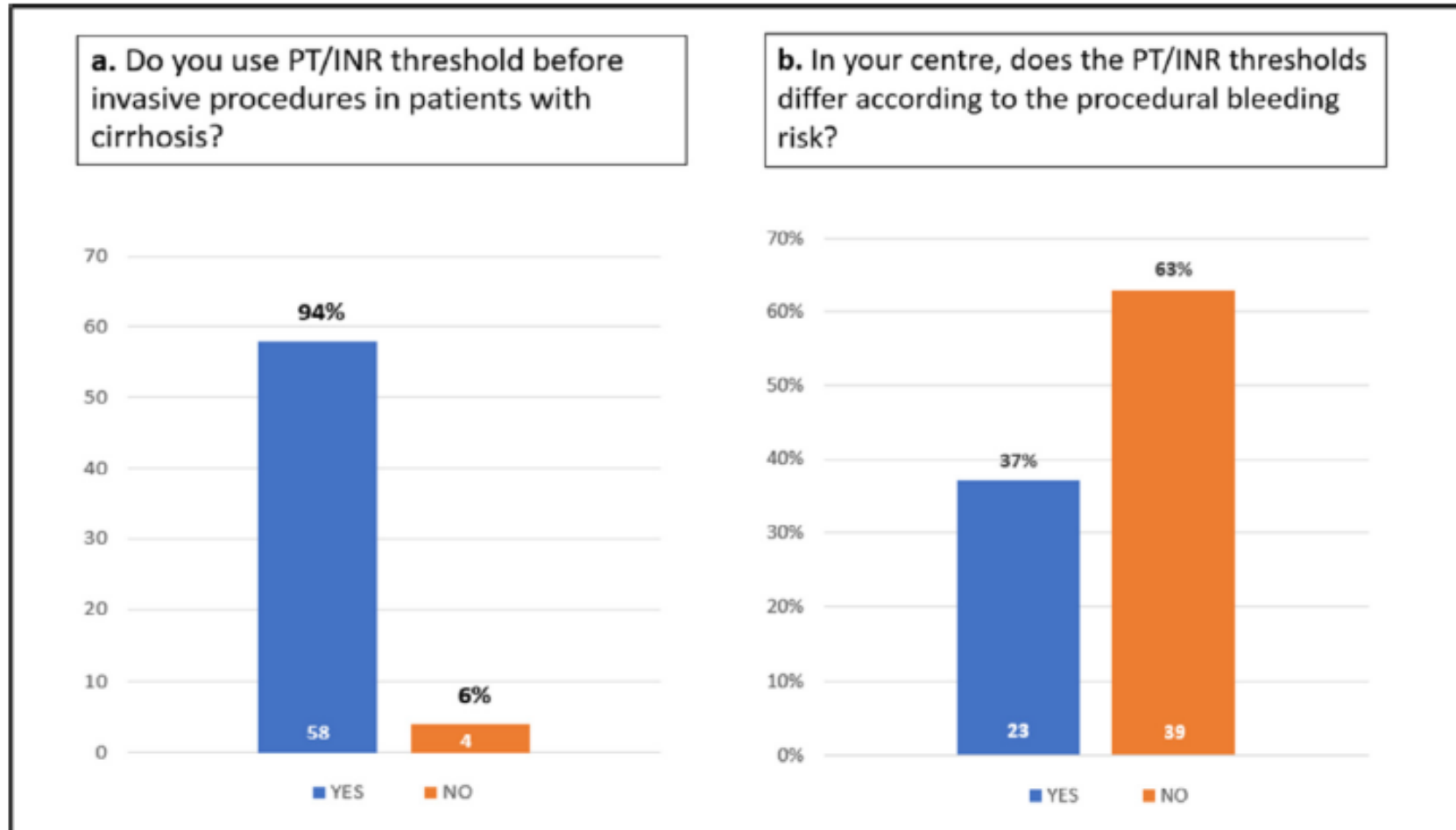
## Recommendation

- In patients with cirrhosis undergoing invasive procedures with a low risk of bleeding, laboratory evaluation of haemostasis with the aim of predicting post-procedural bleeding is not indicated (**LoE 4, strong recommendation**).














## Recommendation

- In patients with cirrhosis undergoing invasive procedures associated with a high risk of bleeding, laboratory evaluation of haemostasis is generally not indicated to predict post-procedural bleeding, although it may serve to provide a baseline status of the patient and to assist the physician in the case of bleeding events (**LoE 4/5, weak recommendation**).

# Estimation of bleeding risk in cirrhosis undergoing procedures in Italy



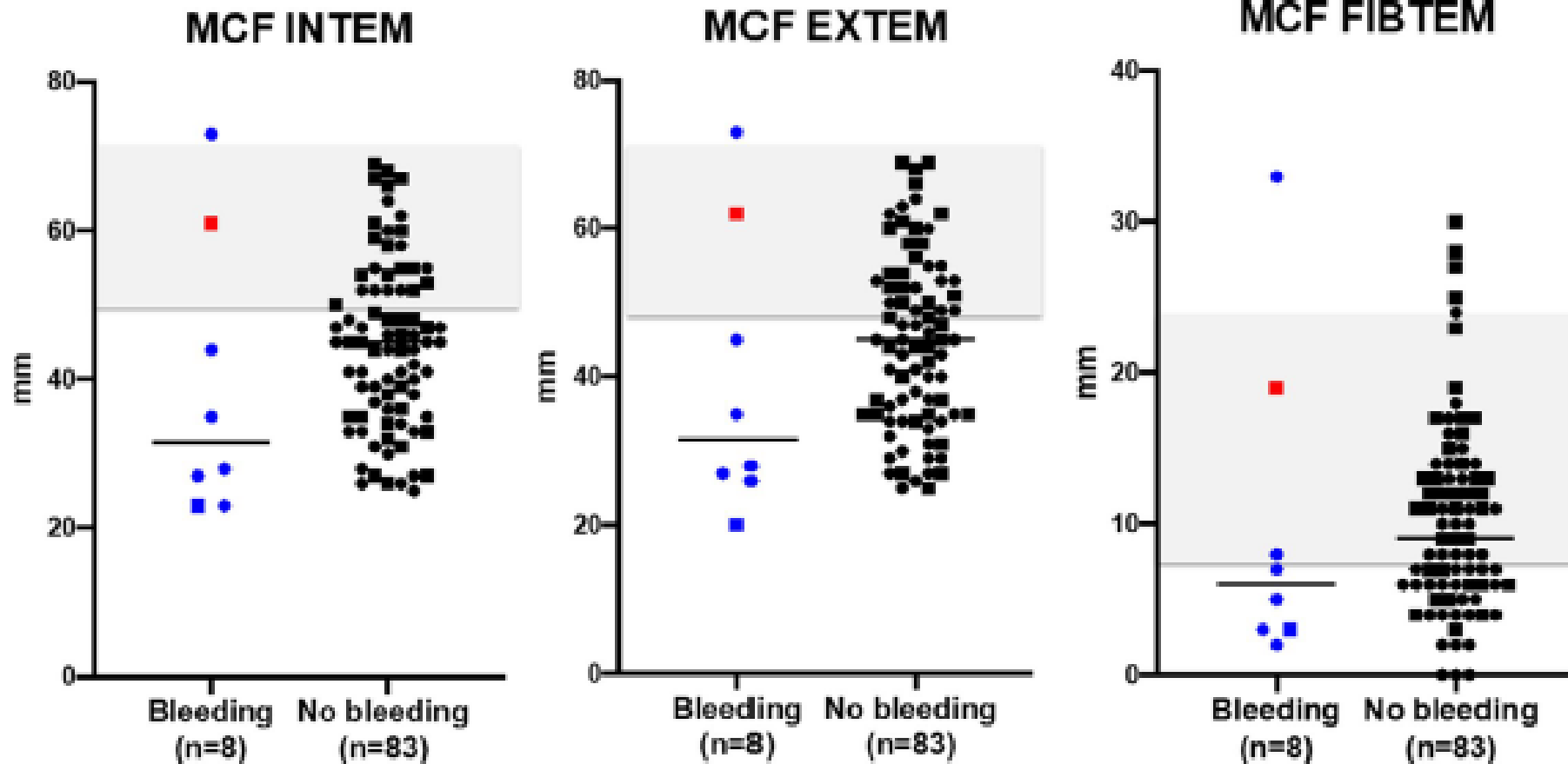
# Predicting bleeding after liver biopsy using comprehensive clinical and laboratory investigations: A prospective analysis of 302 procedures

Julien Bissonnette<sup>1</sup>  | Alix Riescher-Tuczkiwicz<sup>1</sup>  |  
 Elia Gigante<sup>1</sup>  | Carole Bourdin<sup>2</sup>  | Larbi Boudaoud<sup>2</sup>  | Heithem Soliman<sup>1</sup>  |  
 François Durand<sup>1</sup>  | Maxime Ronot<sup>3</sup>  | Dominique Valla<sup>1</sup>  | Valérie Vilgrain<sup>3</sup>  |  
 Emmanuelle de Raucourt<sup>2</sup>  | Pierre-Emmanuel Rautou<sup>1</sup>  

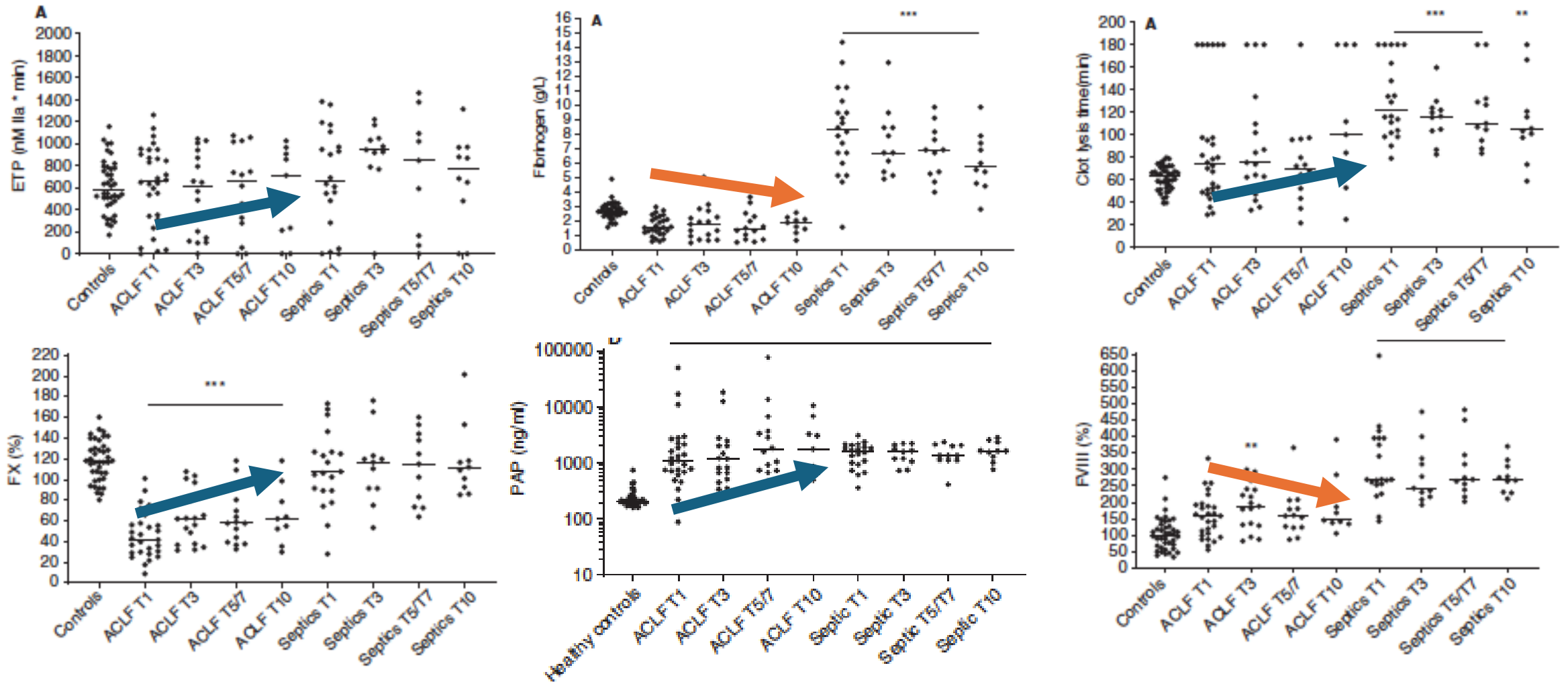
- 302 patients → 173 underwent percutaneous and 129 transjugular liver biopsy.
- 21 bleeding episodes (7%); 20 based on ultrasonographic criteria, 1 on laboratory criteria.
- None of the hemostasis tests and no item of the clinical questionnaire were associated with liver biopsy-related bleeding in the overall study group.
- Same results percutaneous/ transjugular liver biopsy, or on patients with cirrhosis.
- Pain 2 h after liver biopsy was more frequent in patients with liver biopsy-related bleeding.

Laboratory	n	No liver biopsy-related bleeding	n	Liver biopsy-related bleeding	p-value
<i>Laboratory features</i>					
Activated partial thromboplastin time ratio	280	1.1 (1.0–1.3)	21	1.1 (0.9–1.1)	.37
Fibrinogen (g/L)	279	2.8 (2.2–3.7)	21	3.3 (2.3–3.7)	.44
Factor II (%)	281	94 (66–118)	21	90 (74–124)	.59
Factor V (%)	281	98 (73–119)	21	101 (78–126)	.61
Factor VII (%)	281	80 (50–100)	21	73 (60–95)	.96
Factor VIII (%)	266	154 (133–197)	21	155 (139–194)	.99
Factor IX (%)	264	89 (63–108)	21	89 (72–117)	.61
Factor X (%)	281	91 (67–115)	21	92 (75–114)	.80
Factor XI (%)	264	78 (56–101)	21	79 (58–104)	.85
VWF antigen (%)	256	261 (187–391)	21	251 (161–379)	.51
PFA-100 ADP (sec)	266	101 (80–131)	20	104 (94–131)	.40
PFA-100 Epinephrin (sec)	263	139 (111–183)	20	131 (119–154)	.57
<i>Clot lysis time (min)</i>					
- >180	278	267	20	19	.82
- ≤180		11		1	
<i>Thromboelastometry</i>					
EXTEM Clotting time (sec)	203	69 (60–79)	15	70 (59–79)	.75
EXTEM Clot formation time (sec)	203	99 (74–137)	15	100 (77–177)	.74
EXTEM Clot firmness (mm)	203	60 (53–66)	15	59 (46–66)	.50
INTEM Clotting time (sec)	199	183 (165–202)	15	172 (166–182)	.09
INTEM Clot formation time (sec)	199	90 (66–125)	15	73 (65–155)	.81
INTEM Clot firmness (mm)	199	57 (50–64)	15	61 (49–65)	.85
FIBTEM Clot firmness (mm)	202	16 (12–21)	15	12 (10–23)	.57
APTEM Clotting time (sec)	201	65 (58–77)	15	64 (55–71)	.50
APTEM Clot firmness (mm)	201	59 (51–65)	14	60 (44–65)	.72
<i>Thrombin generation assay</i>					
In the absence of thrombomodulin					
- Lag time (min)	261	4.4 (3.9–5.4)	18	4.7 (4.2–5.1)	.85
- Time to peak (min)	261	7.5 (6.7–8.8)	18	7.4 (6.8–8.4)	.78
- Peak height (nM)	261	184 (136–232)	18	189 (148–246)	.47
- ETP (nM*min)	257	1047 (858–1257)	18	989 (817–1499)	.88
- Velocity index (nM/min)	260	61 (42–86)	18	60 (42–100)	.61
- Time to tail (min)	257	24 (22–26)	18	22 (21–27)	.19
In the presence of thrombomodulin					
- Lag time (min)	238	5.8 (4.9–8)	16	6.6 (5.8–7.7)	.29
- Time to peak (min)	239	8.6 (7.4–10.9)	16	9.1 (7.8–10.5)	.55
- Peak height (nM)	239	112 (63–157)	16	93 (73–132)	.85
- ETP (nM*min)	238	504 (283–708)	16	430 (312–651)	.66
- Velocity index (nM/min)	238	46 (24–70)	16	43 (24–59)	.84
- Time to tail (min)	236	23 (21–26)	16	23 (21–26)	.47

# In cirrhosis/ACLF, ROTEM was not predictive of bleeding

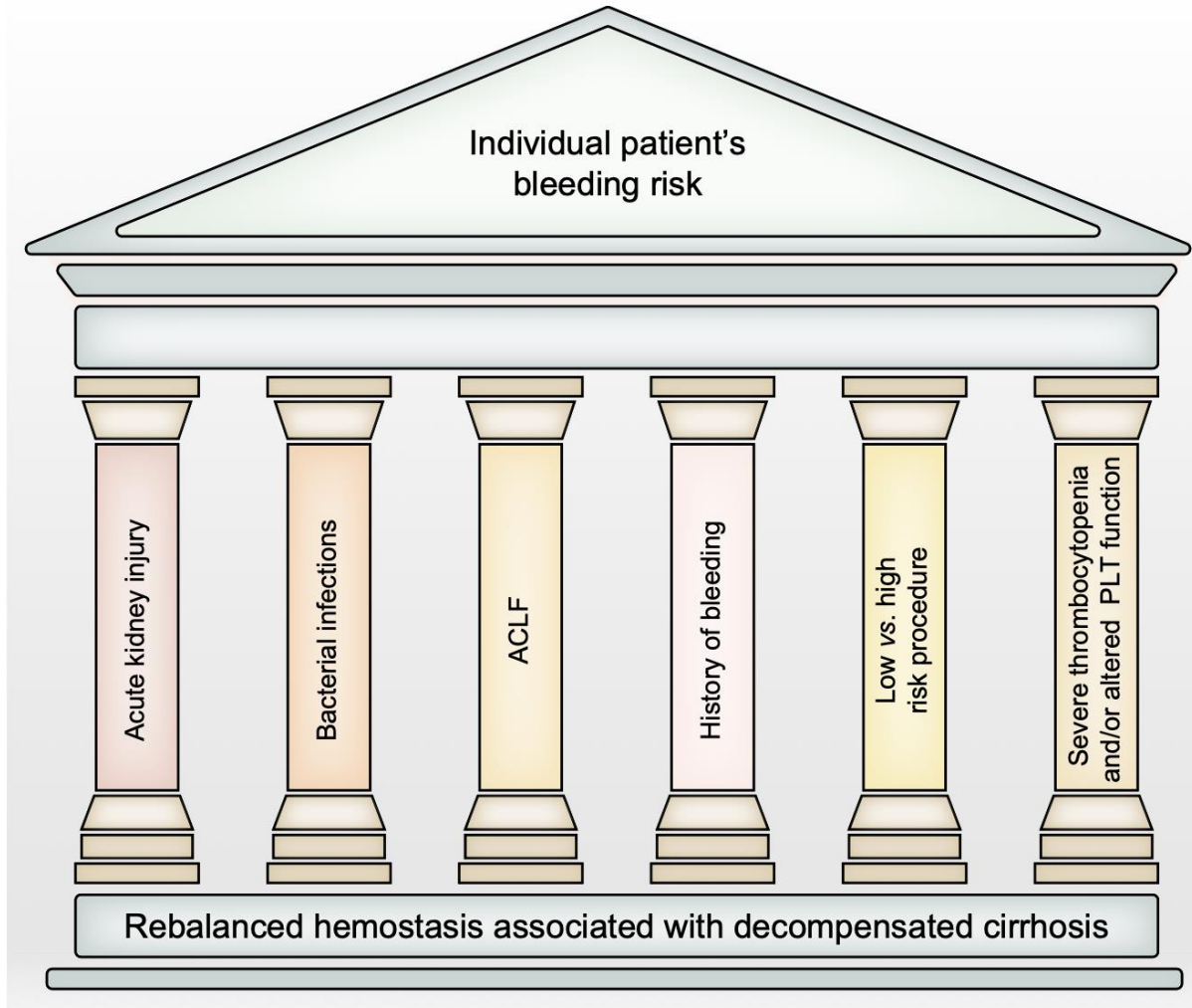


# Hemostasis in ACLF is a highly dynamic condition



# Toward a more comprehensive view

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## Acute kidney injury, but not sepsis, is associated with higher procedure-related bleeding in patients with decompensated cirrhosis

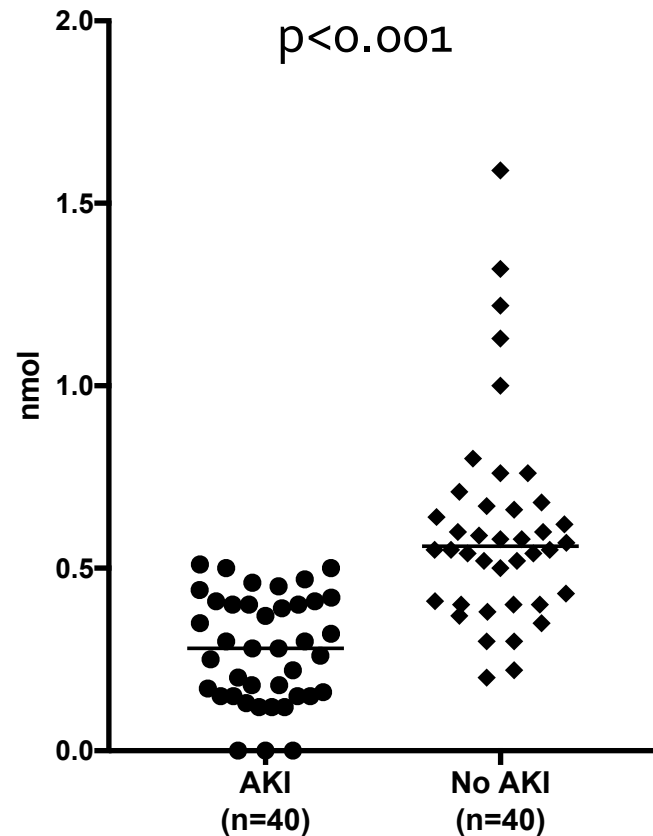
Adelina Hung<sup>1</sup>  | Guadalupe Garcia-Tsao<sup>1,2</sup>

On multivariate analysis (logistic regression), the **presence of AKI** at time of paracentesis was the only independent predictor of bleeding

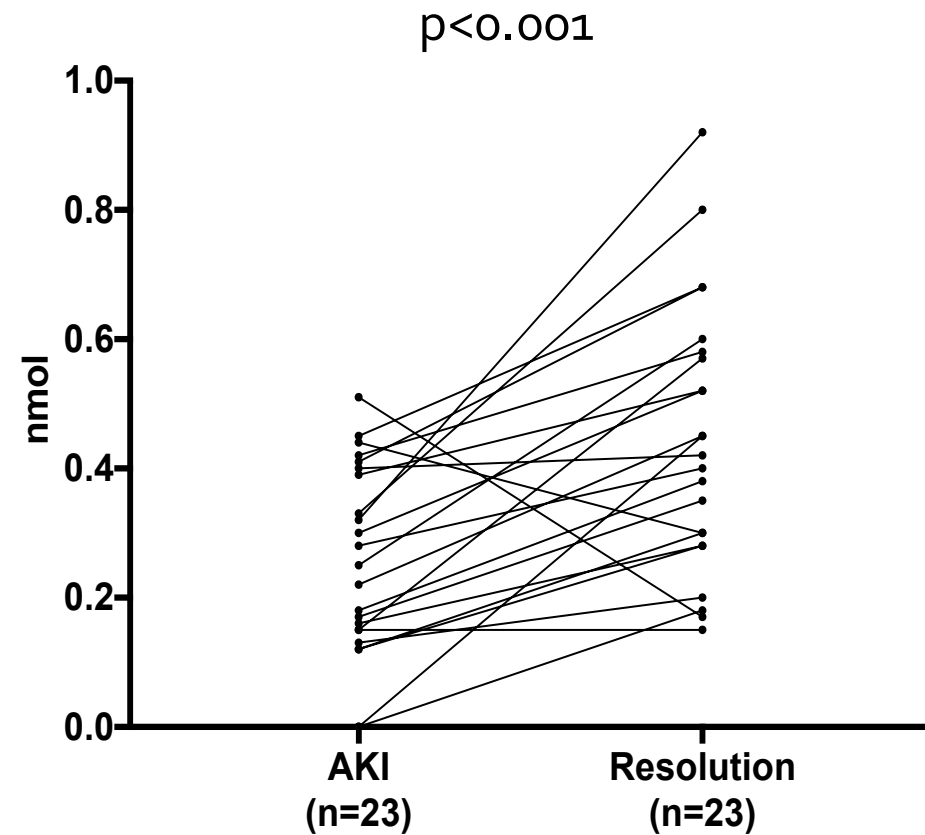
Variable	Odds Ratio	95% CI	P-value
<b>AKI</b>	<b>4.268</b>	<b>1.349 – 13.501</b>	<b>0.014</b>
Sepsis	1.701	0.533 – 5.429	0.370
Volume removed >2L	2.424	0.741 – 7.923	0.143
AST	1.003	0.996 – 1.010	0.432

# AKI in decompensated cirrhosis is associated with a reversible platelet dysfunction

Platelet secretion at baseline

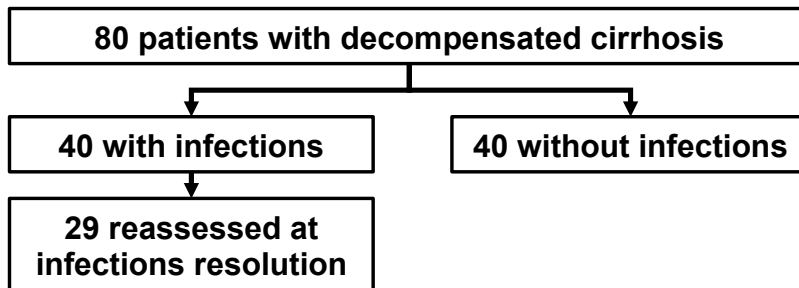


Platelet at resolution of AKI



# Global hemostatic profiling in decompensated cirrhosis with bacterial infections

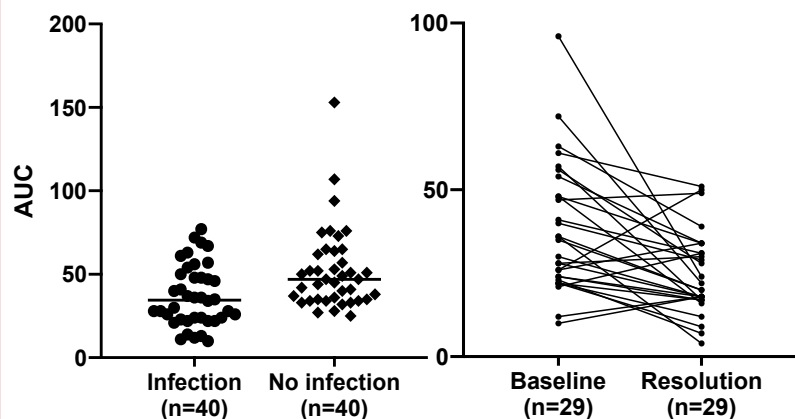
The effect of bacterial infections on the hemostatic balance in hospitalized patients with decompensated cirrhosis is unknown



Extensive hemostatic assessment including platelets, coagulation, and fibrinolysis

## PLATELETS

ADP-induced aggregation was lower in infections and further deteriorated at resolution



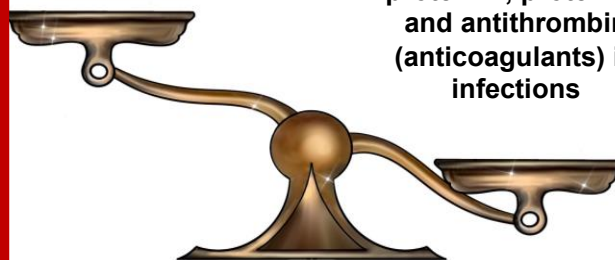
## COAGULATION

*Bleeding*

*Thrombosis*

Lower FVII in infections

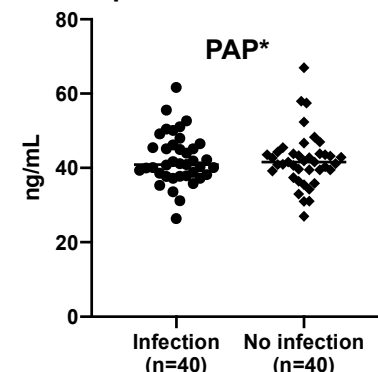
Significantly lower protein C, protein S, and antithrombin (anticoagulants) in infections



At resolution of infections, coagulation factors returned to levels of patients without infection

## FIBRINOLYSIS

No difference in fibrinolysis activation between patients with and without infections



\*Plasmin-antiplasmin complex is a marker for global fibrinolysis activation

At resolution of infections, fibrinolysis remained unchanged

Bacterial infections in decompensated cirrhosis are associated with impaired whole blood platelet aggregation (pro-hemorrhagic) and reduced level of natural anticoagulants (pro-thrombotic), which may unbalance hemostasis and increase the risk of both bleeding and thrombosis

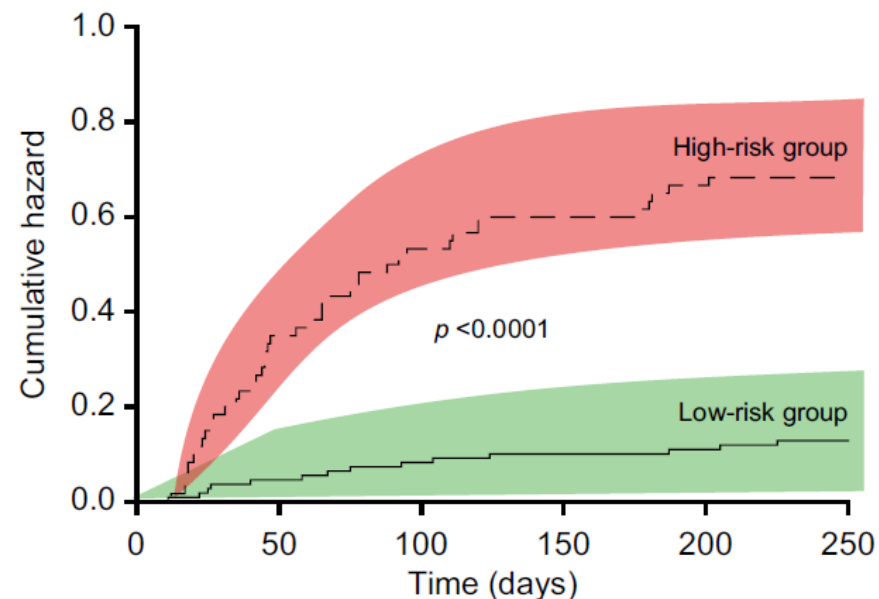
## Severity of systemic inflammation is the main predictor of ACLF and bleeding in people with acutely decompensated cirrhosis

1. In a prospective study including people with AD of cirrhosis, C-reactive protein (CRP), Child-Pugh, and CLIF-C AD score-but NOT hyper-coagulability and fibrinolysis activation-were independent predictors of ACLF within 1 year.
2. The Padua model, which was validated in an independent cohort of people with AD from Vienna and Frankfurt, accurately identified people at increased risk of ACLF

The Padua AD model

		CLIF-C AD score					
		<50		50-60		>60	
Child-Pugh class	CRP (mg/L)	B	C	B	C	B	C
<10	Low	Low	Low	Low	Low	Low	Low
10-50	Low	Low	Low	Low	High	Low	High
>50	Low	High	High	High	High	High	High

Risk of ACLF according to high vs. low risk



3. Bleeding during follow-up was associated with CRP level and progression to ACLF-but NOT baseline coagulopathy; thrombosis was associated with CRP level and anti-fibrinolytic factor PAI-1 level >50 ng/ml

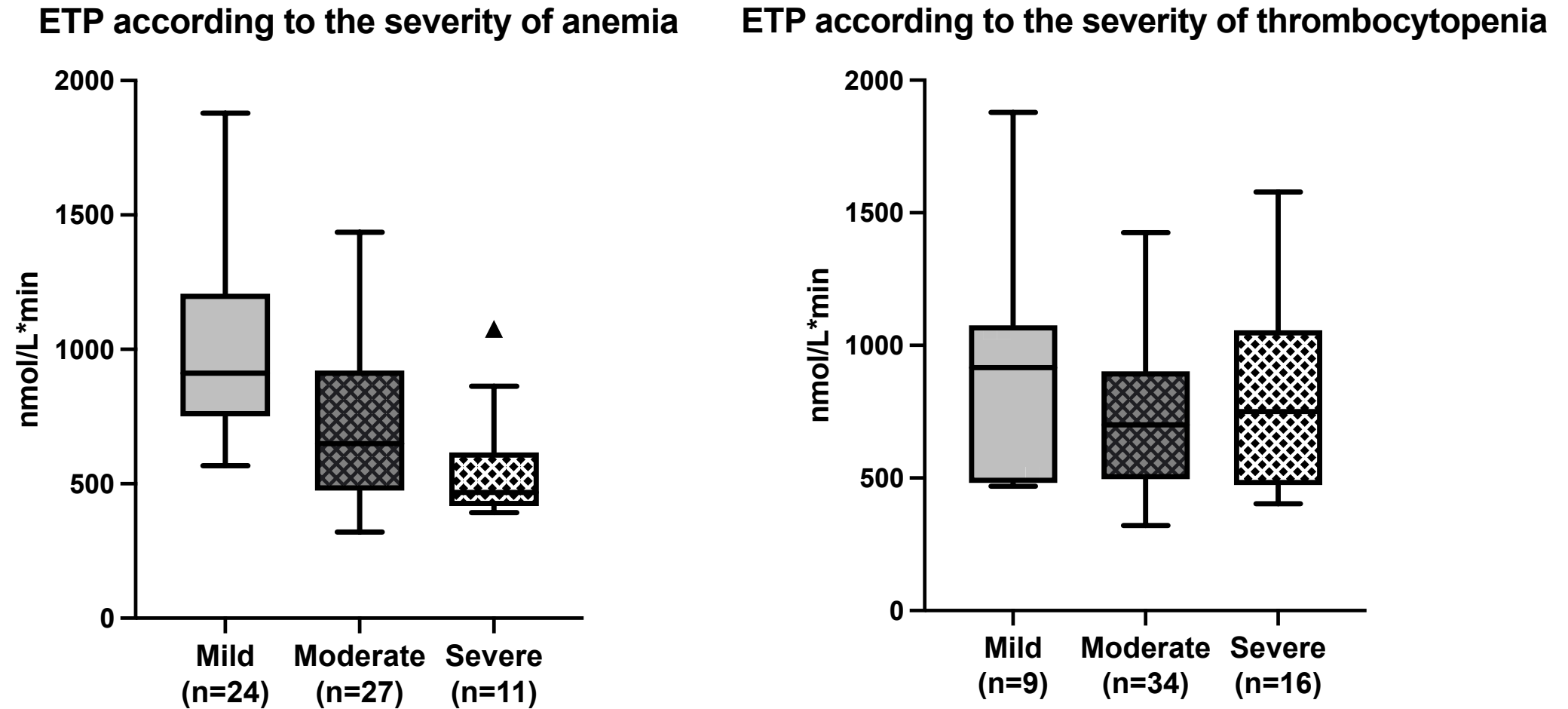
# ACLF was associated with increased risk of procedure-related bleeding in the in the PROC-BLeeD cohort

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		Non bleeding patients (n = 1105)	Bleeding patients (n = 82)	P value
CLF grade 0 (no ACLF)	827 (78.7)	783 (80.3)	44 (57.9)	<.001
ACLF (grades 1, 2, and 3)	224 (21.3)	192 (19.7)	32 (42.1)	<.001
ACLF grade 1	112 (10.7)	102 (10.5)	10 (13.2)	.498
ACLF grade 2	84 (8.0)	67 (6.9)	17 (22.4)	<.001
ACLF grade 3	28 (2.7)	23 (2.4)	5 (6.6)	.022

Relative risk, 2.05; 95% CI, 1.32–3.19; *P* = .001

# Anemia was associated with a more profound impairment in whole blood TG



# Distinguish between low and high-risk procedure

	Low-bleeding risk	No consensus	High-bleeding risk
	<ul style="list-style-type: none"> <li>Transjugular liver biopsy</li> <li>Hepatic venous pressure gradient measurement</li> <li>Diagnostic and therapeutic paracentesis</li> </ul>	<ul style="list-style-type: none"> <li>Transcatheter arterial chemoembolization or radioembolization</li> <li>Tunneled ascitic drain placement</li> <li>Laparoscopic liver biopsy</li> <li>Percutaneous liver biopsy</li> <li>Portal recanalization</li> <li>Transjugular intrahepatic portosystemic shunt</li> <li>Percutaneous ablation of liver cancer</li> </ul>	<ul style="list-style-type: none"> <li>Cholecystostomy or percutaneous biliary drain placement</li> </ul>
	<ul style="list-style-type: none"> <li>ERCP without sphincterotomy</li> <li>ERCP with biliary or pancreatic stent placement without sphincterotomy</li> <li>Hemostasis with plasma argon</li> <li>Video capsule</li> <li>Ultrasound without fine-needle aspiration</li> <li>Enteral stent deployment</li> <li>Polypectomy &lt; 1 cm (upper and lower endoscopy)</li> <li>Diagnostic upper endoscopy or balloon assisted enteroscopy</li> <li>Push enteroscopy</li> <li>Flexible sigmoidoscopy (with or without biopsy)</li> <li>Diagnostic colonoscopy (with or without biopsy)</li> </ul>	<ul style="list-style-type: none"> <li>ERCP with papillary balloon dilatation without sphincterotomy</li> <li>Endoscopy with radiofrequency ablation</li> <li>Variceal ligation</li> <li>Therapeutic assisted balloon enteroscopy</li> <li>Endoscopy with ultrasound with fine needle aspiration</li> <li>Glue injection of gastric varices</li> <li>Endoscopy with stricture dilatation (balloon, pneumatic or bougie)</li> </ul>	<ul style="list-style-type: none"> <li>ERCP with biliary or pancreatic sphincterotomy</li> <li>Endoscopy with mucosal resection</li> <li>Submucosal dissection</li> <li>Cystogastrostomy</li> <li>Polypectomy &gt; 1 cm (upper and lower endoscopy)</li> <li>Peroral endoscopic myotomy</li> <li>Ampullary resection</li> <li>Percutaneous gastrostomy or jejunostomy placement</li> </ul>
	<ul style="list-style-type: none"> <li>Central venous catheter placement</li> <li>Peripherally inserted central catheter line placement</li> <li>Central line removal</li> <li>Cardiac catheterization</li> <li>Transesophageal echocardiography</li> <li>Diagnostic coronary angiography</li> <li>Inferior vena cava filter placement</li> </ul>	<ul style="list-style-type: none"> <li>Arterial line placement</li> <li>Therapeutic coronary angiography</li> <li>Angiography or venography with intervention</li> </ul>	
	<ul style="list-style-type: none"> <li>Thoracentesis</li> <li>Bronchoscopy without biopsy</li> </ul>	<ul style="list-style-type: none"> <li>Tunneled pleural drain placement</li> <li>Bronchoscopy with biopsy</li> <li>Therapeutic bronchoscopy</li> </ul>	<ul style="list-style-type: none"> <li>Intrathoracic organ biopsy</li> </ul>
	<ul style="list-style-type: none"> <li>Cystoscopy</li> <li>Ureteroscopy</li> <li>Colposcopy with cervical biopsy</li> <li>Diagnostic hysteroscopy</li> </ul>	<ul style="list-style-type: none"> <li>Transjugular kidney biopsy</li> <li>Hysteroscopy with biopsy</li> <li>Lithotripsy (kidney, bladder, ureter)</li> <li>Amniocentesis</li> </ul>	<ul style="list-style-type: none"> <li>Prostate biopsy</li> <li>Percutaneous kidney biopsy</li> <li>Nephrostomy tube placement</li> </ul>
	<ul style="list-style-type: none"> <li>Dental cleaning</li> <li>Intra-articular injection</li> <li>Lymph node percutaneous biopsy</li> <li>Skin biopsy</li> <li>Drainage catheter exchange</li> </ul>	<ul style="list-style-type: none"> <li>Intra-articular puncture</li> <li>Dental extraction</li> <li>Lumbar puncture</li> </ul>	<ul style="list-style-type: none"> <li>Epidural catheter placement</li> <li>Central nervous system procedure</li> <li>Non liver intraabdominal solid-organ biopsy</li> </ul>

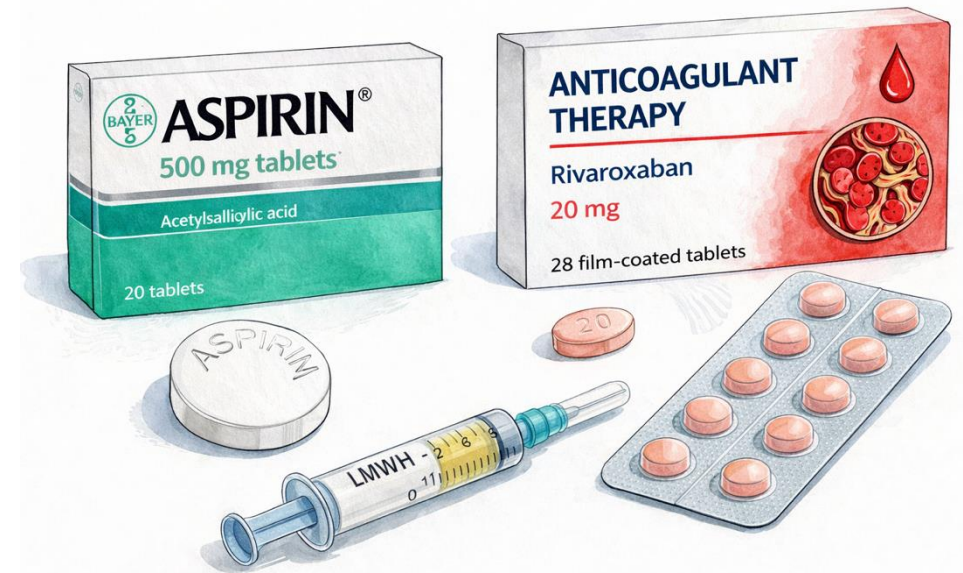
# Antithrombotic drugs

## ANTIPLATELET

1. The effect of **antiplatelet drugs** on procedural bleeding risk is **NOT well documented**.
2. **Clopidogrel** was associated with a **higher incidence of post-procedural bleeding** in the PROC-BLeeD prospective study (no multivariable analysis).
3. **No firm conclusion.**

## ANTICOAGULANT

1. In patients undergoing **EVL**, **LMWH** seems **not associated** with increased risk of bleeding.
2. Bleeding risk increased in patients with cirrhosis chronic liver disease treated with anticoagulant than in patients without anticoagulants.
3. Patients with platelet count  $<50 \times 10^9/L$  may be at higher risk.



Semmler G et al, Liver Int 2021  
Kundumadam S et al, Clin Transl Gastroenterol 2020  
Lieber SR et al, J Clin Gastroenterol 2022

# From prediction to prevention

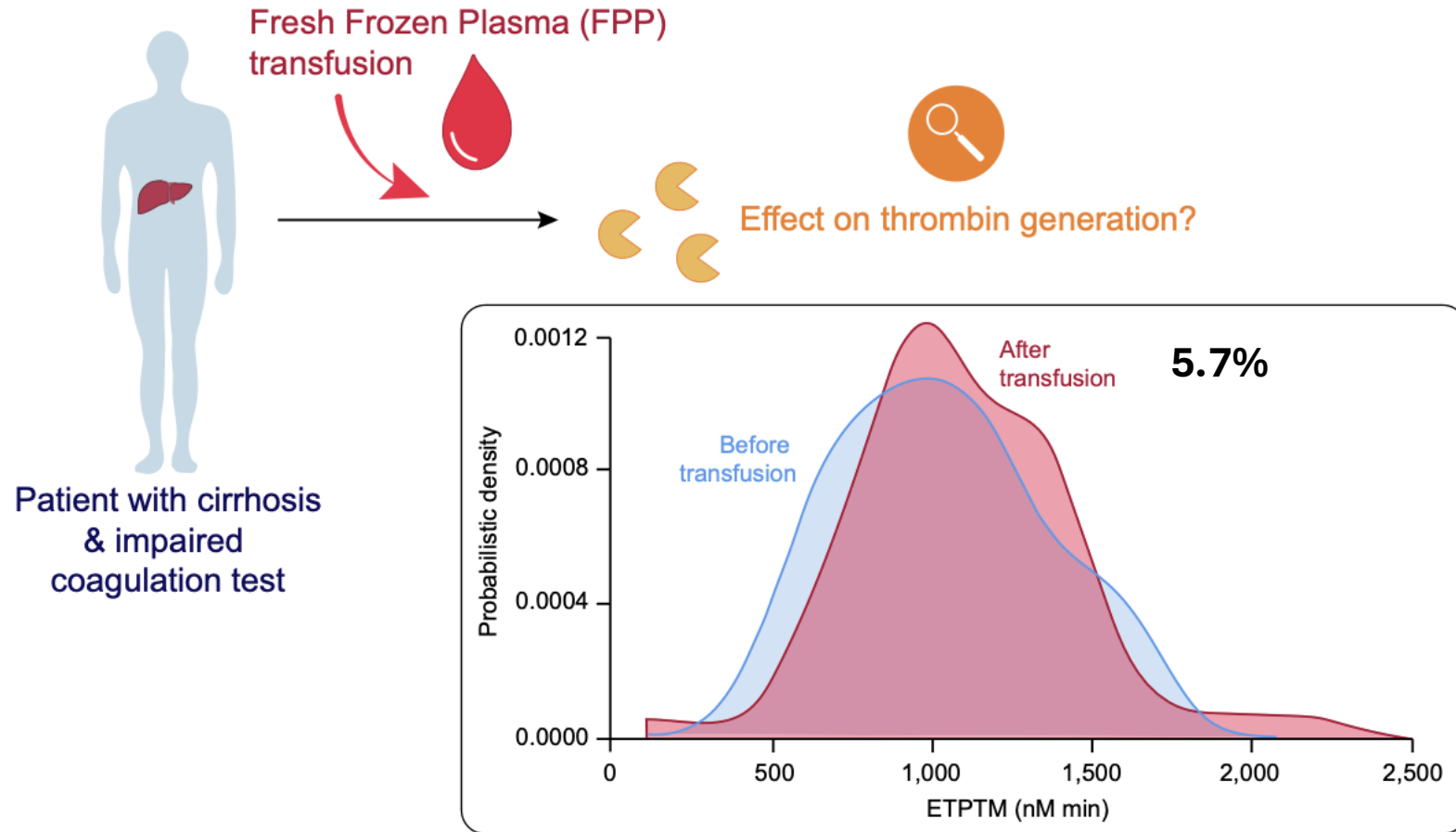
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# Transfusion with cryoprecipitate for very low fibrinogen does NOT affect bleeding in critically ill cirrhosis

Variable	Hazard ratio (HR)	95% CI of HR	Parameter estimate	Standard error	p-Value
Total population					
CLIF-C ACLF score (per unit change)	1.053	1.033–1.074	0.052	0.010	<0.01
Admission to ICU for bleeding	0.416	0.269–0.645	−0.876	0.222	<0.01
Initial fibrinogen level prior to any transfusion (per unit change)	0.999	0.992–1.006	−0.001	0.004	0.68
Transfusion with cryoprecipitate	1.104	0.717–1.699	0.099	0.220	0.65
Population admitted to ICU for bleeding					
CLIF-C ACLF score (per unit change)	1.045	1.005–1.086	0.044	0.020	0.03
Initial fibrinogen level (per unit change)	0.991	0.976–1.005	−0.009	0.007	0.21
Transfusion with cryoprecipitate	1.500	0.532–4.227	0.405	0.529	0.44

# FFP does not improve thrombin generation



- > Enhanced thrombin generation & coagulation tests in a limited number of patients
- > Slight decrease of thrombin generation in 34% of cases

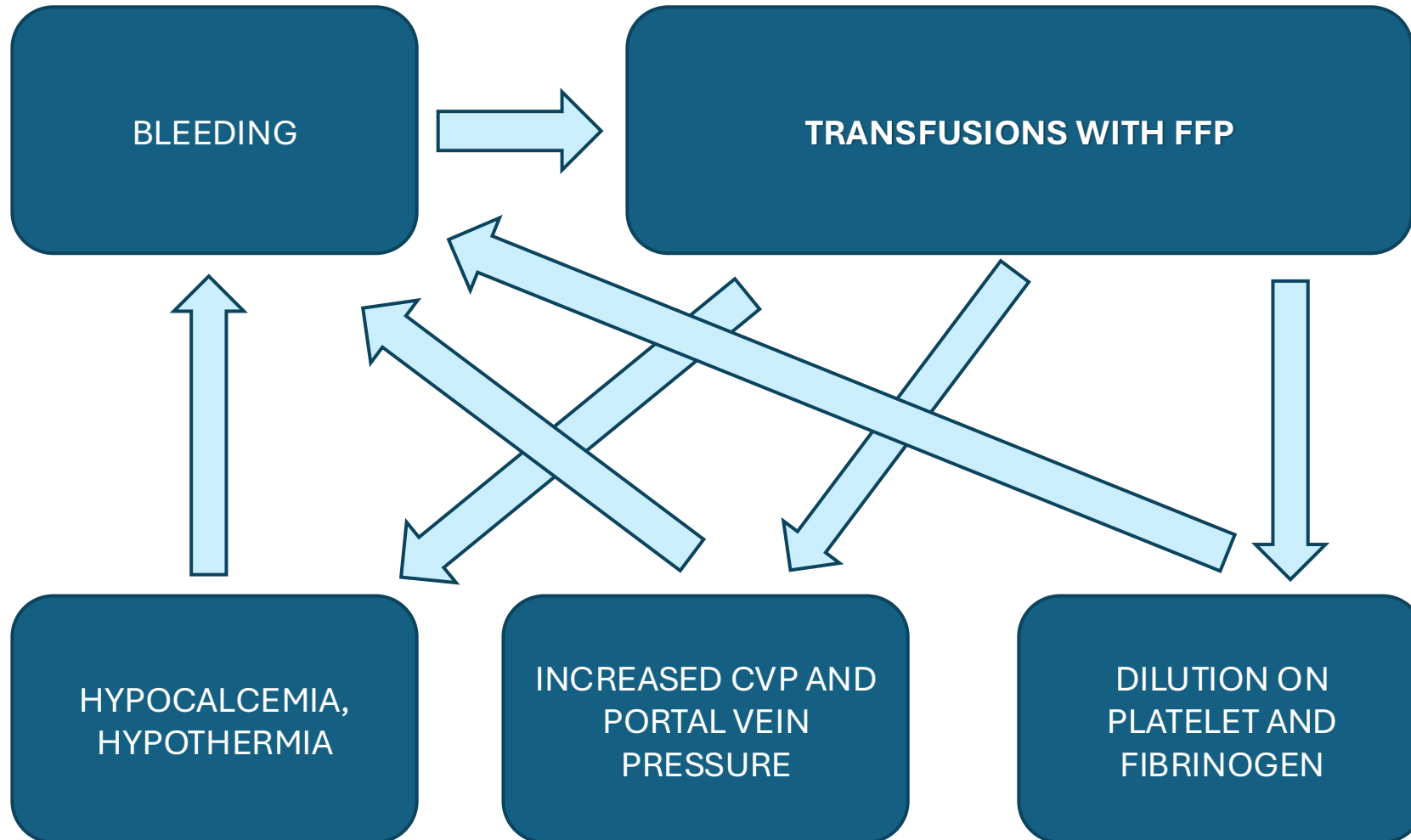
# The issue of volume overload

Author (Year)	Patients	Volume	Target	Correction
Spector 1966	11	0.6-1.8 L	Quick PT >60%	72%
Gazzard 1975	30	0.9 L	PT <3s cont	20%
Mannucci 1976	11	<0.7 L	PT normal	36%
Williamson 1999	11	0.4 L	PT normal	0% <sup>+</sup>
Youssef 2003	100	2-5 units	PT <3s cont	10% <sup>°</sup>

<sup>+</sup> very variable increase in factors; <sup>°</sup> none with 2 units

# Dilutional coagulopathy


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# Recommendations of selected societies for correction of coagulation tests prior to high-risk procedures in cirrhosis


	BSG 2020 <sup>50</sup>	ACG 2020 <sup>51</sup>	AASLD 2021 <sup>38</sup>	AGA 2021 <sup>52</sup>	ISTH 2021 <sup>36</sup>	EASL 2022 <sup>37</sup>
Platelet count $\geq 50 \times 10^9/L$	Do not correct	Do not correct	Do not correct	Do not correct	Do not correct	Do not correct
Platelet count $< 50 \times 10^9/L$	Transvenous approach recommended If not possible (lesional liver biopsy), platelet transfusion or thrombopoietin receptor agonists can be considered	Correct using high doses of platelet infusions; if the procedure is elective, use of thrombopoietin receptor agonists	No routine preprocedural correction	If severe thrombocytopenia and high-risk procedure discussion with a hematologist	Might correct in case of very high-risk surgery (eg, neurosurgery and intraocular surgery) and platelet count $< 30-50 \times 10^9/L$	If the platelet count is $20-50 \times 10^9/L$ and local hemostasis is not possible, correction may be considered If the platelet count is $< 20 \times 10^9/L$ and local hemostasis not possible, correction should be considered
PT/INR	If INR $> 1.4$ , transvenous route recommended For percutaneous lesional biopsies, the INR should be $< 2.0$ Fresh frozen plasma not recommended	Do not correct	Do not correct	Do not correct	Do not evaluate routinely	Do not correct
APTT	Not mentioned	Not mentioned	Not mentioned	Not mentioned	Do not evaluate routinely	Not mentioned
Fibrinogen	No specific recommendation	No specific recommendation	Do not correct	Do not correct	Do not evaluate routinely	Do not correct
Viscoelastic tests	No specific recommendation	May be useful	Do not use routinely	No recommendation	Do not use routinely	Not possible to advise for or against their use

# Optimize patient conditions before procedures




↓


**LOWER BLEEDING RISK**



### TREAT INFECTION


- Early recognition and prompt antibiotics
- Adequate source control when indicated





### TREAT ANEMIA (not transfusion)


- Iron supplementation (oral or IV)
- Erythropoiesis-stimulating agent (ESA)
- Vitamin B12 / Folate repletion if deficient





### TREAT AKI

- Optimize hemodynamics and volume status
- Avoid nephrotoxins
- Consider albumin and vasoconstrictors (e.g. terlipressin)



# Thromboelastography-Guided vs Standard-of-Care or On-Demand Platelet Transfusion in Patients with Cirrhosis and Thrombocytopenia Undergoing Procedures: A Randomized Controlled Trial

## Study Population



Patients with cirrhosis  
Platelet counts  $<50 \times 10^3/\text{mm}^3$   
Undergoing high-risk  
procedures

## Randomization arms



TEG-Guided  
transfusion



Empirical  
transfusion



On-demand  
transfusion



## Study Results



TEG reduced prophylactic transfusions



No procedure-related mortality or major bleeding



Outcomes of On-demand transfusion similar to TEG-guided transfusion

Journal of Vascular and  
Interventional Radiology

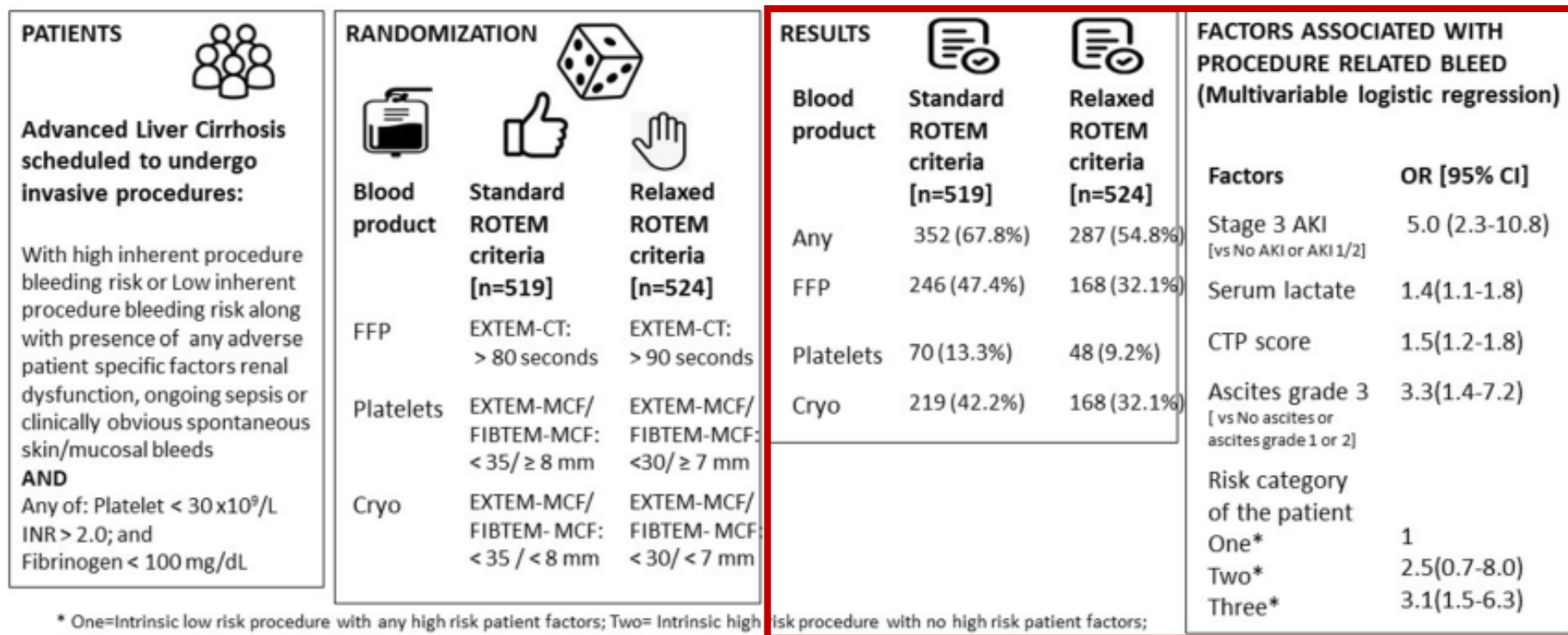
JVIR



## Comparison of relaxed versus standard cut-offs of rotational thromboelastometry for guiding blood product use before invasive procedures in advanced cirrhosis: a randomized controlled trial

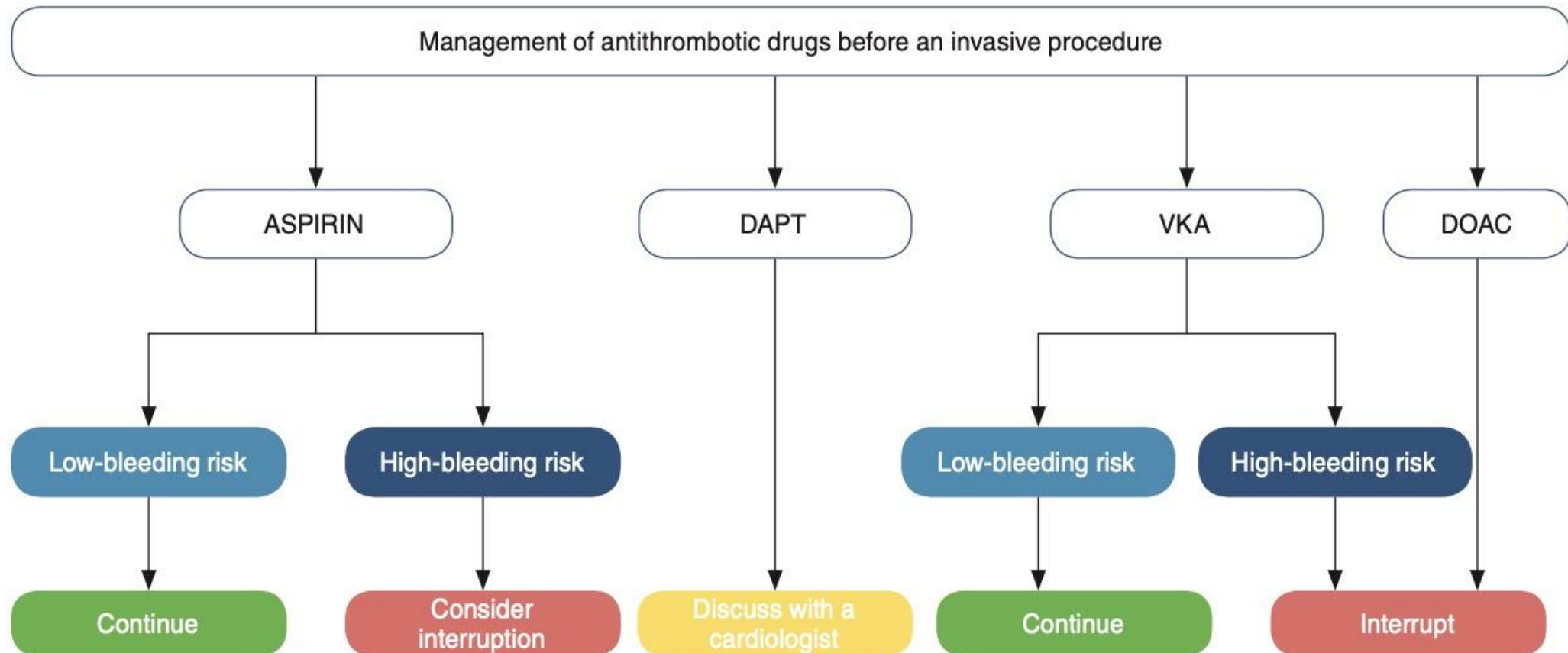
Manoj Kumar<sup>1</sup> · Tushar Madke<sup>1</sup> · Amar Mukund<sup>2</sup> · Yashwant Patidar<sup>5</sup> · Saggere Muralikrishna Shasthry<sup>1</sup> · Chhagan Bihari<sup>3</sup> · Prashant Agarwal<sup>4</sup> · Ankur Jindal<sup>1</sup> · Meenu Bajpai<sup>5</sup> · Rakhi Maiwall<sup>1</sup> · Ashok Choudhary<sup>1</sup> · Vijayraghavan Rajan<sup>1</sup> · Vinod Arora<sup>1</sup> · Harsh Vardhan Thevathia<sup>1</sup> · Babu Lal Meena<sup>1</sup> · Satender Pal Singh<sup>1</sup> · Ashish Maheshwari<sup>5</sup> · Ankit Bhardwaj<sup>6</sup> · Guresh Kumar<sup>7</sup> · Shiv K. Sarin<sup>1</sup>

Received: 29 January 2025 / Accepted: 27 April 2025  
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\* One=Intrinsic low risk procedure with any high risk patient factors; Two= Intrinsic high risk procedure with no high risk patient factors; and Three= Intrinsic high risk procedure with any high risk patient factors

# Management of antithrombotic drugs in the periprocedural period in patients with cirrhosis



# Hemostatic prophylaxis is NOT recommended/discouraged

In patients with cirrhosis undergoing invasive procedures, correction of a prolonged INR with **FFP** is **not recommended** to decrease the rate of procedure-related clinically relevant bleeding (LoE 2, strong recommendation).

In patients with cirrhosis undergoing invasive procedures, routine use of **PCCs** to decrease the rate of procedure-related clinically relevant bleeding **is discouraged** (LoE 3, weak recommendation).

In patients with cirrhosis undergoing invasive procedures, routine use of **tranexamic acid** to decrease the rate of procedure-related clinically relevant bleeding **is discouraged** (LoE 4, weak recommendation).

In patients with cirrhosis undergoing invasive procedures, routine correction of **fibrinogen deficiency** to decrease the rate of procedure-related clinically relevant bleeding **is discouraged** (LoE 4, strong recommendation).

Infusion of **platelet concentrates** or use of **TPO-R agonists** is **not recommended when platelet count is above  $50 \times 10^9/L$**  or when bleeding can be treated by local haemostasis (LoE 3/4, strong recommendation).

In patients undergoing **high-risk procedures** in whom local haemostasis is not possible and **platelet count is between  $20 \times 10^9/L$  and  $50 \times 10^9/L$**  infusion of platelet concentrates, or TPO-R agonists should **not be routinely performed but may be considered** on a case-by-case basis (LoE 3/4, strong recommendation).

In patients undergoing **high-risk procedures** in whom local haemostasis is not possible and **platelet count is very low ( $20 \times 10^9/L$ )**, infusion of platelet concentrates or TPO-R agonists **should be considered on a case-by-case basis** (LoE 3/4, strong recommendation).

# Predicting bleeding does necessarily mean that we will be able to avoid these bleeding...

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But we suggest it remains important to:

- Optimize patient management, especially in acute settings.
- Guide tailored interventions,
- Optimize procedural planning,
- Facilitate alternative strategies for invasive procedures
- Support patient awareness and informed consent.

# Take home messages

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1. Prediction of procedure-related bleeding in cirrhosis remains challenging.
2. Comprehensive assessment including liver and non-liver related factors is key.
3. Further research is needed to understand how to move from prediction to prevention.