



Troubles de l'hémostase dans la cirrhose : évaluation, prévention et traitement des hémorragies post-procédure invasive

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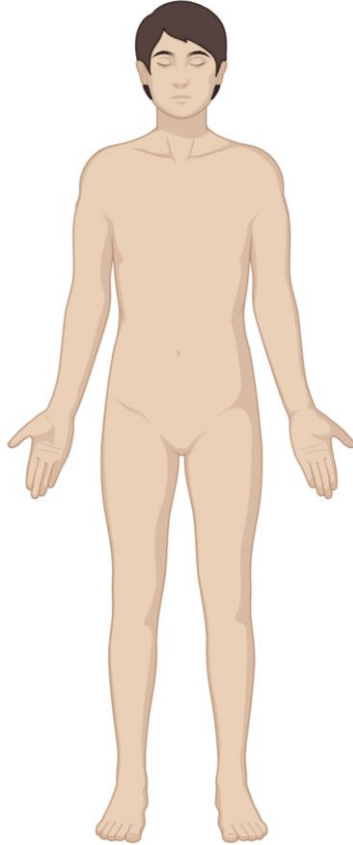
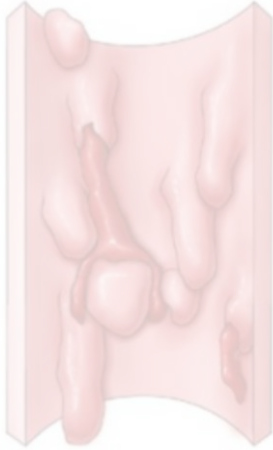


Conflicts of interest

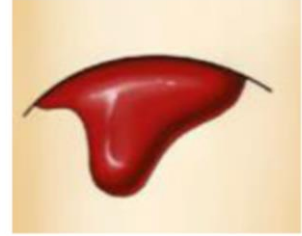
- I do not have a financial relationship relevant to that presentation
- I am not discussing off-label investigative use of a drug/device/product

Bleeding in patients with cirrhosis

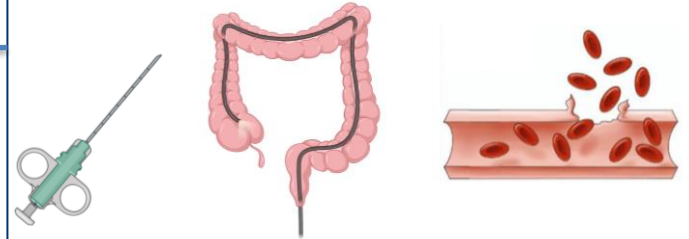
Portal hypertension



Haemostasis related



Post-procedure



Invasive procedures in patients with cirrhosis

- Coagulation changes in patients with cirrhosis
- Management of invasive procedures in cirrhosis
- Management of anticoagulants and antiplatelet agents

Coagulation in cirrhosis

Primary hemostasis:

platelet aggregation

Coagulation:

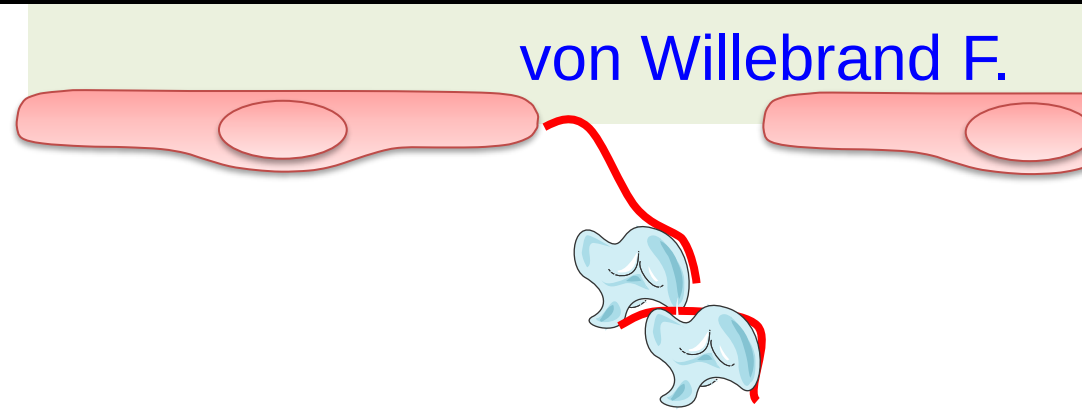
fibrin formation

Fibrinolysis:

fibrin lysis

Coagulation in cirrhosis

Primary hemostasis:
platelet aggregation



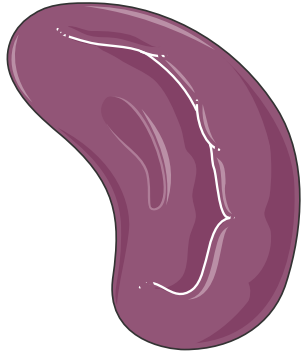
Thrombocytopenia

↑ von Willebrand F.
↑ Multimer size

Favors bleeding

Favors thrombosis

Thrombocytopenia and cirrhosis

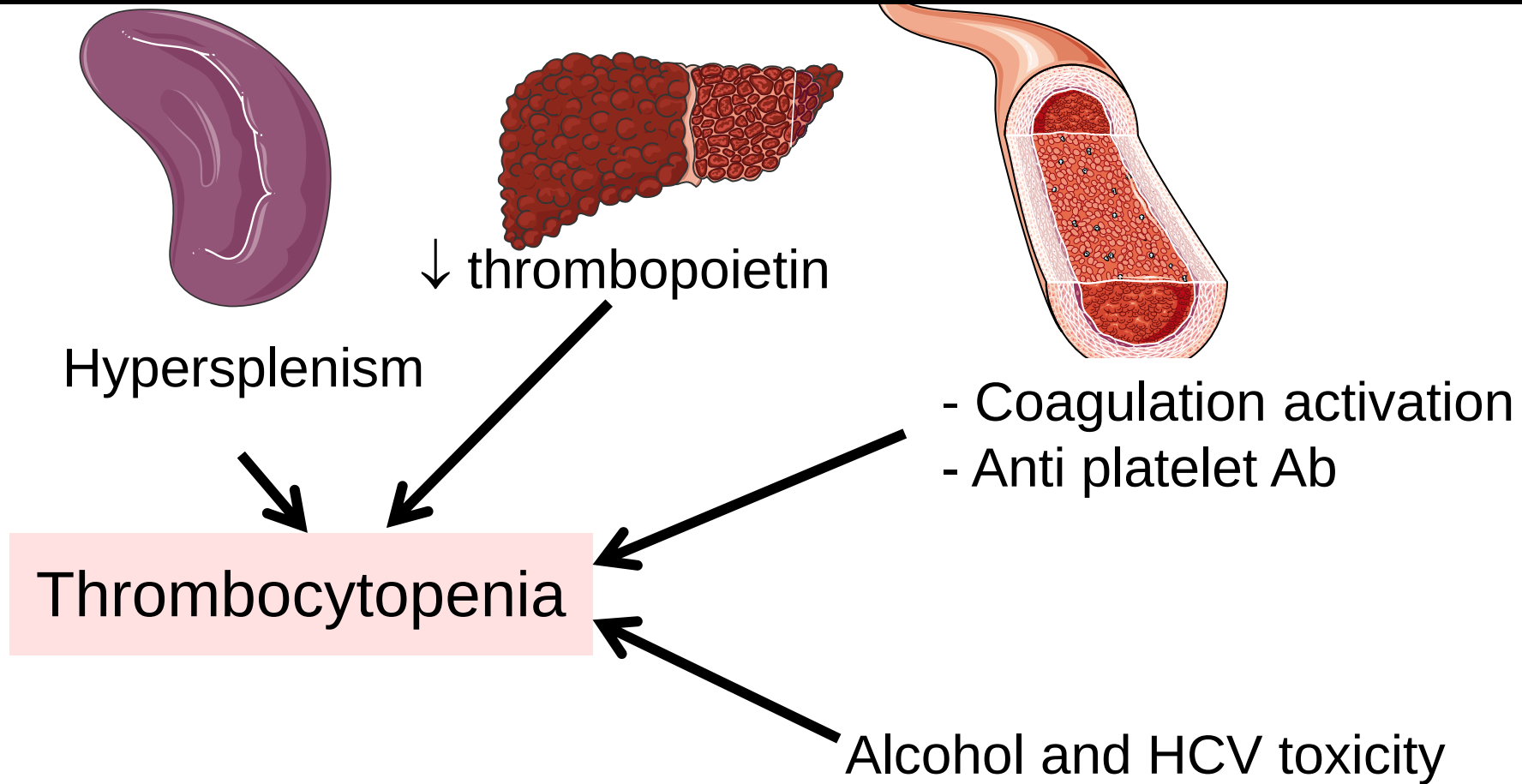


Hypersplenism



Thrombocytopenia

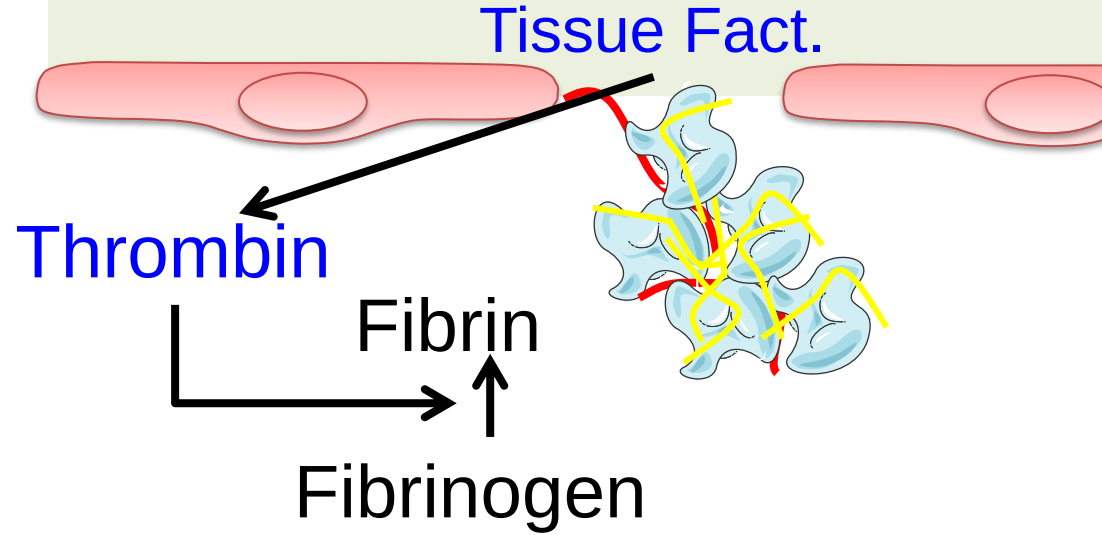
Thrombocytopenia and cirrhosis



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:

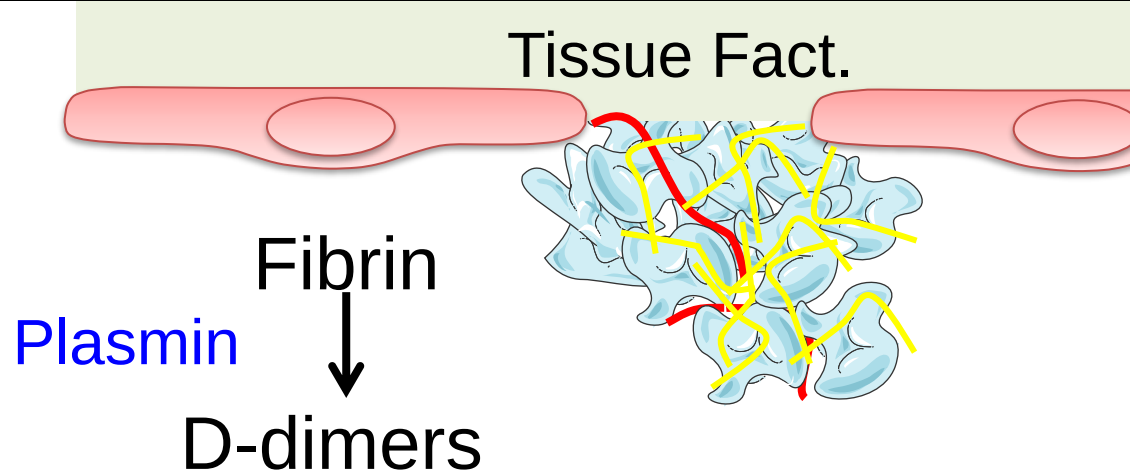
platelet aggregation

Coagulation:

fibrin formation

Fibrinolysis:

fibrin lysis



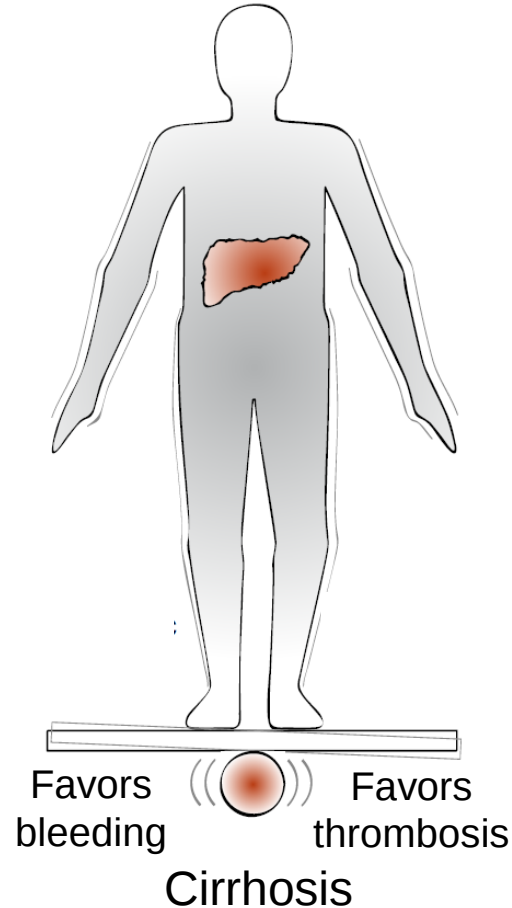
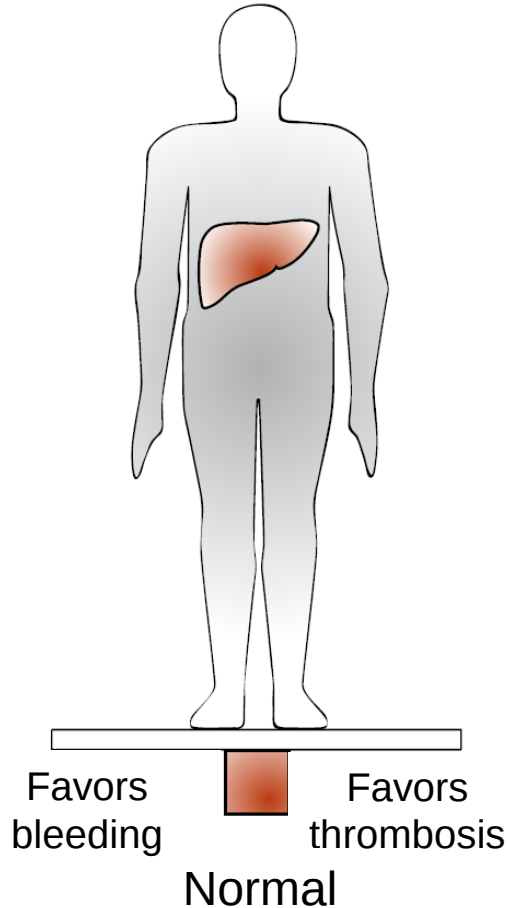
↑ tPA

Favors bleeding

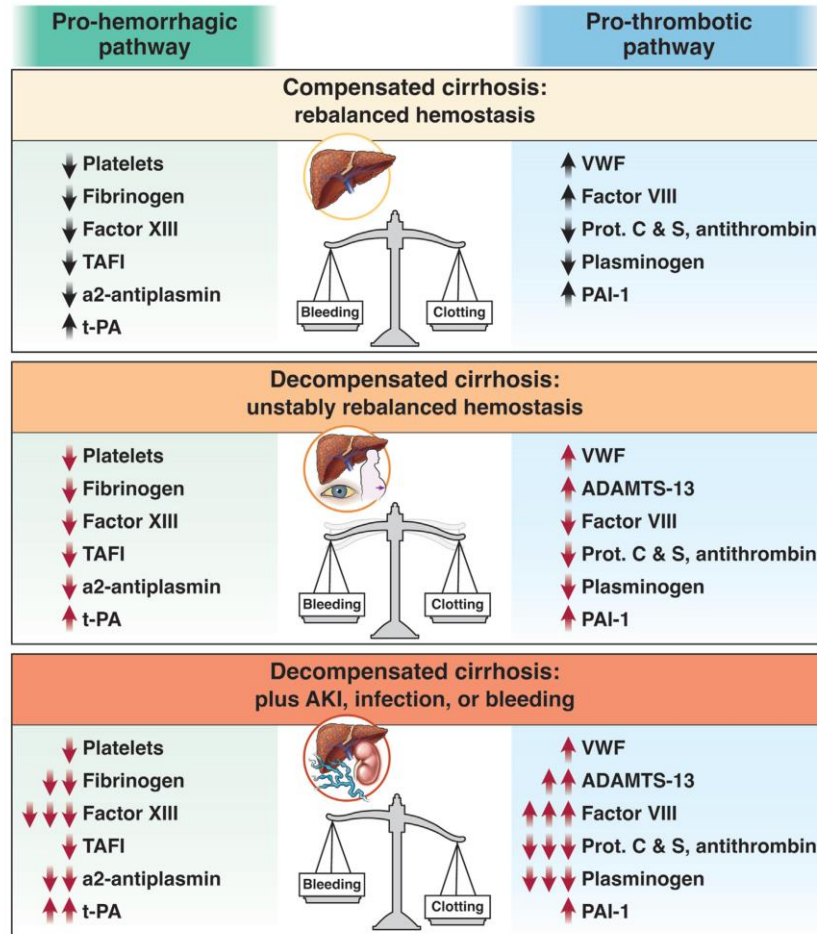
↓ plasminogen, α_2
antiplasmin, ↑ PAI-1

Favors thrombosis

Coagulation in cirrhosis



Coagulation changes with cirrhosis progression



Coagulation in cirrhosis



Invasive procedures in patients with cirrhosis

- Coagulation changes in patients with cirrhosis
- Management of invasive procedures in cirrhosis
- Management of anticoagulants and antiplatelet agents

Invasive procedures in patients with cirrhosis

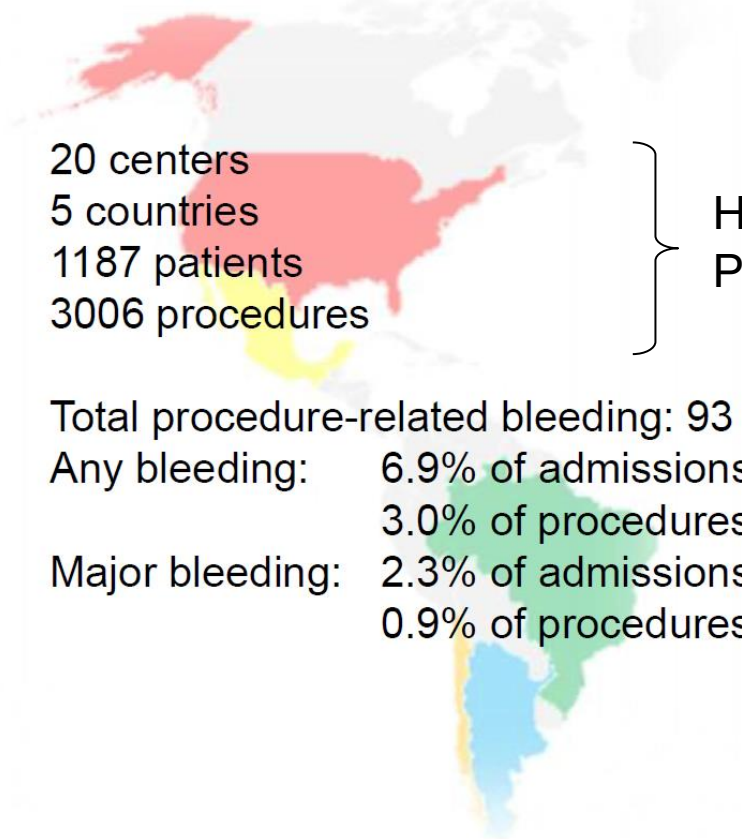
- The patient
- The procedure
- The laboratory

Prediction: the patient

When the procedure is scheduled

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

Predictors of bleeding in hospitalized patients with cirrhosis



20 centers
5 countries
1187 patients
3006 procedures

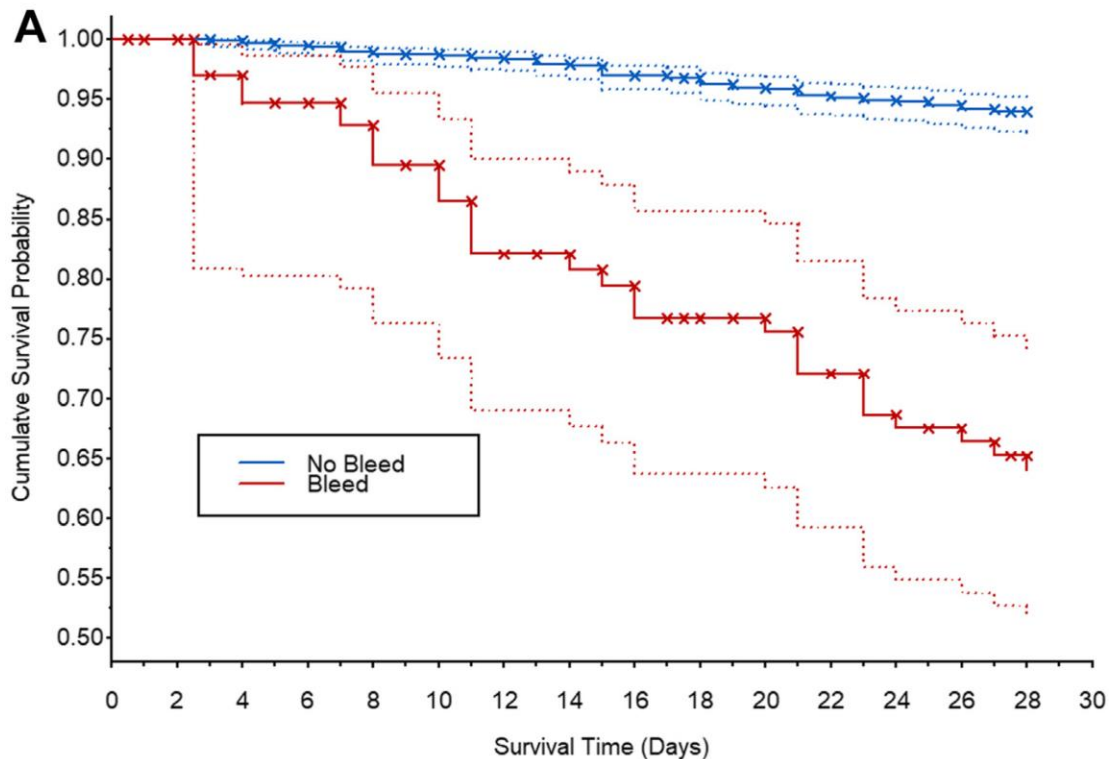
Hospitalized patients with cirrhosis
Prospectively enrolled

Total procedure-related bleeding: 93
Any bleeding: 6.9% of admissions
3.0% of procedures
Major bleeding: 2.3% of admissions
0.9% of procedures

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



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 $> 1.5\%$



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 ≥ 50 × 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 × 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



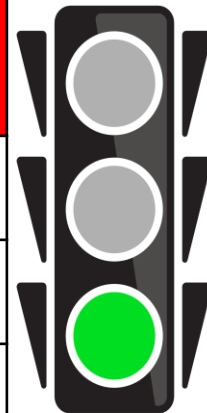
Consensus for 52 procedures

35 at low risk of bleeding

17 at high risk of bleeding

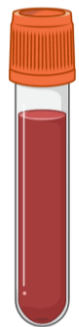
Suggested thresholds

	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

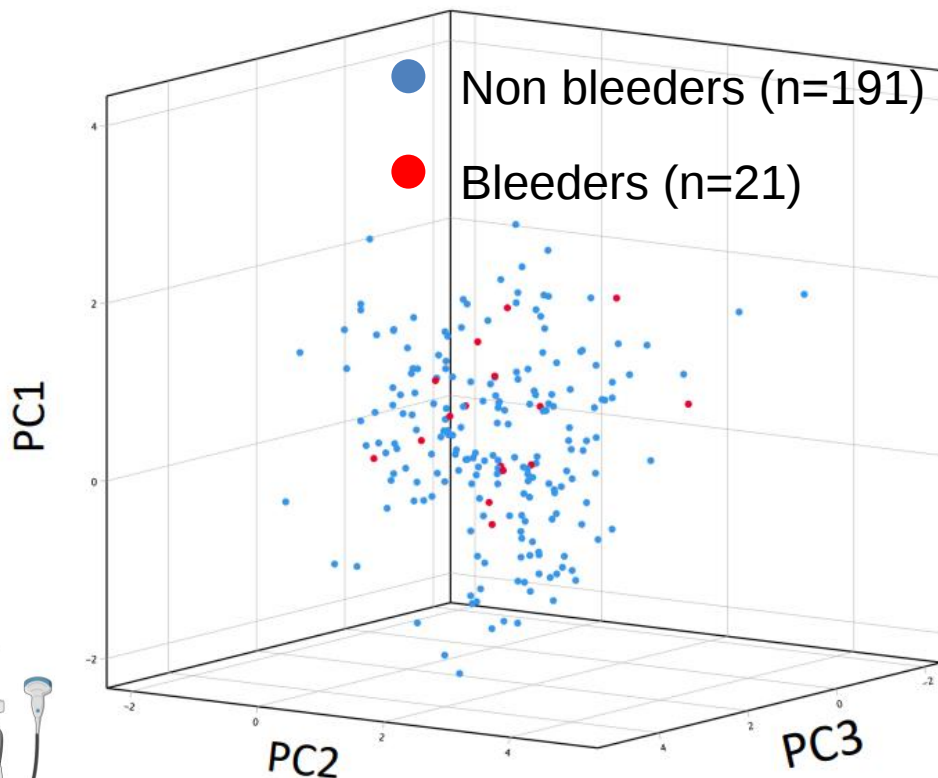
302 patients undergoing liver biopsy



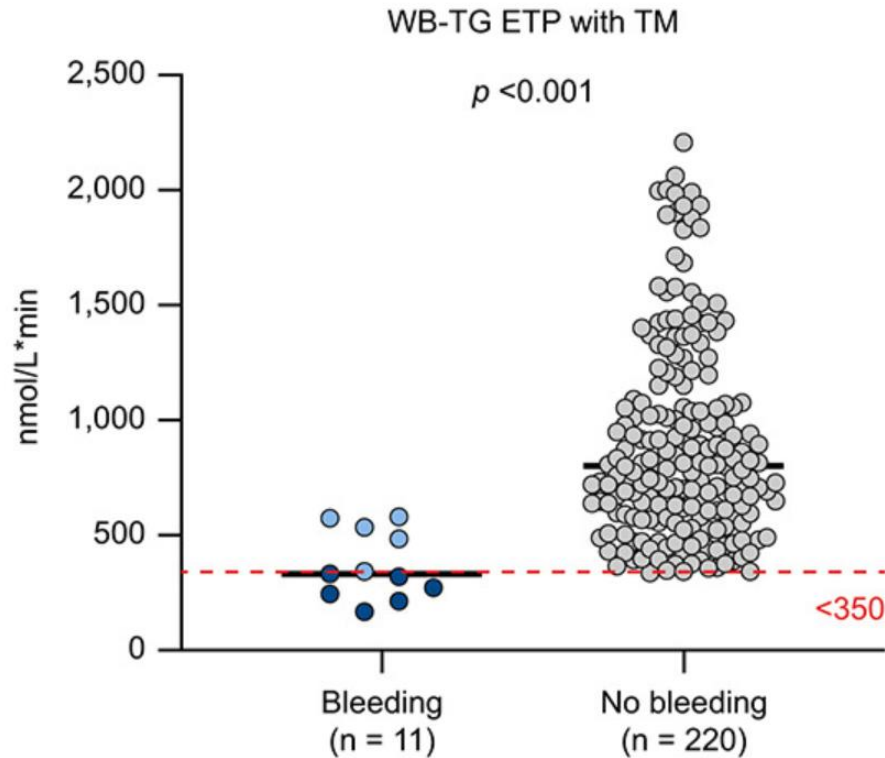
- PT, aPTT, platelet, coag factors
- PFA-100
- Thromboelastography
- Thrombin generation assays
- Plasma clot lysis time
- Clinical questionnaire



Endpoint: liver hematoma or ↓ Hb



Whole blood thrombin generation assay: some potential?



Major Clinically relevant non-major

Zanetto, et al. J Hepatol 2025

Going beyond the limits: interest of thromboelastography?

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



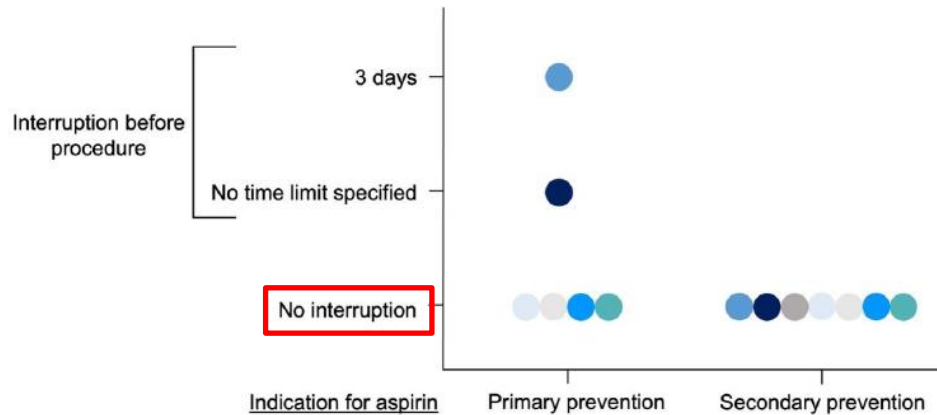
	SOC (n=30)	TEG guided (n=30)
PLT transfusion	46%	17%
FFP transfusion	66%	10%
Bleeding	3%	0%
Allergic reaction	3%	0%

Invasive procedures in patients with cirrhosis

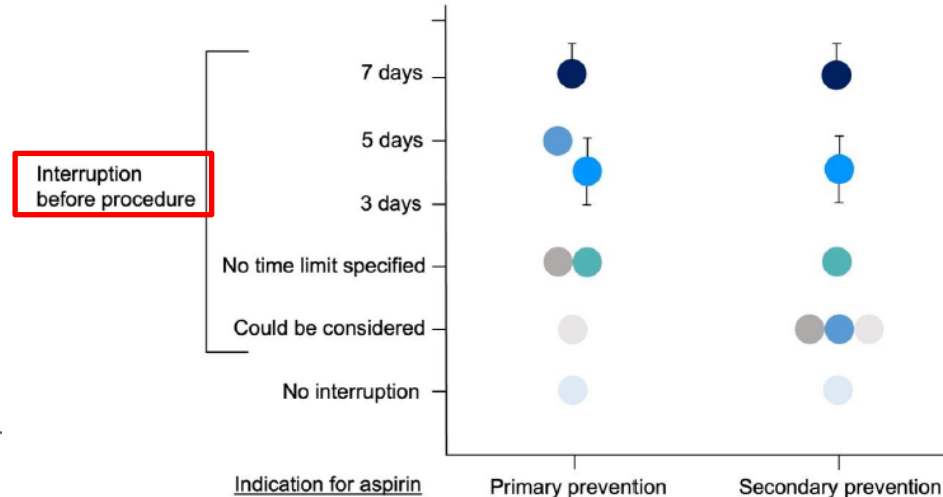
- Coagulation changes in patients with cirrhosis
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Management of aspirin before invasive procedures

Low-risk procedure

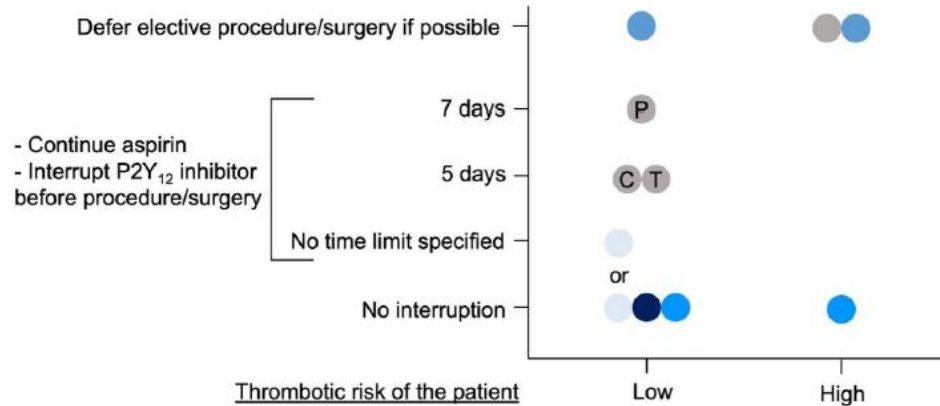


High-risk procedure

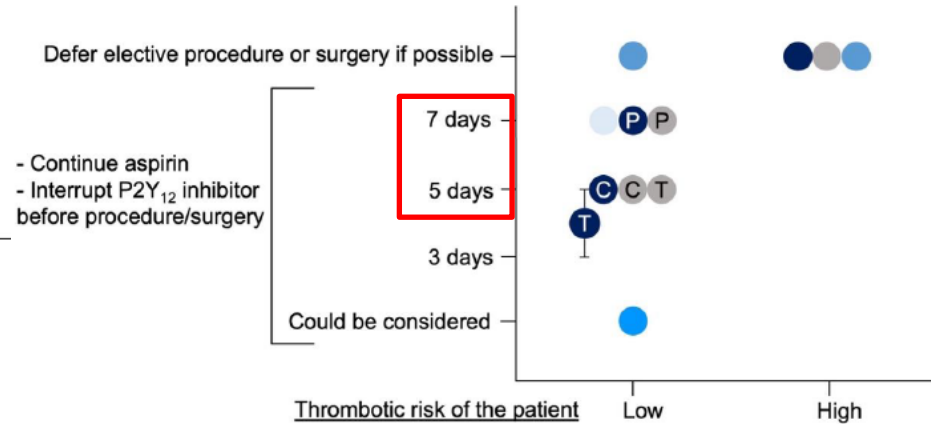


Management of DAPT before invasive procedures

Low-risk procedure



High-risk procedure



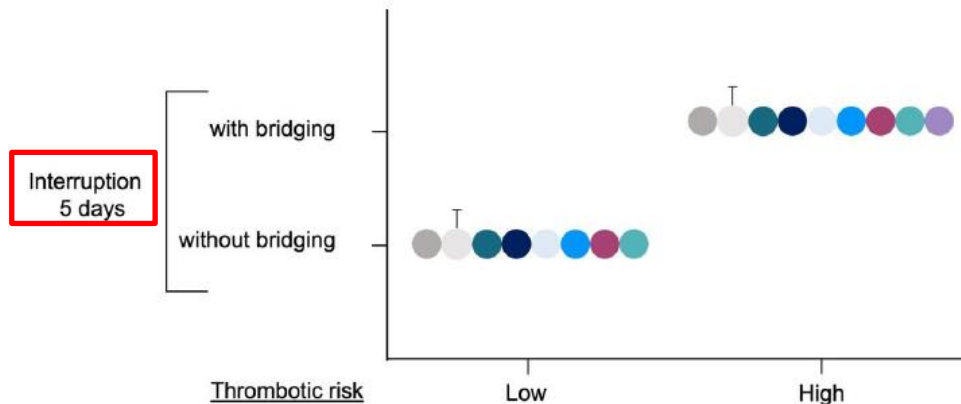
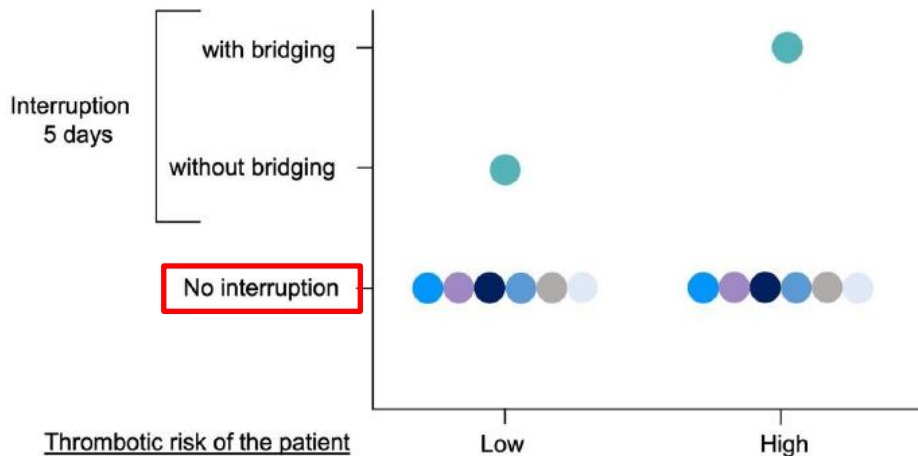
Halvorsen, 2022³⁰ Barkun, 2022⁹⁵ Kietai, 2023⁹⁴ Veitch, 2021⁹² Joglar, 2024⁹⁷

Patel, 2019⁵ Lester, 2024⁹⁵ Douketis, 2022⁹³ Vahanian, 2022⁹⁶

Management of VKA before invasive procedures

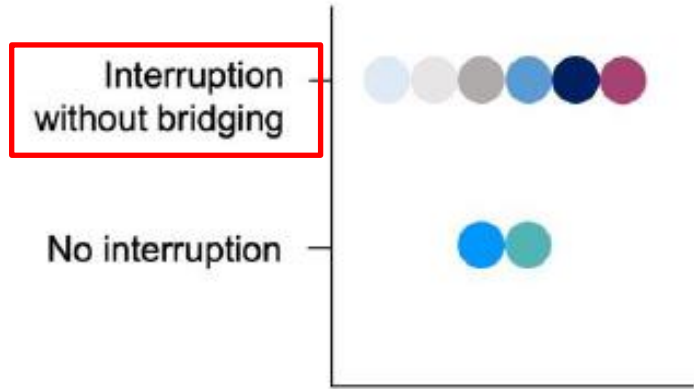
Low-risk procedure

High-risk procedure

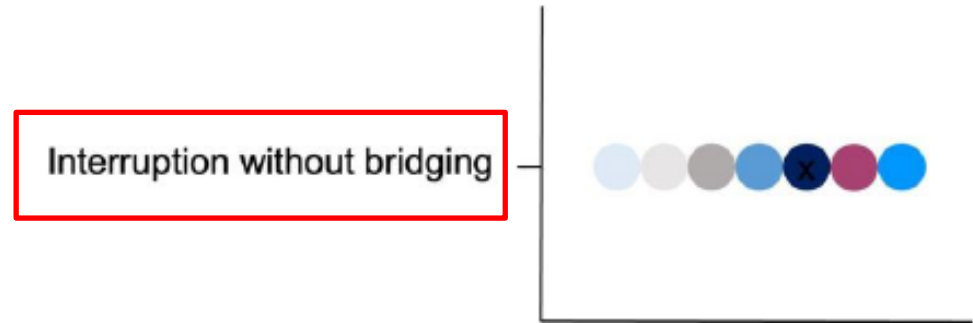


Management of DOACs before procedure

Low-risk procedure



High-risk procedure



Management of DOACs and VKA before procedures

		Day -5	Day -4	Day -3	Day -2	Day -1		Day +1	Day +2	Day +3
LOW-BLEEDING RISK	RIVAROXABAN APIXABAN EDOXABAN DABIGATRAN (CrCl ≥ 50 mL/min)					STOP	STOP			
	DABIGATRAN (CrCl 30-50 mL/min)				STOP	STOP	STOP			
	WARFARIN									
HIGH-BLEEDING RISK	RIVAROXABAN APIXABAN EDOXABAN DABIGATRAN (CrCl ≥ 50 mL/min)				STOP	STOP	STOP	STOP		
	DABIGATRAN (CrCl 30-50 mL/min)		STOP	STOP	STOP	STOP	STOP	STOP		
	WARFARIN	STOP	STOP	STOP	STOP	STOP	STOP*			

Treatment of post-procedure bleeding

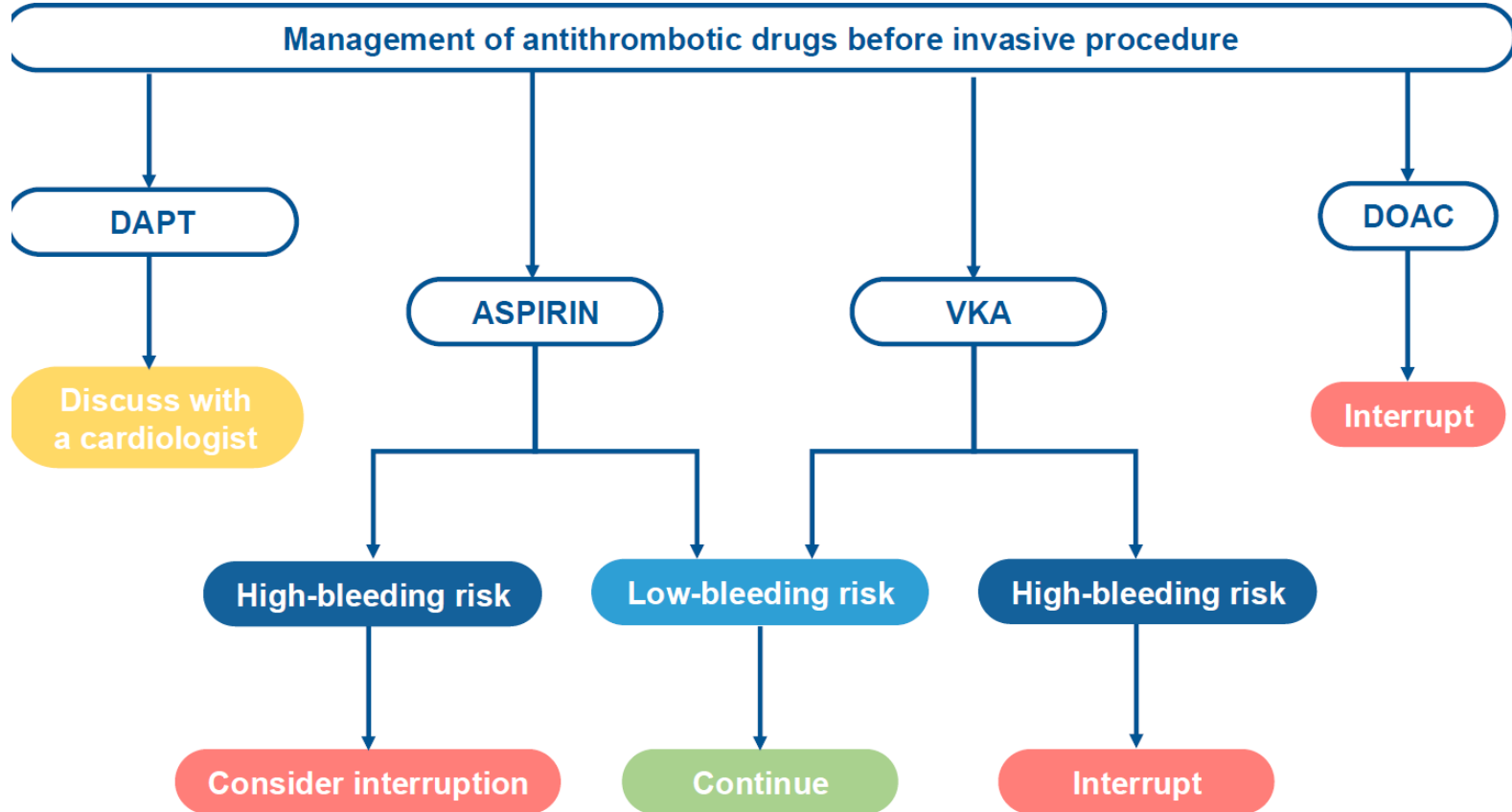
Local treatment +++

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

Conclusion #1

- **Cirrhosis:** fragile balance of haemostasis
- **Predict: be careful if**
 - ✓ platelets $< 50'000/\text{mm}^3$
 - ✓ “we can not put the finger”

Conclusion #2



Networks for vascular liver diseases



European
Reference
Network

Hepatological Diseases
(ERN RARE-LIVER)



VALDIG

VASCULAR LIVER DISEASE GROUP



French network for vascular liver diseases

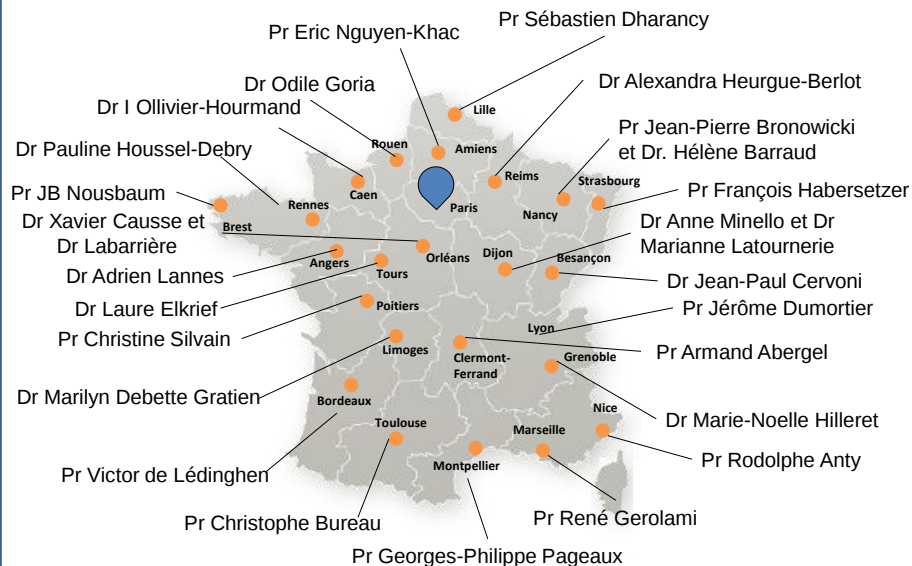


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MALADIES VASCULAIRES
DU FOIE



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DU FOIE DE L'ADULTE ET DE L'ENFANT

Centre de compétence maladies vasculaires du foie



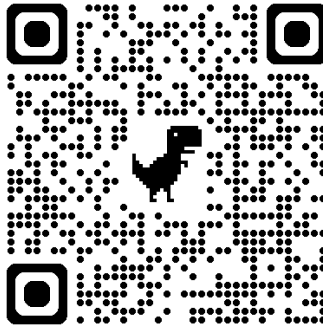
crmvmf.foie@bjn.aphp.fr

European vascular liver diseases network

EURO-VALDI-NET

Start Date: 01/11/2024

End Date: 01/11/2028





Hepatology unit, Beaujon Hospital
Reference center for vascular liver diseases



Inserm U1149 www.rautoulab.com/
Team "vessels in liver diseases"



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