Thrombose splanchnique

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Médecine interne
CHUM

Conférence CanVECTOR

Conflit d’intérêt

- Aucun
- Je ferai des recommandations hors indication

Objectifs

- Utiliser les guides cliniques pour les thromboses intra-abdominales
- Intégrer les notions des études récentes
- Instituer une anticoagulothérapie appropriée

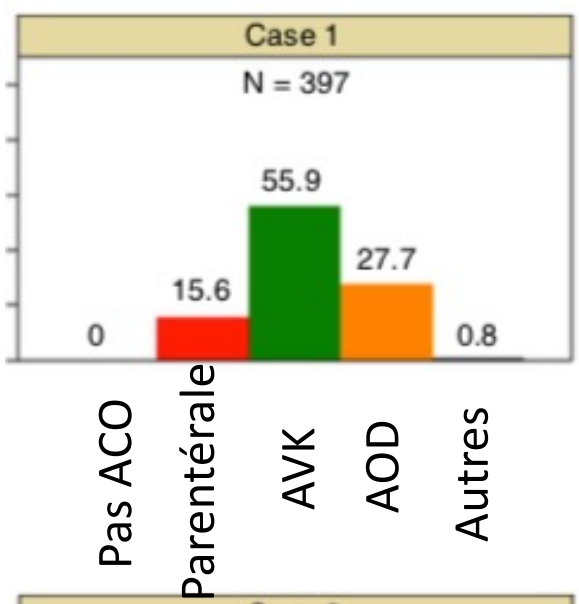
Plan

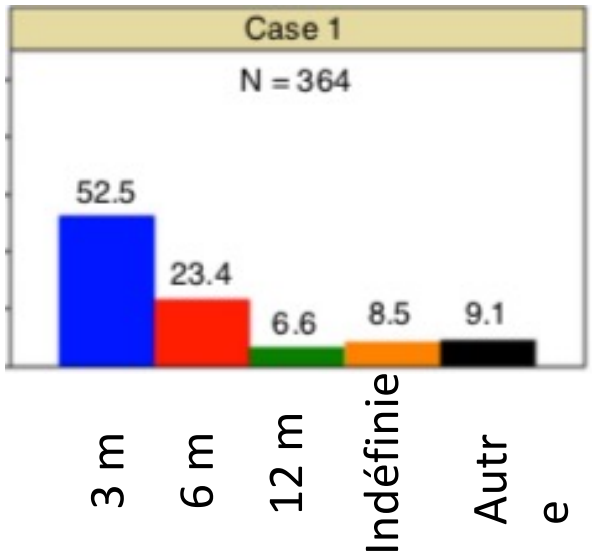
- Introduction
- Épidémiologie
- Lignes directrices
  - Données supportant les recommandations
- Données récentes
- Place des anticoagulants oraux directs

Je n'aborderai pas les thromboses des veines sus-hépatiques (Budd-Chiari), les traitements invasifs, ni la présentation clinique et investigations

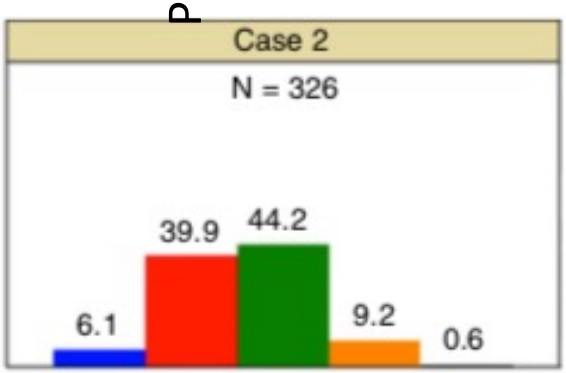
En pratique

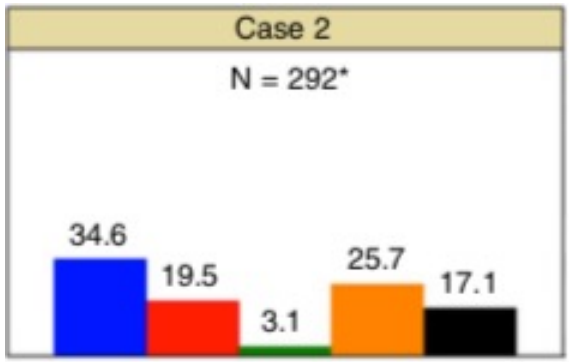
Thrombose splanchnique en présence d'un facteur provoquant





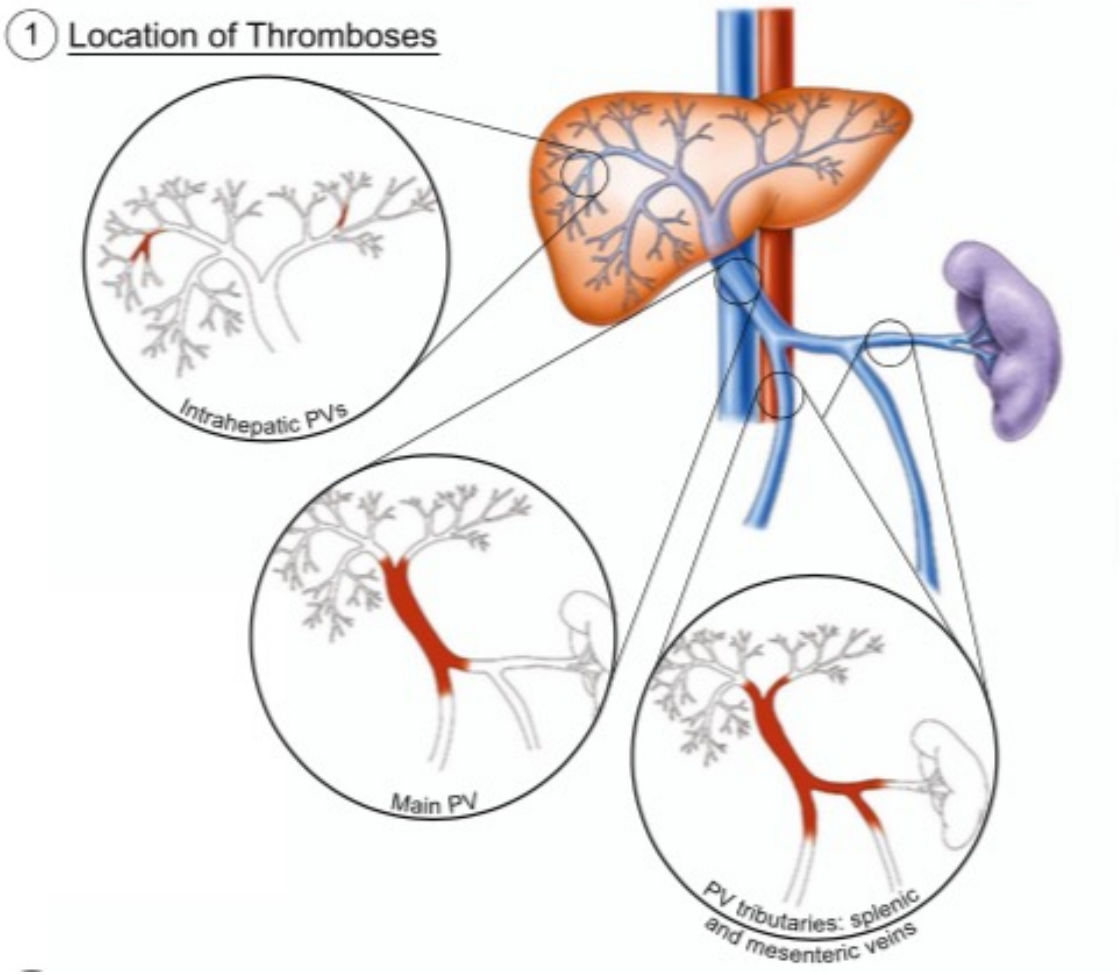
Thrombose porte chez patient cirrhotique Child Pugh B avec varices œsophagiennes grade 2





Tiré de Riva, N., et al. (2020)

Localisation



Tiré de Northup, P. G., et al. (2021)

Prévalence à l'autopsie thrombose portale :

- Sans cirrhose 0.05%
- Cirrhose : 6.59%

Incidence à 1 an après Dx cirrhose 3.2 à 4.1%

Incidence 1.73 et 3.78/100 000 p-a (femmes et hommes)

Northup, P. G., et al. (2021)
Riva, N. and W. Ageno (2020)

Aiguë VS chronique

TABLE 5. Recommended Standardized Nomenclature for Description of PVT in Both the Clinical and Research Setting

Descriptor	Definition
Time course	
Recent/aiguë	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

Tiré de Northup, P. G., et al. (2021)

Facteurs de risque

Incidence 1 an post-chirurgie abdominale : 2.68%

Table I Risk Factors For Splanchnic Vein Thrombosis

Risk Factors For SVT		
Persistent Acquired Risk Factors	**Transient Acquired Risk Factors**	**Inherited Risk Factors**
Liver cirrhosis 25%	Intra-abdominal Inflammations/infections	Factor V Leiden mutation
Solid cancer 25%	Abdominal surgery	Prothrombin G20210A mutation
Myeloproliferative neoplasm 10%	Hormonal therapy	JAK2V617F mutation
Inflammatory bowel disease	Pregnancy or puerperium	Protein C deficiency
Antiphospholipid syndrome		Protein S deficiency
Other hematologic disease (e.g. PNH)		Antithrombin deficiency
Autoimmune disease (e.g. Behçet's disease)		

Abbreviations: PNH, paroxysmal nocturnal haemoglobinuria; SVT, splanchnic vein thrombosis.

Tiré de Valeriani, E., et al. (2019)

1/3 >1 facteurs de risque

15 à 27% non provoqué

Zhang, B., et al. (2020)

Évidences

Current Outcome of Portal Vein Thrombosis in Adults: Risk and Benefit of Anticoagulant Therapy

BERTRAND CONDAT,* FABIENNE PESSIONE,* SOPHIE HILLAIRE,* MARIE-HELENE DENNINGER,‡ MARIE-CLAUDE GUILLIN,‡ MARC POLIQUIN,* ANTOINE HADENGUE,* SERGE ERLINGER,* and DOMINIQUE VALLA*

Saignements (IC 95%)/100 p-a	Évènements thrombotiques (IC 95%)/100 p-a
12.5 (10 à 15)	5.5 (3.8 à 7.2)

Pas d'association entre risque/sévérité de saignement GI et traitement anticoagulant

Récidive d'évènements thrombotiques réseau portal

	Anticoagulation (/100 p-a)	Sans anticoagulation (/100 p-a)	Risque relatif (IC 95%)
Population complète	0.64	1.87	2.9 (0.6 à 14)
État prothrombotique	0.82	5.19	6.3 (1.3 à 30.4)

Condat, B., et al. (2001)

Acute Portal Vein Thrombosis Unrelated to Cirrhosis: A Prospective Multicenter Follow-up Study

Aurelie Plessier,[1] Sarwa Darwish-Murad,[2] Manuel Hernandez-Guerra,[3] Yann Consigny,[1] Federica Fabris,[4] Jonel Trebicka,[5] Jorg Heller,[5] Isabelle Morard,[6] Luc Lasser,[7] Philippe Langlet,[7] Marie-Hélène Denninger,[8] Dominique Vidaud,[8] Bertrand Condat,[1] Antoine Hadengue,[6] Massimo Primignani,[4] Juan-Carlos Garcia-Pagan,[3] Harry L. A. Janssen,[2] and Dominique Valla[1] for the European Network for Vascular Disorders of the Liver (EN-Vie)

Vaisseaux	Taux recanalisation 1 an
Veine porte/branches principales	38%
Veine mésentérique supérieure	61%
Veine splénique	54%

Saignement : 9/95 patients (''sévère'' chez 5 patients)

Pas de recanalisation thrombose porte après 6 mois post-initiation anticoagulation

Plessier, A., et al. (2010)

Original Investigation

Long-term Clinical Outcomes of Splanchnic Vein Thrombosis
Results of an International Registry

Walter Ageno, MD; Nicoletta Riva, MD; Sam Schulman, MD; Jan Beyer-Westendorf, MD; Soo Mee Bang, MD; Marco Senzolo, MD; Elvira Grandone, MD; Samantha Pasca, MD; Matteo Nicola Dario Di Minno, MD; Rita Duce, MD; Alessandra Malato, MD; Rita Santoro, MD; Daniela Poli, MD; Peter Verhamme, MD; Ida Martinelli, MD; Pieter Kamphuisen, MD; Doyeun Oh, MD; Elbio D'Amico, MD; Cecilia Becattini, MD; Valerio De Stefano, MD; Gianpaolo Vidili, MD; Antonella Vaccarino, MD; Barbara Nardo, MD; Marcello Di Nisio, MD; Francesco Dentali, MD

Table 3. Incidence of Outcome Events in Subgroups With Different Risk Factors[a]

Outcome	Liver Cirrhosis (n = 167)	Solid Cancer (n = 136)	Myeloproliferative Neoplasm (n = 49)	Unprovoked SVT (n = 163)	Transient Risk Factors[b] (n = 105)
Major bleeding events	22 Events; 10.0 per 100 patient-years (6.6-15.1)	7 Events; 4.4 per 100 patient-years (2.1-9.3)	3 Events; 3.6 per 100 patient-years (1.1-11.1)	5 Events; 1.7 per 100 patient-years (0.7-4.2)	1 Event; 0.5 per 100 patient-year (0.1-3.7)
Thrombotic events	25 Events; 11.3 per 100 patient-years (7.7-16.8)	12 Events; 7.6 per 100 patient-years (4.3-13.3)	5 Events; 5.9 per 100 patient-year (2.5-14.3)	18 Events; 6.3 per 100 patient-year (4.0-10.0)	6 Events; 3.2 per 100 patient-year (1.4-7.0)
Mortality	45 Events; 16.8 per 100 patient-year (12.5-22.4)	67 Events; 39.5 per 100 patient-years (31.1-50.1)	3 Events; 3.4 per 100 patient-year (1.1-10.4)	7 Events; 2.3 per 100 patient-years (1.1-4.8)	5 Events; 2.5 per 100 patient-years (1.1-6.1)

Tirée de Ageno, W., et al. (2015)

Traitement anticoagulant associé à diminution risque saignement majeur et évènements thrombotiques

Risque évènement thrombotique > risque saignement majeur

Lignes directrices

HEPATOLOGY **2020**

HEPATOLOGY, VOL. 73, NO. 1, 2021

Vascular Liver Disorders, Portal Vein Thrombosis, and Procedural Bleeding in Patients With Liver Disease: 2020 Practice Guidance by the American Association for the Study of Liver Diseases

Patrick G. Northup[1], Juan Carlos Garcia-Pagan[2-4], Guadalupe Garcia-Tsao[5,6], Nicolas M. Intagliata[1], Riccardo A. Superina[7], Lara N. Roberts[8], Ton Lisman[9], and Dominique C. Valla[10,11]

Baveno VII – Renewing consensus in portal hypertension

Roberto de Franchis[1,*], Jaime Bosch[2,3], Guadalupe Garcia-Tsao[4,5], Thomas Reiberger[6,7], Cristina Ripoll[8], on behalf of the Baveno VII Faculty[§]

2022

CHEST **2012** Supplement

ANTITHROMBOTIC THERAPY AND PREVENTION OF THROMBOSIS, 9TH ED: ACCP GUIDELINES

Antithrombotic Therapy for VTE Disease

Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Clive Kearon, MD, PhD; Elie A. Akl, MD, MPH, PhD; Anthony J. Comerota, MD; Paolo Prandoni, MD, PhD; Henri Bounameaux, MD; Samuel Z. Goldhaber, MD, FCCP; Michael E. Nelson, MD, FCCP; Philip S. Wells, MD; Michael K. Gould, MD, FCCP; Francesco Dentali, MD; Mark Crowther, MD; and Susan R. Kahn, MD

Clinical Practice Guidelines

JOURNAL OF HEPATOLOGY

EASL Clinical Practice Guidelines: Vascular diseases of the liver☆

European Association for the Study of the Liver*

2016

ACCP 2012

ACCP 2012[69]				
Type of patients		**Type of anticoagulation**	**Duration of anticoagulation**	
SVT (except BCS)	Incidentally detected (2, C)	Not suggested°		
	Symptomatic (1,B)	LMWH → VKA#	Transient risk factor	3 months
			Persistent risk factor or unprovoked	Extended anticoagulant therapy

Tiré de Valeriani, E., et al. (2019)

Kearon, C., et al. (2012)

Trouvailles fortuites

- Trouvaille fortuite chez 20-30%
- Extrapolation embolie pulmonaire découverte fortuitement?

Cohorte multicentrique prospective : 604 patients → 177 (30%) diagnostiqué fortuitement → 64 (36%) n'ont pas été anticoagulés

	Thrombose fortuite	Thrombose suspectée cliniquement
Saignements majeurs		
Incidence (/100 p-a)	3.3 (1.7-6.3)	3.9 (2.6-5.7)
Thrombose		
Incidence (/100 p-a)	8 (5.2-12.1)	7 (5.2-9.3)

Riva, N., et al. (2016)

AASLD 2020

AASLD 2009[71] Mise à jour 2020				
Type Of Patients		**Type Of Anticoagulation**	**Duration Of Anticoagulation**	
EHPVO	Acute	LMWH → VKA (I,B) AOD	Transient risk factor	At least 3 months[c] (I,B)
			Persistent risk factor	Long-term (I,B)
	Chronic	Not specified	Transient risk factor	Not specified
			Persistent risk factor	Long-term (IIa,C)
BCS		LMWH → VKA (I,B)	Permanent anticoagulant therapy (I,C)	
Cirrhotic		Case by case decision*		

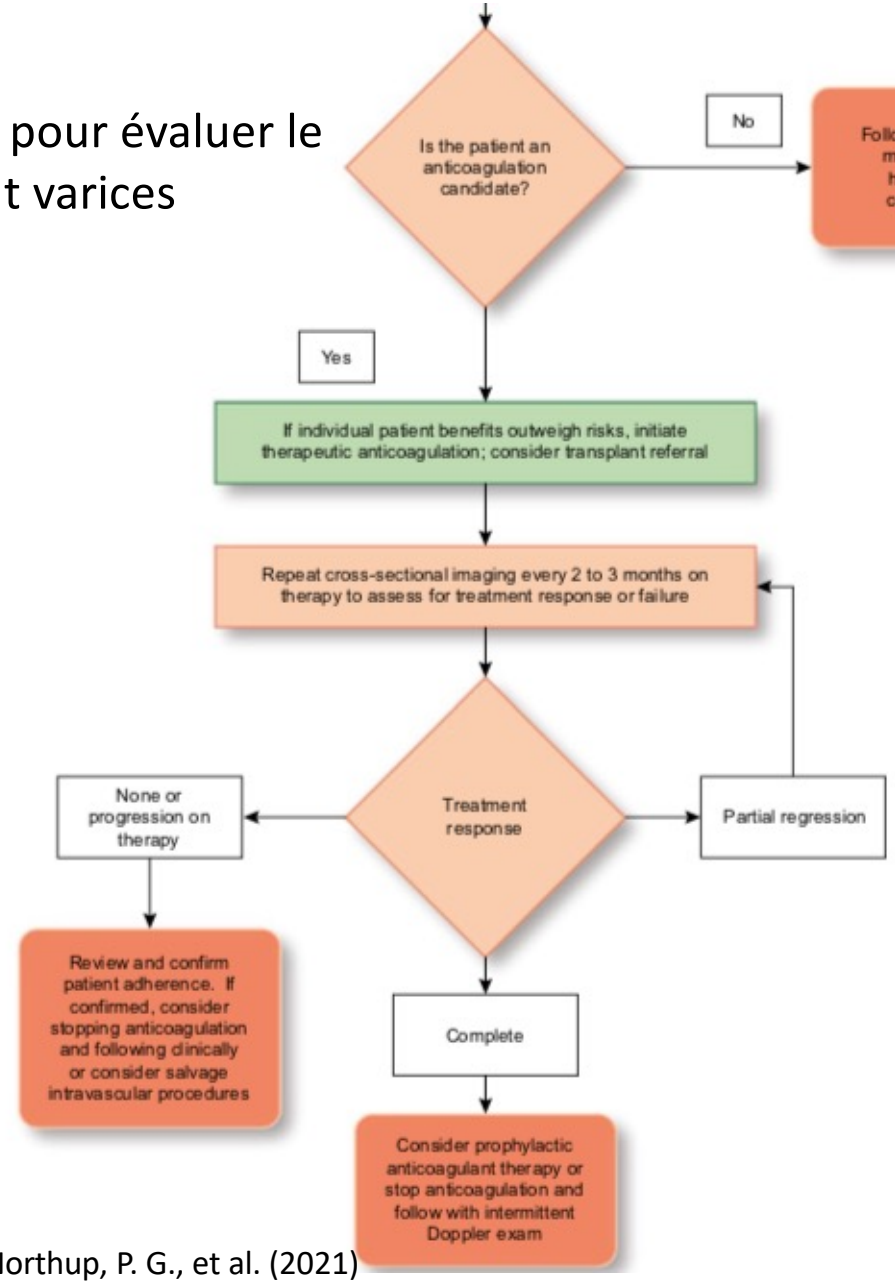
Tiré de Valeriani, E., et al. (2019)

Si occlusion porte complète chronique/cavernome avec collatérales, peu de bénéfices établis d'un traitement anticoagulant.
Prise en charge des complications de l'hypertension portale

Northup, P. G., et al. (2021)

AASLD 2020

OGD pour évaluer le statut varices



- Raisonnable d'observer sans traitement avec imagerie aux 3 mois si :
  - Minimalement occlusive
  - petites branches intra-hépatiques
- Pas de traitement suggéré pour transformation caverneuse

Tiré de Northup, P. G., et al. (2021)

Baveno VII 2022

<table>
<tr><th colspan="2">Thrombose splanchnique</th><th>Type d'anticoagulant</th><th colspan="2">Durée</th><th>Autres</th></tr>
<tr><td rowspan="3">Sans cirrhose</td><td rowspan="2">Récente</td><td rowspan="2">HBPM → AVK
AOD</td><td>Facteur de risque transitoire</td><td>6 mois</td><td rowspan="2">Imagerie à 6 mois
Si absence de recanalisation : dépistage VO</td></tr>
<tr><td>Facteur de risque persistant ou non-provoquée</td><td>Long terme
Si arrêt, utiliser D-dimères à 1 mois pour stratifier risque de récidive</td></tr>
<tr><td>Chronique</td><td>Pas de mention</td><td colspan="2">Long terme si facteur de risque persistant ou non-provoquée</td><td>Débuter anticoagulant une fois que risque saignement GI évalué</td></tr>
<tr><td>Cirrhose</td><td>Anticoagulation :
-Récente avec occlusion complète/partielle
-Sx
-Candidat transplantation
Considérer si minimalement occlusive avec progression ou atteinte VMS</td><td>HBPM
HBPM → AVK
AOD (CP A seulement)</td><td colspan="3">Jusqu'à recanalisation porte (minimum 6 mois)
Jusqu'à transplantation si candidat
Après recanalisation, selon risques/bénéfices</td></tr>
</table>

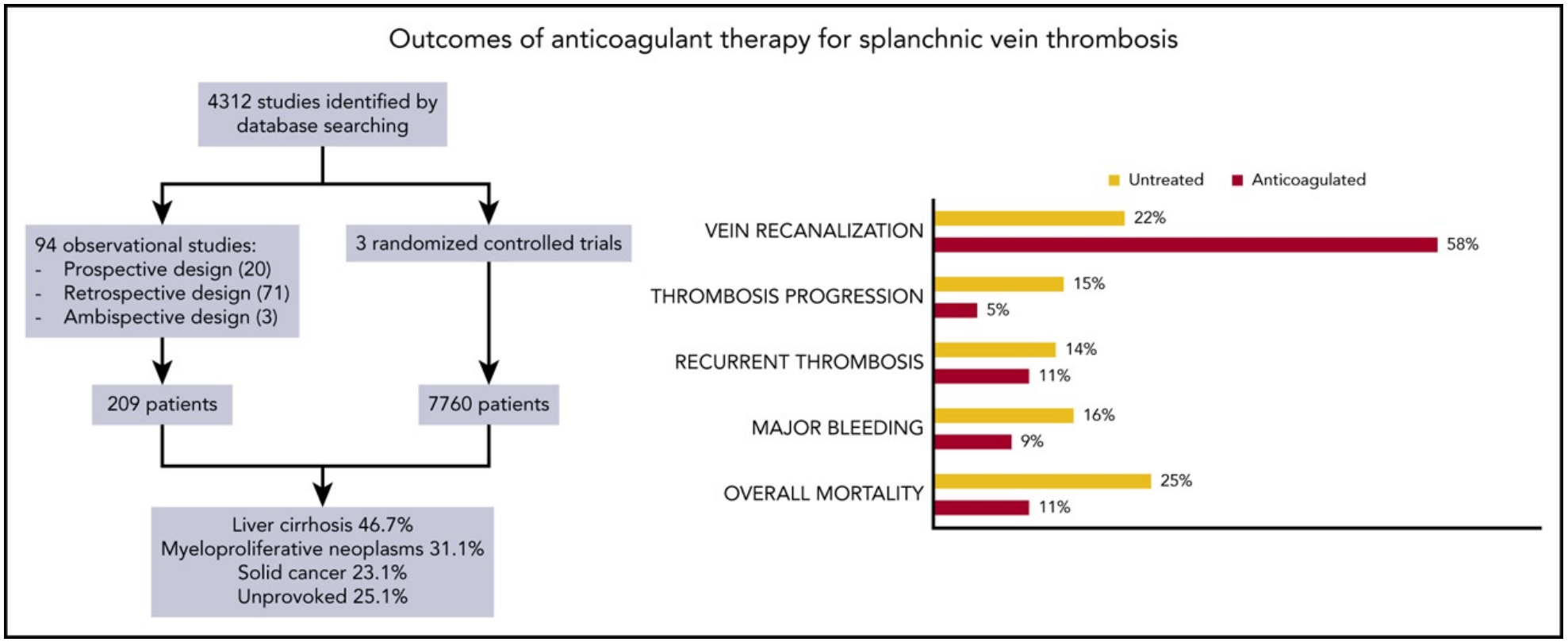
Adapté de Valeriani, E., et al. (2019)
de Franchis, R. (2022)

Données récentes

THROMBOSIS AND HEMOSTASIS

Anticoagulant therapy for splanchnic vein thrombosis: a systematic review and meta-analysis

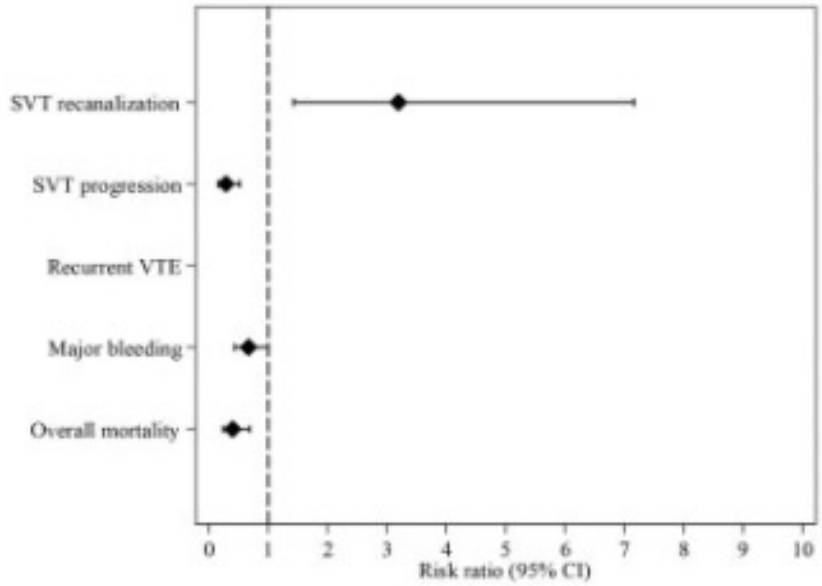
Emanuele Valeriani,[1,2] Marcello Di Nisio,[3] Nicoletta Riva,[4] Omri Cohen,[5,6] Juan-Carlos Garcia-Pagan,[7] Marta Magaz,[7] Ettore Porreca,[1] and Walter Ageno[8]



Tiré de Valeriani, E., et al. (2021)

Anticoagulant Treatment for Splanchnic Vein Thrombosis in Liver Cirrhosis: A Systematic Review and Meta-Analysis

Emanuele Valeriani[1,2] Marcello Di Nisio[3] Nicoletta Riva[4] Omri Cohen[5,6] Ettore Porreca[1]
Marco Senzolo[7] Andrea De Gottardi[8] Marta Magaz[9] Juan-Carlos Garcia-Pagan[9] Walter Ageno[10]



Outcome	Anticoagulated: events (n/N, %)	Untreated: events (n/N, %)	Studies (n)	I^2 (%)	RR (95% CI)
SVT recanalization	195/305 (63.9%)	79/282 (28.0%)	9	80	3.19 (1.42-7.17)
SVT progression	16/224 (7.1%)	44/181 (24.3%)	8	0	0.28 (0.15-0.52)
Recurrent VTE	8/92 (8.7%)	10/57 (17.5%)	1	-	-
Major bleeding	14/218 (6.4%)	20/179 (11.2%)	6	0	0.52 (0.28-0.97)
Overall mortality	21/230 (9.1%)	39/186 (21.0%)	6	0	0.42 (0.24-0.73)

Fig. 4 Radiological and clinical outcomes in treated versus untreated patients with liver cirrhosis. CI, confidence interval; RR, risk ratio; SVT, splanchnic vein thrombosis; VTE, venous thromboembolism.

Tiré de Valeriani, E., et al. (2021)

Place des anticoagulants oraux directs

https://onlinelibrary.wiley.com/doi/10.1111/joim.13205

Rivaroxaban for the treatment of noncirrhotic splanchnic vein thrombosis: an interventional prospective cohort study

Walter Ageno,[1] Jan Beyer Westendorf,[2] Laura Contino,[3] Eugenio Bucherini,[4] Maria Teresa Sartori,[5] Marco Senzolo,[6] Elvira Grandone,[7-9] Rita Santoro,[10] Marc Carrier,[11] Aurélien Delluc,[11] Valerio De Stefano,[12] Fulvio Pomero,[13] Marco Paolo Donadini,[1] Alberto Tosetto,[14] Cecilia Becattini,[15] Ida Martinelli,[16] Barbara Nardo,[17] Laurent Bertoletti,[18] Marcello Di Nisio,[19] Alejandro Lazo-Langner,[20] Alessandro Schenone,[21] and Nicoletta Riva[22]

Issues	3 mois (n = 97) (%; IC 95%)	3 à 6 mois (n = 96)
Saignements majeurs	2 (2.1; 0.6-7.2)	1
Saignement non majeurs	4 (3.1; 1.1-8.7)	2
Récidive thrombose splanchnique symptomatique	2 (2.1; 0.6-7.1)	1
Recanalisation complète	43/91 (47.3; 37.3-57.4)	N/A
Recanalisation partielle	33/91 (36.3; 27.1-46.5)	N/A

Néo œsophage distal et œsophagite sévère

71.9% sous Rivaroxaban

Ageno, W., et al. (2022)

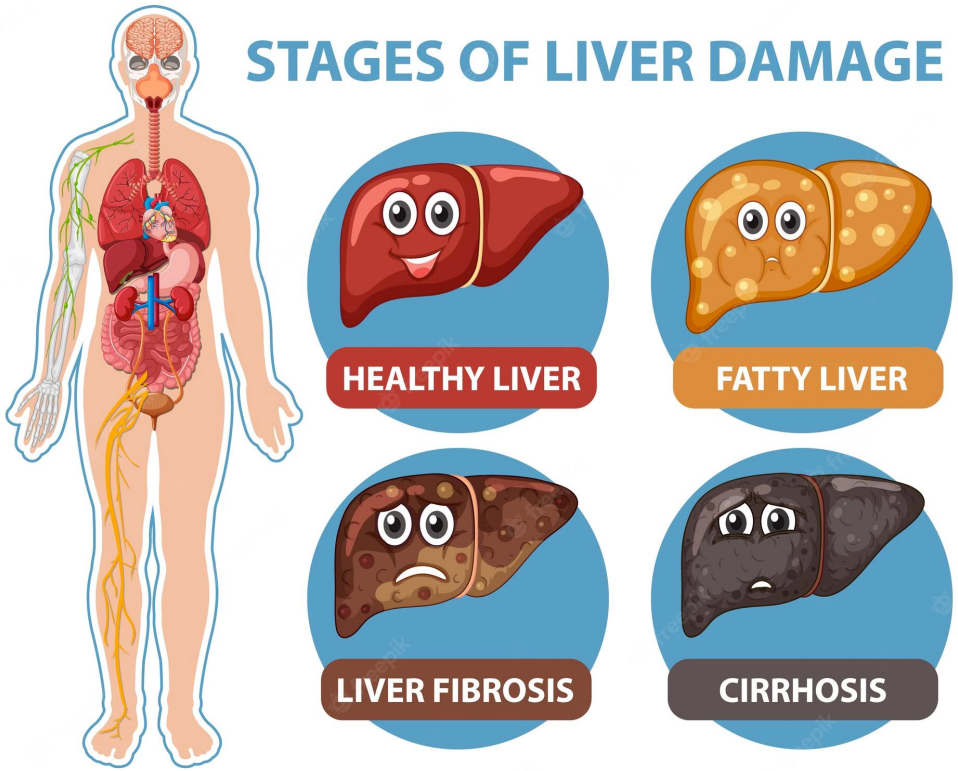
THROMBOSIS AND HEMOSTASIS

Anticoagulant therapy for splanchnic vein thrombosis: a systematic review and meta-analysis

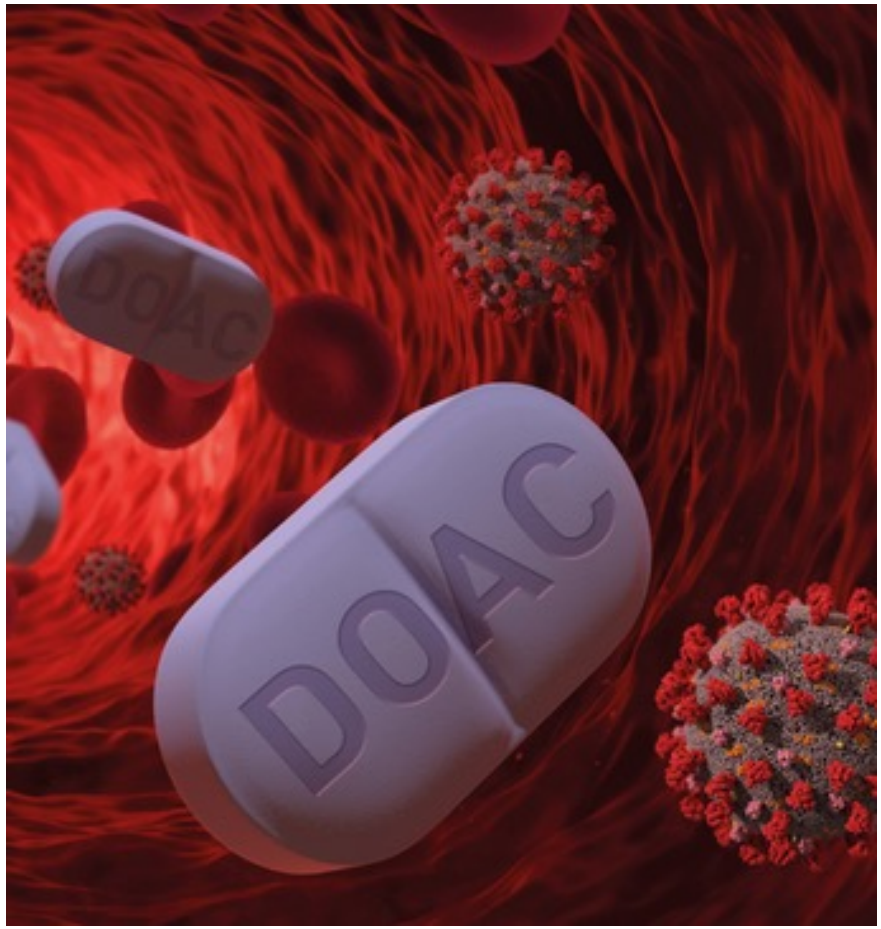
Emanuele Valeriani,[1,2] Marcello Di Nisio,[3] Nicoletta Riva,[4] Omri Cohen,[5,6] Juan-Carlos Garcia-Pagan,[7] Marta Magaz,[7] Ettore Porreca,[1] and Walter Ageno[8]

- AOD : 142 patients
- Analyses des issues selon type d'anticoagulant :
  - Plus de recanalisation avec AOD et HBPM
  - Progression thrombose, récidive TEV, saignement majeur et mortalité similaires entre les types d'anticoagulant.
    - Saignement majeur : 7% AOD VS 11% AVK
    - Récidive TEV : 8% AOD VS 8% AVK

Valeriani, E., et al. (2021)



https://www.freepik.com/free-vector/diagram-showing-stages-liver-damage_24881705.htm



https://onlinelibrary.wiley.com/doi/10.1111/joim.13205

Table 3. Type of Bleeding Events in Cirrhosis Patients on Direct Oral Anticoagulants

	n	Percent	Annualized rate (%)
Any bleeding	45	32.6	25.1
Major bleeding	11	8.0	6.2
Fatal bleeding	0	0	0
Central nervous system bleeding	1	0.7	0.6
Hemoglobin drop ≥2 g/dL or ≥2 units packed red blood cells	10	7.2	6.2
CRNMB	22	15.9	12.2
Minor bleeding	12	8.7	6.7
DOAC discontinuation due to bleeding	29	21	16.5

Tiré de Mort, J. F., et al. (2021)

Complications during DOAC therapy	
Procedure-related bleedings	7 (11.7%, 3.4% of all procedures)
Minor	6
Major	1
Spontaneous bleeding event	38 (28.6%)
≥2 spontaneous bleeding events	4 (3.0%)
Minor	15 (39.5%, 11.3% of all)
Major	23 (60.5%, 17.3% of all)
Fatal	1 (2.6%)

Tiré de Semmler, G., et al. (2021)

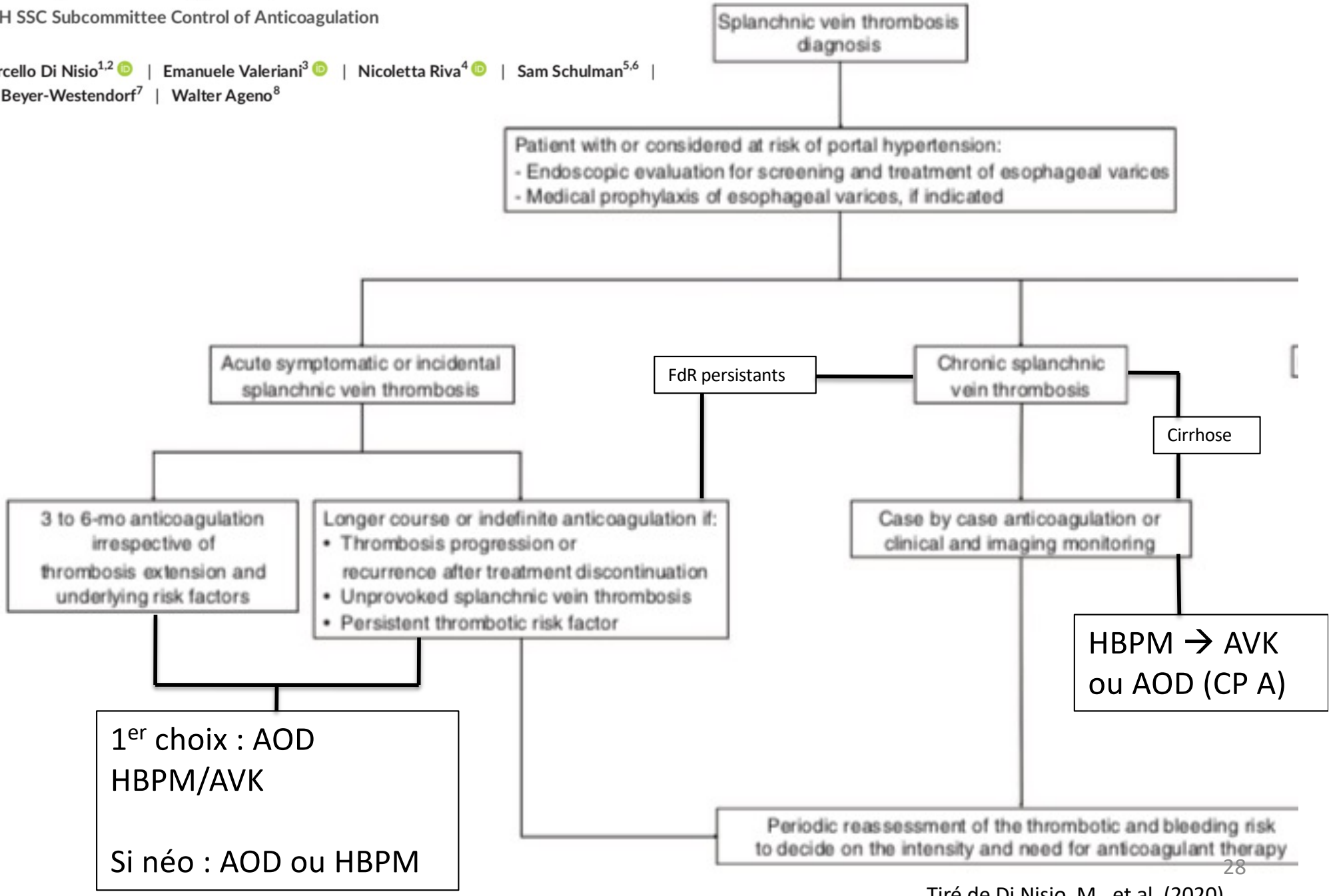
RECOMMENDATIONS AND GUIDELINES

jth

Anticoagulant therapy for splanchnic vein thrombosis

ISTH SSC Subcommittee Control of Anticoagulation

Marcello Di Nisio[1,2] | Emanuele Valeriani[3] | Nicoletta Riva[4] | Sam Schulman[5,6] | Jan Beyer-Westendorf[7] | Walter Ageno[8]



Tiré de Di Nisio, M., et al. (2020)

Messages clés (1)

- Maladie hétérogène en raison des populations
  - Cirrhose
  - Cancer
  - Facteurs de risque transitoires
- Anticoagulation pour toutes les thromboses récentes
  - Durée selon facteurs provoquant (transitoires VS permanents)

Messages clés (2)

- Si chronique, probablement bénéfices si facteurs de risque persistants
- Cirrhose :
  - Évaluation OGD nécessaire pré-anticoagulation
  - Candidat transplantation → anticoagulation à favoriser
  - Risque/bénéfice semble plus restreint lorsque transplantation non envisagée.
- Place des AOD :
  - En l'absence de cirrhose, données rassurantes sur l'efficacité et sécurité en thrombose splanchnique
  - En cirrhose, peu de données
    - À considérer si Child A et éviter si Child B-C

Questions/Commentaires/discussion

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Merci à Dr Julien Bissonnette hépatologue CHUM pour ses commentaires

Références

1. Riva, N., et al. (2020). "Anticoagulation in splanchnic and cerebral vein thrombosis: An international vignette-based survey." Res Pract Thromb Haemost **4(7): 1192-1202.**
2. Northup, P. G., et al. (2021). "Vascular Liver Disorders, Portal Vein Thrombosis, and Procedural Bleeding in Patients With Liver Disease: 2020 Practice Guidance by the American Association for the Study of Liver Diseases." Hepatology **73(1): 366-413.**
3. Riva, N. and W. Ageno (2020). "Cerebral and Splanchnic Vein Thrombosis: Advances, Challenges, and Unanswered Questions." J Clin Med **9(3).**
4. Valeriani, E., et al. (2019). "Splanchnic Vein Thrombosis: Current Perspectives." Vascular Health & Risk Management **15: 449-461.**
5. Zhang, B., et al. (2020). "Incidence of Splanchnic Vein Thrombosis After Abdominal Surgery: A Systematic Review and Meta-analysis." Journal of Surgical Research **245: 500-509.**
6. Kearon, C., et al. (2012). "Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines." Chest **141(2 Suppl): e419S-e496S.**
7. Riva, N., et al. (2016). "Clinical history and antithrombotic treatment of incidentally detected splanchnic vein thrombosis: a multicentre, international prospective registry." Lancet Haematol **3(6): e267-275.**
8. de Franchis, R., et al. (2022). "Baveno VII - Renewing consensus in portal hypertension." J Hepatol **76(4): 959-974.**
9. (2016). "EASL Clinical Practice Guidelines: Vascular diseases of the liver." J Hepatol **64(1): 179-202.**
10. Condat, B., et al. (2001). "Current outcome of portal vein thrombosis in adults: risk and benefit of anticoagulant therapy." Gastroenterology **120(2): 490-497.**
11. Plessier, A., et al. (2010). "Acute portal vein thrombosis unrelated to cirrhosis: a prospective multicenter follow-up study." Hepatology **51(1): 210-218.**
12. Ageno, W., et al. (2015). "Long-term Clinical Outcomes of Splanchnic Vein Thrombosis: Results of an International Registry." JAMA Internal Medicine **175(9): 1474-1480.**
13. Valeriani, E., et al. (2021). "Anticoagulant therapy for splanchnic vein thrombosis: a systematic review and meta-analysis." Blood **137(9): 1233-1240.**
14. Valeriani, E., et al. (2021). "Anticoagulant Treatment for Splanchnic Vein Thrombosis in Liver Cirrhosis: A Systematic Review and Meta-Analysis." Thromb Haemost **121(7): 867-876.**
15. Ageno, W., et al. (2022). "Rivaroxaban for the treatment of noncirrhotic splanchnic vein thrombosis: an interventional prospective cohort study." Blood Adv **6(12): 3569-3578.**
16. Mort, J. F., et al. (2021). "Rates of Bleeding and Discontinuation of Direct Oral Anticoagulants in Patients With Decompensated Cirrhosis." Clin Gastroenterol Hepatol **19(7): 1436-1442.**
17. Semmler, G., et al. (2021). "Safety of direct oral anticoagulants in patients with advanced liver disease." Liver Int **41(9): 2159-2170.**
18. Hoolwerf, E. W., et al. (2018). "Direct oral anticoagulants in patients with liver cirrhosis: A systematic review." Thromb Res **170: 102-108.**
19. Hanafy, A. S., et al. (2019). "Randomized controlled trial of rivaroxaban versus warfarin in the management of acute non-neoplastic portal vein thrombosis." Vascul Pharmacol **113: 86-91.**
20. Di Nisio, M., et al. (2020). "Anticoagulant therapy for splanchnic vein thrombosis: ISTH SSC Subcommittee Control of Anticoagulation." J Thromb Haemost **18(7): 1562-1568.**