Places des AOD dans les thromboses splanchniques (hors EP et TVP)

SFTH 2025, Masters Class #8

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Liens d’intérêt potentiels

Sur les 5 dernières années :

- Investigateur d’essais thérapeutiques financés ou co-financés par : ACTELION, ANTHOS, BAYER, BMS-PFIZER, DAICHII-SANKYO, LEO-PHARMA, MSD.

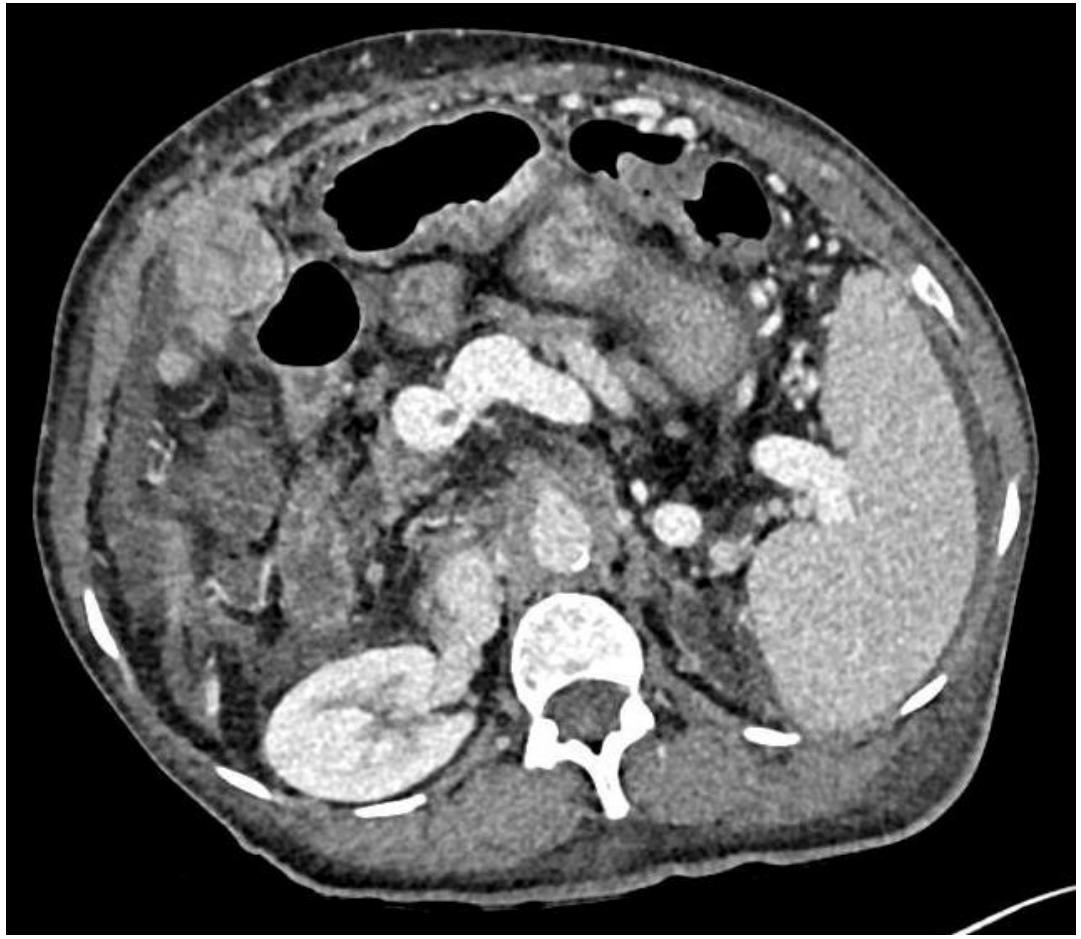
- Invité à des congrès par : ACTELION, ASPEN, BAYER, BMS-PFIZER, LEO-PHARMA, MSD.

- Orateur dans des symposiums financés ou co-financés par : ACTELION, ASPEN, BAYER, BMS-PFIZER, LEO-PHARMA, MSD, SANOFI.

This presentation is independent from the activity as vice-chair for the “Venous Thromboembolism” program of the ISTH, and do not engage the ISTH.

Proposition de cas clinique

- **homme** de **55** ans atteint de **cirrhose**, découverte d'une **thrombose portale aiguë** avec obstruction de 60 % du tronc portal, sur **douleurs abdominales** et **rectorragies** (minimes)



Proposition de cas clinique

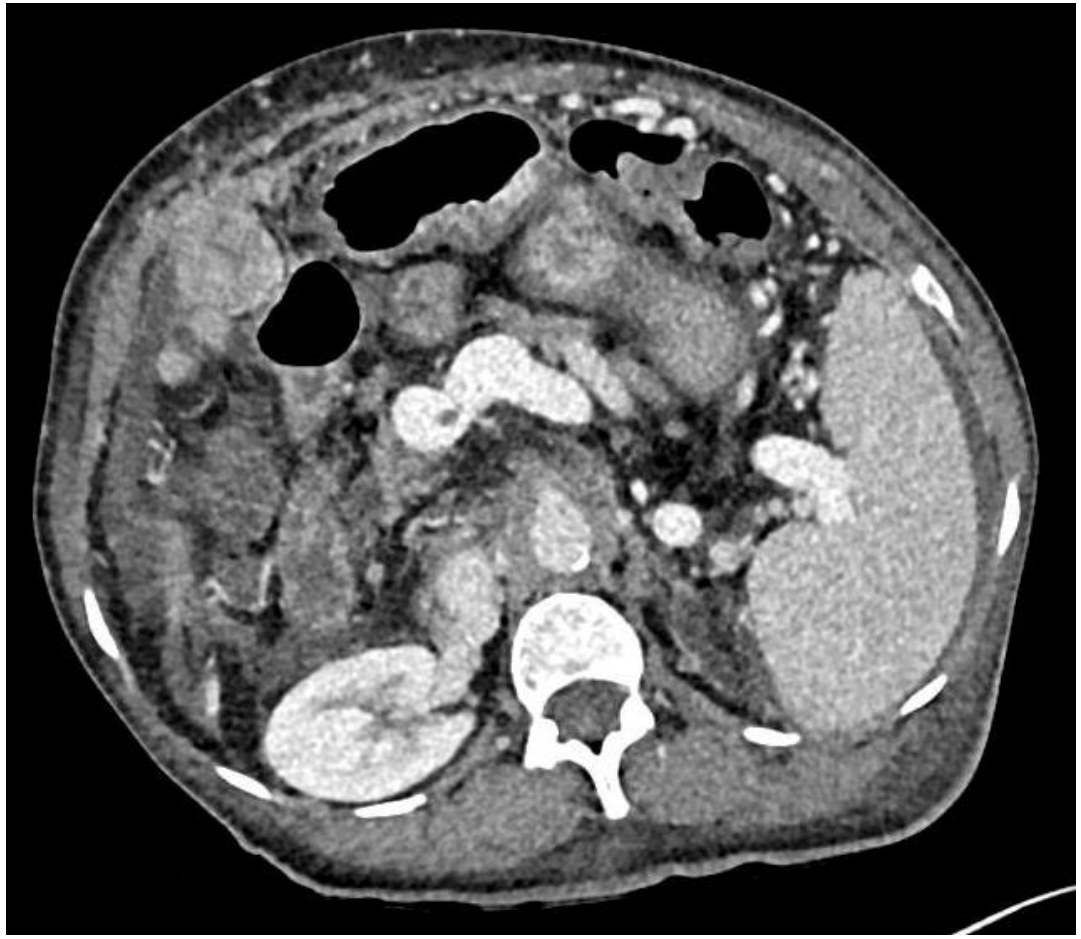
- **homme** de **55** ans atteint de **cirrhose**, découverte d'une **thrombose portale aiguë** avec obstruction de 60 % du tronc portal, sur **douleurs abdominales** et **rectorragies** (minimes)

- **Questions de prise en charge** :
  1. Avez-vous besoin d'autres renseignements ?
  2. Si vous initiez un traitement anticoagulant : lequel et comment ?
  3. Si vous initiez un traitement anticoagulant : combien de temps ?
  4. Si vous décidez de ne pas initier de traitement anticoagulant : quelle gestion faites vous ?

Proposition de cas clinique

- **homme** de **55** ans atteint de **cirrhose**, découverte d'une **thrombose portale aiguë** avec obstruction de 60 % du tronc portal, sur **douleurs abdominales** et **rectorragies** (minimes)

Cause de cirrhose ?
Hypertension portale (VO ? ++) ?
Co-prescription ?



Hb ?
Plaquettes ?
Hémostase ?
Créatinine ?
Bilan hépatique ?

Evolution après thrombose digestive

Cohorte ISTH

- **604** patients suivi prospectivement, avec thrombose digestive objectivée
- Prise en charge thérapeutique laissée **libre** à l'investigateur (rien ou : HBPM ou HBPM/relais AVK)

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)

Abbreviation: SVT, splanchnic vein thrombosis.

[a] Some patients had more than 1 risk factor.

[b] Transient risk factors included recent surgery, intra-abdominal infection, use of hormone therapy, pregnancy/puerperium, and abdominal trauma.

→ Taux de récidive faible sous anticoagulant (excepté cancer solide)

→ Taux d'hémorragie élevé sous anticoagulant (et même sans anticoagulant)

→ Situation la plus complexe : **cirrhose**

Ageno W et al JAMA int med 2015

Evolution après thrombose digestive

- 604 patients suivi prospectivement, avec thrombose digestive objectivée
- Prise en charge thérapeutique laissée libre à l'investigateur (prioritaire HBPM ou HBPM/relais AVK)

Figure 1. Cumulative Incidence of Major Bleeding and Thrombotic Events in the Entire Cohort of Patients With Splanchnic Vein Thrombosis

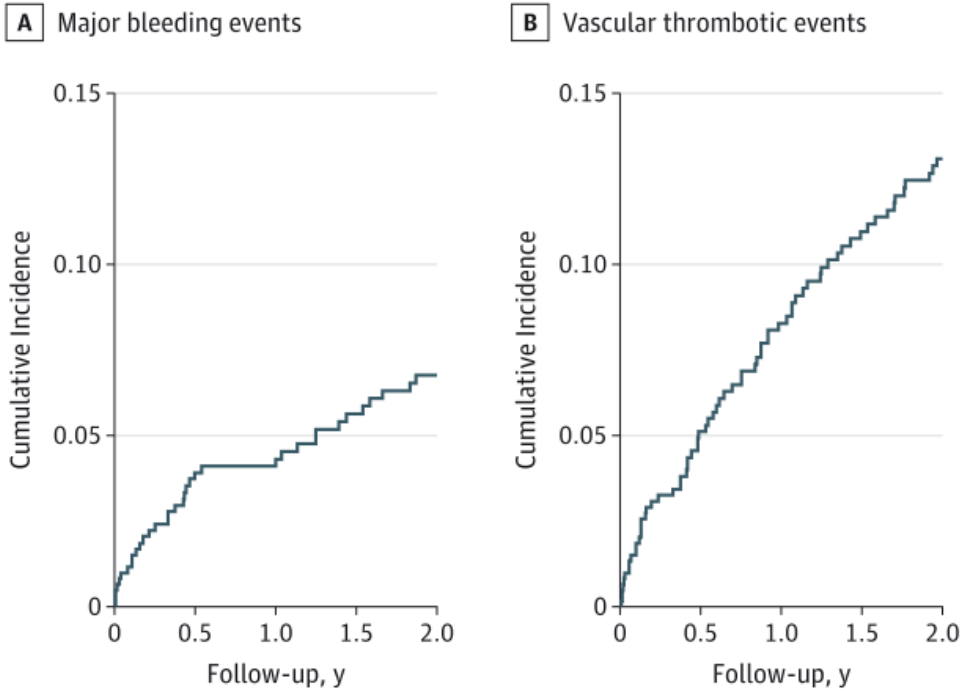
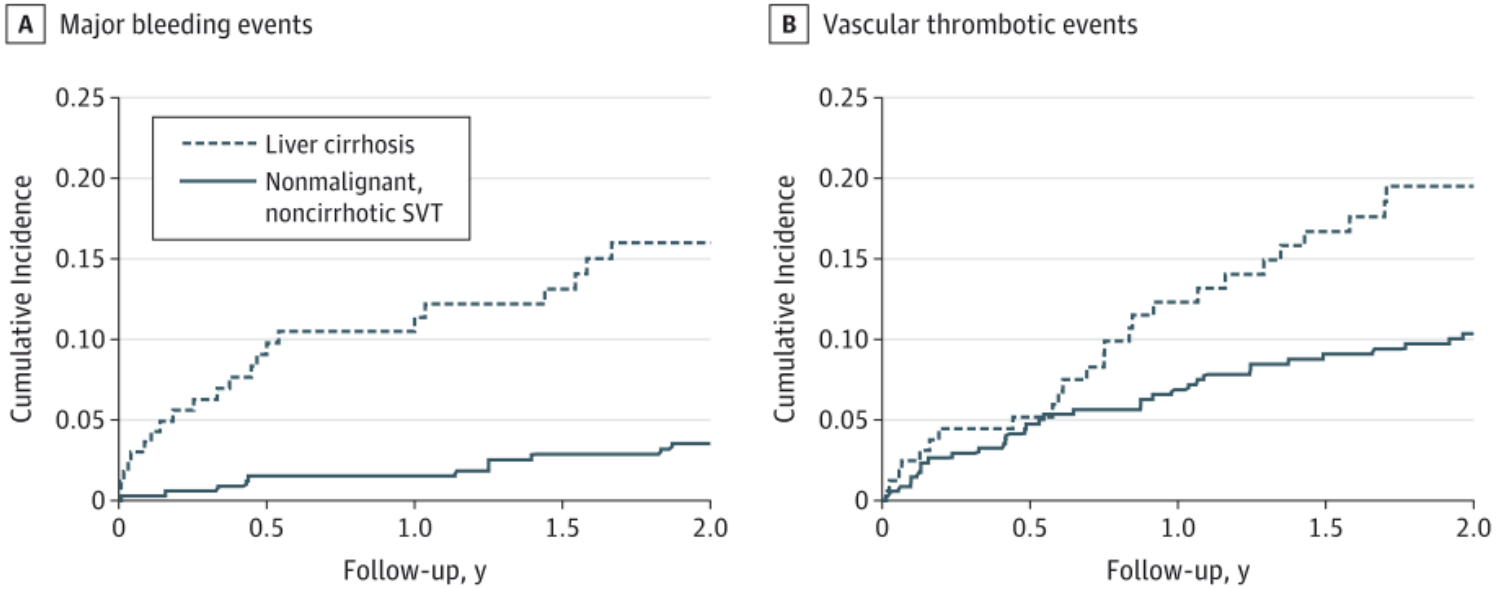


Figure 2. Cumulative Incidence of Major Bleeding and Thrombotic Events in Patients With Liver Cirrhosis and Nonmalignant, Noncirrhotic Splanchnic Vein Thrombosis (SVT)

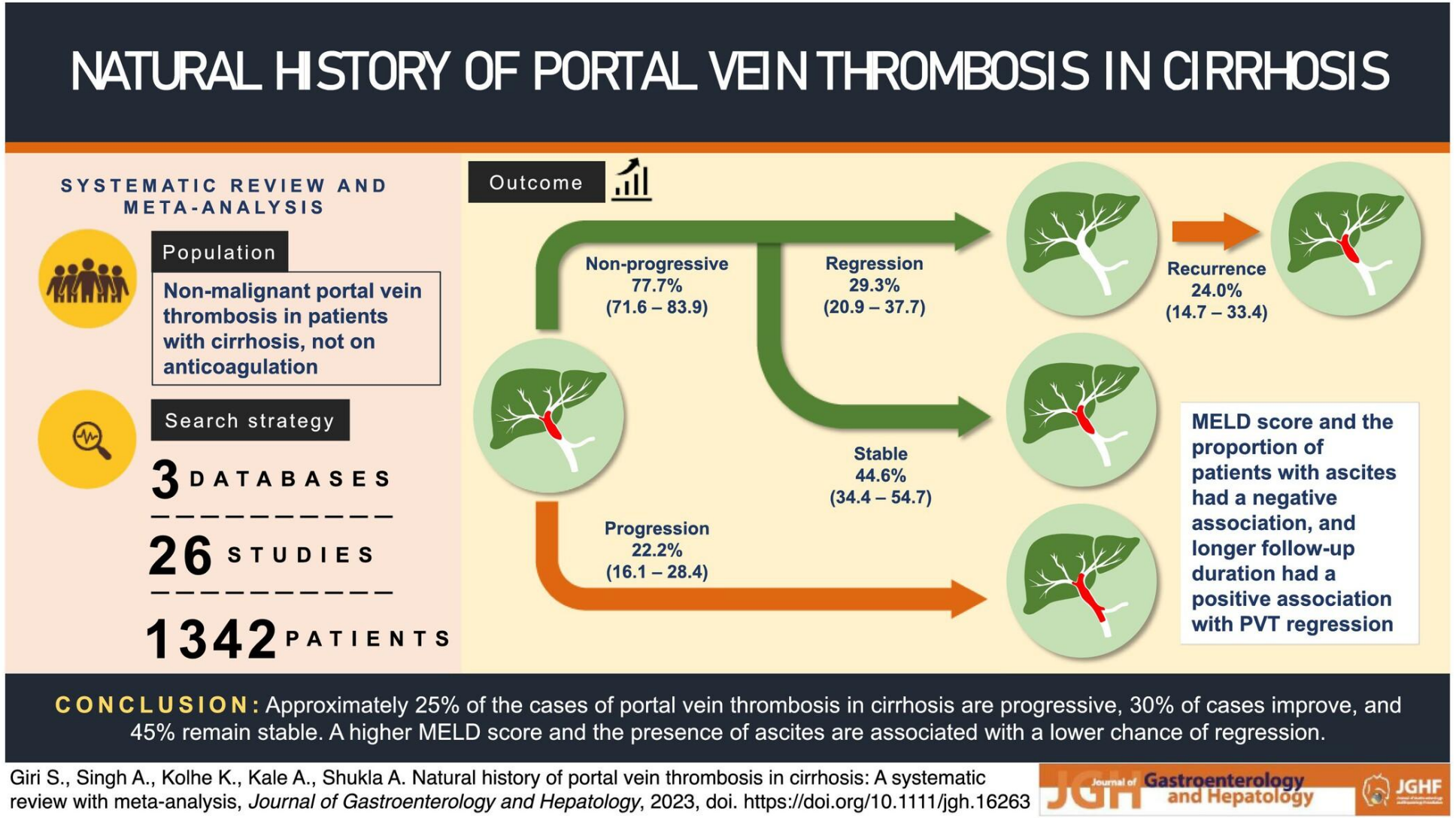


Ageno W et al JAMA int med 2015

Evolution après thrombose digestive

Méta-analyse

Evolution sans AC chez les cirrhotiques

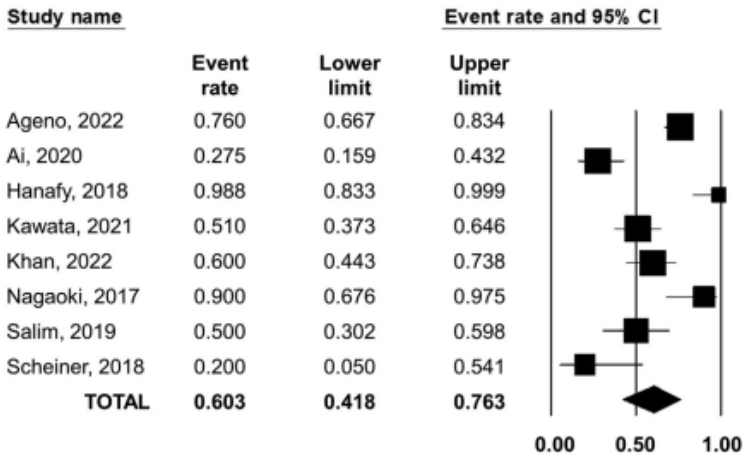


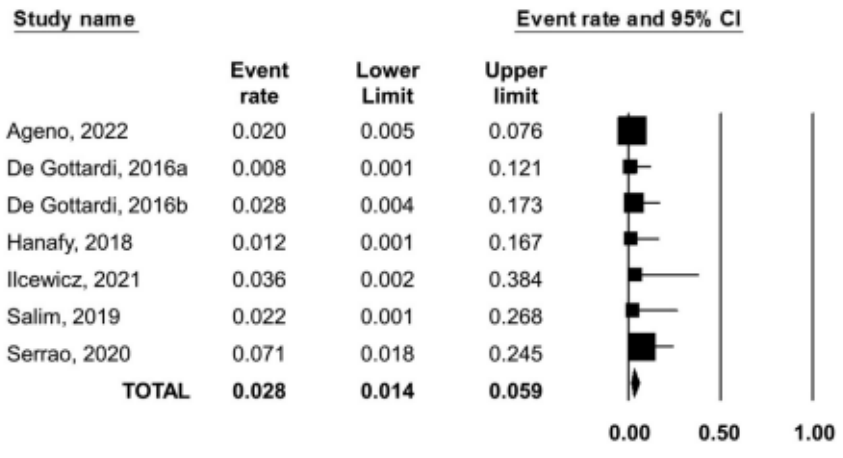
Giri S., Singh A., Kolhe K., Kale A., Shukla A. Natural history of portal vein thrombosis in cirrhosis: A systematic review with meta-analysis, *Journal of Gastroenterology and Hepatology*, 2023, doi. https://doi.org/10.1111/jgh.16263

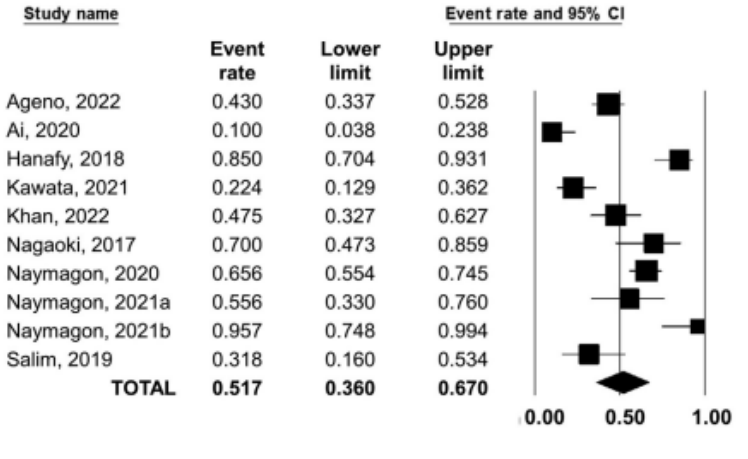
AOD et Thromboses digestives

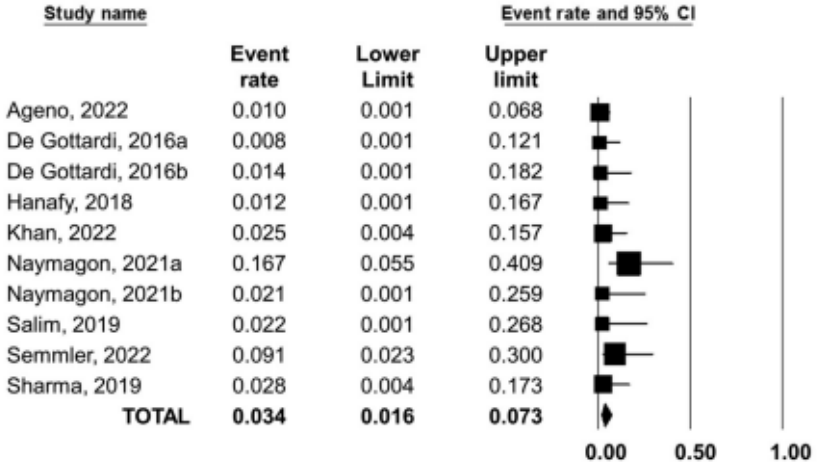
Méta-analyses des études

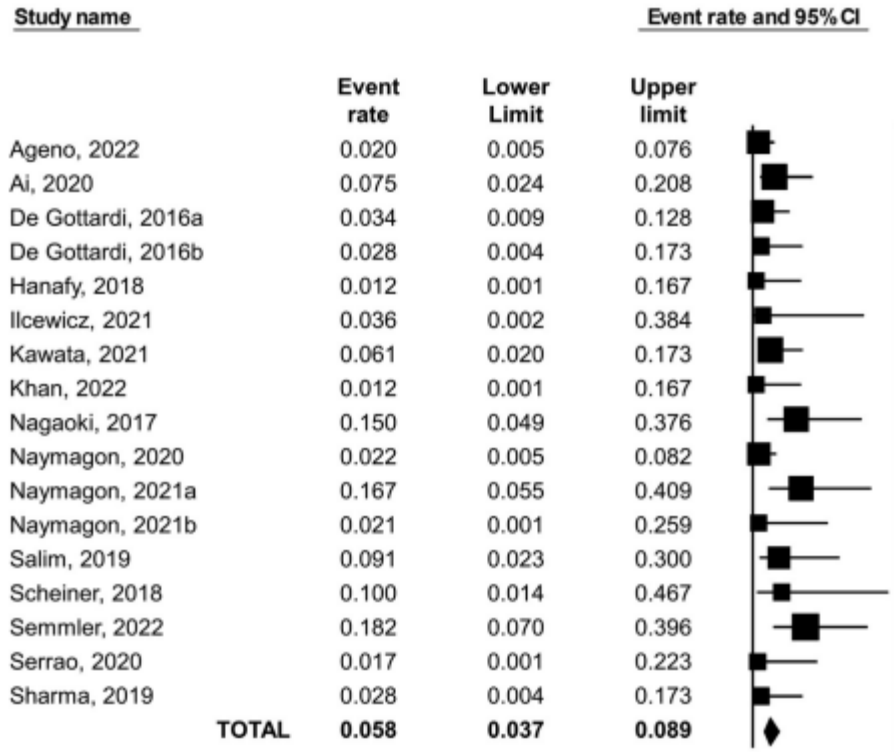
2 prospectives ; 1 seul RCT











Taux de re-canalisation (complète en bas) ≈50%

Episode de MTEV (en haut) Décès (en bas) ≈3%

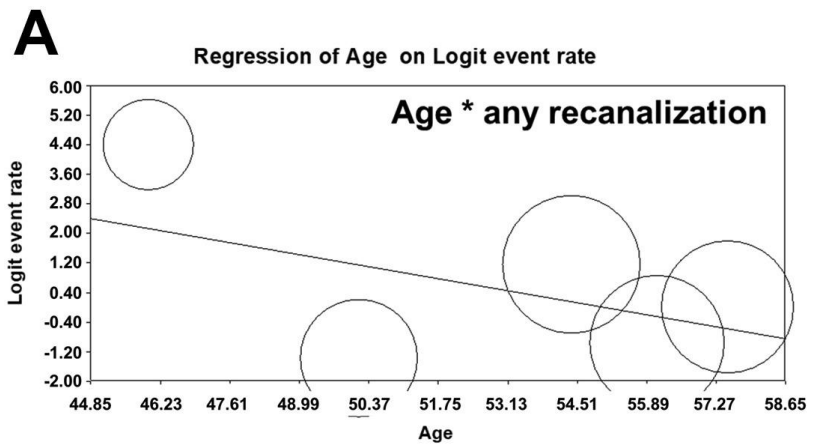
Hémorragie majeure ≈6%

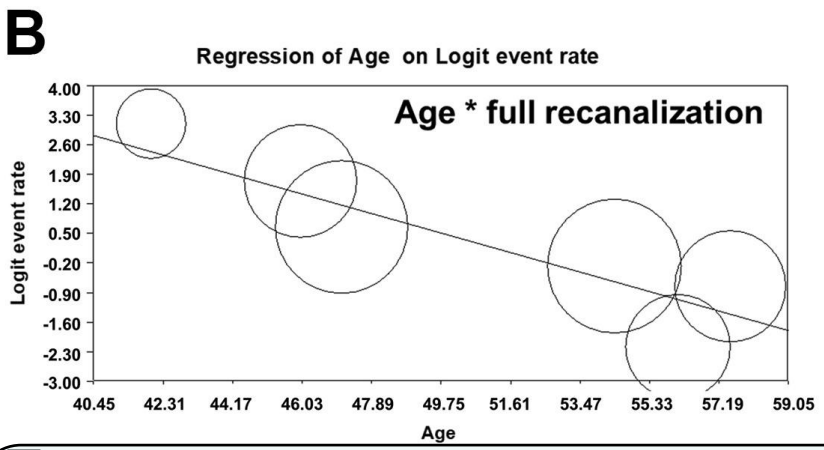
Calcaterra et al JTH 2024

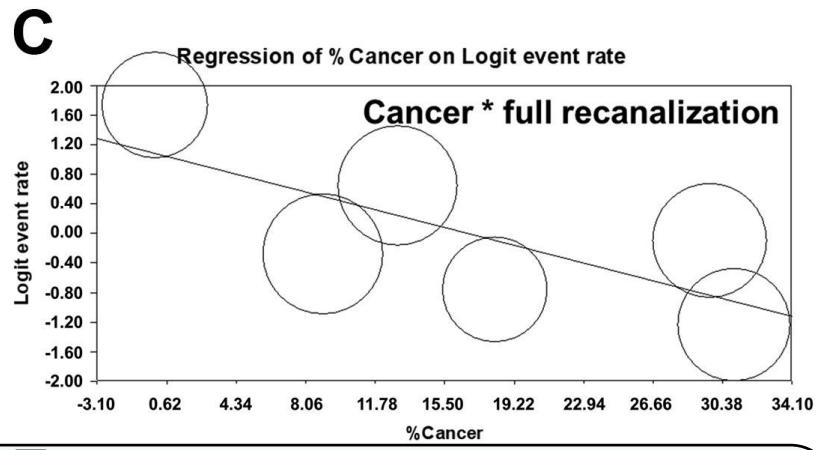
AOD et Thromboses digestives

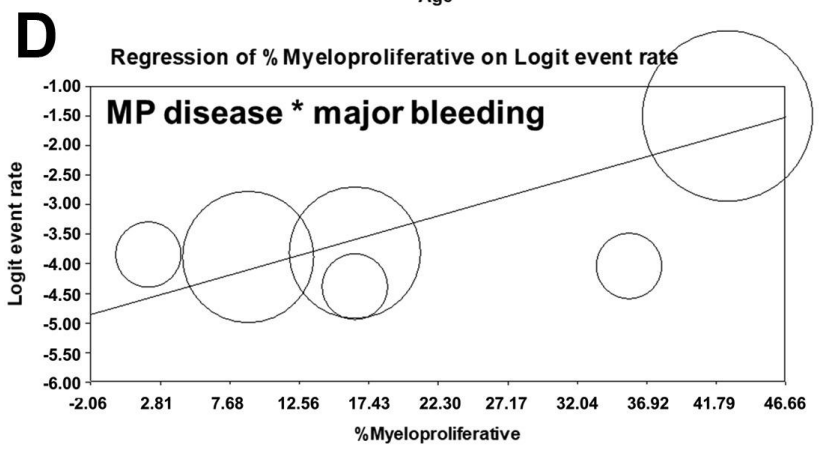
Méta-analyses des études

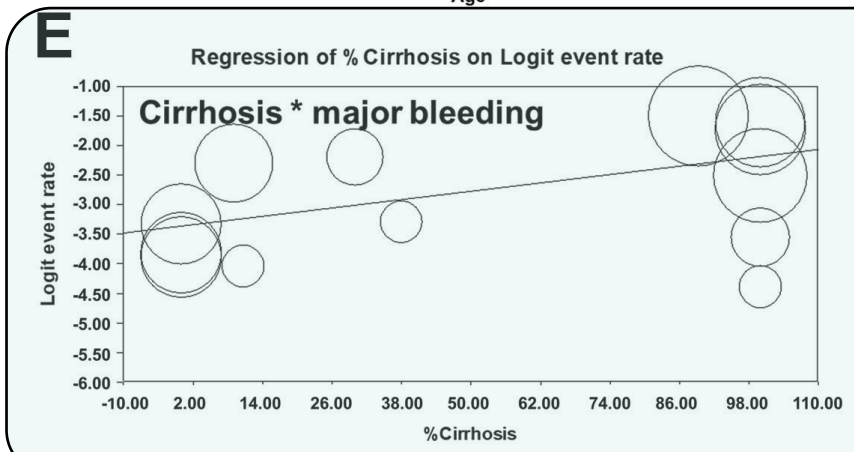
2 prospectives ; 1 seul RCT

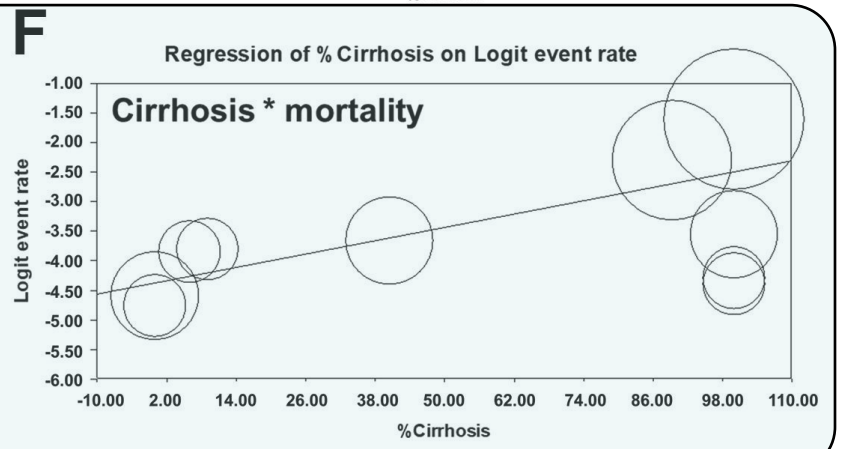












Calcaterra et al JTH 2024

AOD vs AVK dans Thromboses digestives

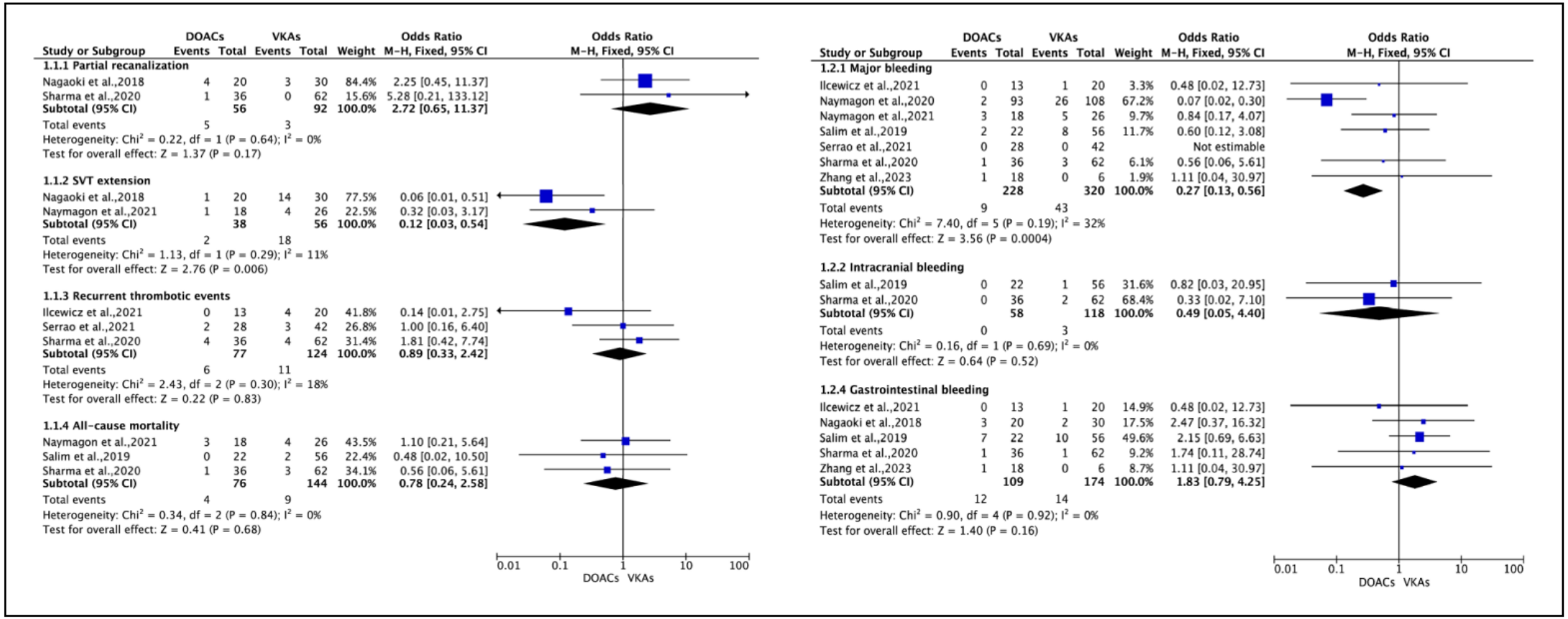


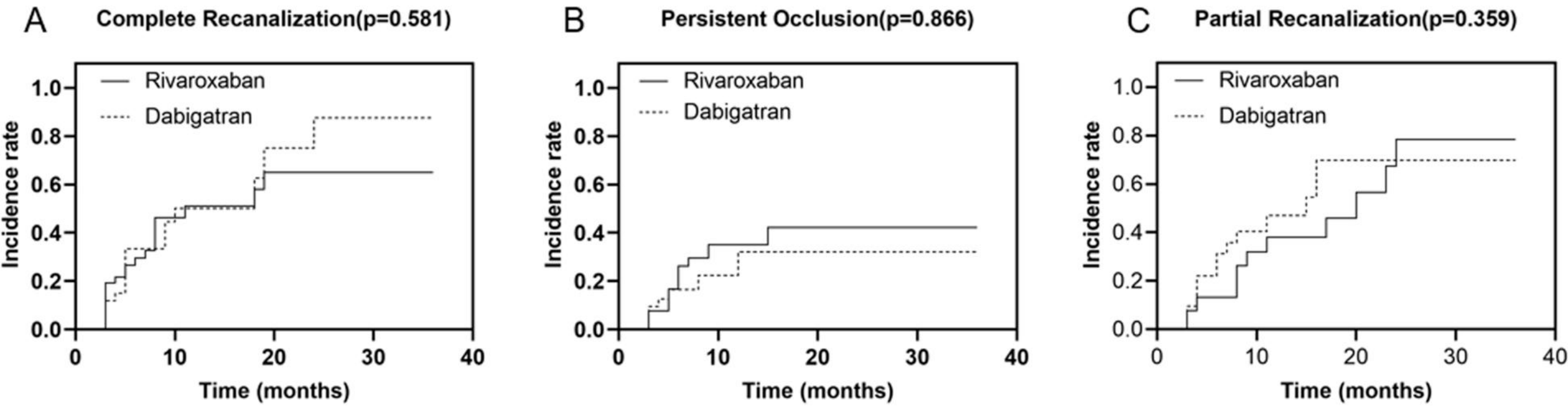
Figure 2. The outcomes between DOACs versus VKAs in patients with SVT (fixed-effects model). DOACs = direct oral anticoagulants; VKAs = vitamin K antagonists; SVT = splanchnic vein thrombosis; RD = risk difference; CI = confidence interval.

Wan et al CATH 2024

Rivaroxaban et Dabigatran en cas de cirrhose

Analyse retrospective

- 💣Comparaison rétrospective monocentrique : 55 riva et 42 dabi, exclusion : Child C, DFG<50.
- profils d'efficacité et de tolérance comparables chez les patients cirrhotiques, en particulier ceux dont la fonction hépatique est de grade A et B selon Child-Pugh. Amélioration significative des scores de Child-Pugh



Zhou et al BMC Gastroenterol 2023

En résumé :

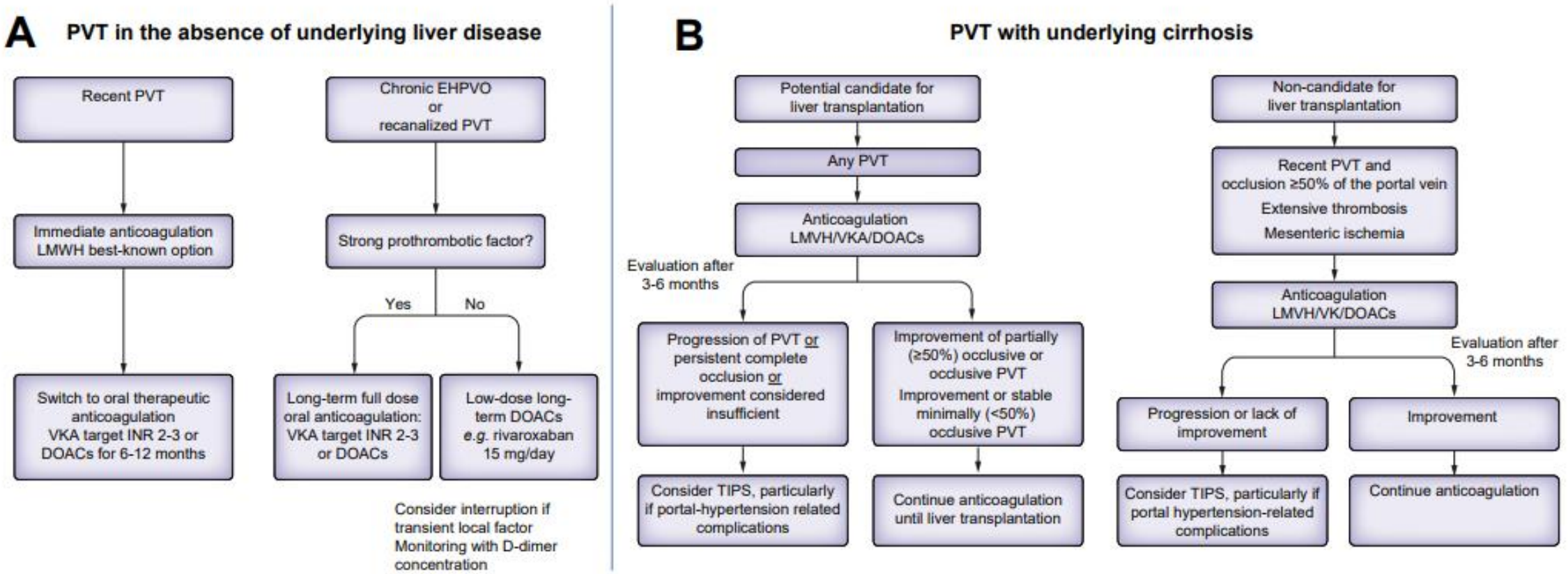
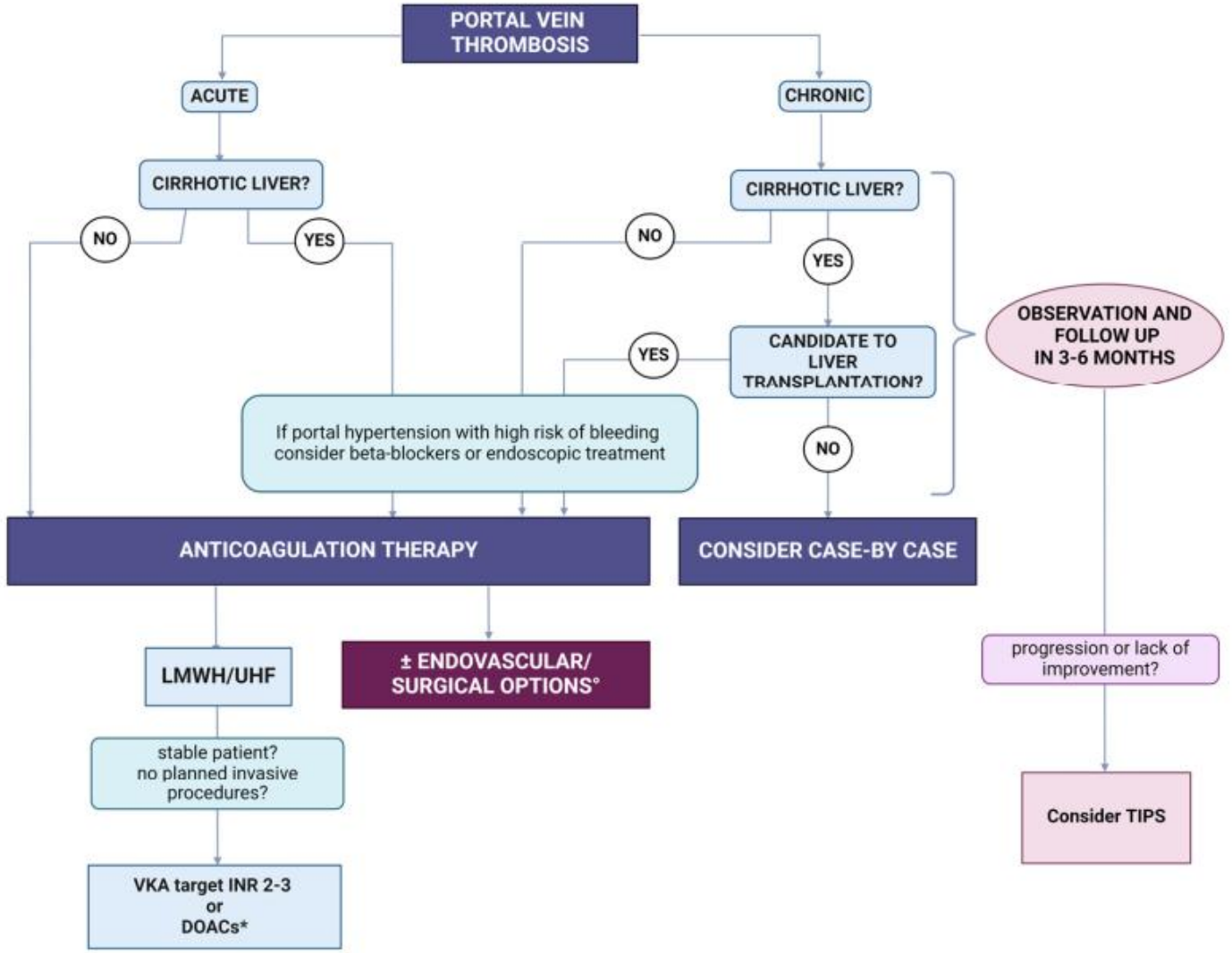


Fig. 3. Proposed algorithm for anticoagulant therapy in patients with portal vein thrombosis with and without cirrhosis. DOACs, direct-acting oral anticoagulants; EHPVO, extrahepatic portal vein obstruction; LMWH, low-molecular-weight heparin; PVT, portal vein thrombosis; TIPS, transjugular intrahepatic portosystemic shunt; VKAs, vitamin K antagonists.

Elkrief L et al JEHP report 2023

En résumé :



°Consider case by case for intestinal infarction, acute abdomen or bleeding.
*Avoid DOACs in Child-Turcotte-Pugh class C. Consider apixaban or dabigatran with caution in Child-Turcotte-Pugh class B.
Abbreviations: DOACs, direct oral anticoagulants; LMWH, low molecular weight heparin; TIPS, transjugular intrahepatic portosystemic shunt; VKA, vitamin K antagonist.

Boccatonda A et al JCM 2024

En résumé :

Table 2. Considerations for the choice of anticoagulant to treat splanchnic vein thrombosis and suggestion of doses (adapted from[149]).

Considerations	Low-molecular-weight heparin	Vitamin K antagonists	Direct oral anticoagulants			
			Apixaban	Rivaroxaban	Edoxaban	Dabigatran
Liver function						
Child-Pugh class A	No action needed	No action needed Target INR 2-3	No action needed 5 mg *twice a day*	No action needed 20 mg *once a day*	No action needed 60 mg *once a day*	No action needed 150 mg *twice a day*
Child-Pugh class B	No action needed	Possible Target INR 2-3	Use with caution 2.5 mg *twice a day*	Use with caution 15 mg *once a day*	Use with caution 30 mg *once daily*	Use with caution 110 mg *twice a day*
Child-Pugh class C	No action needed	Possible Target INR 2-3	Contraindicated	Contraindicated	Contraindicated	Contraindicated
Renal function						
eGFR 30-50 ml/min	No action needed	Possible Target INR 2-3	No action needed 5 mg *twice a day*	Use with caution 15 mg *once a day*	Use with caution 30 mg *once daily*	Use with caution 110 mg *twice a day*
eGFR <30 ml/min	Use with caution	Possible Target INR 2-3	Use with caution 2.5 mg *twice a day*	Use with caution 15 mg *once a day*	Use with caution 30 mg *once daily*	Contraindicated
eGFR <15 ml/min	Contraindicated	Possible Target INR 2-3	Contraindicated	Contraindicated	Contraindicated	Contraindicated
Other considerations						
Drug-drug interaction Other medication with P-gp protein or Cyto-chrome 3A4 metabolism	No action needed	No action needed Target INR 2-3	No action needed	Use with caution 15 mg *once a day*	No action needed	Use with caution 110 mg *twice a day*
History of peptic ulcer disease with or without gastrointestinal bleeding			No action needed	Use with caution *Consider* 15 mg *once a day*	No action needed	Use with caution *Consider* 110 mg *twice a day*
Specific consideration		Monitoring may be difficult in patients with liver insufficiency Factor II concentration may be useful in this setting				Contraindicated in patients with antiphospholipid syndrome No data on pharmacokinetics after TIPS placement

eGFR, estimated glomerular filtration rate; INR, international normalised ratio; P-gp, Permeability glycoprotein; TIPS, transjugular intrahepatic portosystemic shunt.

Elkrief L et al JEHP report 2023

En résumé :

DOACs in specific SVT patients

- Hepatic dysfunction
  → DOACs contraindicated if Child-Pugh class C (rivaroxaban if Child-Pugh classes B-C)
- Severe renal insufficiency
  → DOACs contraindicated if CrCl <15 mL/min* (dabigatran if CrCl <30 mL/min)
- Thrombocytopenia
  → DOACs not recommended if platelet count $<50\times10^9$/L

- Luminal GI cancer
  → Higher risk of GI bleed, poor absorption, CHT interference, vomiting/nausea
- MVT complicated by bowel ischemia
  → Potential DOACs malabsorption
- Chronic SVT or portal cavernoma
  → Case-by-case evaluation
- Gastroesophageal varices
  → Not a contraindication to anticoagulant therapy (consider EGDS, beta-blockers, EBL)
  → Frequently associated with severe liver disease

- Incidentally detected SVT
  → Similar rates of event than symptomatic SVT

Riva RPTH 2021

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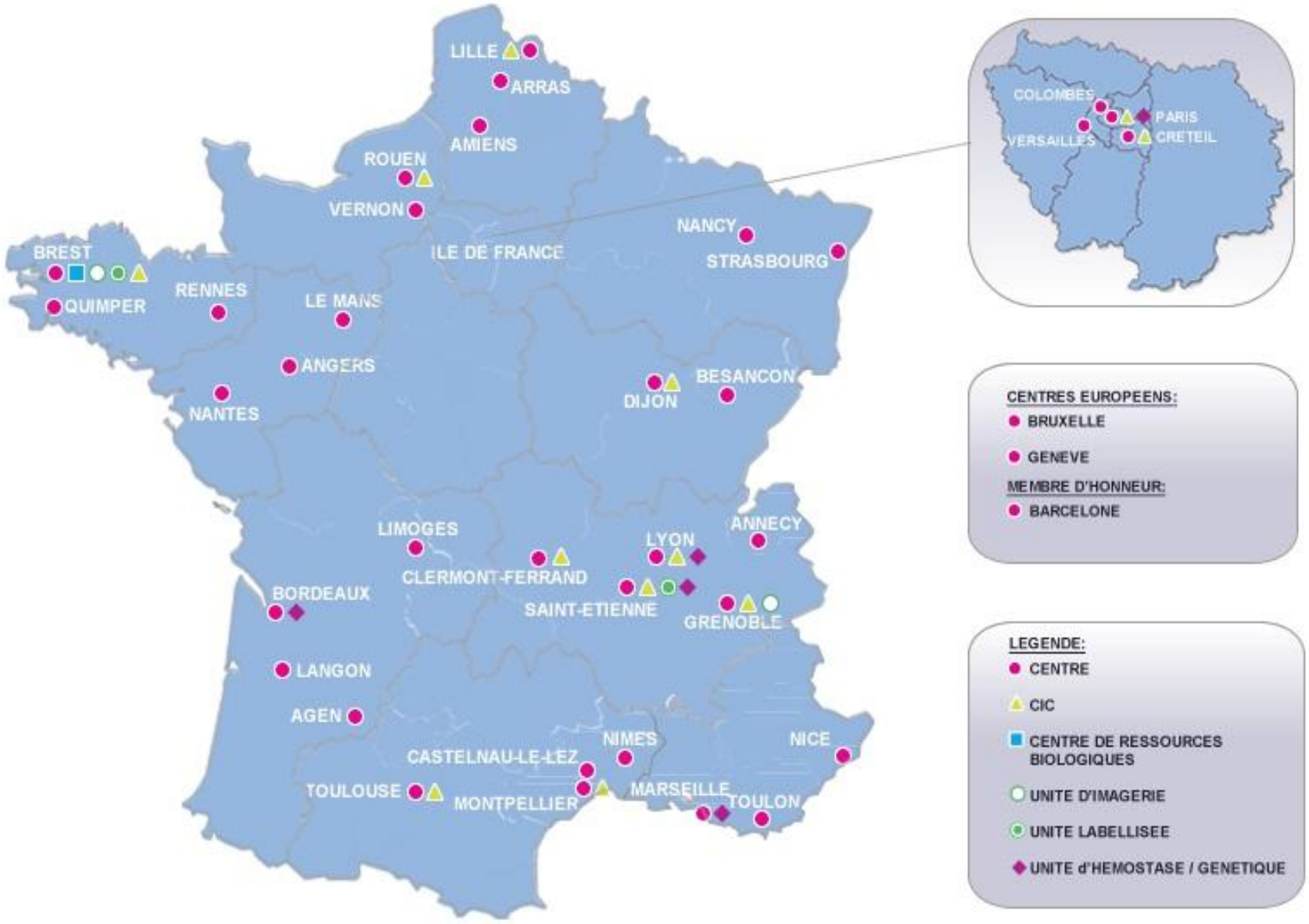

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