PVT without cirrhosis: what place for anticoagulation?

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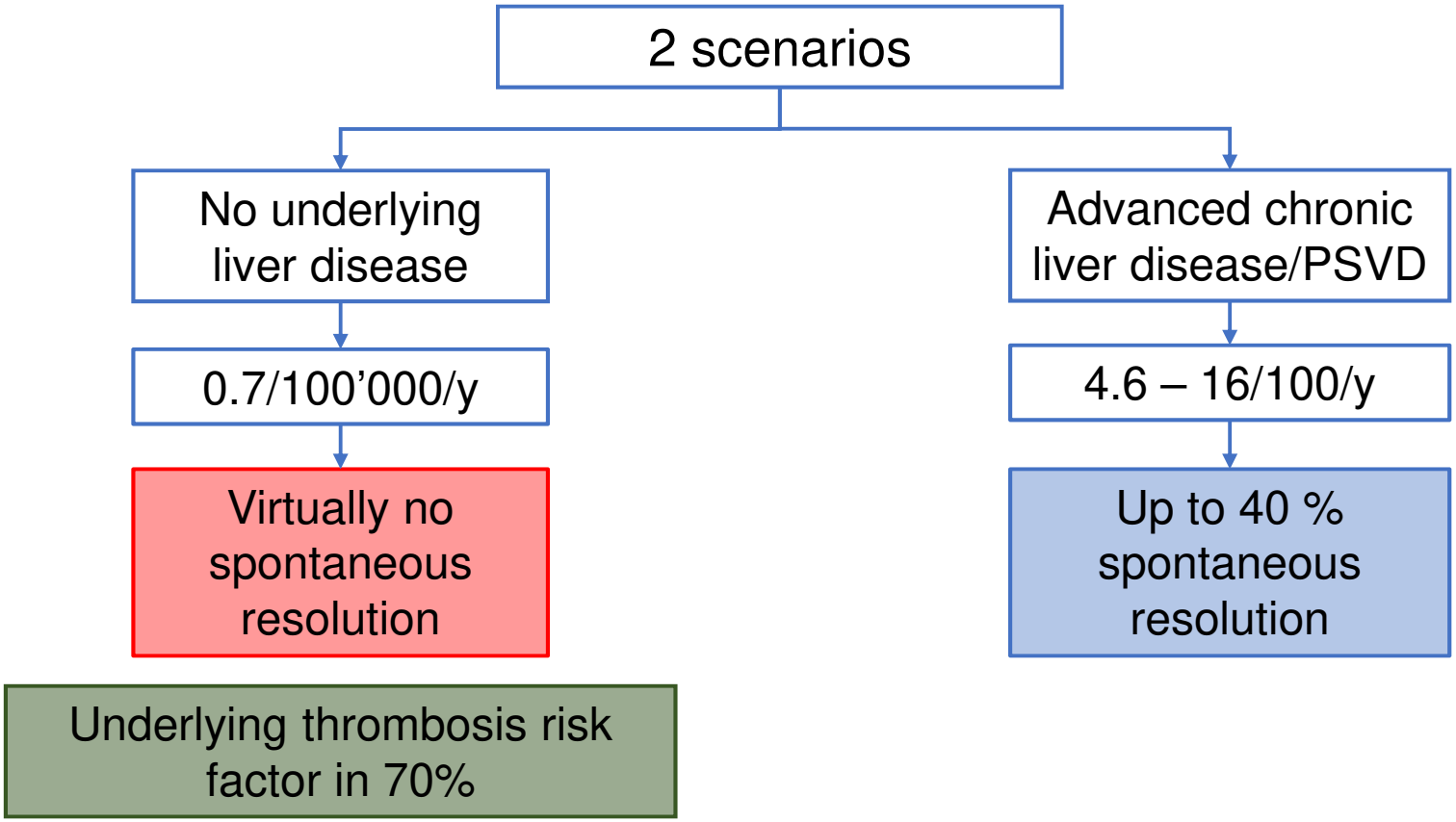
Outline

PVT
Hemodynamic and clinical impact

Anticoagulants
What and when

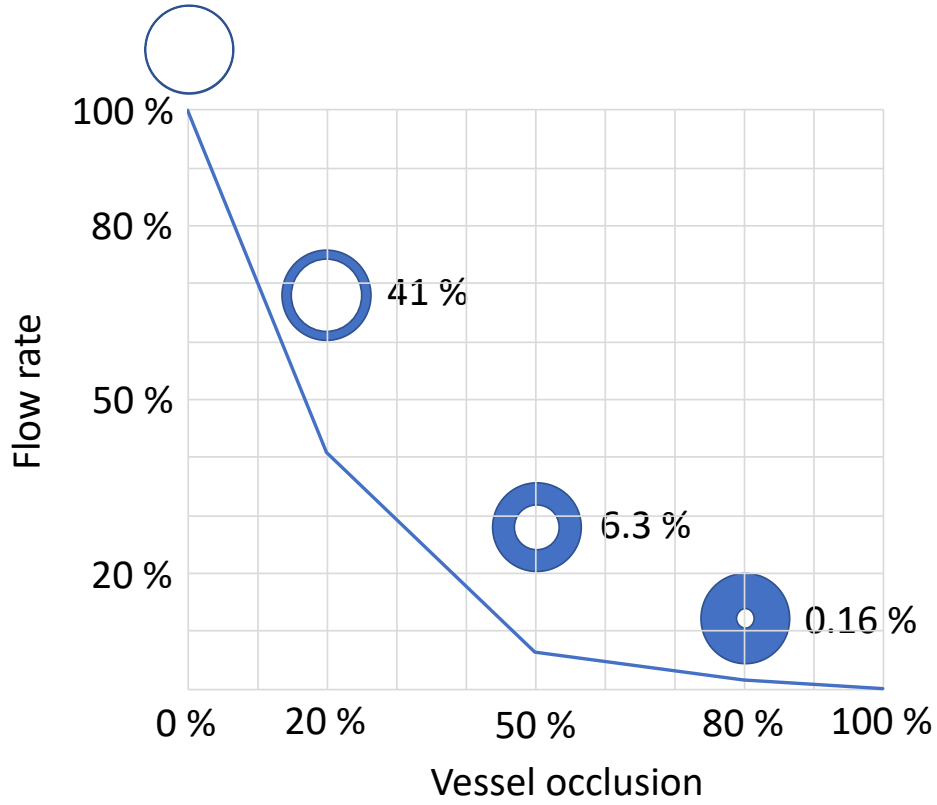
Anticoagulants
Pros and Cons

Portal vein thrombosis: what is the outcome?



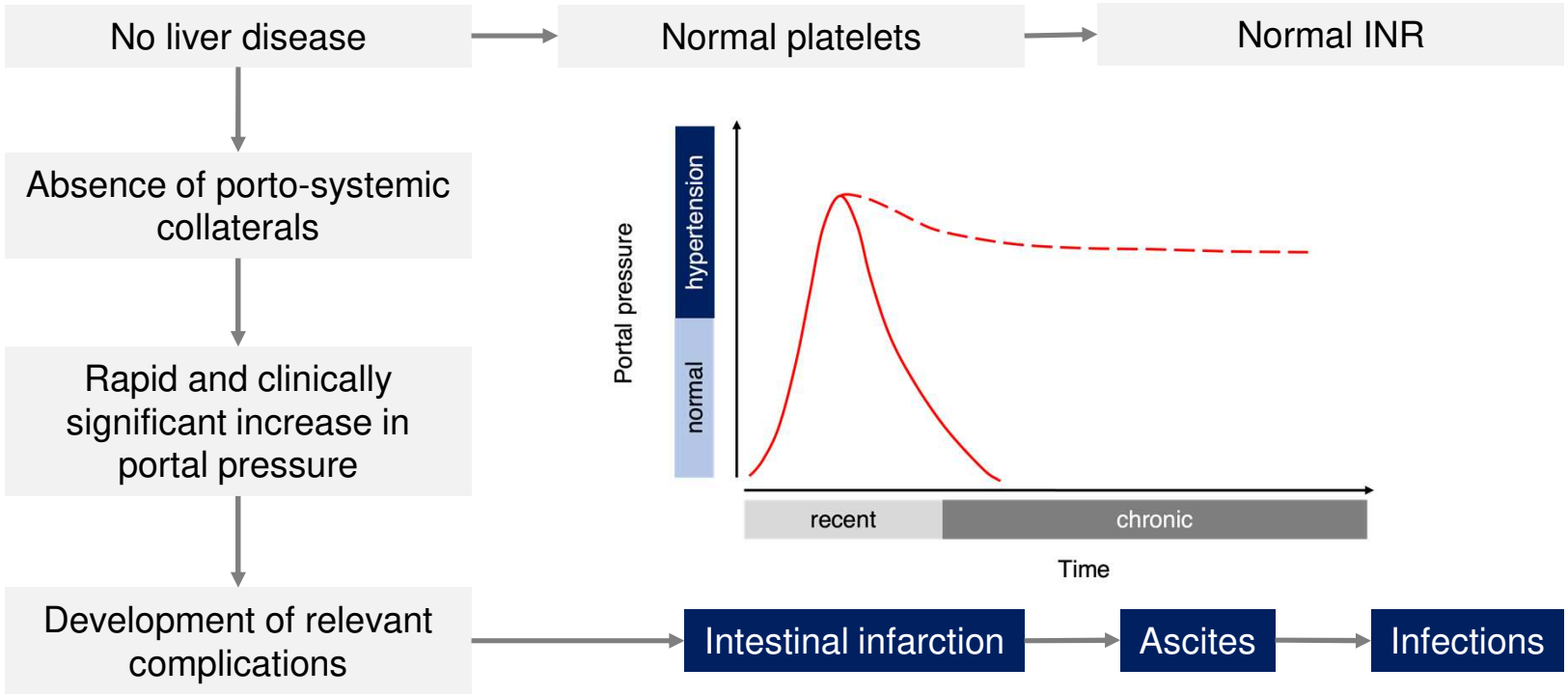
Intagliata, Gastro, 2019; Faccia; WJG, 2019; Northup, Hepatology, 2020

Haemodynamic consequences



Hernández-Gea, J Hepatol, 2019

Recent obstructive portal vein thrombosis



Hernández-Gea, J Hepatol, 2019

Goals of treatment

- To prevent extension to mesenteric or splenic vein
- To prevent complications of intestinal ischemia
- To achieve recanalization and avoid portal hypertension

Northup, Hepatology, 2020

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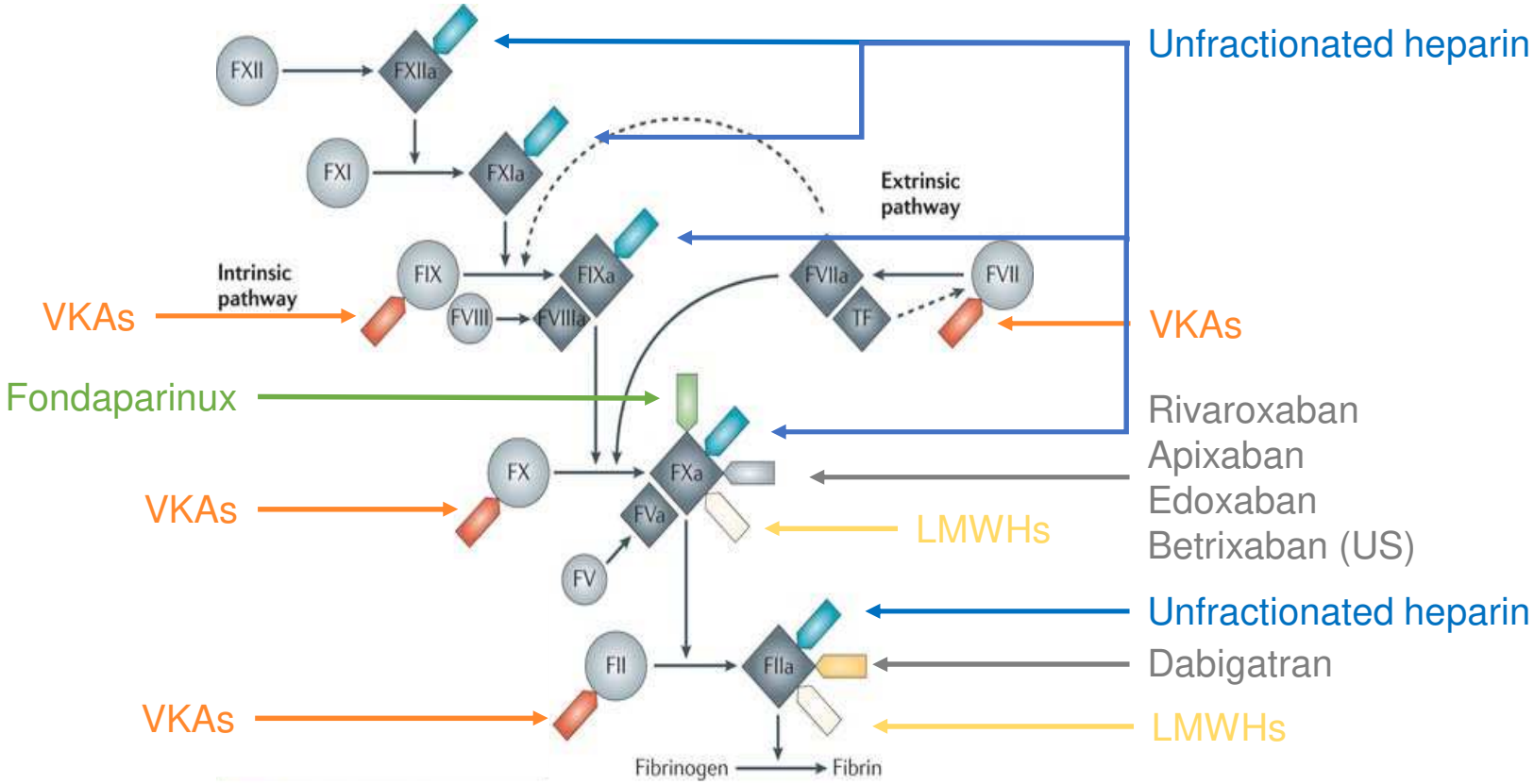
Anticoagulants and mechanisms of action



adapted from Perzborn, Nat Rev Drug Discovery, 2011; Weinberg, SeminLiver Dis, 2019

First line treatment of PVT: anticoagulation

Unfractionated heparin or LMWH	Represent the mainstay of initial therapy
Fondaparinux	Insufficient data available
Vitamin K antagonists	Are used after recovery from the acute event
DOACs	Increasingly coming on stage, despite scarcity of data on efficacy

First line treatment: anticoagulation

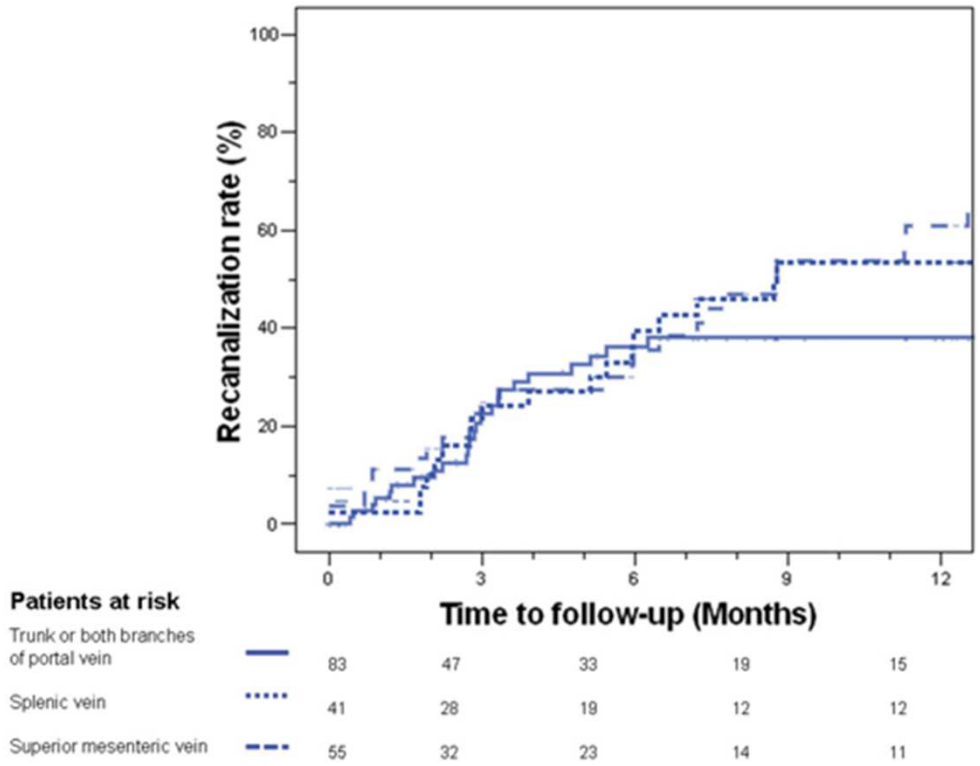
Advantages

Large set of data and experience (in particular in non-spalnchnic venous thrombosis).
Non-invasive treatment.
Increasingly documented efficacy and safety.
Antidotes available.

Drawbacks

Monitoring needed for VKAs.
Systemic treatment probably not needed.
Risk of bleeding.
Low rate of recanalization.

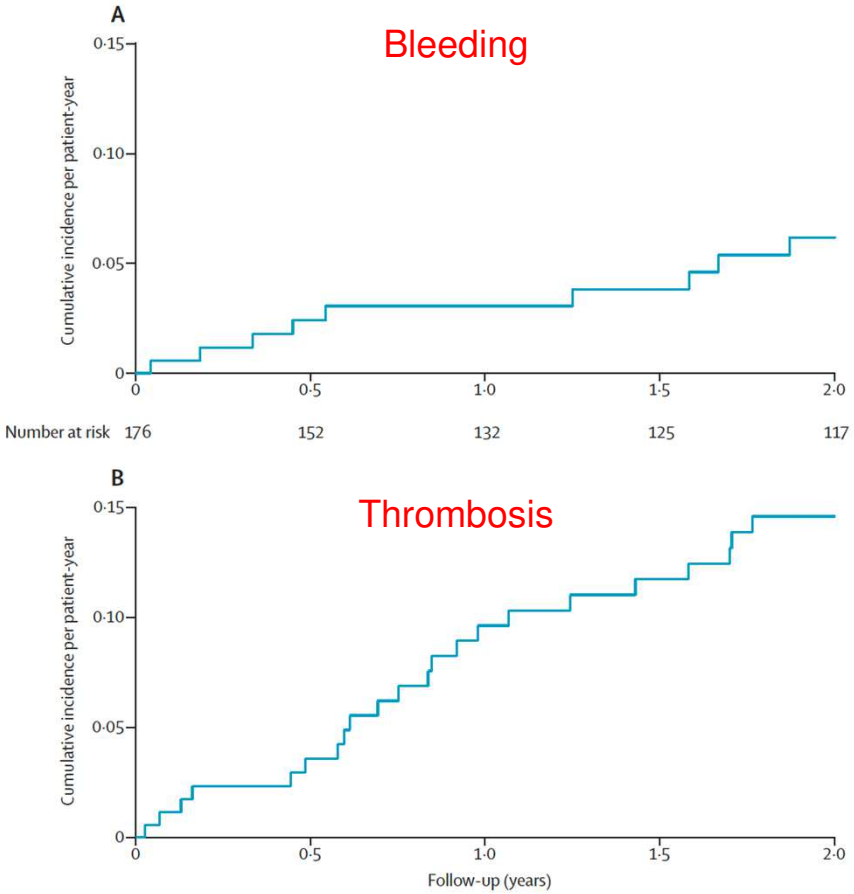
Patients without liver disease: recanalization

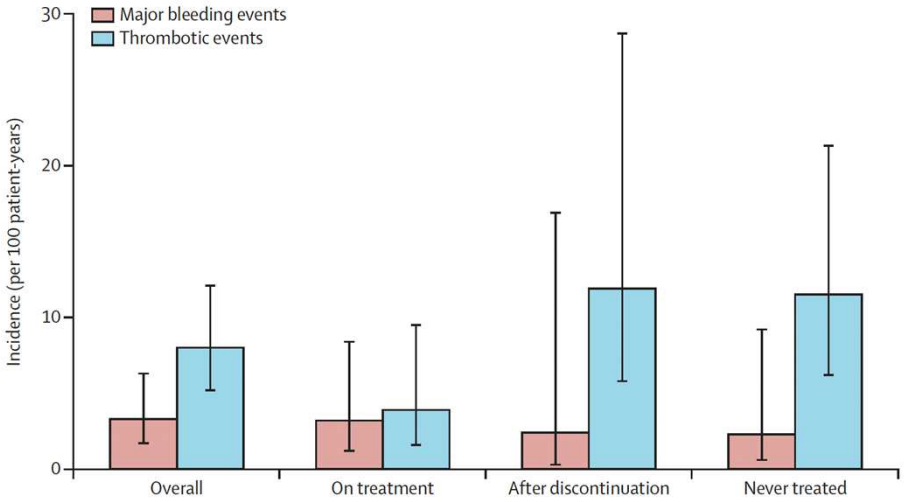


- Complete recanalization in 38%
- Progression and intestinal ischemia in 2%
- Bleeding 8%

Plessier, Hepatology, 2010

Patients with/without liver disease: outcome

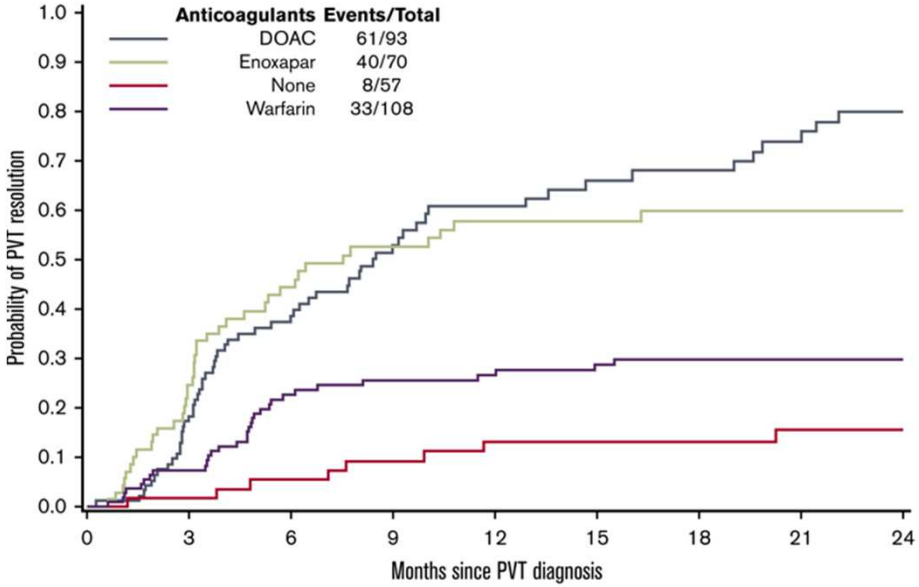




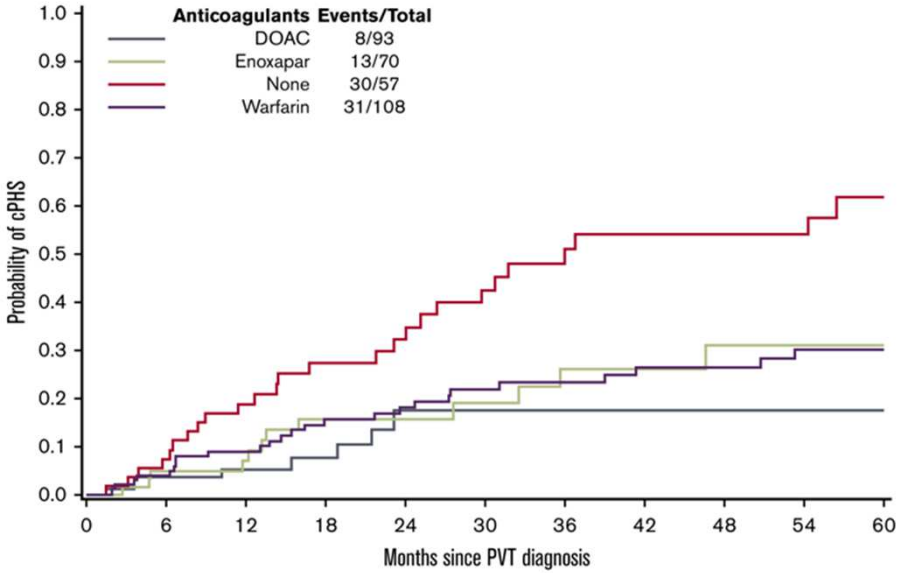
Riva, Lancet Haematol, 2016

Patients without liver disease

Complete resolution



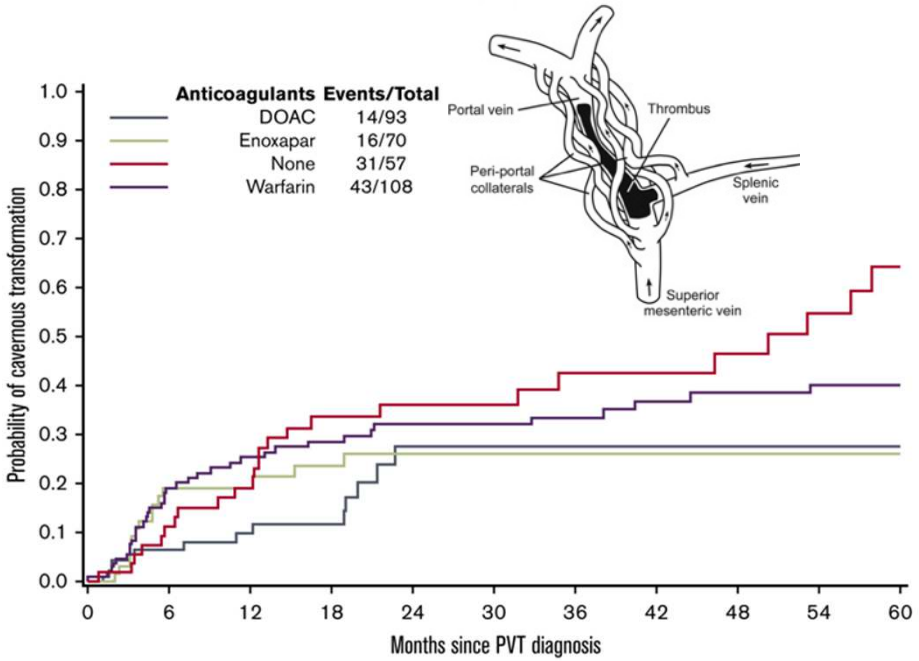
Symptoms of PHT



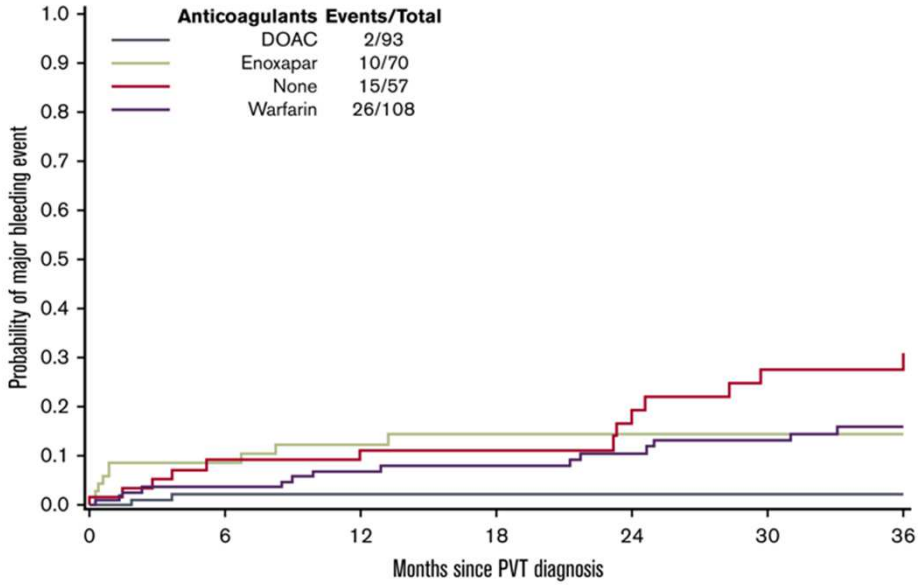
Naymagon, Blood Advances, 2020

Patients without liver disease

Cavernous transformation



Major bleeding



Naymagon, Blood Advances, 2020

The RIPORT study

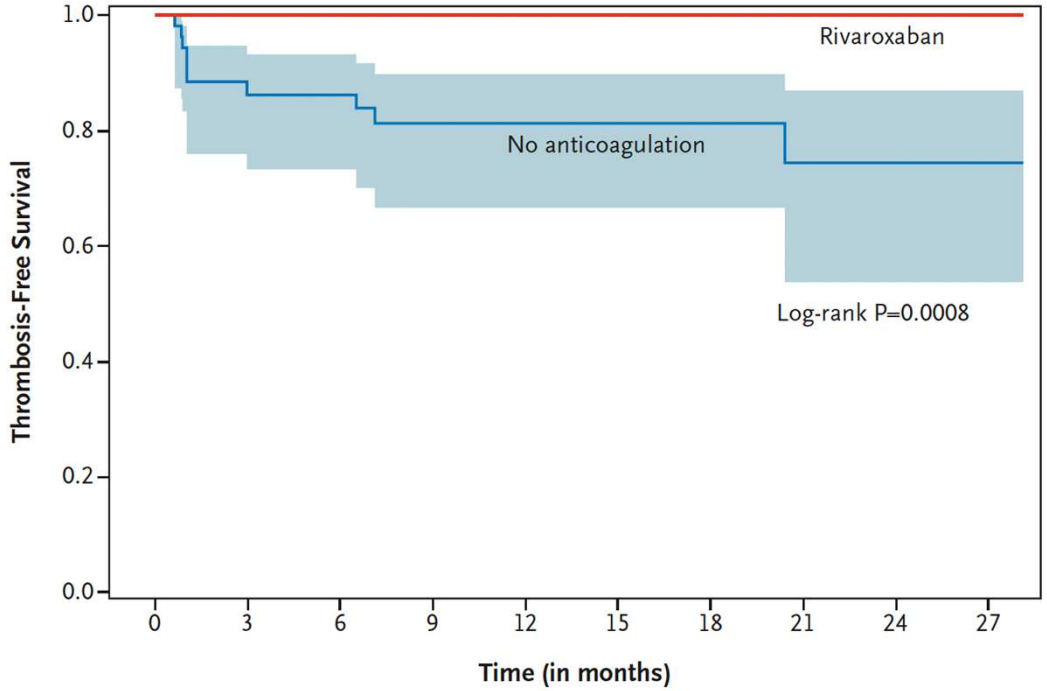
- **Inclusion criteria**:
  - portal cavernoma or
  - recent portal vein thrombosis >6 months,

  without major-risk factors for recurrent thrombosis

- **Exclusion criteria**:
  - myeloproliferative diseases
  - antiphospholipid syndrome or
  - homozygous or composite heterozygous G20210A factor II and G1691A factor V mutations
  - personal or 1st degree unprovoked family history of venous thrombosis
  - past mesenteric infarction

Plessier, NEJM Evidence, 2022

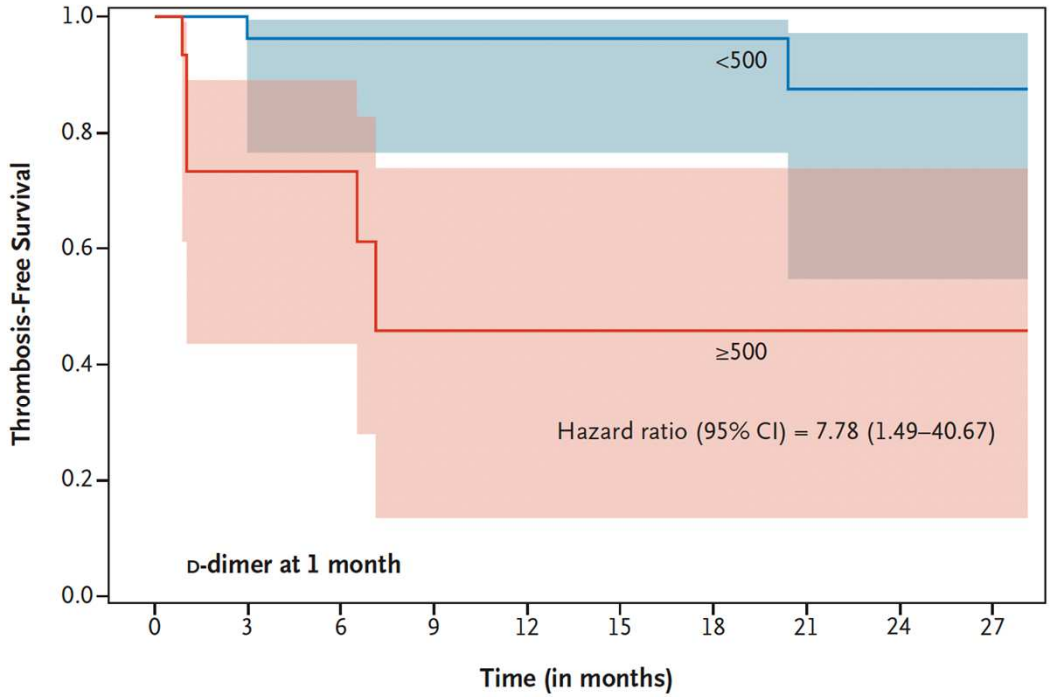
Patients without liver disease



No. at Risk										
No anticoagulation	56	40	36	26	23	12	12	11	11	8
Rivaroxaban	55	45	39	32	25	17	17	17	17	12

Plessier, NEJM Evidence, 2022

Patients without liver disease



No. at Risk										
<500	32	26	26	21	20	11	11	10	10	7
≥500	16	10	6	3	2	1	1	1	1	1

Plessier, NEJM Evidence, 2022

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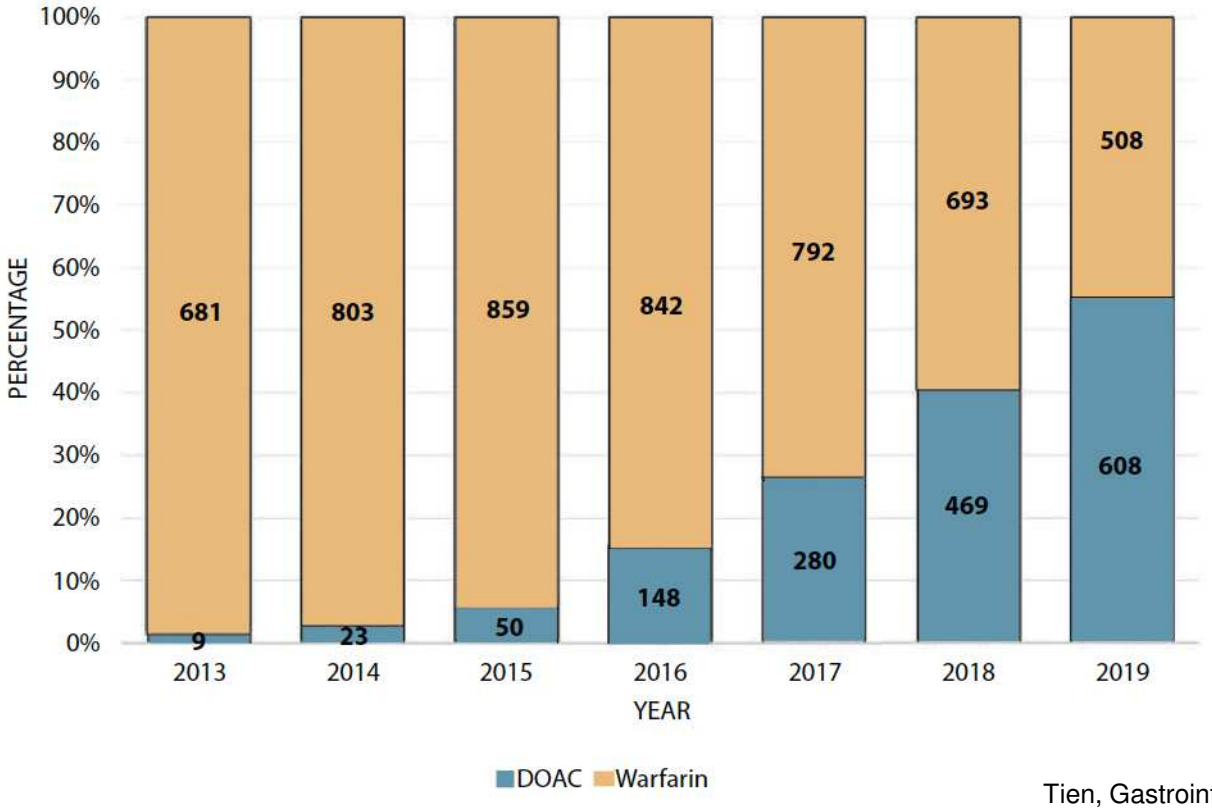
Use of DOACs vs VKAs in patients undergoing endoscopy



Tien, Gastrointestinal Endoscopy, 2020

Reasons to use DOACs rather than VKAs

Demonstrated superiority or non-inferiority to prior standards

Fewer/no monitoring requirements

Less frequent follow-ups

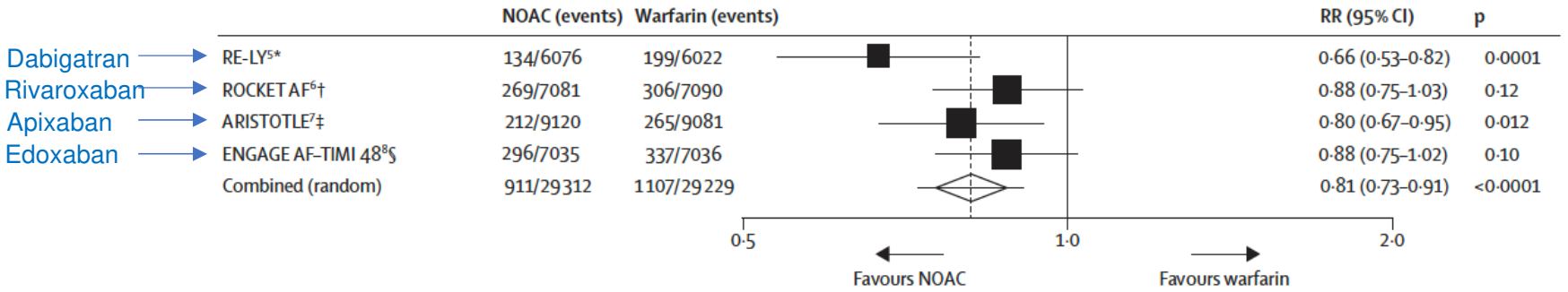
Fewer drug and food interactions

Rapid onset and offset of effects

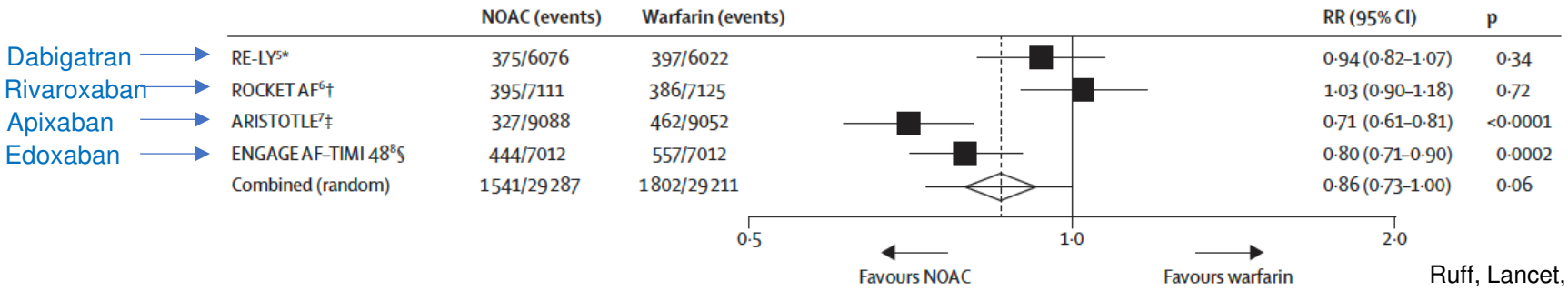
Antidotes available

Efficacy and safety DOACs vs VKAs

Stroke or systemic embolic events



Major bleeding



Ruff, Lancet, 2014

Efficacy and safety DOACs vs VKAs

MAJOR BLEEDING OVERALL

- apixaban and edoxaban are better
- no advantage of dabigatran or rivaroxaban over VKAs

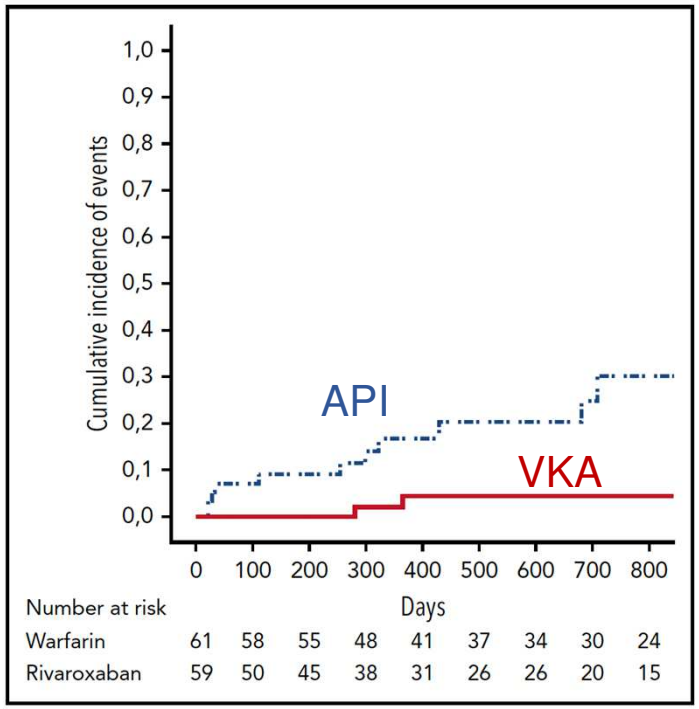
MAJOR GI BLEEDING

- incidence is higher with dabigatran or rivaroxaban

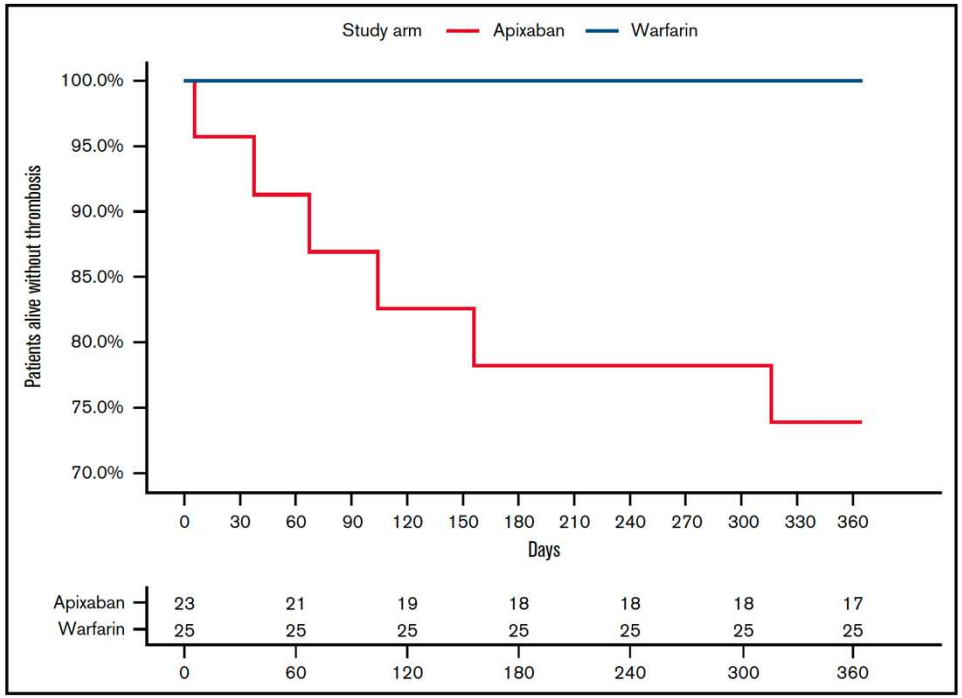
MAJOR INTRACRANIAL BLEEDING

- lower incidence with all DOACs

Efficacy and safety DOACs vs VKAs in APS



Pengo, Blood, 2018



Woller, Blood Adv, 2022

DOACs in patients with chronic kidney disease

Renal insufficiency: increased risk of bleeding or TE *per se*

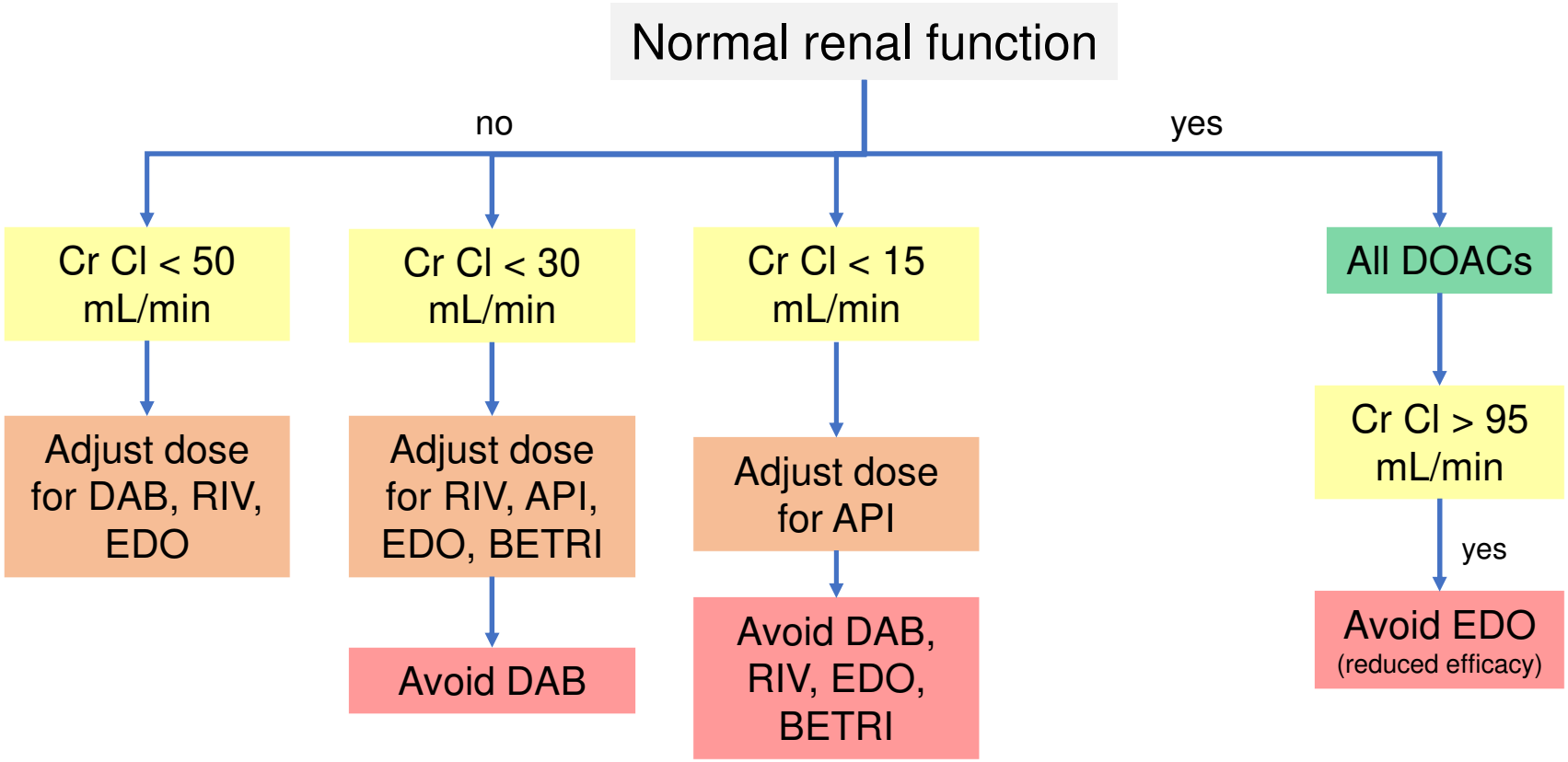
DOACs are eliminated by the kidney to varying degrees

Dose adaptation is necessary

Regular monitoring of the renal function to adjust the dose

Renal elimination: DAB 80%, EDO 50%, RIVA 35%, API 27%, BETRI 10%

DOACs in patients with chronic kidney disease



Chen, J Am Heart Assoc, 2020

Take home messages

Anticoagulation for PVT with normal liver ≠ with cirrhosis

Anticoagulation first line treatment

LMWH ≠ VKA ≠ DOACs

Consider anticoagulation for longer than 6 months,
restart if D-dimers > 500

Challenges and open issues

Therapeutic vs prophylactic dose?

Stopping and restarting rules?

Is there a role for primary prevention in at risk situations?