



Non-cirrhotic PVT

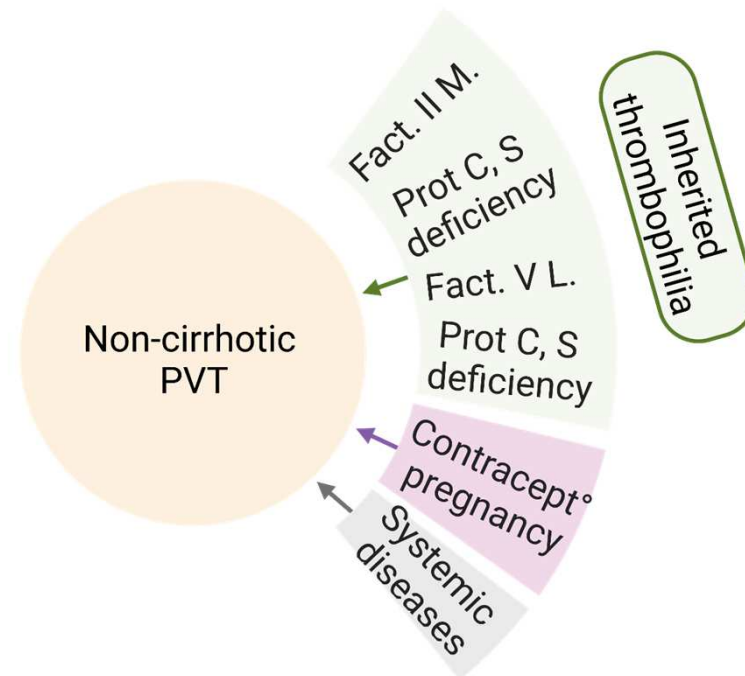
Causes and underlying mechanisms

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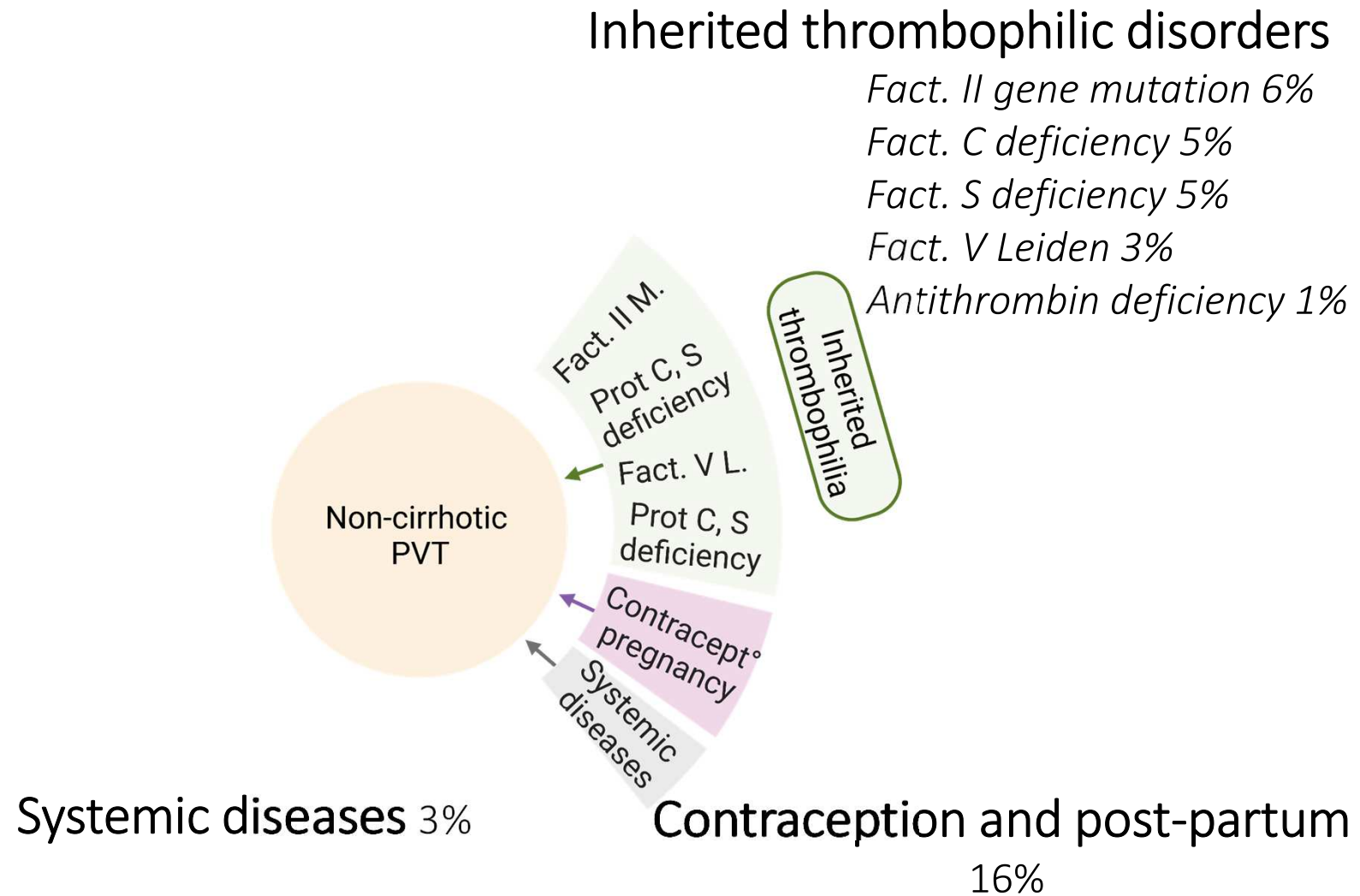
Causes of non-cirrhotic portal vein thrombosis

0.35–2.5 cases per 100,000 per year

15 to 36% → Multiple factors



Causes of non-cirrhotic portal vein thrombosis



Hernández-Gea V, J Hepatol, 2019

Causes of non-cirrhotic portal vein thrombosis

CMV diseases

Other risk factor 50%

Fact. II mutation 22% (vs. 4% in CMV neg patients)

De Broucker C, J Hepatol, 2022

Obesity

25% in NC-PVT with 1 or more risk factor

45% in Idiopathic NC-PVT

Bureau C, J Hepatol, 2016

Inherited thrombophilic disorders

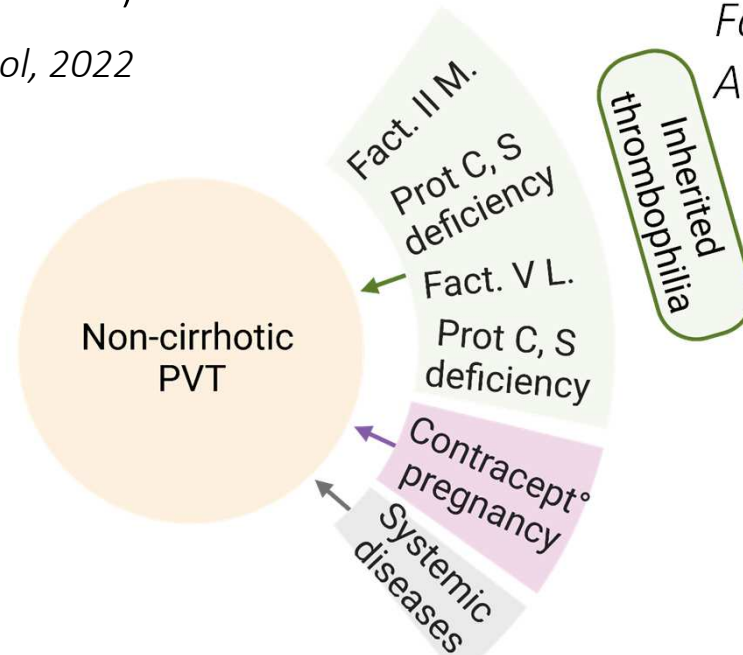
Fact. II gene mutation 6%

Fact. C deficiency 5%

Fact. S deficiency 5%

Fact. V Leiden 3%

Antithrombin deficiency 1%



Systemic diseases 3%

Contraception and post-partum

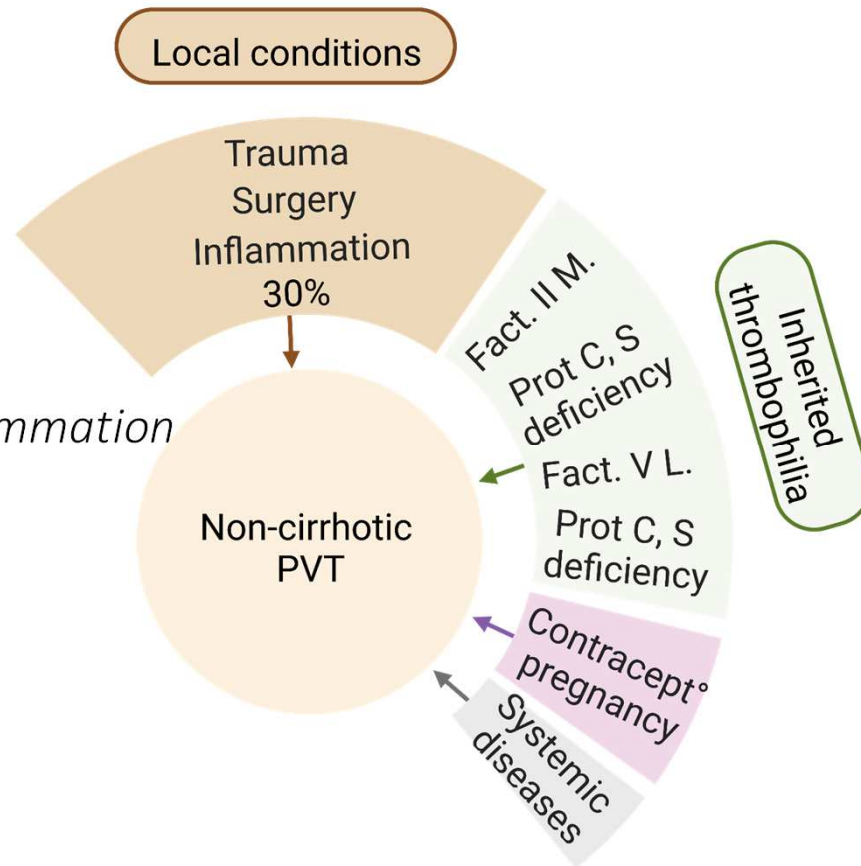
16%

Hernández-Gea V, J Hepatol, 2019

Causes of non-cirrhotic portal vein thrombosis

Local risk factor

- Abdominal trauma
- Intra-abdominal surgery
- Inflammatory intra-abdominal lesions
 - Acute pancreatitis*
 - Biliary or intestinal infection or inflammation*

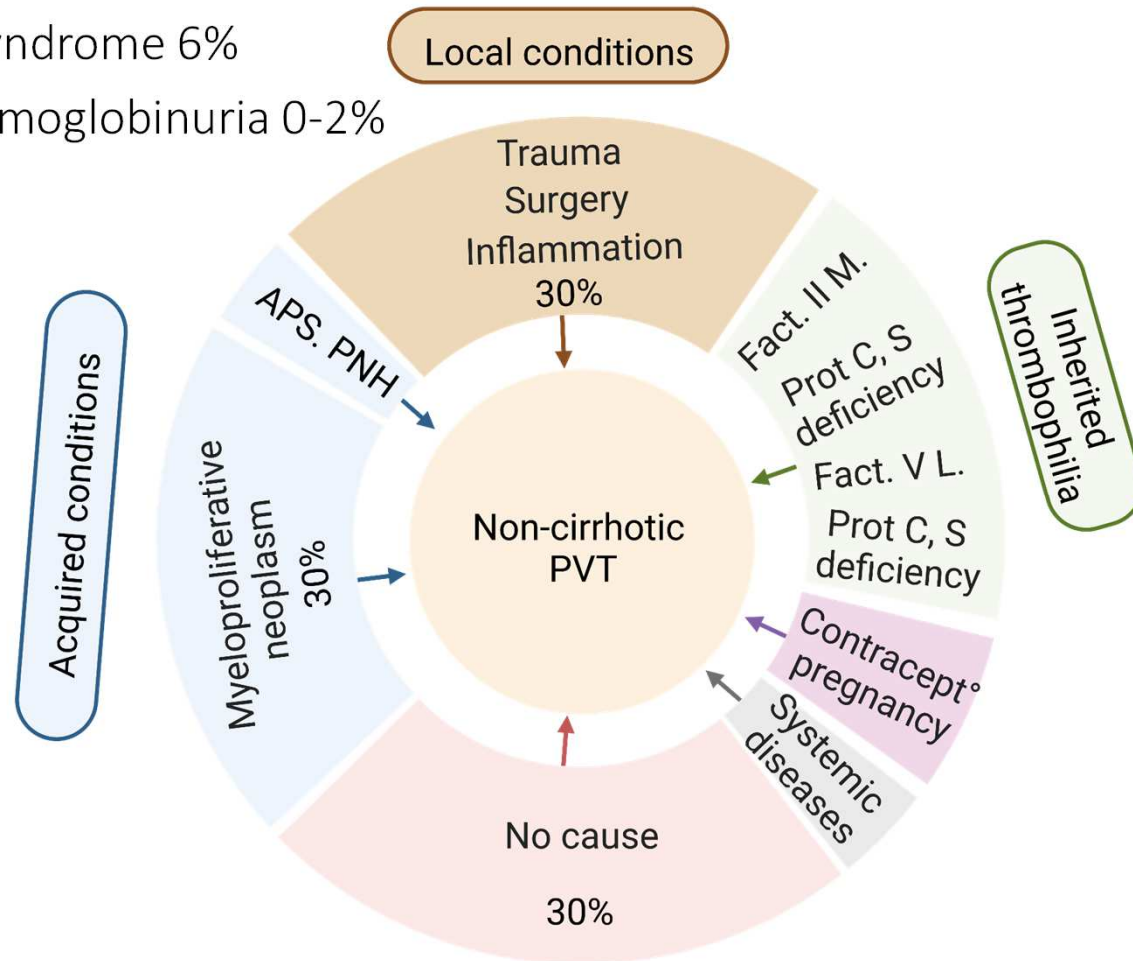


Causes of non-cirrhotic portal vein thrombosis

Other acquired thrombophilic diseases

Antiphospholipid syndrome 6%

Paroxysmal nocturnal haemoglobinuria 0-2%



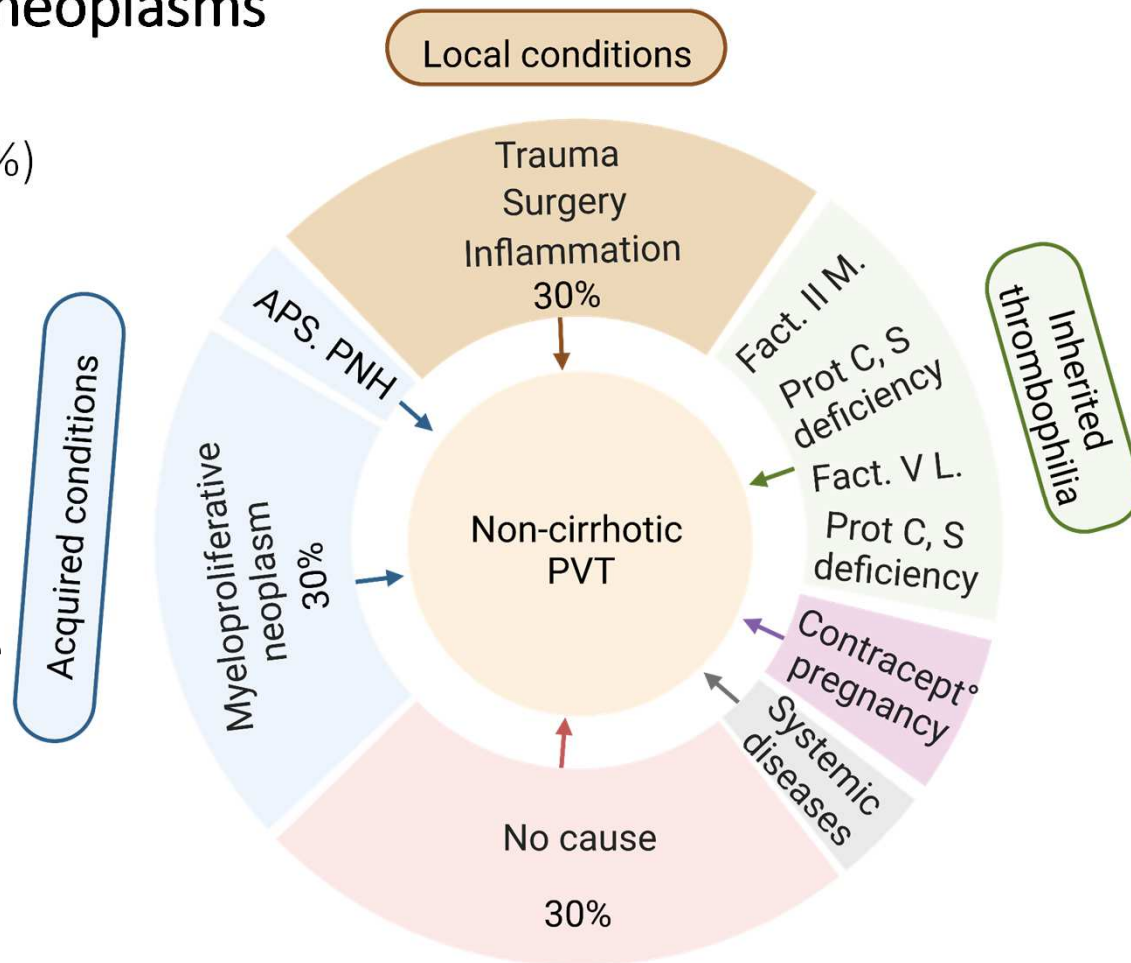
Causes of non-cirrhotic portal vein thrombosis

Myeloproliferative neoplasms

JAK2 Mutations (87%)

CALR Mutations (2-10%)

→ No clear mechanisms before recently



Myeloproliferative neoplasms and NC-PVT

→ More female and younger

	PV Without PVT	PV with PVT
Female	37%	67%
Age (median)	57	47

How J et al., BJH 2018

→ Less CALR mutations

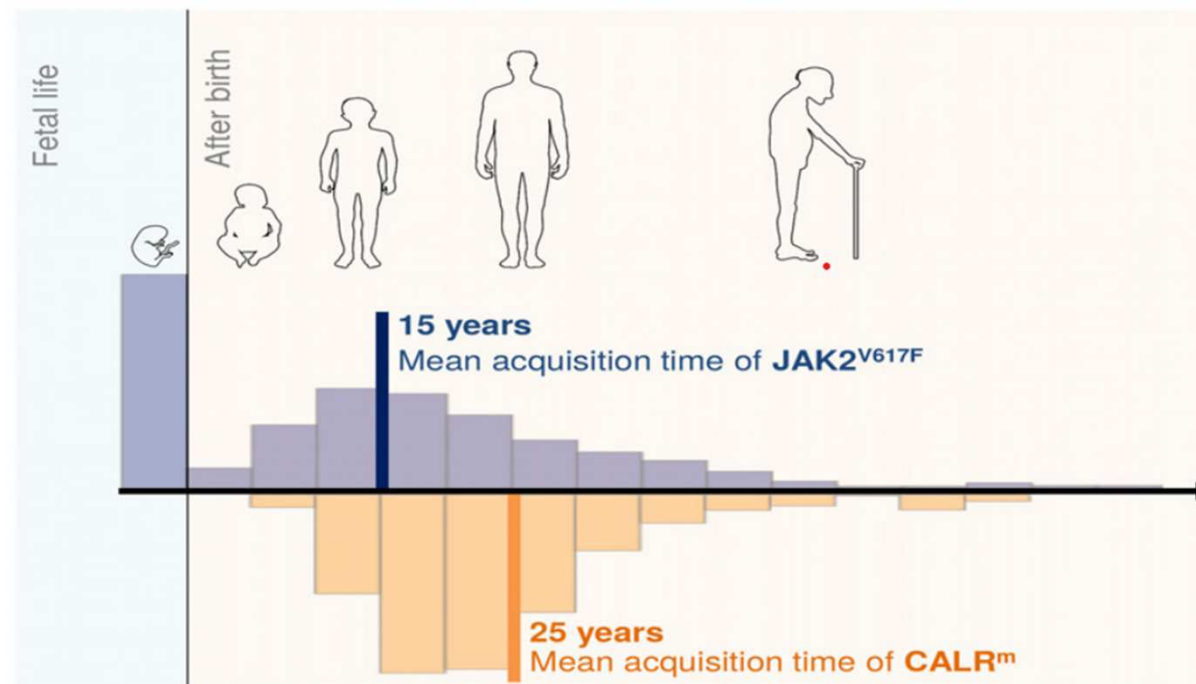
	JAK2 negative MPN Without PVT	JAK2 negative MPN with PVT
CALR	67-88 %	9-30 %

*Klampf T et al.,
NEJM, 2013*

*Poisson J et al.,
J Hepatol, 2017*

Myeloproliferative neoplasms and NC-PVT

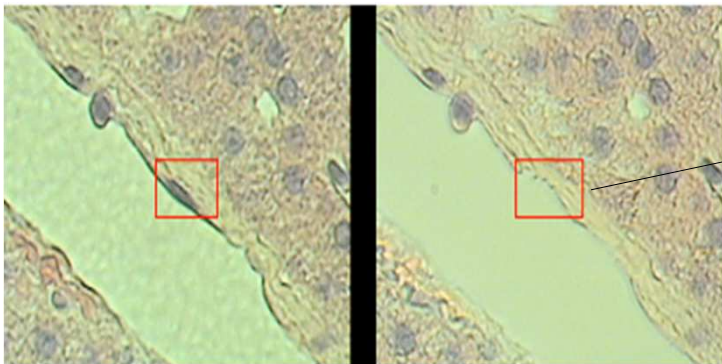
→ JAK2 mutation appears earlier in life than CALR mutations



Myeloproliferative neoplasms and NC-PVT

→ $JAK2^{V617F}$ in endothelial cells

Splenic and hepatic vein



$JAK2^{V617F}+$

Sozer, Blood 2009; Rosti, Blood 2012

Endothelial progenitor $JAK2^{V617F}+$

Teofili, Blood, 2011; Helman, BJH, 2016

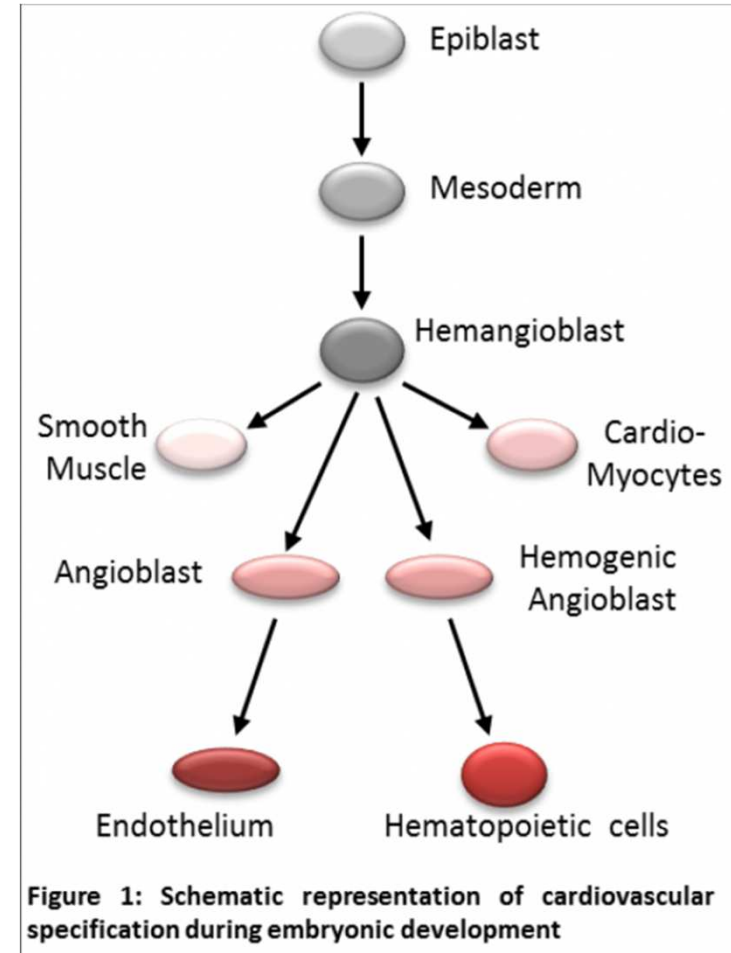
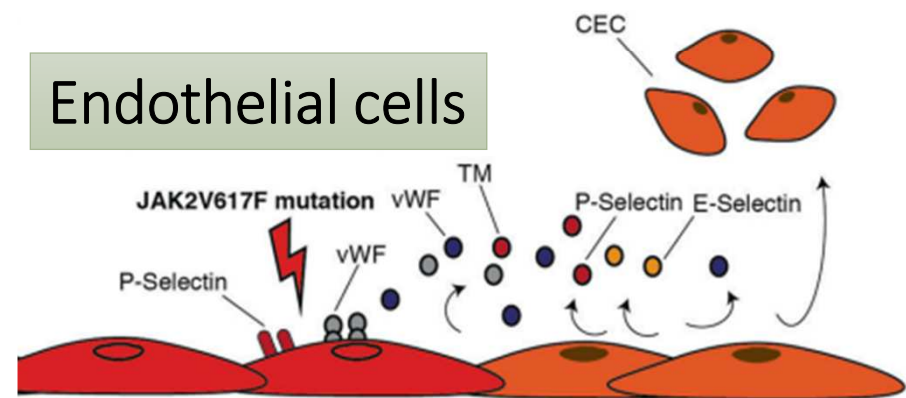


Figure 1: Schematic representation of cardiovascular specification during embryonic development

Mechanisms of venous thrombosis in MPN

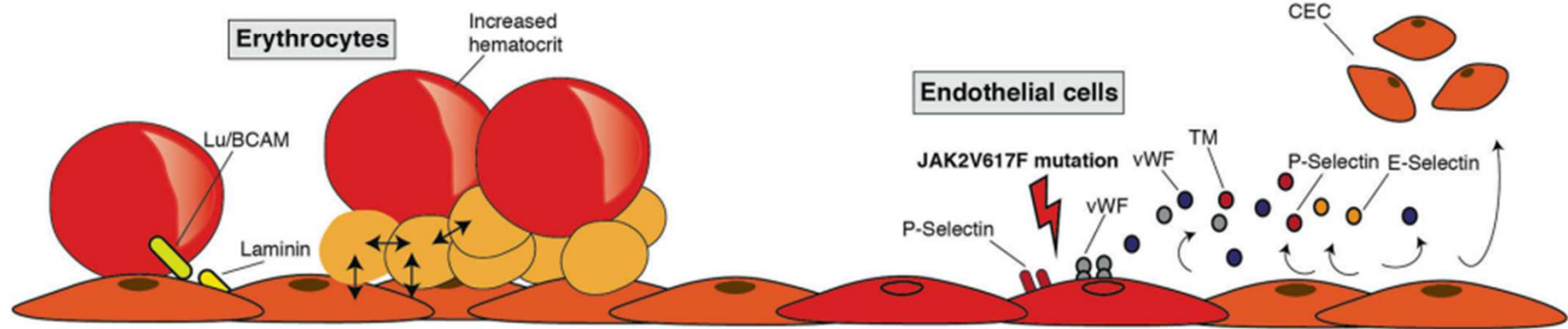


MPN : Myeloproliferative neoplasms

Guy A, Poisson J, James C, *Leukemia*, 2021

Mechanisms of venous thrombosis in MPN

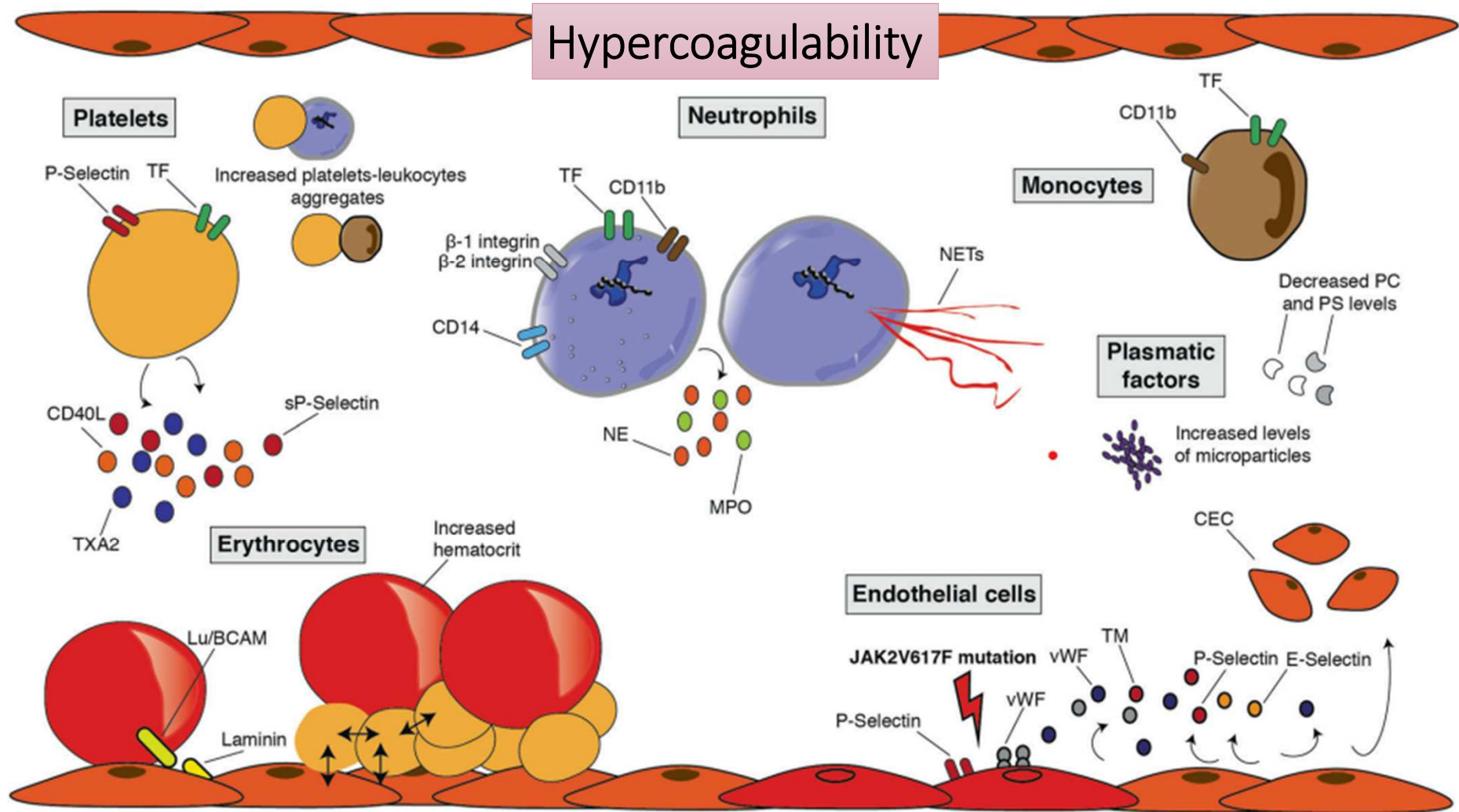
Disturbed blood flow



MPN : Myeloproliferative neoplasms

Guy A, Poisson J, James C, *Leukemia*, 2021

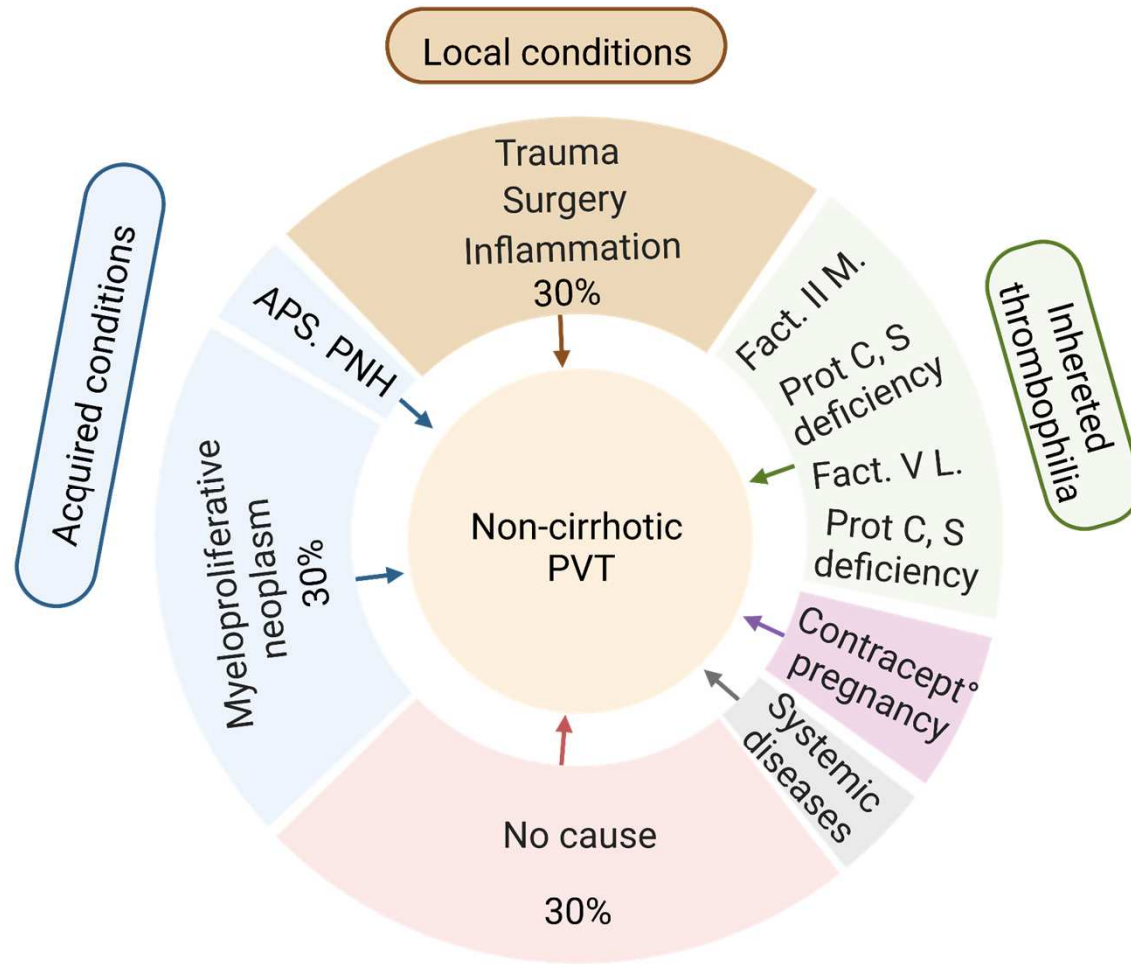
Mechanisms of veinous thrombosis in MPN



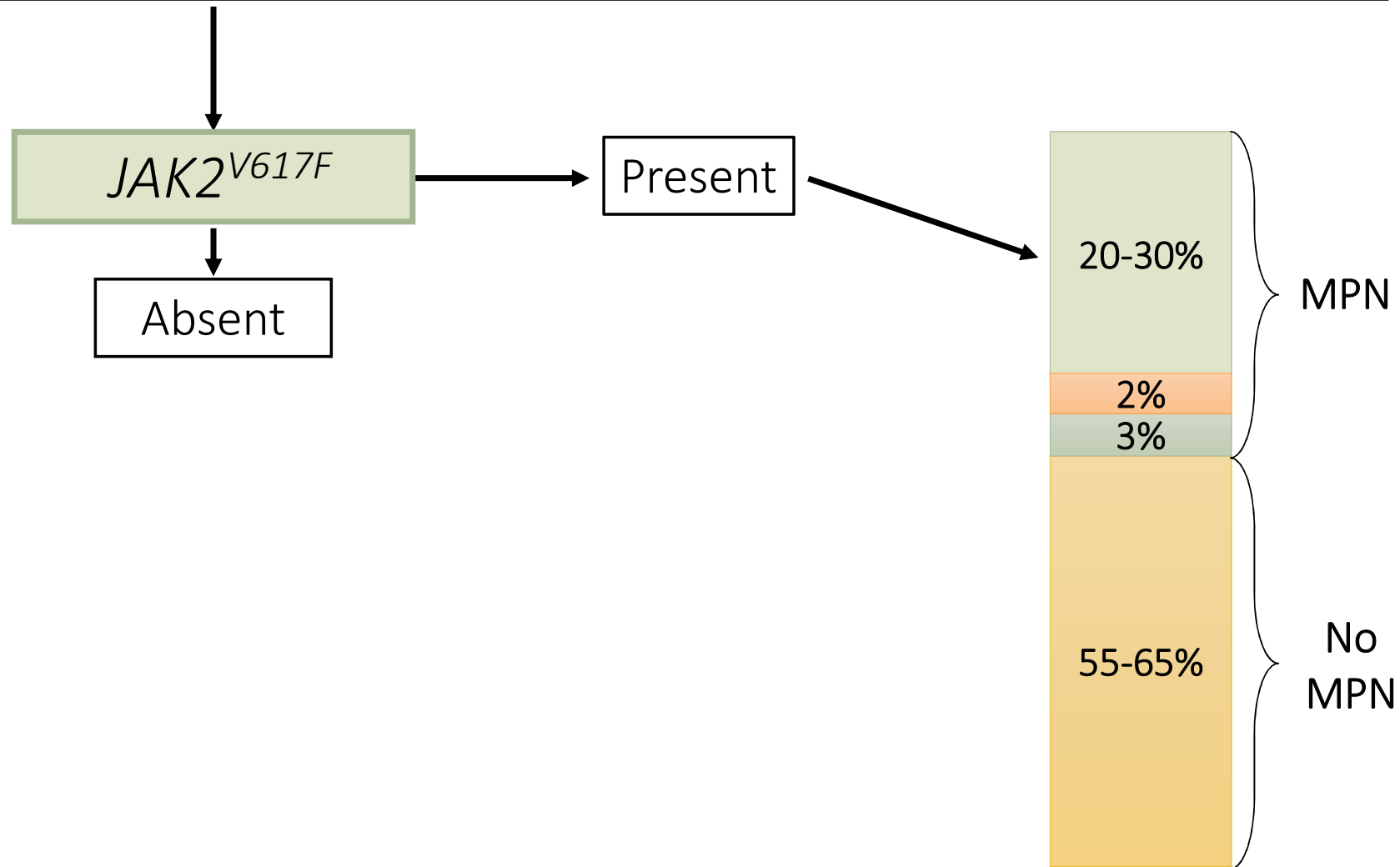
MPN : Myeloproliferative neoplasms

Guy A, Poisson J, James C, *Leukemia*, 2021

Improving causes diagnosis

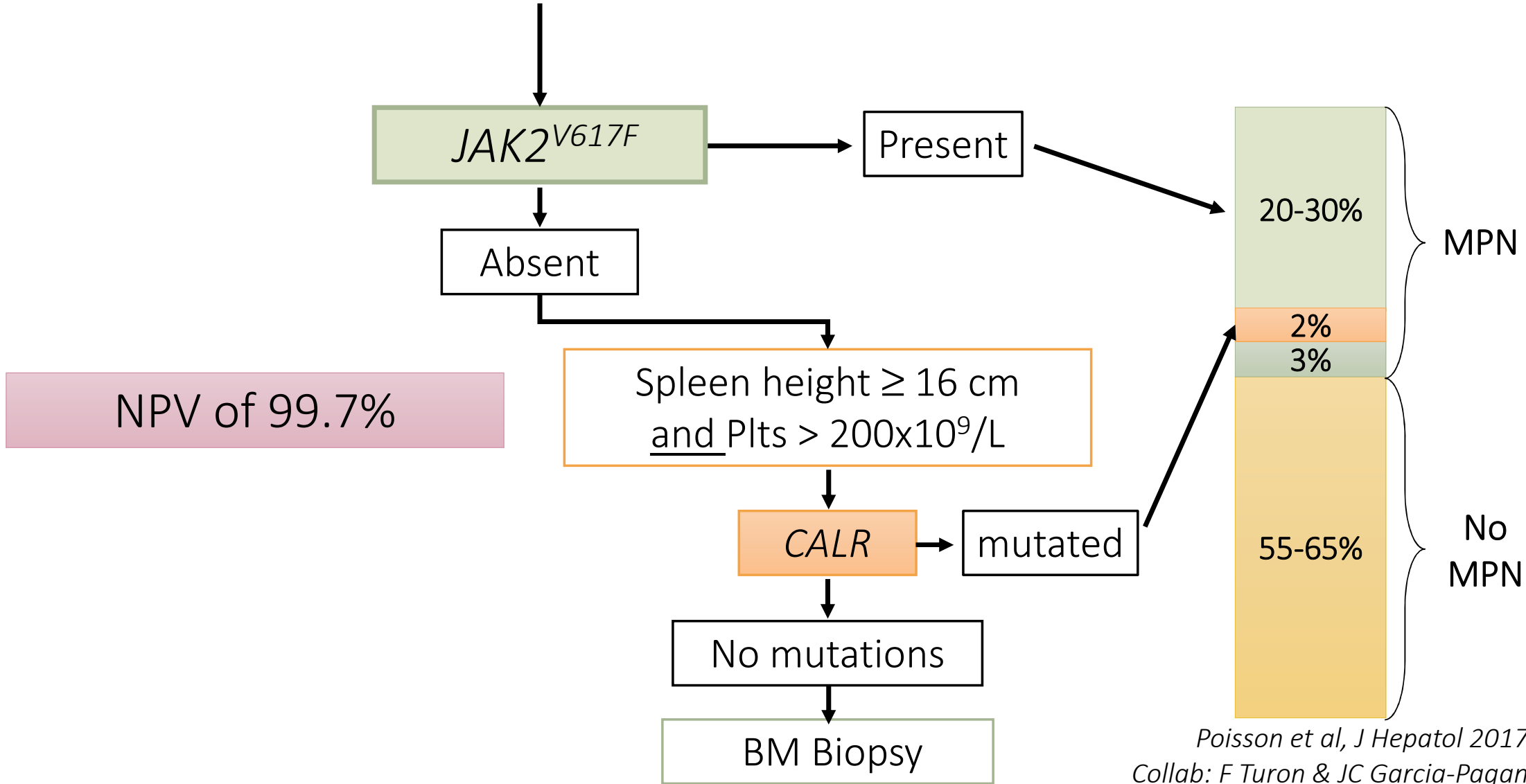


Splanchnic vein thrombosis and CALR mutations



Poisson et al, J Hepatol 2017
Collab: F Turon & JC Garcia-Pagan

Splanchnic vein thrombosis and CALR mutations



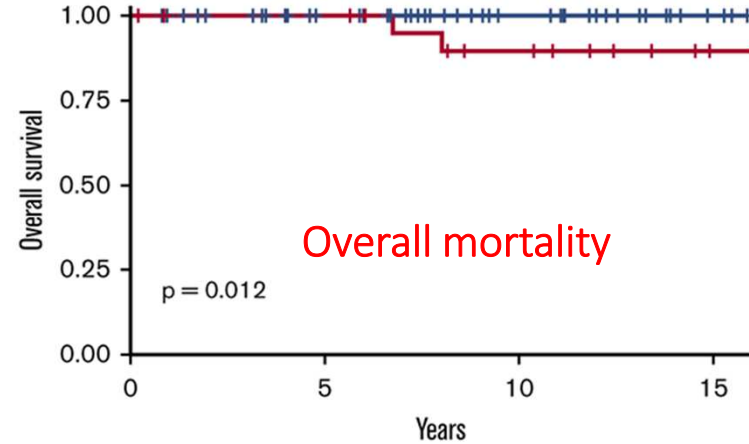
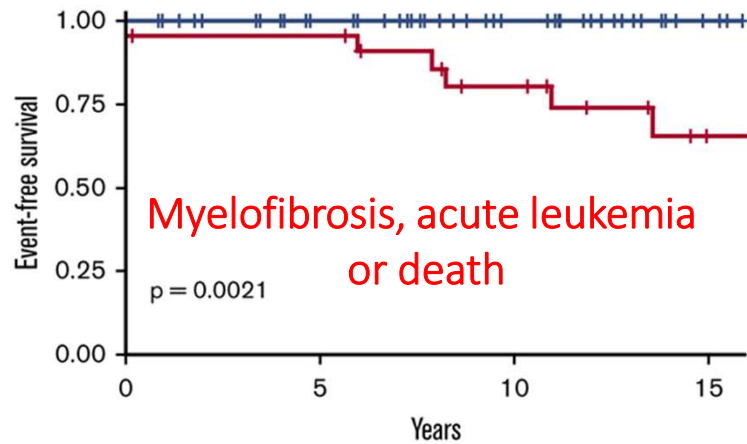
NC-PVT and molecular profiling in myeloproliferative neoplasms

Molecular profiling of patients with myeloproliferative neoplasm and splanchnic vein thrombosis identifies high risk patients with:

JAK2V167F \geq 50%

and/or

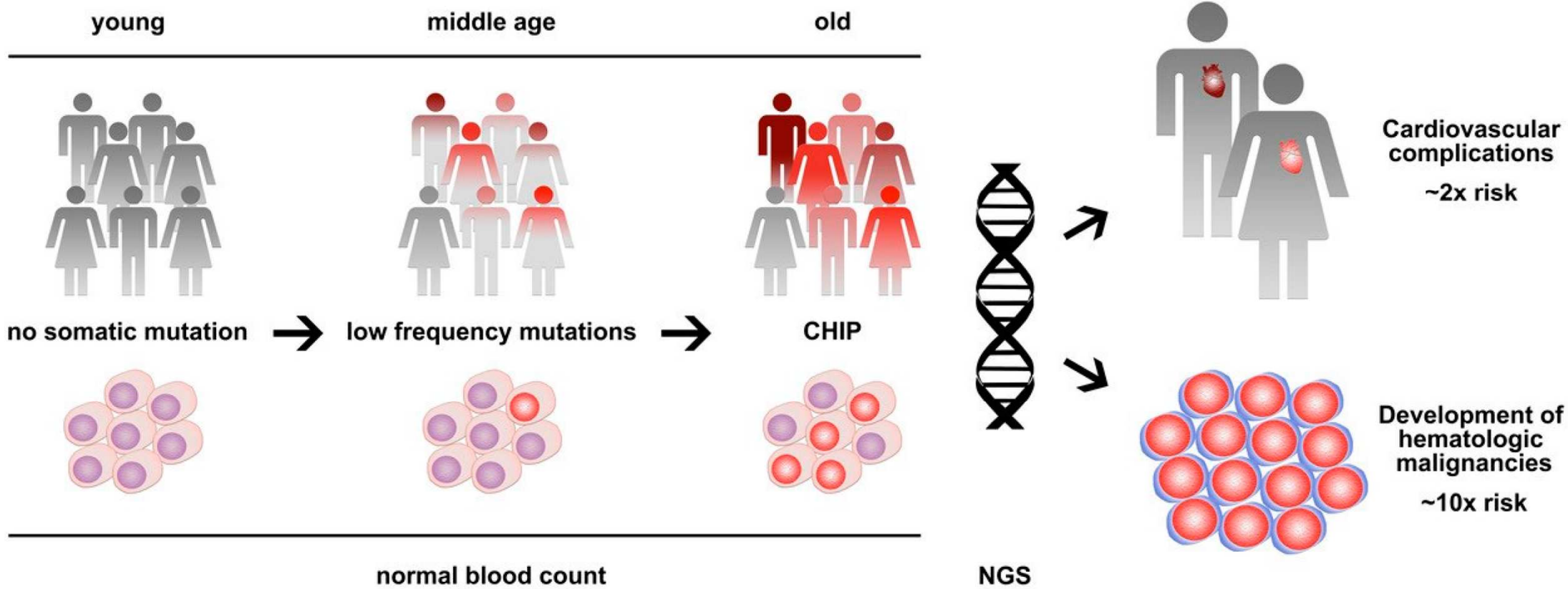
Chromatin Spliceosome Tp53 mutation



Low risk	57	44	29	14
High risk	23	21	14	7

Low risk	57	44	29	14
High risk	23	21	15	8

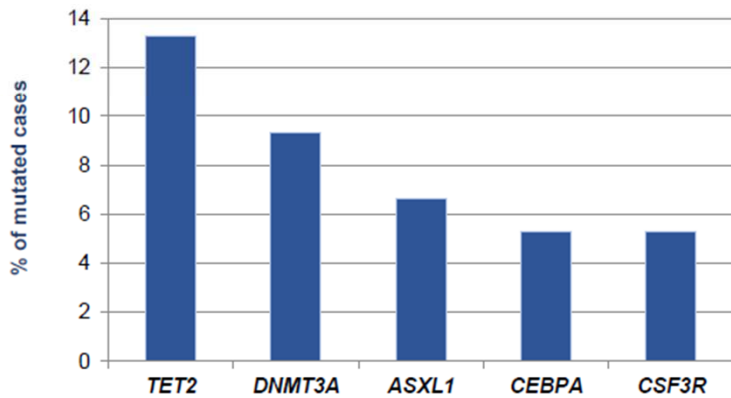
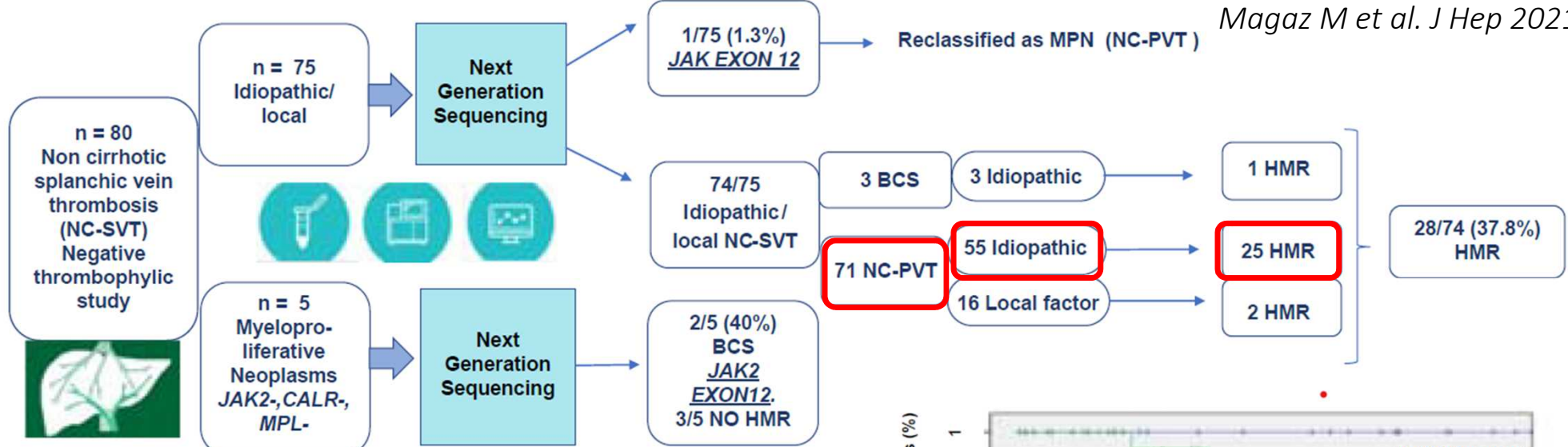
Clonal hematopoiesis of indeterminate potential (CHIP)



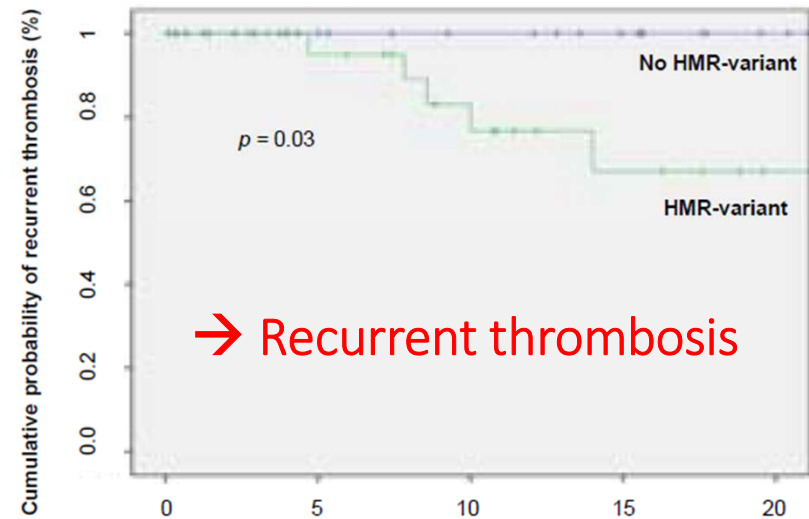
High-molecular-risk (HMR) variants :
TET2, DNMT3A, ASXL1, Tp53...

NC-PVT and clonal hematopoiesis

Magaz M et al. J Hep 2021

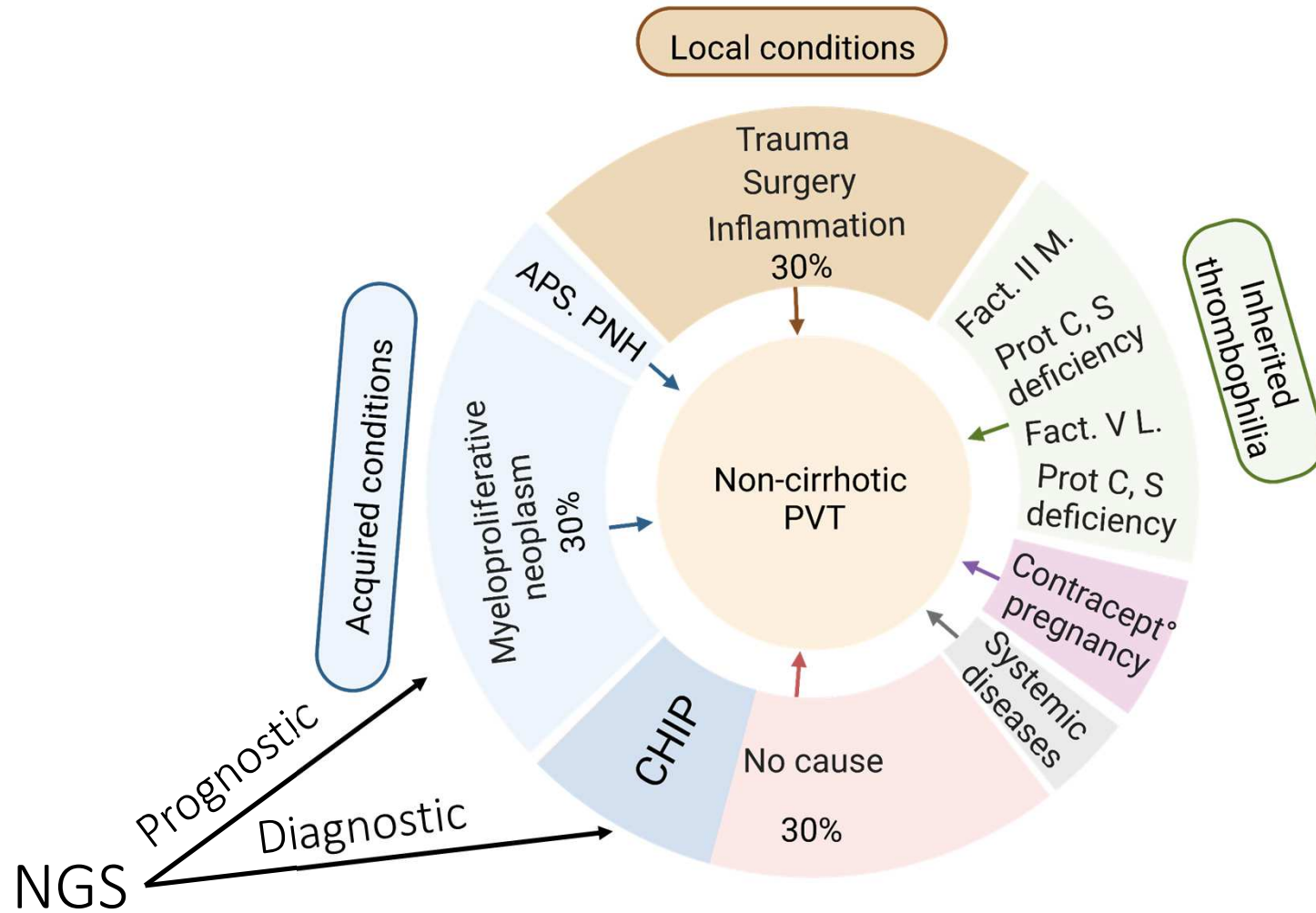


Most frequent High molecular risk-variants (HMR) High-molecular-risk (HMR)



→ Recurrent thrombosis

Improving NC-PVT causes diagnosis



Thank you



