Vénás thromboemboliák diagnózisa és kezelése

Haematológia szintentartó 2025

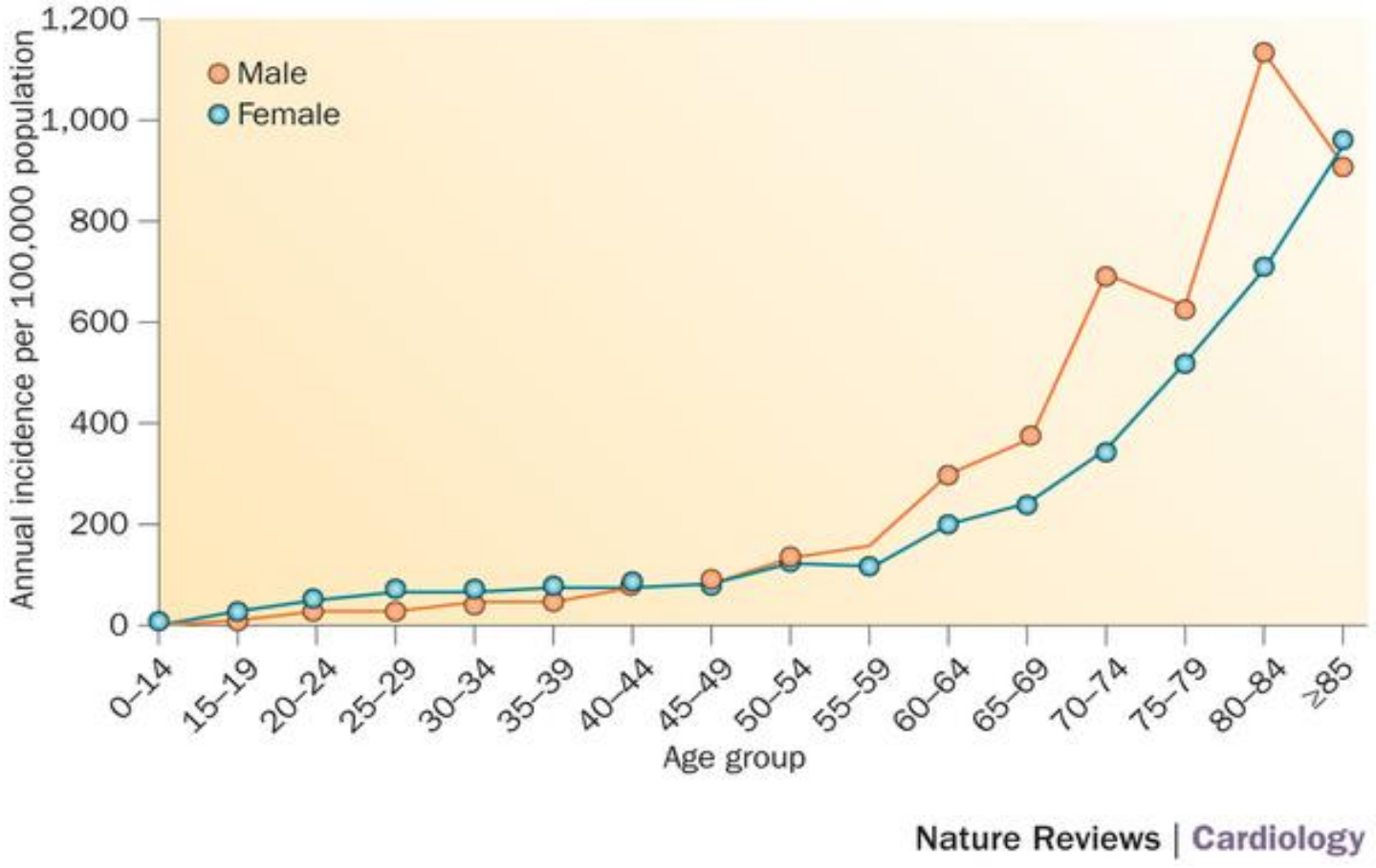
Dr. Tóth Orsolya

terv

- Diagnózis - ajánlások
- Kezelés
  - Mi a legkritikusabb faktor a VTE (hosszútávú…) kezelésében?
  - APS
  - Daganat asszociált thrombosis
  - Splanchnikus vénák thrombosisa
  - Cerebralis vénás thrombosis

A VTE gyakorisága a korral nő – 60 éves kortól drámai növekedés

A fejlett országokban minden 12. ember elszenved az élete folyamán egy VTE eseményt
A VTE-n átesettek kb. 20%-a meghal egy éven belül
Erős provokáló faktor a major sebészeti beavatkozás és az aktív rosszindulatú daganat, de a legtöbb esemény nem provokált!



VTE - Diagnózis

- ASH 2018: **American Society of Hematology 2018 guidelines for management of venous thromboembolism: diagnosis of venous thromboembolism**

- 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS)

PE diagnózisa –ESC GL

- Az akut PE tünetei nem specifikusak (dyspnoe, mellkasi fájdalom, collapsus, haemoptysis, haemodinamikai instabilitás…)
- Gyakrabban jut eszünkbe ez a diagnózis
- Egyre szélesebb körben tudjuk használni a non-invazív diagnosztikus modalitásokat (CTPA könnyen hozzáférhető)

- Gyakrabban indul kivizsgálás PE irányában – a diagnosztika végén kb a betegek 5%-nál igazolódik a diagnózis (1980-as években: 50%!)

- Valamennyi diagnosztikus eszköz használatánál figyelembe kell venni a preteszt probability-t!

Recommendations for diagnosis (1)

Recommendations	Class	Level
Suspected PE with haemodynamic instability		
In suspected high-risk PE, as indicated by the presence of haemodynamic instability, bedside echocardiography or emergency CTPA (depending on availability and clinical circumstances) are recommended for diagnosis.	I	C
It is recommended that i.v. anticoagulation with UFH, including a weight-adjusted bolus injection, be initiated without delay in patients with suspected high-risk PE.	I	C

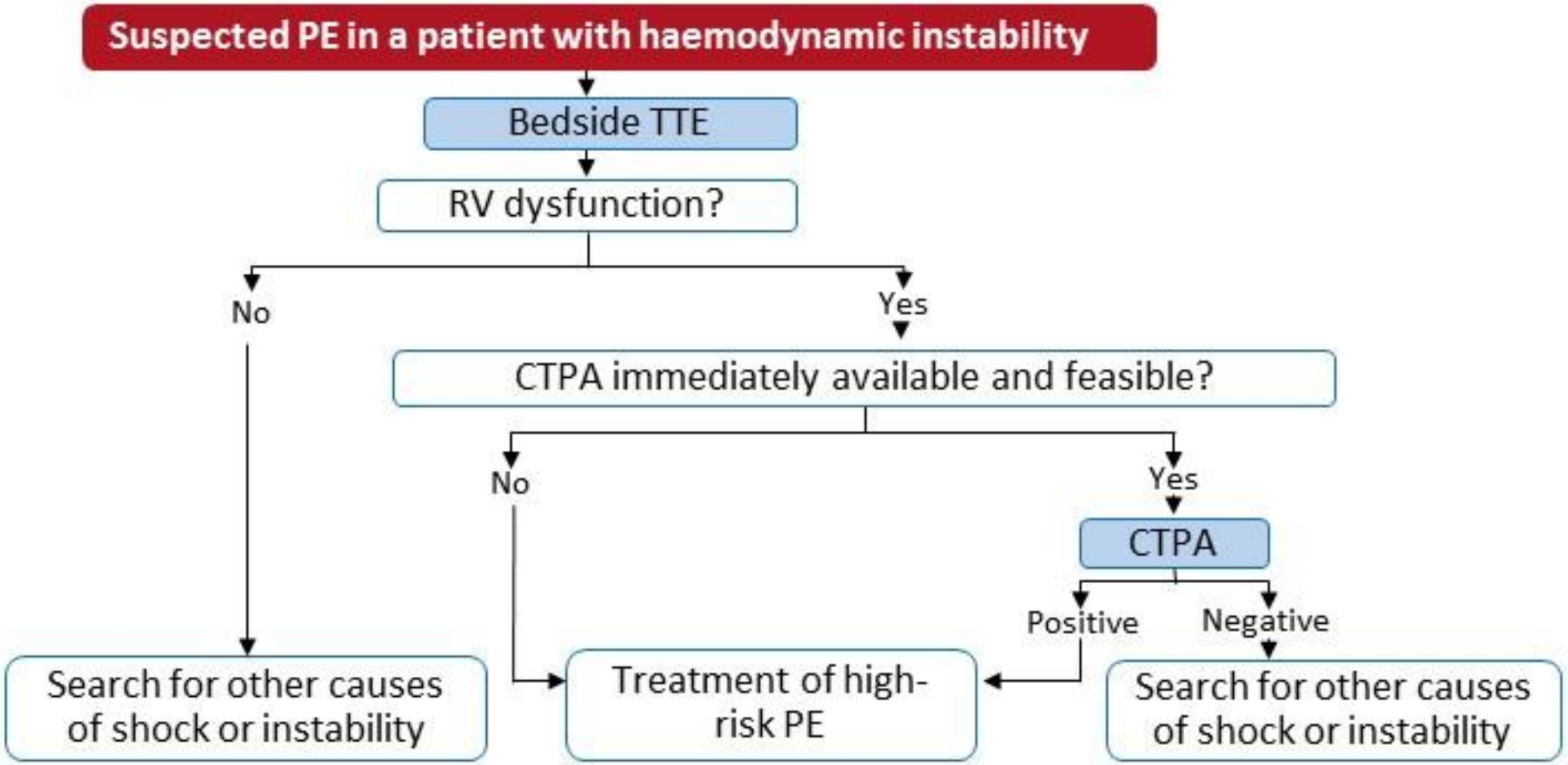
CTPA = computed tomography pulmonary angiography.

Table 4 Definition of haemodynamic instability

(1) Cardiac arrest	(2) Obstructive shock	(3) Persistent hypotension
Need for cardiopulmonary resuscitation	Systolic BP <90 mmHg, or vasopressors required to achieve a BP ≥90 mmHg despite adequate filling status	Systolic BP <90 mmHg, or systolic BP drop ≥40 mmHg, either lasting longer than 15 minutes and not caused by new-onset arrhythmia, hypovolaemia, or sepsis
	And	
	End-organ hypoperfusion (altered mental status; cold, clammy skin; oliguria/anuria; increased serum lactate)	

(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Figure 3 Diagnostic algorithm for suspected high-risk PE



CTPA = computed tomography pulmonary angiography; RV = right ventricular; TTE = transthoracic echocardiography

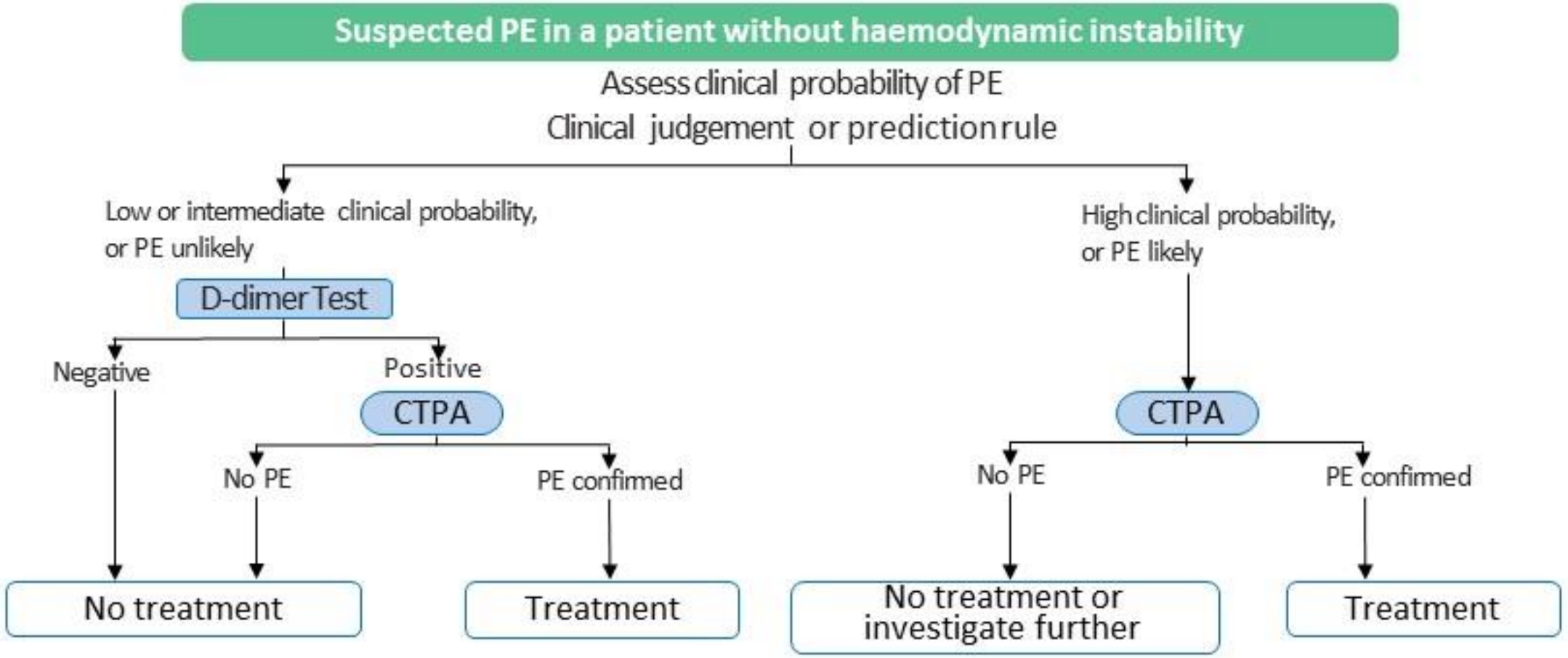
2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations for diagnosis (2)

Recommendations	Class	Level
Suspected PE without haemodynamic instability		
The use of validated criteria for diagnosing PE is recommended.	I	B
Initiation of anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE while diagnostic work-up is in progress.	I	C
Clinical evaluation		
It is recommended that the diagnostic strategy be based on clinical probability, assessed either by clinical judgement or by a validated prediction rule.	I	A

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Figure 4 Diagnostic algorithm for suspected PE without haemodynamic instability



CTPA = computed tomography pulmonary angiography

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Table 5 Revised Geneva clinical prediction rule for PE (1)

Items	Clinical decision rule points	
	Original version	Simplified version
Previous PE or DVT	3	1
Heart rate		
75–94 b.p.m.	3	1
≥95 b.p.m.	5	2
Surgery or fracture within the past month	2	1
Haemoptysis	2	1

DVT = deep vein thrombosis.

Table 5 Revised Geneva clinical prediction rule for PE (2)

	Original version	Simplified version
Active cancer	2	1
Unilateral lower limb pain	3	1
Pain on lower limb deep venous palpation and unilateral oedema	4	1
Age >65 years	1	1

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Table 5 Revised Geneva clinical prediction rule for PE (3)

Clinical probability		
Three-level score		
Low	0–3	0–1
Intermediate	4–10	2–4
High	≥11	≥5
Two-level score		
PE unlikely	0–5	0–2
PE likely	≥6	≥3

Recommendations for diagnosis (3)

Recommendations	Class	Level
D-dimer		
Plasma D-dimer measurement, preferably using a highly sensitive assay, is recommended in outpatients/emergency department patients with low or intermediate clinical probability, or PE-unlikely, to reduce the need for unnecessary imaging and irradiation.	I	A
As an alternative to the fixed D-dimer cut-off, a negative D-dimer test using an age-adjusted cut-off (age x 10 µg/L, in patients >50 years) should be considered for excluding PE in patients with low or intermediate clinical probability, or PE-unlikely.	IIa	B

Recommendations for diagnosis (4)

Recommendations	Class	Level
D-dimer (cont'd)		
As an alternative to the fixed or age-adjusted D-dimer cut-off, D-dimer levels adapted to clinical probability should be considered for excluding PE.	IIa	B
D-dimer measurement is not recommended in patients with high clinical probability, as a normal result does not safely exclude PE, even when using a highly sensitive assay.	III	A
CTPA		
It is recommended to reject the diagnosis of PE (without further testing) if CTPA is normal in a patient with low or intermediate clinical probability, or PE-unlikely.	I	A

CTPA = computed tomography pulmonary angiography.

Recommendations for diagnosis (5)

ESC European Society of Cardiology

Recommendations	Class	Level
CTPA (cont'd)		
It is recommended to accept the diagnosis of PE (without further testing) if CTPA shows a segmental or more proximal filling defect in a patient with intermediate or high clinical probability.	I	B
It should be considered to reject the diagnosis of PE (without further testing) if CTPA is normal in a patient with high clinical probability or PE-likely.	IIa	B
Further imaging tests to confirm PE may be considered in case of isolated subsegmental filling defects.	IIb	C
CT venography is not recommended as an adjunct to CTPA.	III	B

CTPA = computed tomography pulmonary angiography.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations for diagnosis (6)

ESC European Society of Cardiology

Recommendations	Class	Level
V/Q scintigraphy		
It is recommended to reject the diagnosis of PE (without further testing) if the perfusion lung scan is normal.	I	A
It should be considered to accept the diagnosis of PE (without further testing) if the V/Q scan yields high probability for PE.	IIa	B
A non-diagnostic V/Q scan should be considered as exclusion of PE when combined with a negative proximal CUS in patients with low clinical probability, or PE-unlikely.	IIa	B
V/Q SPECT		
V/Q SPECT may be considered for PE diagnosis.	IIb	B

V/Q = ventilation-perfusion; SPECT = single photon emission computed tomography.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations for diagnosis (7)

ESC European Society of Cardiology

Recommendations	Class	Level
Lower-limb compression ultrasonography (CUS)		
It is recommended to accept the diagnosis of VTE (and PE) if a CUS shows a proximal DVT in a patient with clinical suspicion of PE.	I	A
If CUS shows only a distal DVT, further testing should be considered to confirm PE.	IIa	A
If a positive proximal CUS is used to confirm PE, assessment of PE severity should be considered to permit risk-adjusted management.	IIa	C
Magnetic resonance angiography (MRA)		
MRA is not recommended for ruling out PE.	III	A

DVT = deep vein thrombosis; VTE = venous thromboembolism.

Table 6 Imaging tests for diagnosis of PE (1)

	Strengths	Weaknesses/limitations
CTPA	• Readily available around the clock in most centres • Excellent accuracy • Strong validation in prospective management outcome studies • Low rate of inconclusive results (3–5%) • May provide alternative diagnosis if PE excluded • Short acquisition time	• Radiation exposure • Exposure to iodine contrast: – limited use in iodine allergy and hyperthyroidism – risks in pregnant and breast-feeding women – contraindicated in severe renal failure • Tendency to overuse because of easy accessibility • Clinical relevance of CTPA diagnosis of subsegmental PE unknown

CTPA = computed tomography pulmonary angiography.

Table 6 Imaging tests for diagnosis of PE (2)

V/Q = ventilation-perfusion; SPECT = single photon emission computed tomography.

	Strengths	Weaknesses/limitations
Planar V/Q scan	• Almost no contraindications • Relatively inexpensive • Strong validation in prospective management outcome studies	• Not readily available in all centres • Interobserver variability in interpretation • Results reported as likelihood ratios • Inconclusive in 50% of cases • Cannot provide alternative diagnosis
V/Q SPECT	• Almost no contraindications • Lowest rate of non-diagnostic tests (<3%) • High accuracy according to available data • Binary interpretation ("PE" vs "no PE")	• Variability of techniques • Variability of diagnostic criteria • Cannot provide alternative diagnosis • No validation in prospective management outcome studies
Pulmonary angiography	• Historical gold standard	• Invasive procedure • Not readily available in all centres

(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Table 6 Imaging tests for diagnosis of PE (3)

	Radiation issues
CTPA	• Radiation effective dose 3–10 mSv • Significant radiation exposure to young female breast tissue
Planar V/Q scan	• Lower radiation than CTPA, effective dose approximately 2 mSv
V/Q SPECT	• Lower radiation than CTPA, effective dose approximately 2 mSv
Pulmonary angiography	• Highest radiation, effective dose 10–20 mSv

CTPA = computed tomography pulmonary angiography; V/Q = ventilation-perfusion; SPECT = single photon emission computed tomography.

ASH 2018 – PE dg

- Alacsony PTP (prevelancia ≤ 5%):
  - **D-dimer** teszt használata ***javasolt*** a PE ***kizárására***. (high sensitivity test)
  - Pozitív DD: V/Q scan vagy CTPA (előbbi preferált)
  - Pulmonary Embolism Rule-out Criteria (PERC) – ha neg., még DD sem kell!
  - Genfi kritériumok: csak ambuláns betegeken validált, osztályos betegeken nem; utóbbi esetében a DD teszt használata is limitált – gyakori a pozitív eredmény
- Közepes PTP (prevelancia ca 20%) ld mint fent
- Magas PTP (prevelancia ≥50%)
  - Egyből CTPA, ha az kontraindikált vagy nem diagnosztikus (vagy pl negatv, de még mindig azt gondoljuk, hogy a betegnek PE-je van), VQ scan vagy prox. CUS
- Rekurrens PE – itt is érdemes a betegeket unlikely – likely kategóriákba osztani és a fentiek szerint eljárni

ASH 2018 – MVT dg

Alsó végtag - Wells score for DVT

- Alacsony PTP/prevelancia ≤10%
  - Negatív DD: kizárja a MVT
  - Pozitív DD: kompressziós UH
- Közepes PTP /prevelancia ca 25%
  - Egyből proximalis vagy teljes végtag UH
- Magas PTP/prevelancia ≥50%)
  - Egyből proximalis és/vagy teljes végtag UH
  - Negatív esetben, ha nem igazolódik alternatv diagnózis, ismételni kell a vizsgálatot (serial testing)

Felső végtag: dichotomizált Constans score (where score ≤1 is unlikely and ≥2 is likely)

The Constans Clinical Decision Score:

Select Criteria:

Patient Characteristics	Score
Venous Material Present [Central venous catheter or Pacemaker thread]	
Yes ○	1 Point
No ○	0 Point
Localised Pain	
Yes ○	1 Point
No ○	0 Points
Unilateral Oedema	
Yes ○	1 Point
No ○	0 Points
Other Diagnosis at least as plausible	
Yes ○	-1 Points
No ○	0 Points

Interpretation

Score	UEDVT Probability[1]
-1 or 0 Points	**Low** 12% probability of UEDVT
1 Point	**Intermediate** 20% probability of UEDVT
2 - 3 Points	**High** 70% probability of UEDVT

Diagnózis -MVT

- Mélyvénás (mélyvéna-) thrombosis vs felületes thrombosis…
  - Felületes thr. mellett 6-44%-ban kimutatható VTE; a MVT akár a másik oldali végtagon is jelentkezhet; PE akár 30%-ban!

Terápiás ajánlás: 45 napig 1x2,5 mg fondaparinux vagy 10 mg rivaroxaban vagy LMWH

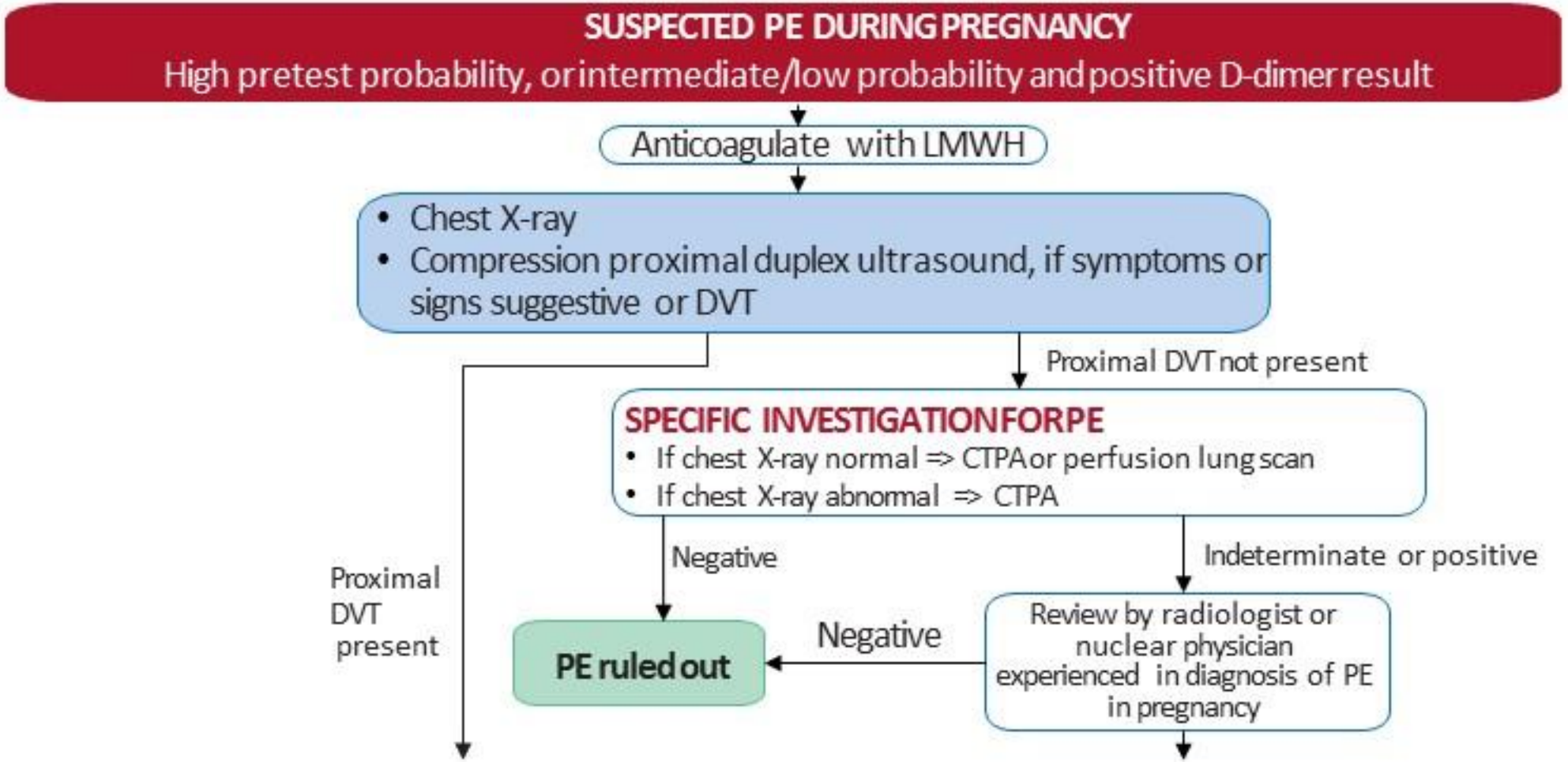
- Distalis vs proximalis thrombosis ….
  - V. poplitea-tól felfelé proximalis!
  - Lábszár izomvénái – distalis

Distalis: lehet sorozat UH-t is választani antikoagulálás helyett

VTE dg várandósság alatt

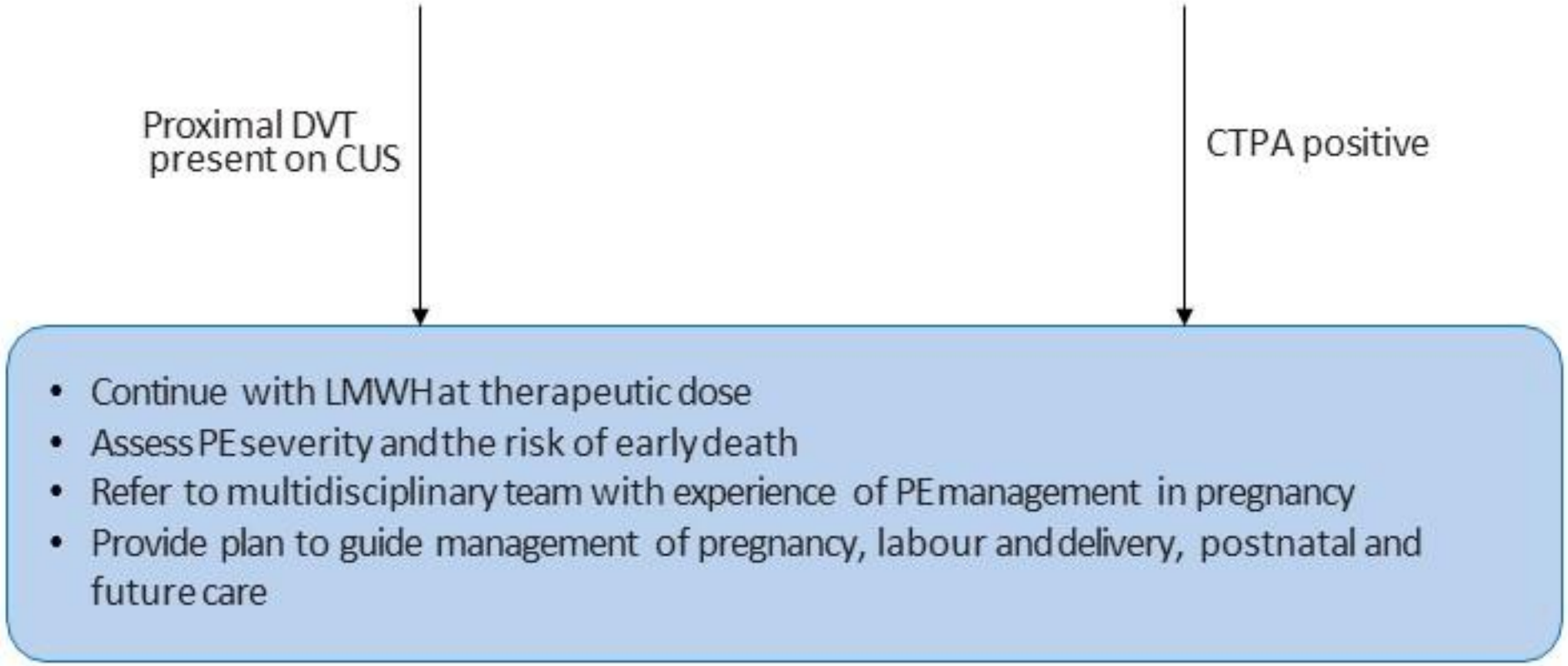
- DD jellemzően nő a várandósság alatt
- Szeretnénk elkerülni a rtg sugárzást
- De itt is fontos a pontos diagnózis

Figure 6 Diagnostic work-up for suspected PE during pregnancy and up to 6 weeks postpartum (1)



2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Figure 6 Diagnostic work-up for suspected PE during pregnancy and up to 6 weeks postpartum (2)



CTPA = computed tomography pulmonary angiography; CUS = compression venous ultrasound; DVT = deep vein thrombosis; LMWH = low molecular weight heparin.

(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations for pulmonary embolism in pregnancy (1)

ESC European Society of Cardiology

Recommendations	Class	Level
Diagnosis		
Formal diagnostic assessment with validated methods is recommended if PE is suspected during pregnancy or in the postpartum period.	I	B
D-dimer measurement and clinical prediction rules should be considered to rule out PE during pregnancy or the postpartum period.	IIa	B
In a pregnant patient with suspected PE (particularly if she has symptoms of DVT), venous CUS should be considered to avoid unnecessary irradiation.	IIa	B

CUS = compression venous ultrasound; DVT = deep vein thrombosis.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations for pulmonary embolism in pregnancy (2)

Recommendations	Class	Level
Perfusion scintigraphy or CTPA (with a low-radiation dose protocol) should be considered to rule out suspected PE in pregnant women; CTPA should be considered as the first- line option if the chest X-ray is abnormal.	IIa	C
Treatment		
Therapeutic, fixed dose of LMWH based on early pregnancy body weight is the recommended therapy for PE in the majority of pregnant women without haemodynamic instability.	I	B
Thrombolysis or surgical embolectomy should be considered for pregnant women with high-risk PE.	IIa	C

CTPA = computed tomography pulmonary angiography; LMWH = low molecular weight heparin.

Recommendations for pulmonary embolism in pregnancy (3)

ESC European Society of Cardiology

Recommendations	Class	Level
It is not recommended to insert a spinal or epidural needle unless at least 24 hours have passed since the last therapeutic dose of LMWH.	III	C
It is not recommended to administer LMWH within 4 hours of removal of an epidural catheter.	III	C
NOACs are not recommended during pregnancy or lactation.	III	C
Amniotic fluid embolism		
Amniotic fluid embolism should be considered in a pregnant or postpartum woman with otherwise unexplained cardiac arrest, sustained hypotension, or respiratory deterioration, especially if accompanied by disseminated intravascular coagulation.	IIa	C

LMWH = low molecular weight heparin; NOAC(s) = non-vitamin K antagonist oral anticoagulant(s).

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Table 9 Classification of PE based on early mortality risk

ESC European Society of Cardiology

Early mortality risk		Indicators of risk			
		Haemo-dynamic instability	Clinical parameters of PE severity/ comorbidity: PESI III–V or sPESI ≥1	RV dysfunction on TTE or CTPA	Elevated cardiac troponin levels
High		+	(+)	+	(+)
Interme-diate	**Intermediate–high**	-	+	+	+
	Intermediate–low	-	+	One (or none) positive	
Low		-	-	-	Assessment optional; if assessed, negative

CTPA = computed tomography pulmonary angiography; PESI = Pulmonary Embolism Severity Index; TTE = transthoracic echocardiography.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Table 8 Original and simplified PESI (1)

Parameter	Original version	Simplified version
Age	Age in years	1point (if age >80 years)
Male sex	+10 points	–
Cancer	+30 points	1point
Chronic heart failure	+10 points	1point
Chronic pulmonary disease	+10 points	
Pulse rate ≥110b.p.m.	+20 points	1point
Systolic BP <100mmHg	+30 points	1point

BP = blood pressure; PESI = Pulmonary Embolism Severity Index.

(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Table 8 Original and simplified PESI (2)

Parameter	Original version	Simplified version
Respiratory rate >30 breaths per min	+20 points	–
Temperature <36 °C	+20 points	–
Altered mental status	+60 points	–
Arterial oxyhaemoglobin saturation <90%	+20 points	1point

PESI = Pulmonary Embolism Severity Index.

Table 8 Original and simplified PESI (3)

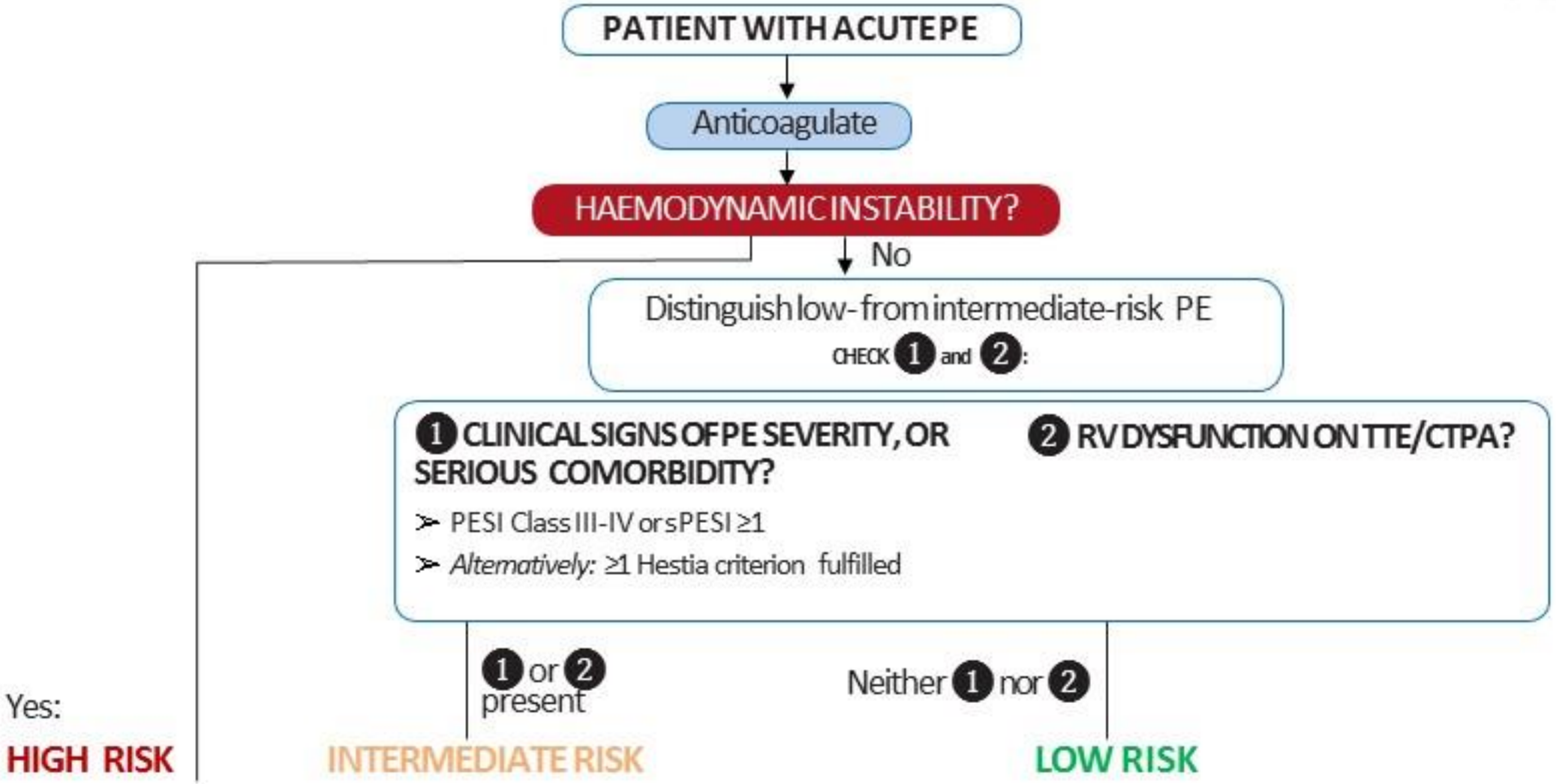
	Risk strata	
	Class I: ≤65 points very low 30-day mortality risk (0–1.6%) **Class II: 66–85 points** low mortality risk (1.7–3.5%)	**0 points** = 30-day mortality risk 1.0% (95% CI 0.0–2.1%)
	Class III: 86–105 points moderate mortality risk (3.2–7.1%) **Class IV: 106–125 points** high mortality risk (4.0–11.4%) **Class V: >125 points** very high mortality risk (10.0–24.5%)	**≥1 point(s)** = 30-day mortality risk 10.9% (95% CI 8.5–13.2%)

PESI = Pulmonary Embolism Severity Index.

(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Figure 5 Risk-adjusted management strategy for acute PE (1)

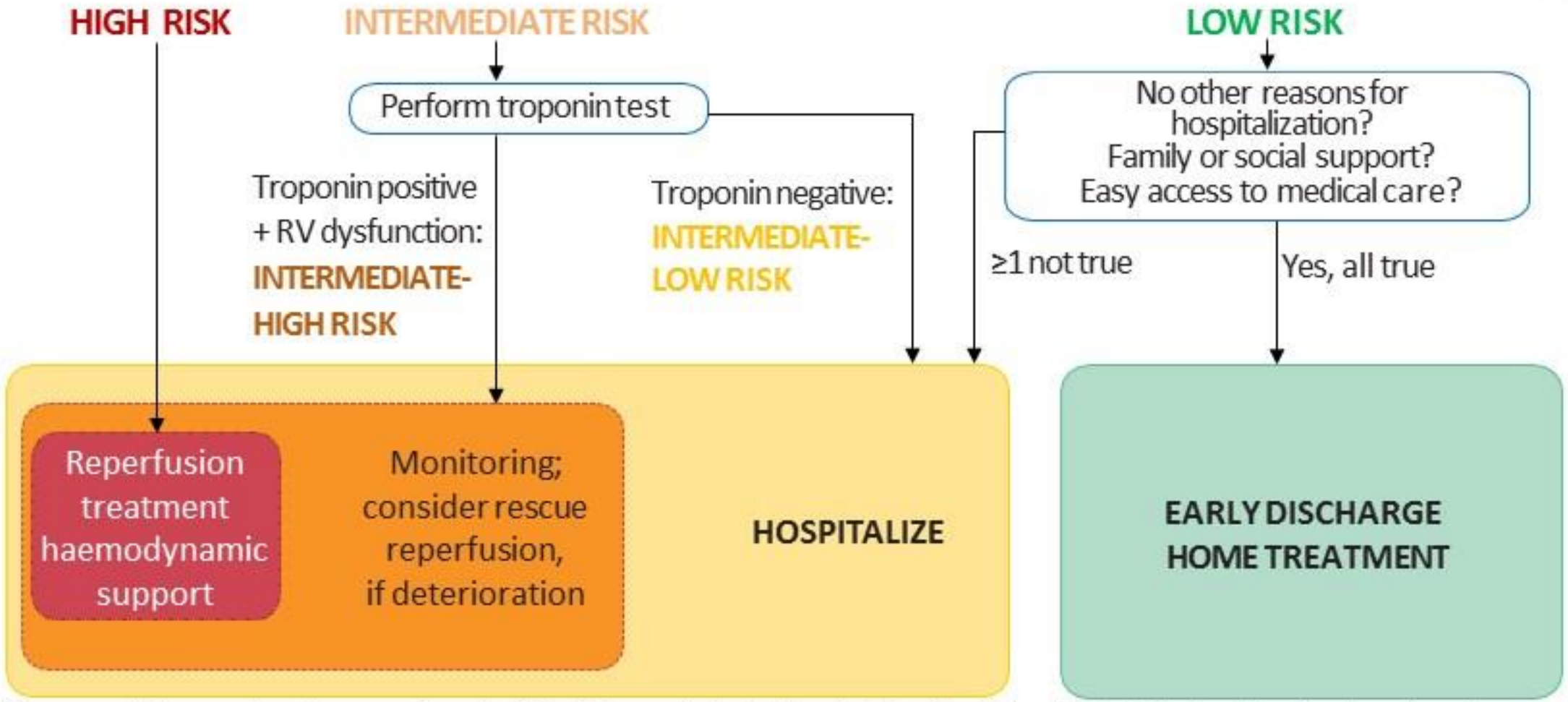
ESC European Society of Cardiology



2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Figure 5 Risk-adjusted management strategy for acute PE (2)

ESC European Society of Cardiology



CTPA = computed tomography pulmonary angiography; PESI = Pulmonary Embolism Severity Index; RV = right ventricular; TTE = transthoracic echocardiography.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations for acute-phase treatment of high-risk PE[a] (1)

Recommendations	Class	Level
It is recommended that anticoagulation with UFH, including a weight-adjusted bolus injection, be initiated without delay in patients with high-risk PE.[a]	I	C
Systemic thrombolytic therapy is recommended for high- risk PE.	I	B
Surgical pulmonary embolectomy is recommended for patients with high-risk PE, in whom thrombolysis is contraindicated or has failed.	I	C

[a] After haemodynamic stabilization of the patient, continue anticoagulation as in intermediate- or low-risk PE.
UFH = unfractionated heparin.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations for acute-phase treatment of high-risk PE (2)

ESC European Society of Cardiology

Recommendations	Class	Level
Percutaneous catheter-directed treatment should be considered for patients with high-risk PE, in whom thrombolysis is contraindicated or has failed.	IIa	C
Norepinephrine and/or dobutamine should be considered in patients with high-risk PE.	IIa	C
ECMO may be considered, in combination with surgical embolectomy or catheter-directed treatment, in patients with PE and refractory circulatory collapse or cardiac arrest.	IIb	C

ECMO = extracorporeal membrane oxygenation.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations for acute-phase treatment of intermediate- or low- risk PE (1)

ESC European Society of Cardiology

Recommendations	Class	Level
Initiation of anticoagulation		
Initiation of anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE, while diagnostic work-up is in progress.	I	C
If anticoagulation is initiated parenterally, LMWH or fondaparinux is recommended (over UFH) for most patients.	I	A
Oral anticoagulants		
When oral anticoagulation is started in a patient with PE who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is recommended in preference to a VKA.	I	A

NOAC = non-vitamin K antagonist oral anticoagulant; LMWH = low molecular weight heparin; VKA = vitamin K antagonist; UFH = unfractionated heparin.

Recommendations for acute-phase treatment of intermediate- or low- risk PE (1)

ESC European Society of Cardiology

Recommendations	Class	Level
Initiation of anticoagulation		
Initiation of anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE, while diagnostic work-up is in progress.	I	C
If anticoagulation is initiated parenterally, LMWH or fondaparinux is recommended (over UFH) for most patients.	I	A
Oral anticoagulants		
When oral anticoagulation is started in a patient with PE who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is recommended in preference to a VKA.	I	A

NOAC = non-vitamin K antagonist oral anticoagulant; LMWH = low molecular weight heparin; VKA = vitamin K antagonist; UFH = unfractionated heparin.

Recommendations for acute-phase treatment of intermediate- or low- risk PE (2)

ESC European Society of Cardiology

Recommendations	Class	Level
Oral anticoagulants		
When patients are treated with a VKA, overlapping with parenteral anticoagulation is recommended until an INR of 2.5 (range 2.0–3.0) is reached.	I	A
NOACs are not recommended in patients with severe renal impairment, during pregnancy and lactation, and in patients with the antiphospholipid antibody syndrome.	III	C

INR = International Normalized Ratio; NOAC(s) = non-vitamin K antagonist oral anticoagulant(s); VKA = vitamin K antagonist.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations for acute-phase treatment of intermediate- or low- risk PE (3)

ESC European Society of Cardiology

Recommendations	Class	Level
Reperfusion treatment		
Rescue thrombolytic therapy is recommended for patients with haemodynamic deterioration on anticoagulation treatment.	I	B
As an alternative to rescue thrombolytic therapy, surgical embolectomy or percutaneous catheter- directed treatment should be considered for patients with haemodynamic deterioration on anticoagulation treatment.	IIa	C
Routine use of primary systemic thrombolysis is not recommended in patients with intermediate- or low-risk PE.	III	B

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations for multidisciplinary PE teams

Recommendations	Class	Level
Set-up of a multidisciplinary team and programme for management of high-risk and (in selected cases) intermediate-risk PE should be considered, depending on the resources and expertise available in each hospital.	IIa	C

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

USZ Universitäts Spital Zürich

Recent advances in VTE treatment

Prof. Stefano Barco, MD
Deputy Director, Department of Angiology, University Hospital Zurich

stefano.barco@usz.ch

22nd Sep 2024 – Zagreb

Pulmonary Embolism Response Team

- Establish a PERT with key specialisms
- Clear flowcharts for more severe PE
- One lead, one telephone number → the lead activates PERT
- Meeting at patient bed or virtually

In Zurich

Intermediate-high risk patients	small PERT (angiology, ICU, ER)	→ **local lysis**
High-risk patients	large PERT (5 specialisms) ECMO-team	→ **catheter-embolectomy**

Recommendations for early discharge, home treatment

Recommendations	Class	Level
Carefully selected patients with low-risk PE should be considered for early discharge and continuation of treatment at home, if proper outpatient care and anticoagulant treatment can be provided.	IIa	A

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Table 13 Hestia exclusion criteria for outpatient management of PE (1)

ESC European Society of Cardiology

Criterion/question
Is the patient haemodynamically unstable?
Is thrombolysis or embolectomy necessary?
Active bleeding or high risk of bleeding?
More than 24 h of oxygen supply to maintain oxygen saturation >90%?
Is PE diagnosed during anticoagulant treatment?
Severe pain needing i.v. pain medication for more than 24 h?

If at least one of the questions is answered with „yes", the patient cannot be discharged early.

(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Table 13 Hestia exclusion criteria for outpatient management of PE (2)

Medical or social reason for treatment in the hospital for more than 24 h (infection, malignancy, no support system)?
Does the patient have a CrCl of <30 mL/min?
Does the patient have severe liver impairment?
Is the patient pregnant?
Does the patient have a documented history of heparin-induced thrombocytopenia?

If at least one of the questions is answered with „yes", the patient cannot be discharged early.
CrCl = creatinine clearance.

Antikoaguláns kezelés

- VTE esetén minden betegnél min. 3 hónapig tartó antikoaguláns kezelés szükséges.

MVT kezelése

- **ANTIKOAGULÁLÁS -** a thrombosis progresszióját akadályozza meg – nem oldja fel (az endogen fibrinolytikus rendszer dolgozik)
- Immobilizáció: NE! - csak fájdalomcsillapítás céljából → ambuláns kezelés lehetséges
- Kompresszió: nem kötelező, nem igazolódott, hogy alkalmas a PTS megelőzésére

MVT kezelése

- **ANTIKOAGULÁLÁS**
- Immobilizáció: csak fájdalomcsillapítás céljából → ambuláns kezelés lehetséges
- Kompresszió a tüntek csökkentésére

- Rekanalisatio: ritkán, proximalis thrombosis esetén, a beteg legyen bevonva a döntésbe (grade 2b); phlegmasia cerulea dolens: végtagmegtartási céllal (thrombectomia vagy katéteres thrombolysis, systemás thrombolysis már nem javasolt a magas vérzéses rizikó miatt)

Mi a legkritikusabb faktor a VTE (hosszútávú…) kezelésében?

- El kell különíteni egymástól a provokált és a nem provokált eseményt!

- gyakori reverzibilis/tranziens erős rizikófaktorok:
  - nagy műtét
  - Trauma
  - Immobilizáció
  - akut belgyógyászati betegség miatti hospitalizáció

Baglin T, Luddington R, Brown K, Baglin C. Incidence of recurrent venous thromboembolism in relation to clinical and thrombophilic risk factors: prospective cohort study. Lancet. 2003 Aug 16;362(9383):523-6. doi: 10.1016/S0140-6736(03)14111-6. PMID: 12932383.

Az antikoaguláns kezelés hossza provokált VTE esetén: 3 hónap

- Meghatározható, tranziens vagy reverzibilis rizikófaktor által provokált VTE esetén a rekurrens VTE aránya alacsony (sebészi és nem sebészi egyaránt)
- Ez független a thrombophilia státusztól!
- Még súlyos thrombophilia esetén sem szükséges élethosszig tartó antikoaguláns kezelés!

- Fontos a provokáló tényezők kikérdezése, dokumentációban rögzítése. (gyakori reverzibilis/tranziens erős rizikófaktorok: nagy műtét, trauma, immobilizáció, akut belgyógyászati betegség miatti hospitalizáció)

Baglin T et al: Incidence of recurrent venous thromboembolism in relation to clinical and thrombophilic risk factors: prospective cohort study. Lancet. 2003 Aug 16;362(9383):523-6. doi: 10.1016/S0140-6736(03)14111-6. PMID: 12932383.
Iorio A et al: Risk of recurrence after a first episode of symptomatic venous thromboembolism provoked by a transient risk factor: a systematic review. Arch Intern Med. 2010 Oct 25;170(19):1710-6. doi: 10.1001/archinternmed.2010.367. PMID: 20975016.
Willem M. Lijfering, MD, PhD. et al: Risk of Recurrent Venous Thrombosis in Homozygous Carriers and Double Heterozygous Carriers of Factor V Leiden and Prothrombin G20210A Circulation Volume 121, Number 15 https://doi.org/10.1161/CIRCULATIONAHA.109.906347

Az antikoaguláns kezelés hossza nem provokált VTE esetén, vagy nem tranziens rizikófaktorok esetén

- **Ezekben az esetekben a 2021-es ACCP guideline javasolja a tartós antikoagulálás („extended phase anticoagulation”) FELAJÁNLÁSÁT – DOAC, vagy aki nem kaphat DOAC-t valamilyen okból, akkor VKA.**
- A VTE recidiva és vérzéses rizikó gondos egyéni mérlegelését javasolják
- Figyelembe kell venni a beteg preferenciáit
- Legalább évente felül kell vizsgálni a döntést!
- Ez is független a thrombophilia státusztól!
- Ha folytatják az antikoagulálást, akkor ajánlott az alacsonyabb dózisú kezelés (pl. 2x2,5 mg apixaban vagy 1x10 mg rivaroxaban)
- Nincs előre meghatározott vége a kezelésnek

Hogyan tudjuk kiválasztani azokat a betegeket, akik jobban járnak a kiterjesztett antikoagulálással?

- De Winter et al, JTH 2023. : Redefining clinical venous thromboembolism phenotypes: a novel approach using latent class analysis
- Data for 3062 patients in the PREFER in VTE registry and for 6593 patients in the Hokusai-VTE trial were analyzed

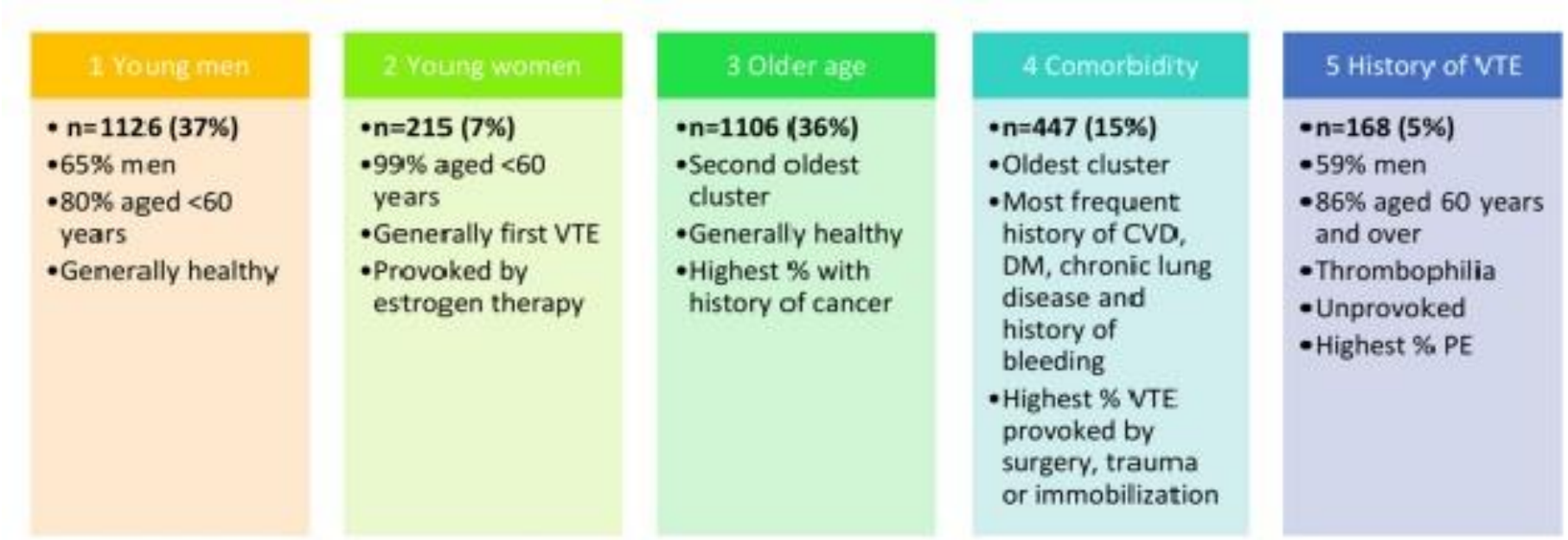
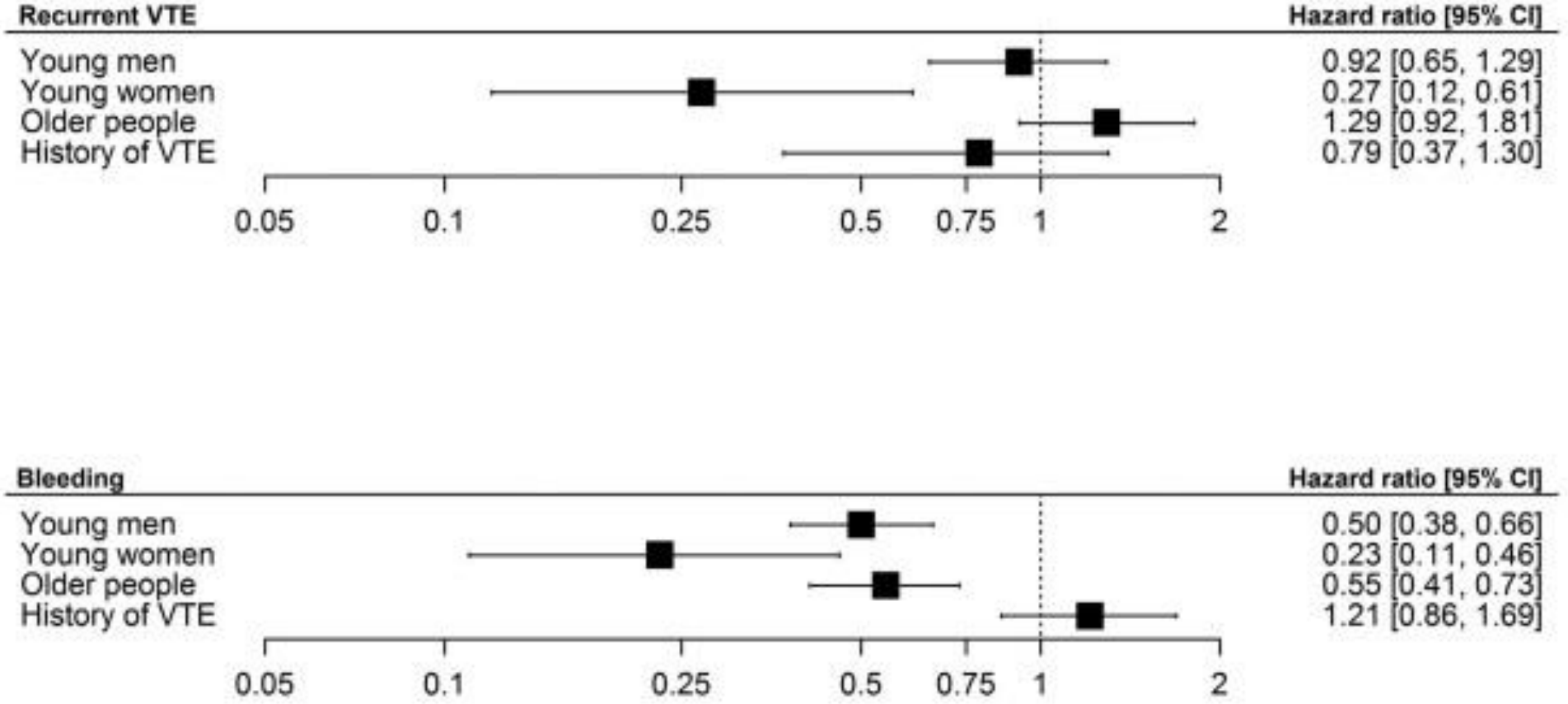


FIGURE 1 Novel clusters among patients with venous thromboembolism (VTE). CVD, cardiovascular disease; DM, diabetes mellitus; PE, pulmonary embolism.

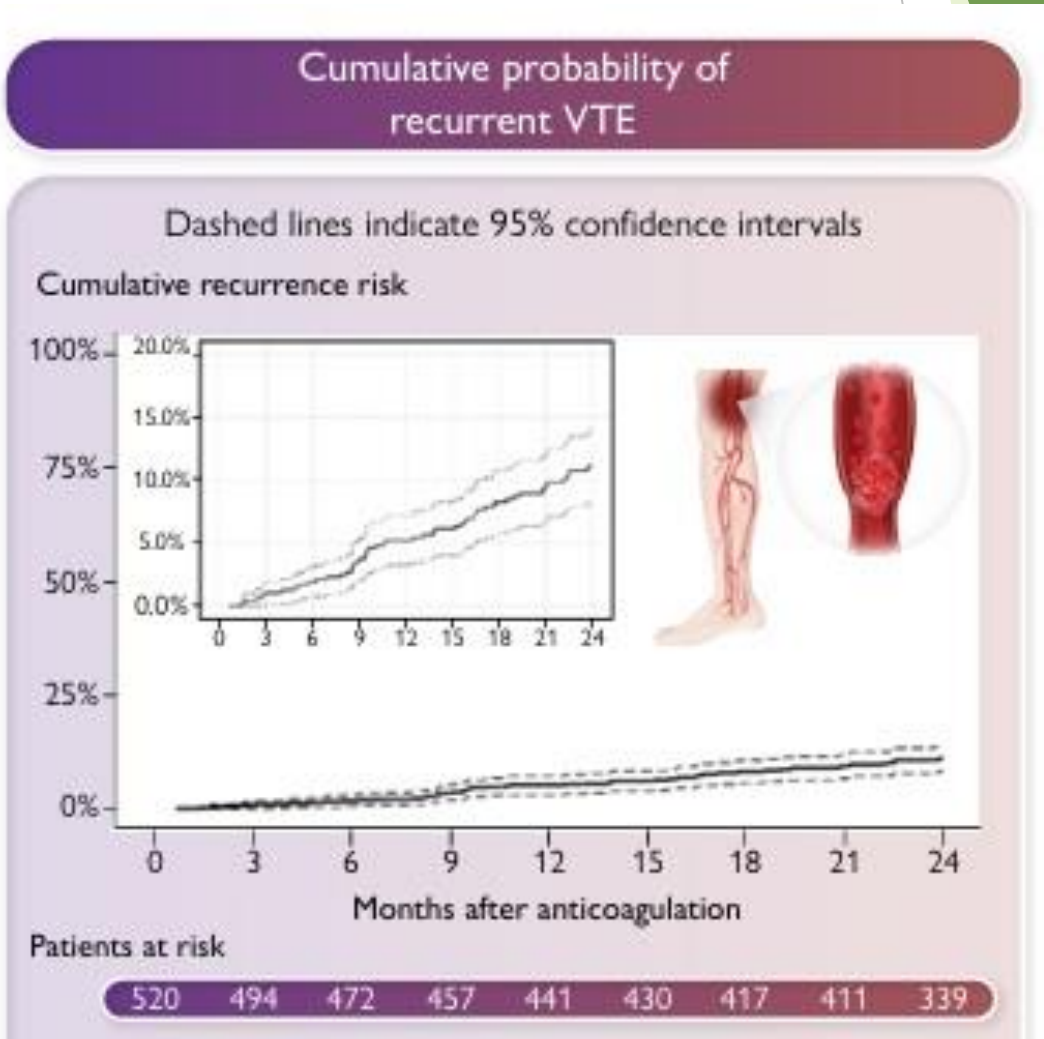
Hogyan tudjuk kiválasztani azokat a betegeket, akik jobban járnak a kiterjesztett antikoagulálással?



Hogyan tudjuk kiválasztani azokat a betegeket, akik jobban járnak a kiterjesztett antikoagulálással?

Paul A. Kyrle et al.: Eur Heart J 2024. The Vienna Prediction Model for identifying patients at low risk of recurrent venous thromboembolism: a prospective cohort study

1. Sex
2. Thrombosis site (e.g., proximal deep-vein thrombosis, distal deep-vein thrombosis, pulmonary embolism)
3. D-dimer levels



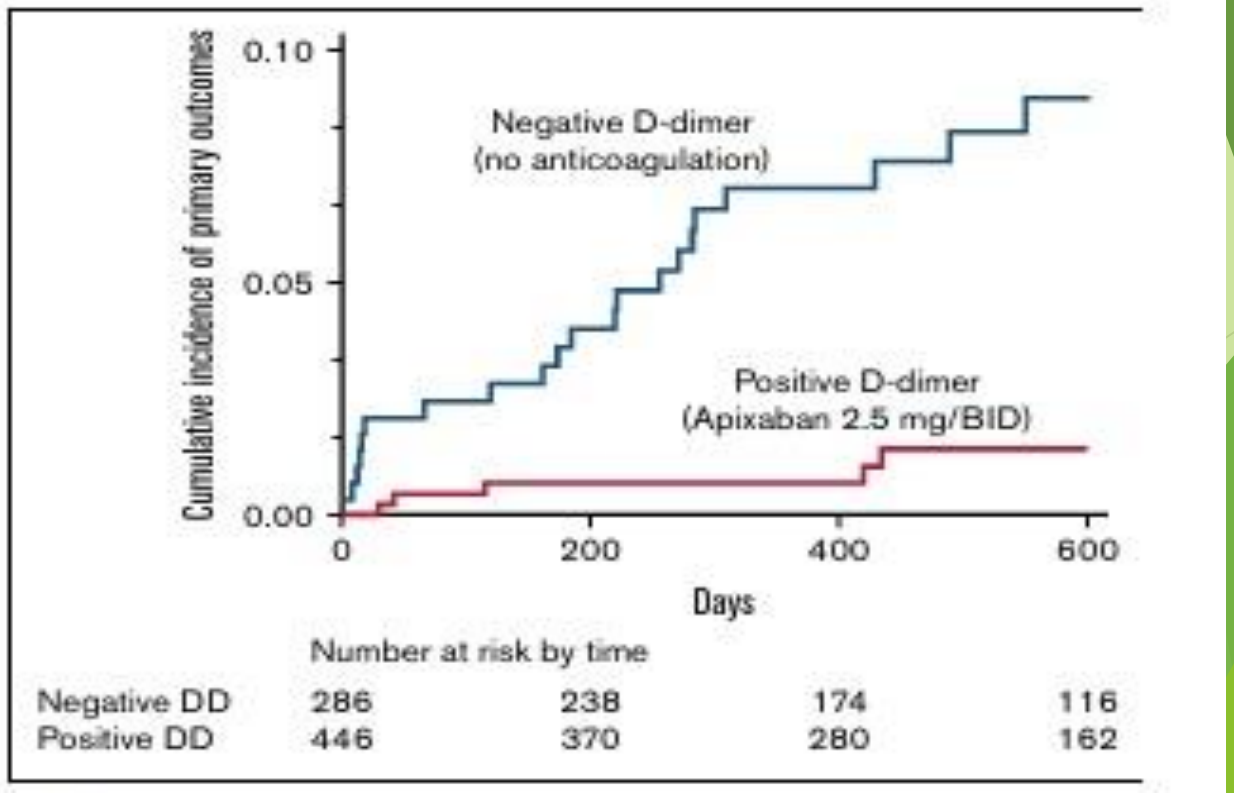
Hogyan tudjuk kiválasztani azokat a betegeket, akik jobban járnak a kiterjesztett antikoagulálással?

Palareti et al.: Blood Adv. 2022. D-dimer and reduced-dose apixaban for extended treatment after unprovoked venous thromboembolism: the Apidulcis study (DD: T0, T15, T30, T60)

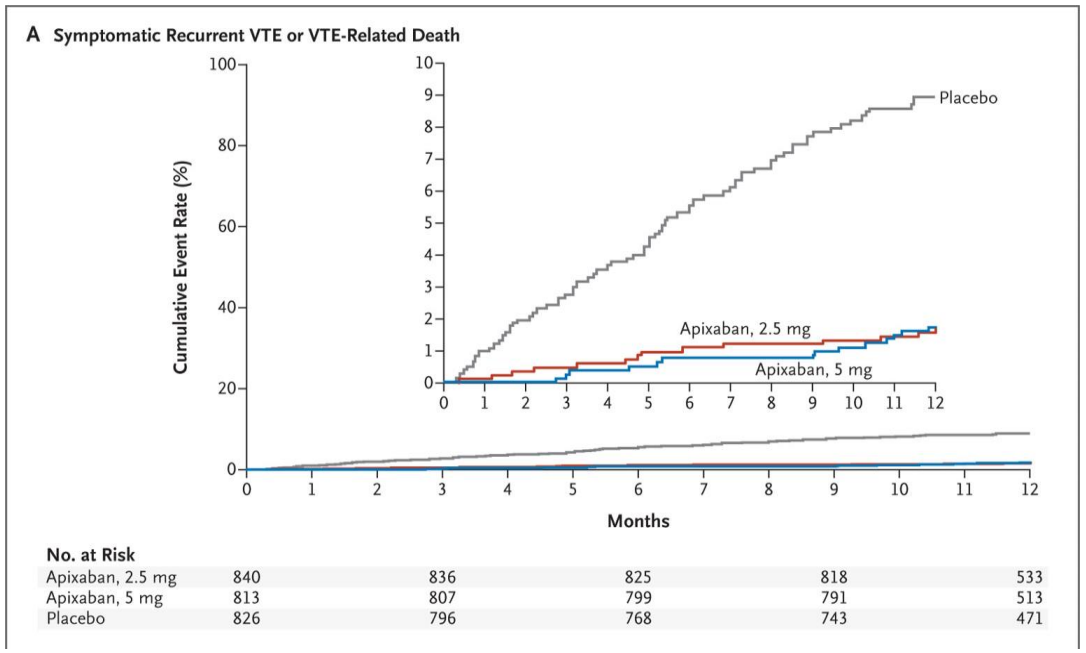
Key Points

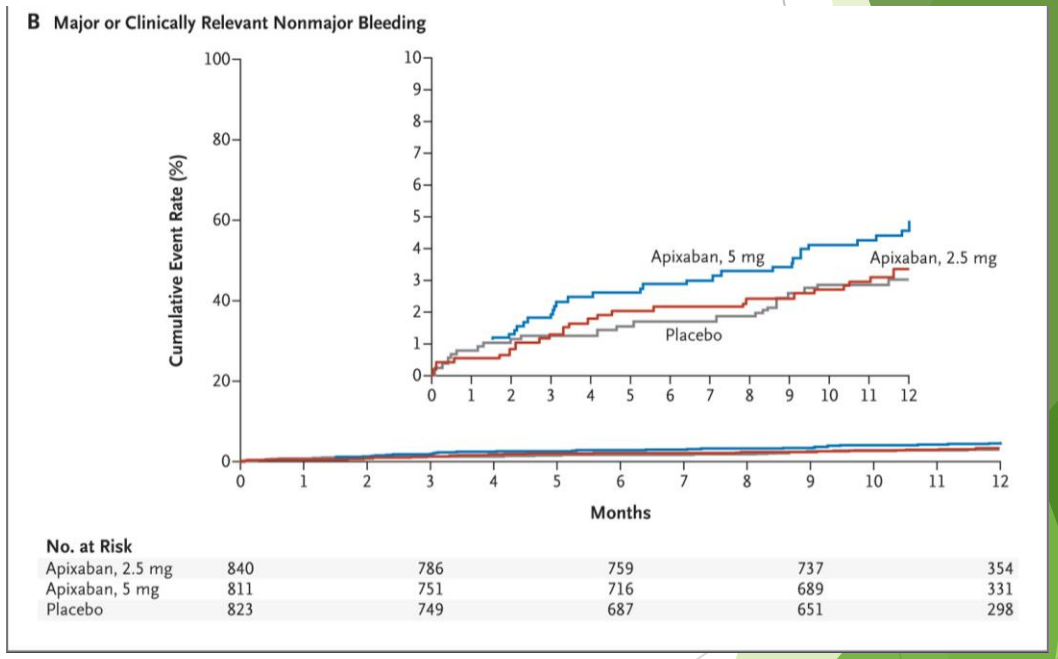
D-dimer testing may help to decide on extended treatment after VTE; this was never assessed since DOACs are available.

Exceedingly more outcomes in patients off anticoagulation for negative D-dimer than in those receiving apixaban for positive testing.



Kiterjesztett antikoagulálás csökkentett dózisú DOAC-kal





Agnelli 2013. NEJM

Table 14 Risk factors for long-term VTE recurrence (1)

ESC European Society of Cardiology

Estimated risk for long-term recurrence	Risk factor category for index PE	Examples
Low (<3% per year)	Major transient or reversible factors associated with >10-fold increased risk for the index VTE event (compared to patients without the risk factor)	•Surgery with general anaesthesia for >30 min •Confined to bed in hospital (only "bathroom privileges") for ≥3 days due to an acute illness, or acute exacerbation of a chronic illness •Trauma with fractures

VTE = venous thromboembolism.

(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Table 14 Risk factors for long-term VTE recurrence (2)

Estimated risk for long-term recurrence	Risk factor category for index PE	Examples
Intermediate (3–8% per year)	Transient or reversible factors associated with ≤10-fold increased risk for first (index) VTE	•Minor surgery (general anaesthesia for <30 min) •Admission to hospital for <3 days with an acute illness •Oestrogen therapy/contraception •Pregnancy or puerperium •Confined to bed out of hospital for ≥3 days with an acute illness

VTE = venous thromboembolism.

Table 14 Risk factors for long-term VTE recurrence (3)

Estimated risk for long-term recurrence	Risk factor category for index PE	Examples
	Non-malignant persistent risk factors	• Leg injury (without fracture) associated with reduced mobility for ≥3 days • Long-haul flight • Inflammatory bowel disease • Active autoimmune disease
	No identifiable risk factor	

VTE = venous thromboembolism.

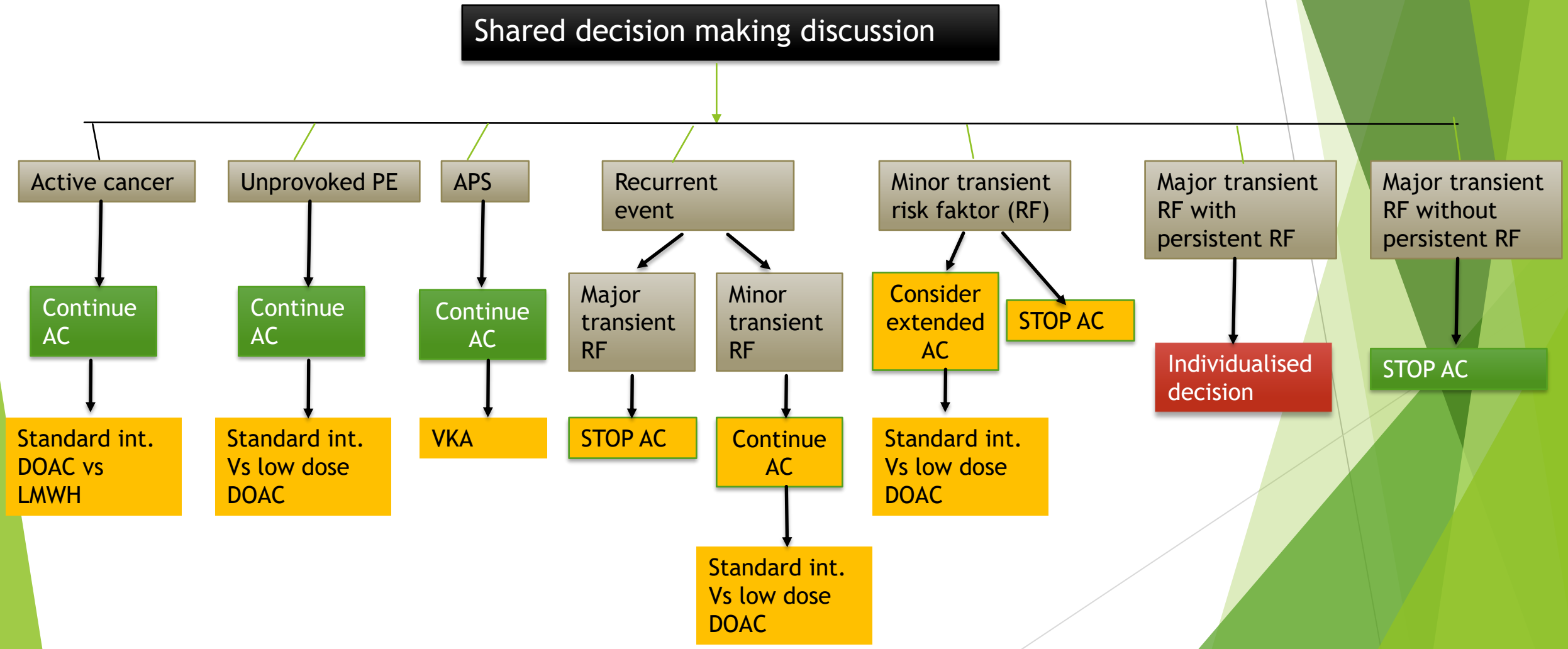
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Table 14 Risk factors for long-term VTE recurrence (4)

Estimated risk for long-term recurrence	Risk factor category for index PE	Examples
High (>8% per year)		•Active cancer •One or more previous episodes of VTE in the absence of a major transient or reversible factor •Antiphospholipid antibody syndrome

VTE = venous thromboembolism.

PE – Harmonisation of guidelines (Zuin et al: International Clinical Practice Guideline Recommendations for Acute Pulmonary Embolism: Harmony, Dissonance, and Silence JACC. 2024 Oct)



Antikoagulálás: melyik gyógyszert válasszuk?

- Jelen ACCP ajánlás szerint DOAC a preferált szer a kezdeti és tartós antikoagulálásra, kivéve, ha a betegnek antiphospholipid szindrómája van (ekkor VKA tartósan).
- Aktív malignitás esetén az oralis FXa gátlók preferáltak az LMWH-val szemben

- Amennyiben az a döntés születik, hogy abbahagyja a beteg az antikoagulálást (pedig indokolt lenne…), aspirin szedését ajánlják, mert…
  - Lehet, hogy elhagytuk az egyébként indokolt aspirint, amikor elkezdtük az antikoagulálást
  - Kis mértékben hozzájárul a recidiva megelőzéséhez

Recommendations for the regimen and duration of anticoagulation after PE in patients *without* cancer (1)

ESC European Society of Cardiology

Recommendations	Class	Level
Therapeutic anticoagulation for at least 3 months is recommended for all patients with PE.	I	A
Patients in whom discontinuation of anticoagulation after 3 months is recommended		
For patients with first PE/VTE secondary to a major transient/reversible risk factor, discontinuation of therapeutic oral anticoagulation is recommended after 3 months.	I	B

VTE = venous thromboembolism.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations for the regimen and duration of anticoagulation after PE in patients *without* cancer (2)

ESC European Society of Cardiology

Recommendations	Class	Level
Patients in whom extension of anticoagulation beyond 3 months is recommended		
Oral anticoagulant treatment of indefinite duration is recommended for patients presenting with recurrent VTE (that is, with at least one previous episode of PE or DVT) not related to a major transient or reversible risk factor.	I	B
Oral anticoagulant treatment with a VKA for an indefinite period is recommended for patients with the antiphospholipid antibody syndrome.	I	B

DVT = deep vein thrombosis; VKA = vitamin K antagonist.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations for the regimen and duration of anticoagulation after PE in patients *without* cancer (3)

ESC European Society of Cardiology

Recommendations	Class	Level
Patients in whom extension of anticoagulation beyond 3 months should be considered		
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE and no identifiable risk factor.	IIa	A
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE associated with a persistent risk factor other than the antiphospholipid antibody syndrome.	IIa	C
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE associated with a minor transient or reversible risk factor.	IIa	C

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations for the regimen and duration of anticoagulation after PE in patients *without* cancer (4)

ESC European Society of Cardiology

Recommendations	Class	Level
NOAC dose in extended anticoagulation		
If extended oral anticoagulation is decided after PE in a patient without cancer, a reduced dose of the NOACs apixaban (2.5 mg *b.i.d.*) or rivaroxaban (10 mg *o.d.*) should be considered after 6 months of therapeutic anticoagulation.	IIa	A
Extended treatment with alternative antithrombotic agents		
In patients who refuse to take or are unable to tolerate any form of oral anticoagulants, aspirin or sulodexide may be considered for extended VTE prophylaxis.	IIb	B

NOAC(s) = non-vitamin K antagonist oral anticoagulant(s); VTE = venous thromboembolism.

Recommendations for the regimen and duration of anticoagulation after PE in patients *without* cancer (5)

ESC European Society of Cardiology

Recommendations	Class	Level
Follow-up of the patient under anticoagulation		
In patients who receive extended anticoagulation, it is recommended to reassess drug tolerance and adherence, hepatic and renal function, and the bleeding risk at regular intervals.	I	C

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations for the regimen and the duration of anticoagulation after PE in patients with active cancer (2)

ESC European Society of Cardiology

Recommendations	Class	Level
For patients with PE and cancer, extended anticoagulation (beyond the first 6 months) should be considered for an indefinite period or until the cancer is cured.	IIa	B
In patients with cancer, managing incidental PE in the same manner as symptomatic PE should be considered, if it involves segmental or more proximal branches, multiple subsegmental vessels, or a single subsegmental vessel in association with proven DVT.	IIa	B

DVT = deep vein thrombosis.

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

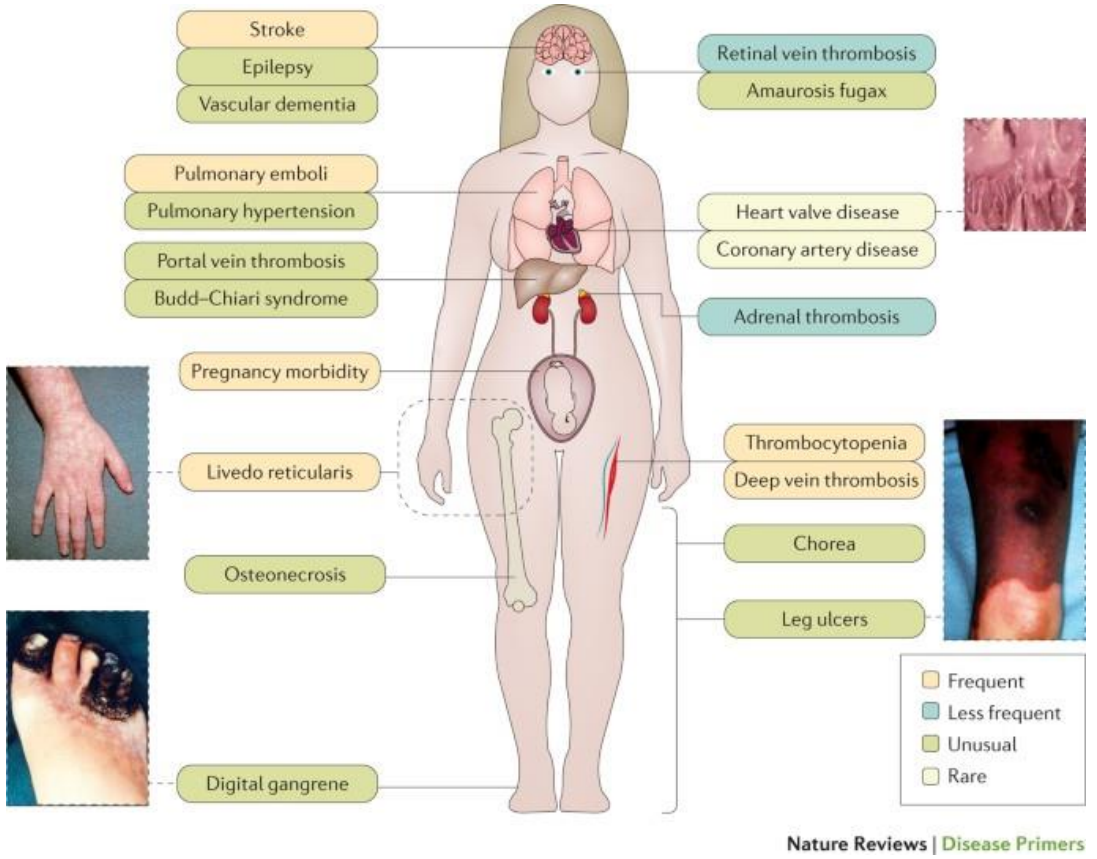
DOAC-ok használata súlyos thrombophilia esetén

- Kevés a bizonyíték, de a teljes dózisú DOAC non-inferior volt a warfarinhoz képest a súlyos thrombophiliák esetén is a nagy tanulmányokban
- Valószínűleg a súlyos PS hiány és bizonyos AT hiányok esetén előfordulhat hatástalanság (treatment failure)
- Low dose DOAC erősen megfontolandó evidencia hiánya miatt
- APS esetén kontraindikáltak

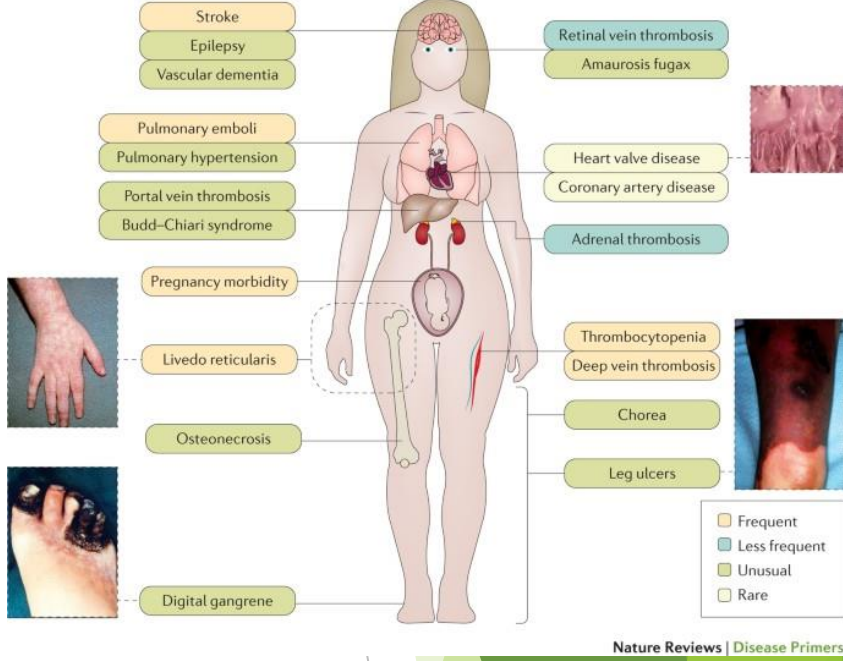
Kovac M, Ignjatovic V, Orlando C, Bereczky Z, Hunt BJ. The use of direct oral anticoagulants in the secondary prevention of venous thromboembolism in patients with severe thrombophilia: communication from the ISTH SSC Subcommittee on Physiological Anticoagulants and Thrombophilia. J Thromb Haemost. 2024 Sep 2:S1538-7836(24)00492-6. doi: 10.1016/j.jtha.2024.08.006. Epub ahead of print. PMID: 39233011.

Antiphospholipid sy – szisztémás betegség

A rekurrens thrombosis adekvát antikoagulálás ellenére komoly problémát jelent az APS esetén- különösen a triple pozitív betegek vannak veszélyben



Antiphospholipid sy



- DIAGNÓZIS: módosított Sapporo kritériumok alapján
- **1. Klinikai kritériumok**
  - Thrombotikus esemény – artériás (TIA, stroke) vagy vénás (VTE) vagy mikrovascularis (pl. CAPS) **VAGY**
  - Várandóssági komplikációk
- **ÉS**
- **2. Laboratóriumi kritériumok**
  - Lupus antikoaguláns és/vagy
  - a-CL és/vagy a-ß2-GPI IgG/IgM pozitivitás
  - Minimum 2 alkalommal, minimum 12 hét különbséggel

DE: 2023 ACR/EULAR APS classification criteria – tanulmányok számára egyelőre

Received: 12 May 2024 | Accepted: 26 June 2024

DOI: 10.1111/bjh.19635

GUIDELINE

BSH Guideline

Guidelines on the investigation and management of antiphospholipid syndrome

Deepa J. Arachchillage[1,2] | Sean Platton[3] | Kieron Hickey[4] | Justin Chu[5] | Matthew Pickering[2,6] | Peter Sommerville[7] | Peter MacCallum[8,9] | Karen Breen[10] | on behalf of the BSH Committee

Az APS diagnózisának felállításához a betegeknek a következőkkel kell rendelkezniük:

- legalább egy, tartósan (legalább 12 hetes különbséggel) pozitív aPL
- nem provokált trombózis, vagy kisebb kockázati tényező által provokált trombózis, vagy terhességi morbiditás (1B).

Kiket teszteljünk APS-re?

Nem provokált, vagy minor rizikófaktorok által provokált thromboembólia, vagy szokatlan helyen fellépő thrombosis (splanchnikus vénák, pl. v. portae, v. mesenterica, v. lienalis, Budd–Chiari sy. és cerebralis vénás sinus thrombosis egyértelmű rizikófaktor nélkül)
Artériás thrombosis <50 év alatt világos rizikófaktorok nélkül
SLE (vagy más, thrombosist vagy terhességi komplikációt okozó autoimmun betegség) az anamnesisben
Másként nem magyarázható **mikrovascularis thrombosis**
Livedo reticularis/livedoid vasculopathia jelenléte esetén
Nem magyarázható **megnyúlt PI vagy APTI** az antikoaguláció megkezdése ELŐTT
Recurrens thrombosis terápiás antikoagulálás ellenére
Thrombocytopenia
Recurrens vetélések/halvaszülés/súlyos pre-eclampsia vagy placenta elégtelenség 34. terhességi hét előtti kezdettel
Szívbillentyű abnormalitások (egyéb ok nélkül)

•Abbreviations: aPL, antiphospholipid antibodies; APS, antiphospholipid syndrome; APTT, activated partial thromboplastin time; PT, prothrombin time; VTE, venous thromboembolism. Adapted from Arachchillage et al.

Laboratóriumi tesztek - ajánlás

- - LA vizsgálat antikoaguláns kezelés alatt nem javasolt(2C).
- - Nem javasolt az LA vizsgálat akut betegeknél vagy akut trombotikus eseményt követő 3 hónapon belül (2B).
- aCL és aß2GPI IgG és IgM vizsgálatokat kell végezni (1B).
- - Két különböző elvű LA-vizsgálatot kell alkalmazni, és az egyéneknél LA-nek kell tekinteni, ha bármelyik teszt pozitív.
- - A laboratóriumoknak az eredmények értelmezése mellett részletes mennyiségi eredményeket kell közölniük minden vizsgált aPL-re vonatkozóan (1A).

APS - Kezelés

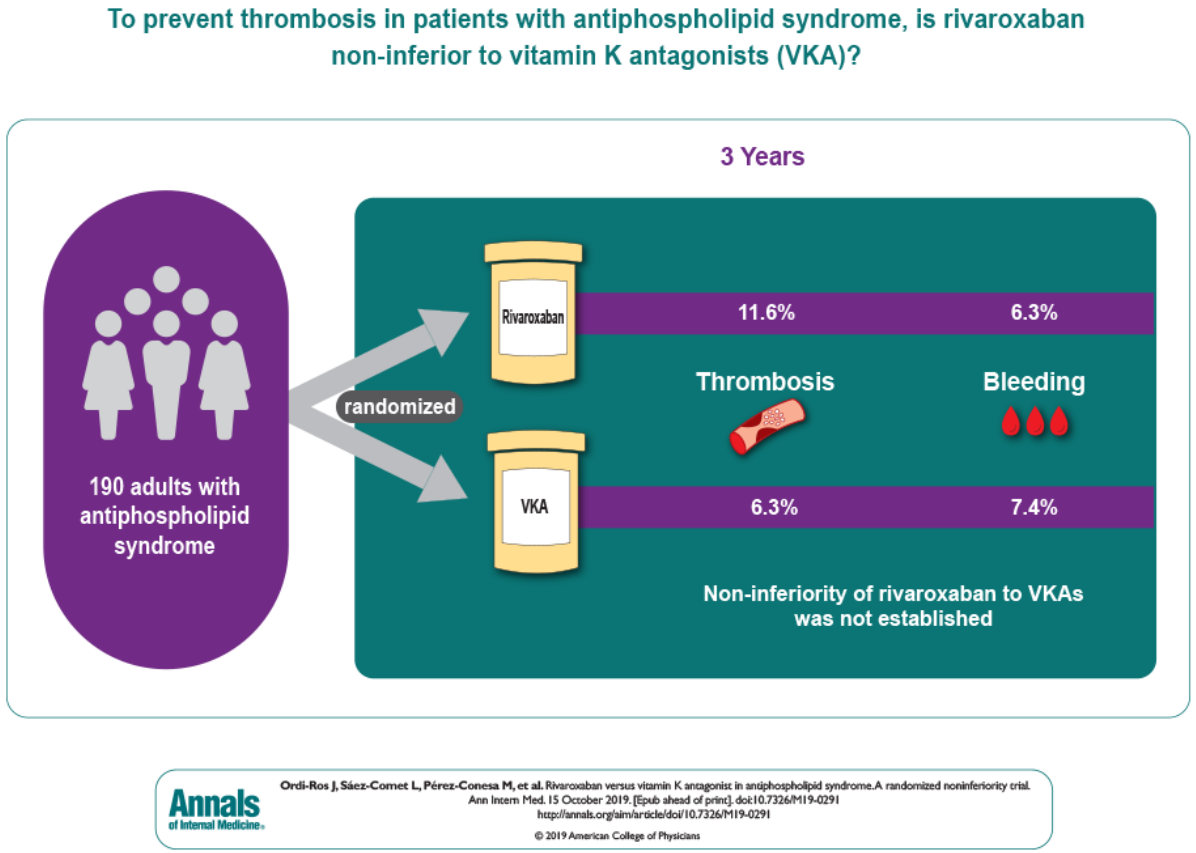
VÉNÁS THROMBOEMBÓLIA

- Tartós antikoagulálás warfarinnal
- Cél INR: 2-3 (két CRT arra a következtetésre jutott, hogy a magasabb terápiás cél INR nem jelentett előnyt)

- Javasolt az APS-ben szenvedő betegeknél a VKA megkezdése előtt alap PI mérése, és ha ez megnyúlt, akkor olyan alternatív PI-reagenseket kell használni, amelyek esetében az alap PI normál (1C).

Az antikoagulálás hatékonysága APS-ban

- Még adekvát antikoaguláns kezelés mellett is fellépnek recidivák
- Legnagyobb veszélyben a triple poz., és artériás thrombosist is elszenvedett betegek vannak (kb 30% recurrens thr. 10 év alatt warfarin mellett)
- Ebben a populcióban a warfarin jobbnak bizonyult a DOAC-nál



VTE – APS kezelése- ajánlások

- A nem provokált vénás trombotikus eseményt mutató APS-betegeknek határozatlan idejű antikoagulációt kell felajánlani (1B).
- A hosszú távú antikoagulációt igénylő APS-ben és VTE-ben szenvedő betegek esetében a VKA-t ajánljuk a 2,0-3,0 cél INR-tartományban (1B). –
- Nem javasolt DOAC-ok bevezetése ismert tripla pozitív APS-ben szenvedő betegeknél (1B).
- Nem javasolt a DOAC-ok bevezetése ismert egy- vagy kétszeresen pozitív APS-ben szenvedő betegeknél (2C).

VTE – APS kezelése- ajánlások

- A háromszoros pozitív APS-ben szenvedő, jelenleg DOAC-ot szedő betegek esetében javasoljuk, hogy a DOAC-ról VKA-ra váltsanak, miután a betegekkel megbeszélték a rendelkezésre álló bizonyítékokat. Azoknak a betegeknek, akik nem kívánnak váltani, a DOAC folytatását javasoljuk az antikoaguláció nélküli kezeléssel szemben (1B).

- Az egy- vagy kétszeres pozitív aPL-ben szenvedő APS-betegek, akik már DOAC-ot kapnak, a beteggel folytatott megbeszélést követően, a klinikai anamnézis, a kezeléshez való ragaszkodás és a korábbi tapasztalatok figyelembevételével, folytathatják a DOAC-ot vagy VKA-ra válthatnak. Azoknak a betegeknek, akik nem kívánnak váltani, a DOAC folytatását javasoljuk az antikoaguláció nélküli kezeléssel szemben (2C).

- Ne változtassuk meg a betegek kezelését, akiknek aPL-szintje csökken vagy negatívvá válik (2C).

Arteriás thr- APS kezelése

- Javasoljuk, hogy az APS-ben és stroke-ban szenvedő betegeket a hematológusok és a stroke-orvosok közösen kezeljék (2C).
- **VKA-val történő véralvadásgátlást** ajánlanak minden APS-ben és stroke-ban szenvedő betegnél (2C).
- Nem javasoljuk a DOAC-ok kezelésre vagy másodlagos profilaxisra történő alkalmazását APS-ben és stroke-ban szenvedő betegeknél (1B).
- VKA-t ajánlanak 2,5 (2,0-3,0) cél INR értékkel APS-ben és első stroke epizódban szenvedő betegeknél (2C). –
- APS-ben és stroke-ban szenvedő betegeknél a VKA-terápia kiegészítését egy vérlemezke-ellenes szerrel fontolják meg, ha további érrendszeri kockázati tényezőkkel rendelkeznek, de nincs jelentős vérzéskockázati tényezőjük (2C).
- DAPT alkalmazása megfontolandó APS-ben szenvedő, stroke-ot kapott betegeknél, ha a VKA alkalmazása ellenjavallt (2C).

- Javasoljuk, hogy minden APS-ben és trombózisban szenvedő betegnél szigorúan ellenőrizzék a kardiovaszkuláris kockázati tényezőket. Ennek magában kell foglalnia a sztatin használatát, kivéve, ha ellenjavallat áll fenn (2C).

Rekurrens thrombosisok kezelése

- Adekvát antikoagulálás melletti recidiva – küldjük centrumba!
- Ha a recidiva DOAC vagy TAG mellett következett be → warfarin (2C). •
- Amennyiben a terápiás INR-en eltöltött idő kielégítő, növeljük meg a cél INR-t 3.0–4.0-re vagy egészítsük ki a kezelést TAG-val. (ekkor cél INR 2.5 (2.0–3.0) marad) (2C).
- Ha emellett is recidiva lép fel, immunmoduláns gyógyszerek használata ajánlott pl hydroxychloroquine (2C). (szemészeti ellenőrzés mellett) illetve egyéb pl. rituximab. (2C).

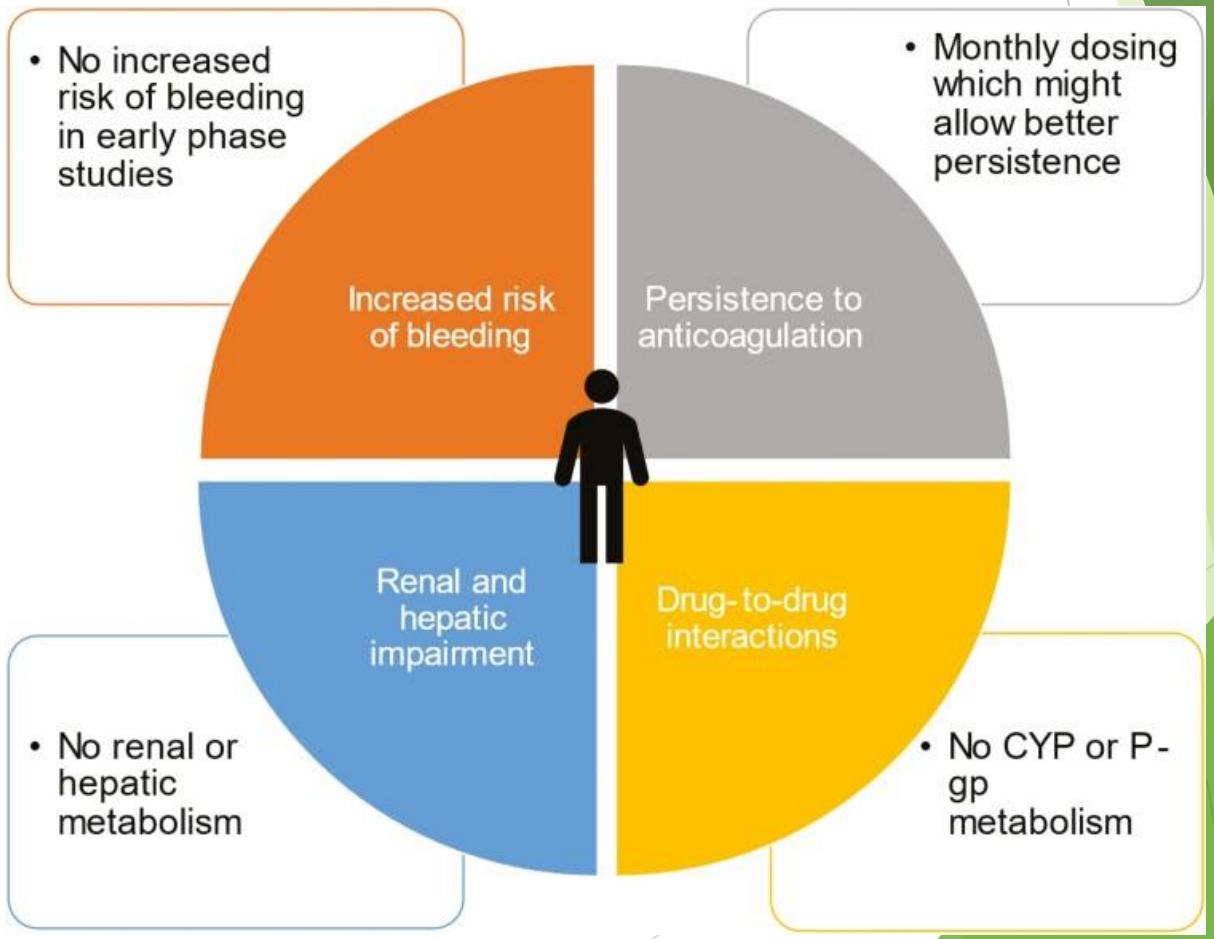
Szülészeti APS kezelése

- Haematológus és szülész együtt kezelje
- Aspirin + LMWH
- VTE esetén terápiás dózisú legyen az LMWH
- Szoros magzati kontroll
- Terv a szüléshez

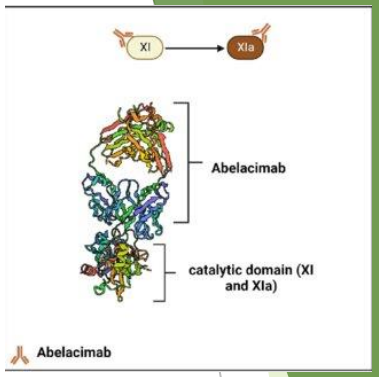
Cancer-associated thrombosis

- ACCP 2021: A rákos megbetegedésben szenvedő, akut VTE-ben szenvedő betegeknél (rákasszociált trombózis) a kezelés megkezdésére és kezelési szakaszára orális Xa-gátlót (apixaban, edoxaban, rivaroxaban) ajánlunk az LMWH helyett (erős ajánlás, közepes bizonyosságú bizonyíték).
- Tartós antikoagulálás javasolt

Ideális gyógyszer CAT-ban….

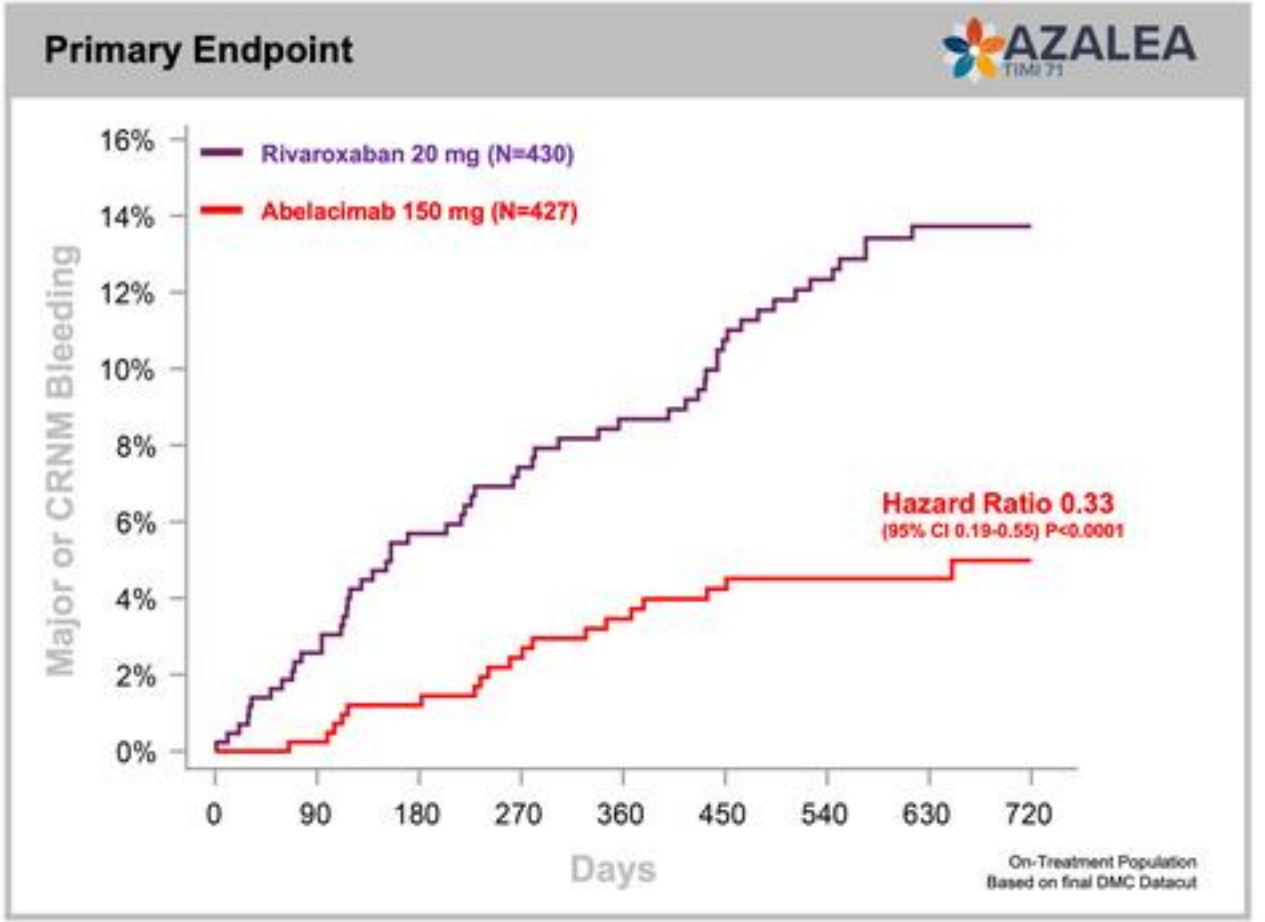


CAT – FXI gátló kezelés -abelacimab



FXI ellenes monoklonalis antitest

AZALEA-TIMI 71 NCT04755283	SC	Atrial fibrillation
ASTER NCT05171049	IV followed by SC	CAT
MAGNOLIA NCT05171075	IV followed by SC	CAT, GI/GU

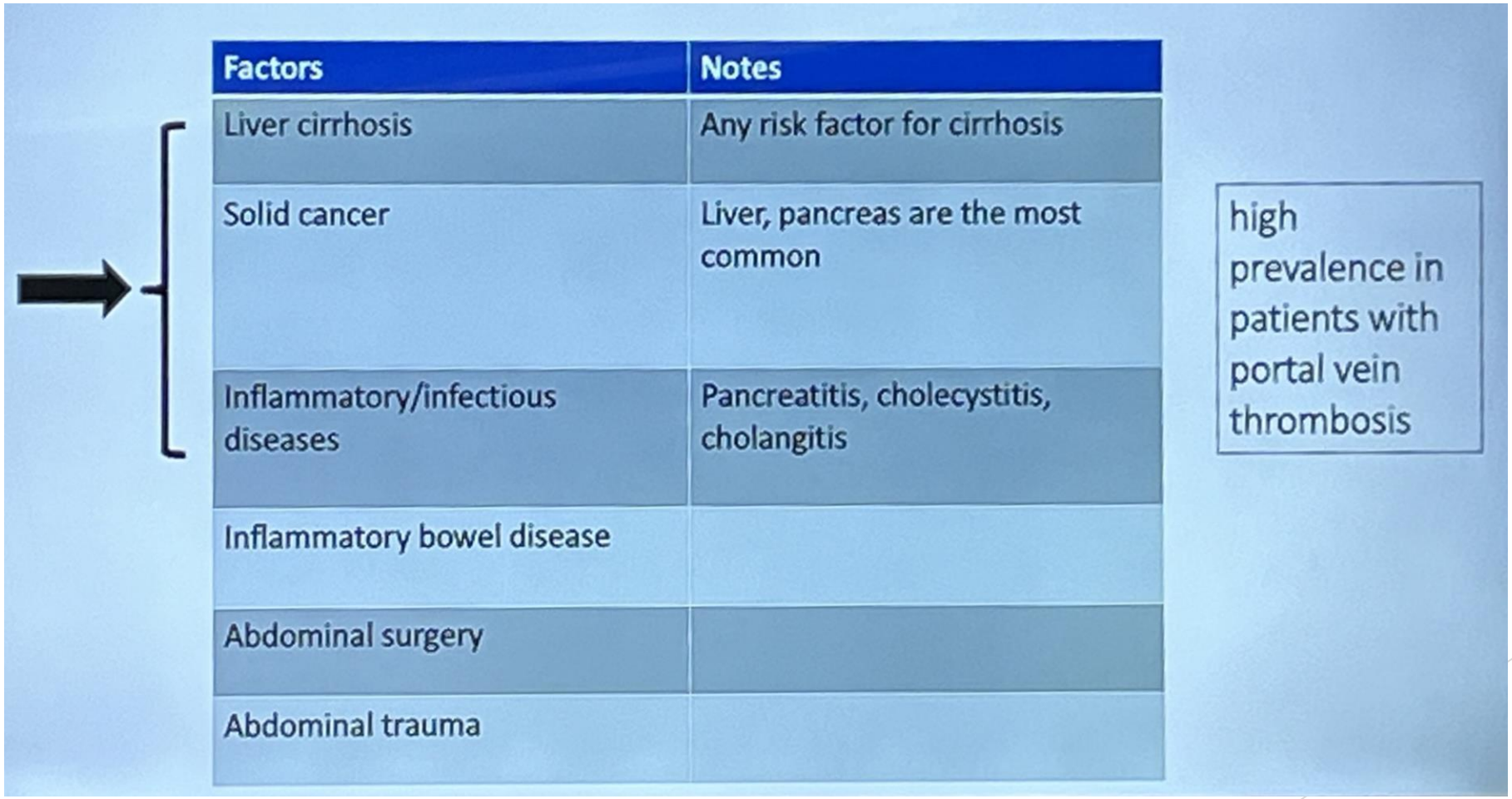


Splanchnikus vénás thrombosis és tünetei

- Sokszor tünetmentes, véletlen lelet
- Leggyakoribb tünet az akut hasi fájdalom, negatív endoscopos lelet mellett
- **V. lienalis thrombosis:** hasi fájdalom, GI vérzés, gyomorvarixok, splenomegalia, thrombocytopenia.
- **V. Portae thrombosis:** cirrhosisban gyakoribb! súlyos hasi fájdalom, hányinger, krónikus esetek: nyelőcső- vagy gyomorvarixok, GI vérzés, splenomegália, ascites és palmáris erythema gyakori. A portalis véna trombózisa összenyomhatja az epevezetékeket → cholangiopathia
- **V. mesentericae thrombosis:** hirtelen fellépő, a klinikai vizsgálattal aránytalan hasi fájdalom, haspuffadás, okkult GI vérzés lehet, bélelhalás.
- **V. hepatica thrombosis:** láz, hasi fájdalom, sárgaság, máj encephalopathiával vagy anélkül

Forrás: https://www.ncbi.nlm.nih.gov/books/NBK553170/

A splanchnicus thrombosissal kapcsolatos lokális faktorok



Factors	Notes
Liver cirrhosis	Any risk factor for cirrhosis
Solid cancer	Liver, pancreas are the most common
Inflammatory/infectious diseases	Pancreatitis, cholecystitis, cholangitis
Inflammatory bowel disease	
Abdominal surgery	
Abdominal trauma	

high prevalence in patients with portal vein thrombosis

A splanchnicus thrombosissal kapcsolatos szisztémás faktorok

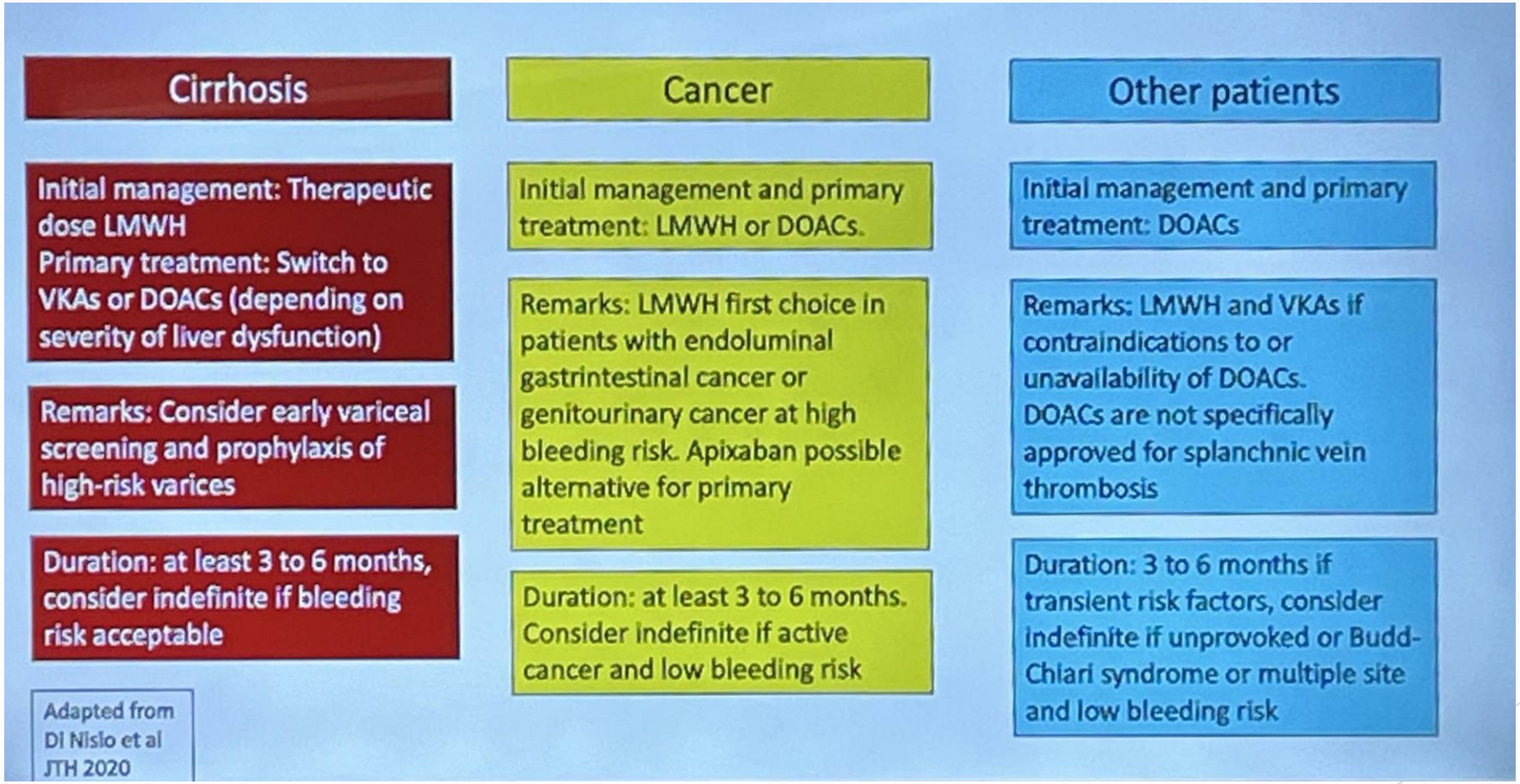
Factors	Notes
Myeloproliferative neoplasms	Polycythemia vera the most common, myelofibrosis rare
Other hematological malignancies	Intra-abdominal lymphomas, acute lymphoblastic leukemia, Multiple myeloma, acute promyelocytic leukemia
Inherited thrombophilia	PG or FVL mutations Protein C, S, AT deficiencies
Antiphospholipid syndrome	
Gender specific risk factors	Hormonal therapy Pregnancy/puerperium
Paroxysmal nocturnal hemoglobinuria	
Autoimmune diseases	E.g. Behcet's disease

Splanchnic vein thrombosis: outcomes after 2-year follow-up

	Liver cirrhosis	Solid cancer	MPN	Unprovoked	Transient risk factors
N	167	136	49	163	105
Major bleeding	10.0% pt-yrs (6.6-15.1)	4.4% pt-yrs (2.1-9.3)	3.6% pt-yrs (1.1-11.1)	1.7% pt-yrs (0.7-4.2)	0.5% pt-yrs (0.1-3.7)
Thrombosis	11.3% pt-yrs (7.7-16.8)	7.6% pt-yrs (4.3-13.3)	5.9% pt-yrs (2.5-14.3)	6.3% pt-yrs (4.0-10.0)	3.2% pt-yrs (1.4-7.0)

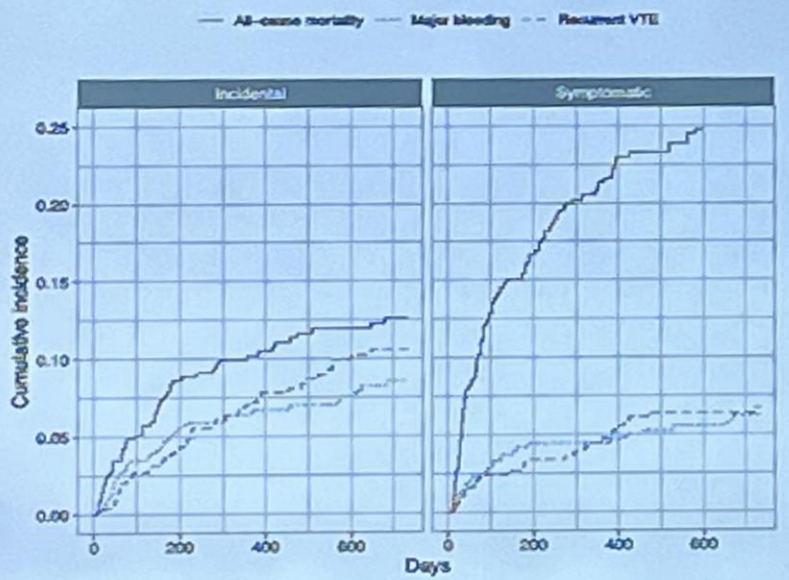
Ageno et al, JAMA Intern Med 2015

ISTH guidance: acute symtomatic SVT



Clinical course and treatment of incidentally detected SVT: individual patient data meta-analysis

Propensity score matching:
incidentally detected vs symptomatic SVT



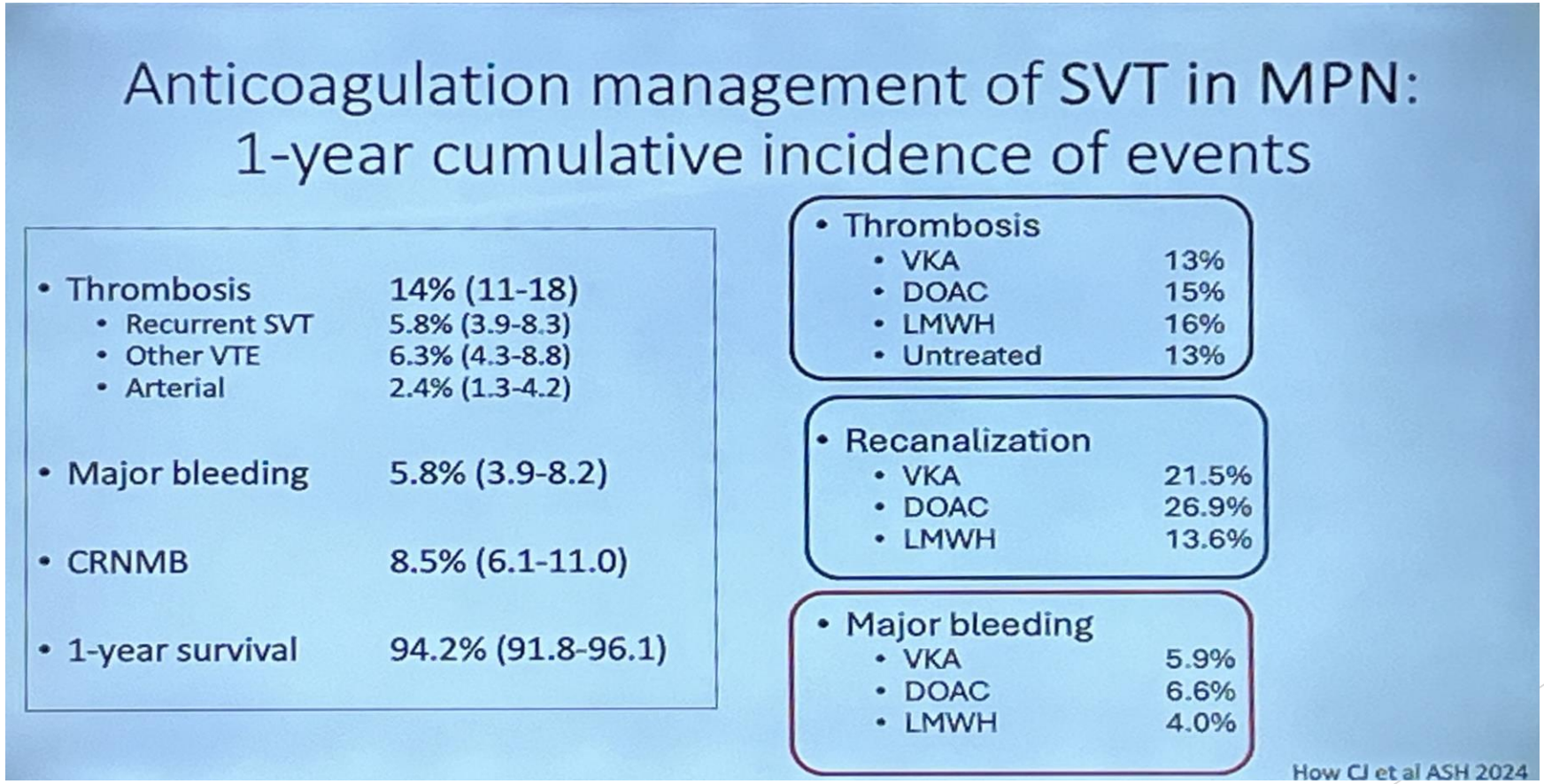
All-cause mortality
IRR 0.5; 95%CI 0.4 to 0.7

Major bleeding
IRR 1.3, 95% CI 0.8 to 2.2

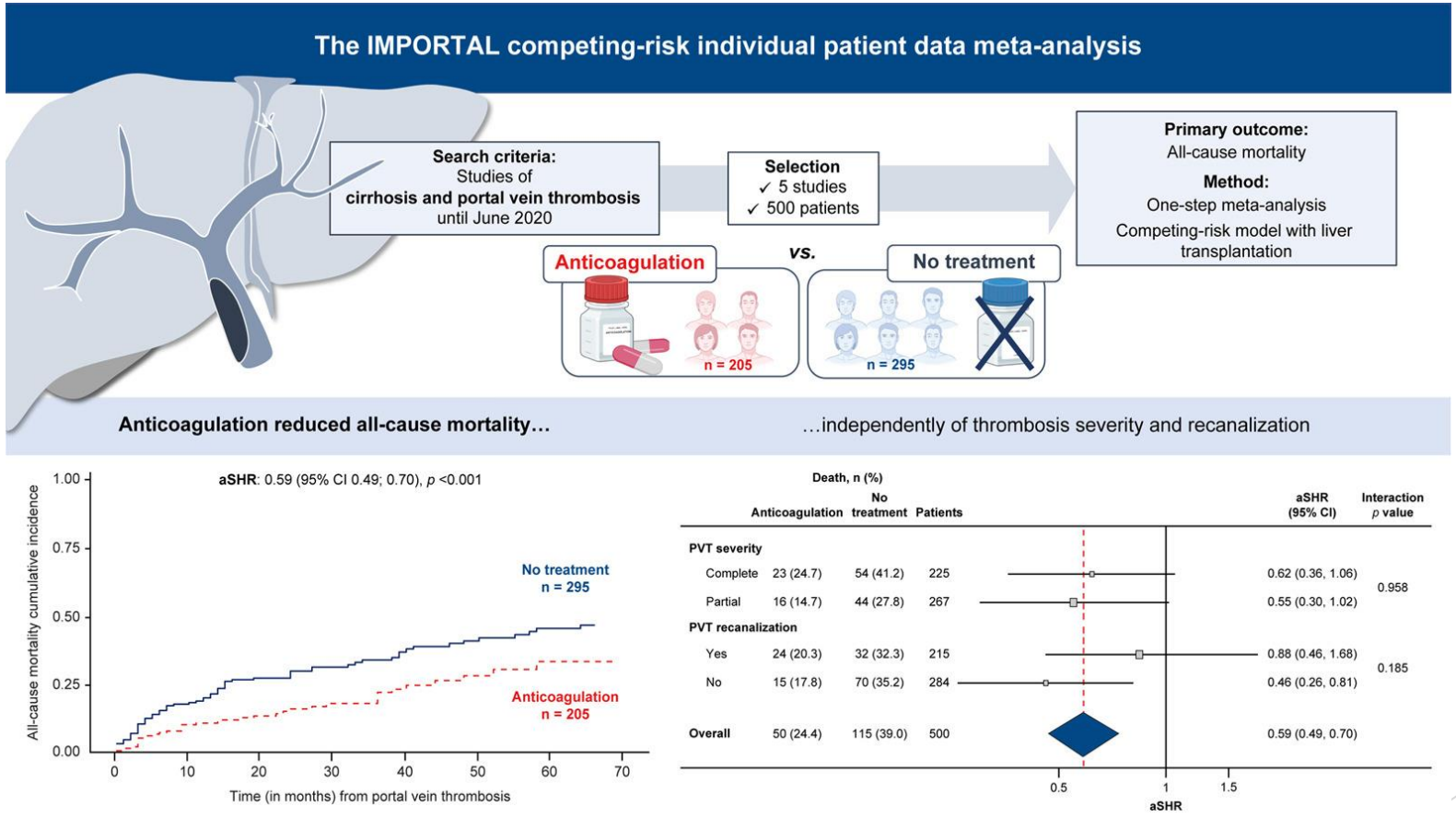
Recurrent VTE
IRR 2.0, 95% CI 1.2 to 3.3

Candeloro M et al J Thromb Hemost 2023

Anticoagulation management of SVT in MPN: 1-year cumulative incidence of events



Anticoagulation improves survival in patients with cirrhosis and portal vein thrombosis: The IMPORTAL competing-risk meta-analysis



- DOI: 10.1016/j.jhep.2023.02.023

SVT összefoglalás

- Az antikoaguláns kezelés hasznos és szükséges
- A nagyobb recanalizációs ráta jobb kimentellel korrelál (DOAC jobb, mint LMWH)
- Véletlenül felfedezett esetekben is javasolt az antikoagulálás
- A vérzéses rizikó fontos tényezője a kezelésnek
- Különböző alapbetegségek - dg - különböző a kezelés

Cerebralis vénás sinus thrombosis tünetei változatosak

- Csak fejfájás
- fejfájás és papillödéma vagy az intrakraniális hipertónia egyéb jelei
- fokális deficitek, például afázia vagy parézis, gyakran epilepsias görcsrohamokkal kombinálva
- Enkefalopátia, kóma, status epilepticus

- Rizikófaktorok: thrombophilia (szokásos megoszlás), cancer, MPN, APS, IBD, obesity, vashiányos anaemia, VITT

Cerebralis vénás sinus thrombosis tünetei változatosak

- Dg: CT venographia v. MR angiographia
- Th: antikoaguláns kezelés (sz.e. dekompressziós műtét; EVT-re nincs evidencia)
  - UFH – pl. ha akut idegsebészeti műtét várható
  - LMWH – VKA – DOAC (DOAC-CVT study: 2025. March Lancet)
  - Ideális időtartam: nem tudjuk (ált 3-12 hónap - Indef? Aki átesett CVT-n, annak magas a rizikója egyéb VTE-re is!) study folyamatban

Köszönöm a figyelmet!