TVP : quel patient traiter au cabinet ? Qui faut-il hospitaliser?

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ESC GUIDELINES

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

The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC)

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Task Force of the ESC, Eur Heart J 2020

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CURRENT OPINION
Pulmonary circulation

Diagnosis and management of acute deep vein thrombosis: a joint consensus document from the European Society of Cardiology working groups of aorta and peripheral vascular diseases and pulmonary circulation and right ventricular function

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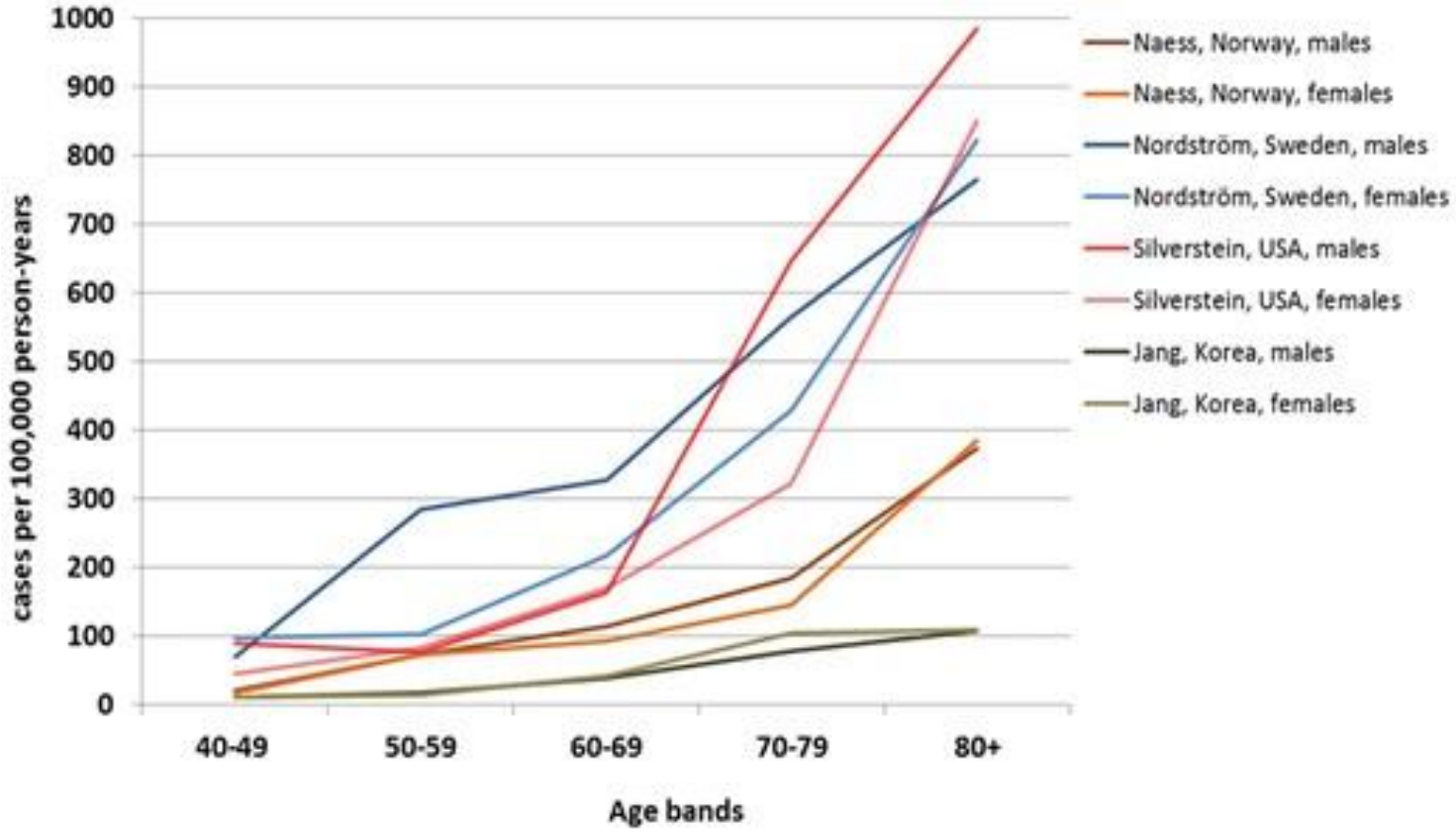
Quelques chiffres en France…

- Incidence MTEV : 180/100.000 habitants/an

- 1/3 d'EP et **2/3 de TVP**
  - **Soit 80.000 TVP par an en France**
  - EP 3ème cause de Sd CV aigu



Mazzolai et al., Eur Heart J 2018

Facteurs prédisposants la MTEV

Strong risk factors (OR > 10)

- Fracture of lower limb
- Hospitalization for HF or atrial fibrillation/flutter (within previous 3 months)
- Hip or knee replacement
- Major trauma
- Myocardial infarction (within previous 3 months)
- Previous VTE
- Spinal cord injury

Moderate risk factors (OR 2–9)

- Arthroscopic knee surgery
- Autoimmune diseases
- Blood transfusion
- Central venous lines
- Intravenous catheters and leads
- Chemotherapy
- Congestive HF or respiratory failure
- Erythropoiesis-stimulating agents
- Hormone replacement therapy (depends on formulation)
- *In vitro* fertilization
- Oral contraceptive therapy
- Post-partum period
- Infection (specifically pneumonia, urinary tract infection, and HIV)
- Inflammatory bowel disease
- Cancer (highest risk in metastatic disease)
- Paralytic stroke
- Superficial vein thrombosis
- Thrombophilia

Weak risk factors (OR < 2)

- Bed rest >3 days
- Diabetes mellitus
- Arterial hypertension
- Immobility due to sitting (e.g. prolonged car or air travel)
- Increasing age
- Laparoscopic surgery (e.g. cholecystectomy)
- Obesity
- Pregnancy
- Varicose veins

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- TVP distale : plus souvent facteur favorisant transitoire
- TVP proximale : plus souvent situation chronique favorisante
- 10% des TVP aux MS

- Risques d'une TVP :
  - Extension, EP, récidive (30% après arrêt de l'anticoagulation, surtout TVP proximale non provoquée)
  - Syndrome post-phlébitique (30-50% après TVP proximale)

Mazzolai et al., Eur Heart J 2018

Table 4. Risk of recurrence after a first episode of unprovoked VTE

Risk factors for DVT recurrence		
Proximal DVT location	Male sex	Persistence of residual vein thrombosis at ultrasound
Obesity	Non-zero blood group	High D-dimer values
Old age	Early PTS development	Role of inherited thrombophilia is controversial

Clinical prediction rules assessing risk of recurrent VTE after first episode of unprovoked VTE[71]			
Score	**Vienna prediction model**	**DASH score**	**HERDOO-2**
Parameters	• D-dimer level at 3 weeks and 3, 9, 15, 24 months after stopping anticoagulation • Male sex • VTE location (Distal DVT, Proximal DVT, PE)	• Abnormal D-dimer 3–5 weeks after stopping anticoagulation • Male sex • Age<50 years • VTE not associated with oestrogen-progestatif therapy in women	• Abnormal D-dimer before stopping anticoagulation • Post thrombotic symptoms (hyperpigmentation, edema and redness) • Age ≥65 years • BMI ≥30
Validation study	Yes	Yes	Yes
Commentaries	Different nomograms are available to calculate risk of VTE recurrence at different time	Patients with low score (≤1) have an annual recurrence rate of 3.1%	It is applicable in women only. Women with low score (≤1) have an annual recurrence rate of 1.3%

Mazzolai et al., Eur Heart J 2018

Diagnostic clinique

- Douleur
- Gonflement/oedème
- Perte du ballant
- Signe de Homans
- Dilatation des veines superficielles
- Rougeur
- Cyanose
- Fièvre inexliquée

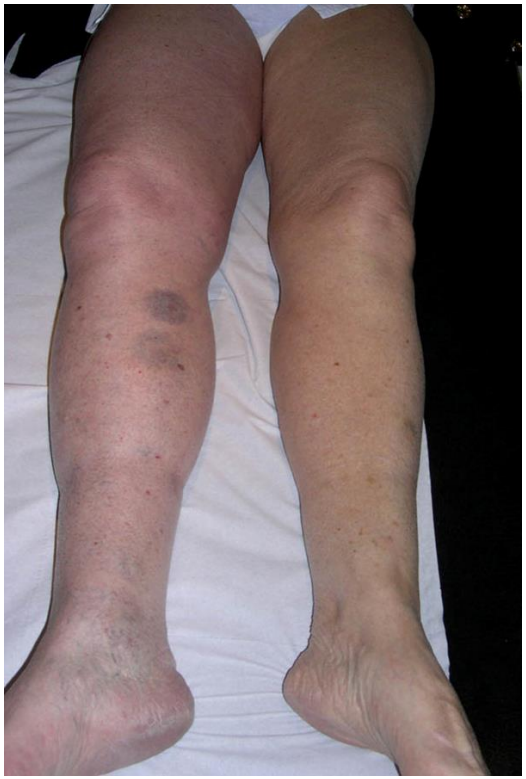
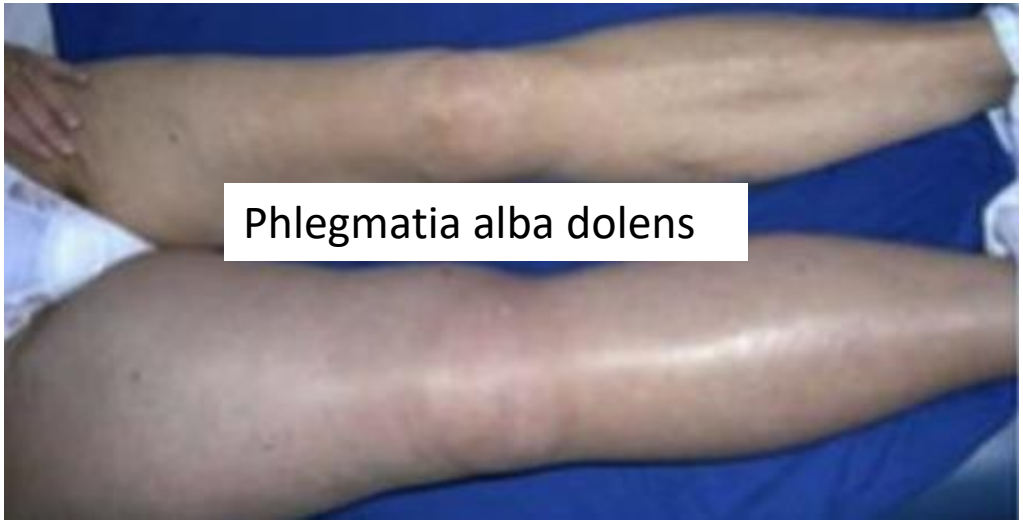
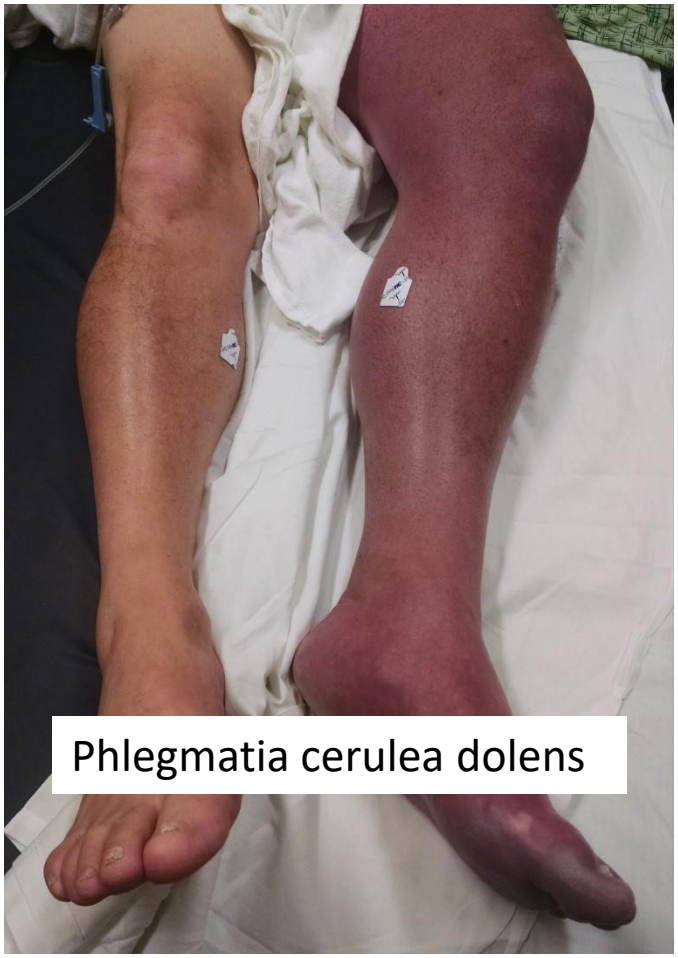


Table 2 The Wells score[12,13]

Clinical variable	Points
Active cancer (treatment ongoing or within previous 6 months or palliative)	+1
Paralysis, paresis or recent plaster immobilization of the lower extremities	+1
Recently bedridden for 3 days or more, or major surgery within the previous 12 weeks requiring general or regional anesthesia	+1
Localized tenderness along the distribution of the deep venous system	+1
Entire leg swelling	+1
Calf swelling at least 3 cm larger than that on the asymptomatic leg (measured 10 cm below the tibial tuberosity)	+1
Pitting edema confined to the symptomatic leg	+1
Collateral superficial veins (non varicose)	+1
Previously documented DVT	+1
Alternative diagnosis at least as likely as DVT	-2
Three-level Wells score	
Low	<1
Intermediate	1–2
High	>2
Two-level Wells score	
Unlikely	≤1
Likely	≥2

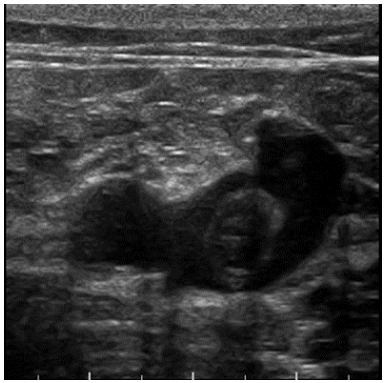
Mazzolai et al., Eur Heart J 2018


Phlegmatia alba dolens


Phlegmatia cerulea dolens

Echo-doppler veineux (compression)

- 4 points ou complet.
- Sensibilité > 90% et spécificité de 95% pour TVP symptomatique proximale.
- TVP retrouvée dans 70% des EP (phlébographie) et 30-50% (EDV).
- Si positif chez patient avec probabilité clinique d'EP : début d'anticoagulation et évaluation du risque.
- A faire si EP retenue.



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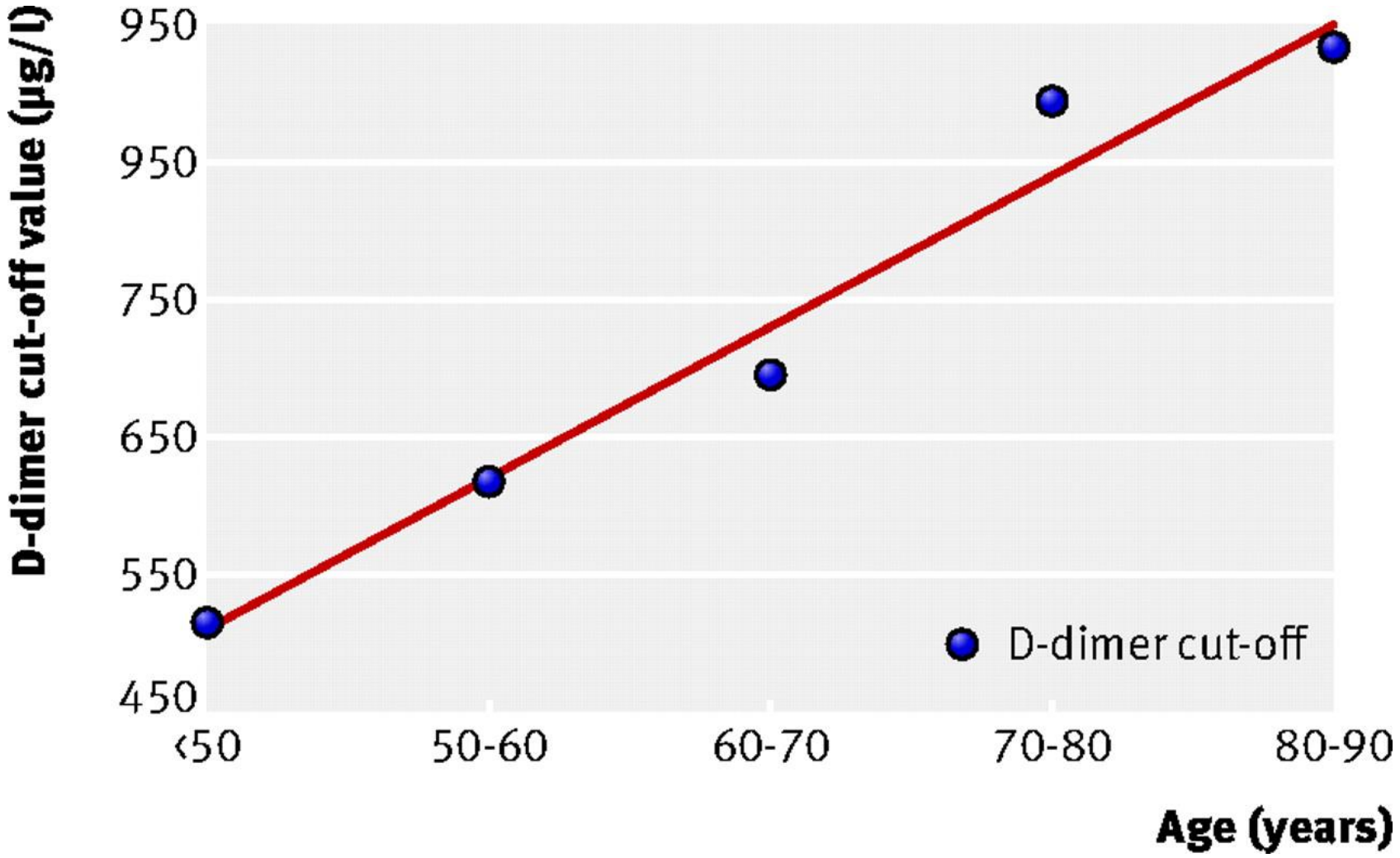
Seuil de positivité des D-dimères



Douma et al., BMJ 2010

Seuil de positivité des D-dimères

Age × 10 chez patients ≥ 50 ans

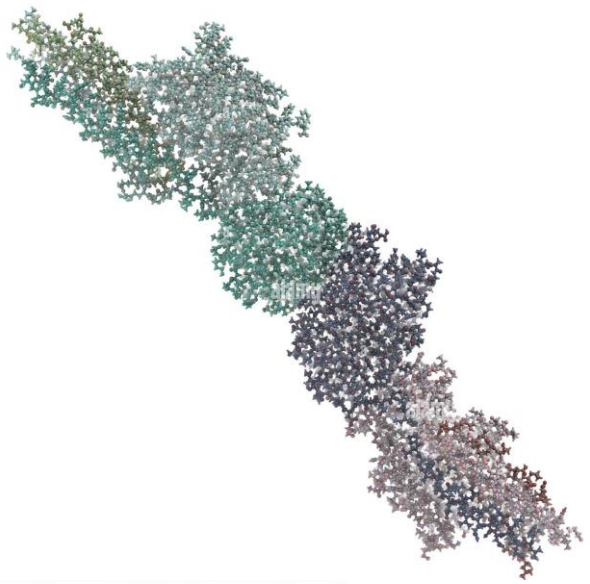
D-Dimer Assay	Low/Intermediate or Unlikely Clinical Probability, No. of Patients	D-Dimer <500 µg/L	3-mo Thromboembolism Risk		D-Dimer ≥500 µg/L and <Age-Adjusted Cutoff	3-mo Thromboembolism Risk	
			No. of Events/ Total Patients	% (95% CI)		No. of Events/ Total Patients	% (95% CI)
VIDAS D-Dimer Exclusion	1345	423	0/417	0.0 (0.0-0.9)	130	0/127	0.0 (0.0-2.9)
Innovance D-Dimer	838	202	1/202	0.5 (0.1-2.8)	103	1/103	1.0 (0.2-5.3)
STA-Liatest D-Dimer	389	132	0/132	0.0 (0.0-2.8)	49	0/47	0.0 (0.0-7.6)
D-Dimer HS 500	185	32	0/31	0.0 (0.0-11.0)	23	0/23	0.0 (0.0-14.3)
Second-generation Tina-quant	128	26	0/26	0.0 (0.0-12.9)	32	0/31	0.0 (0.0-11.0)
Cobas h 232	13	2	0/2	0.0 (0.0-65.8)	0		
Total	2898	817	1/818	0.1 (0.0-0.7)	337	1/331	0.3 (0.1-1.7)

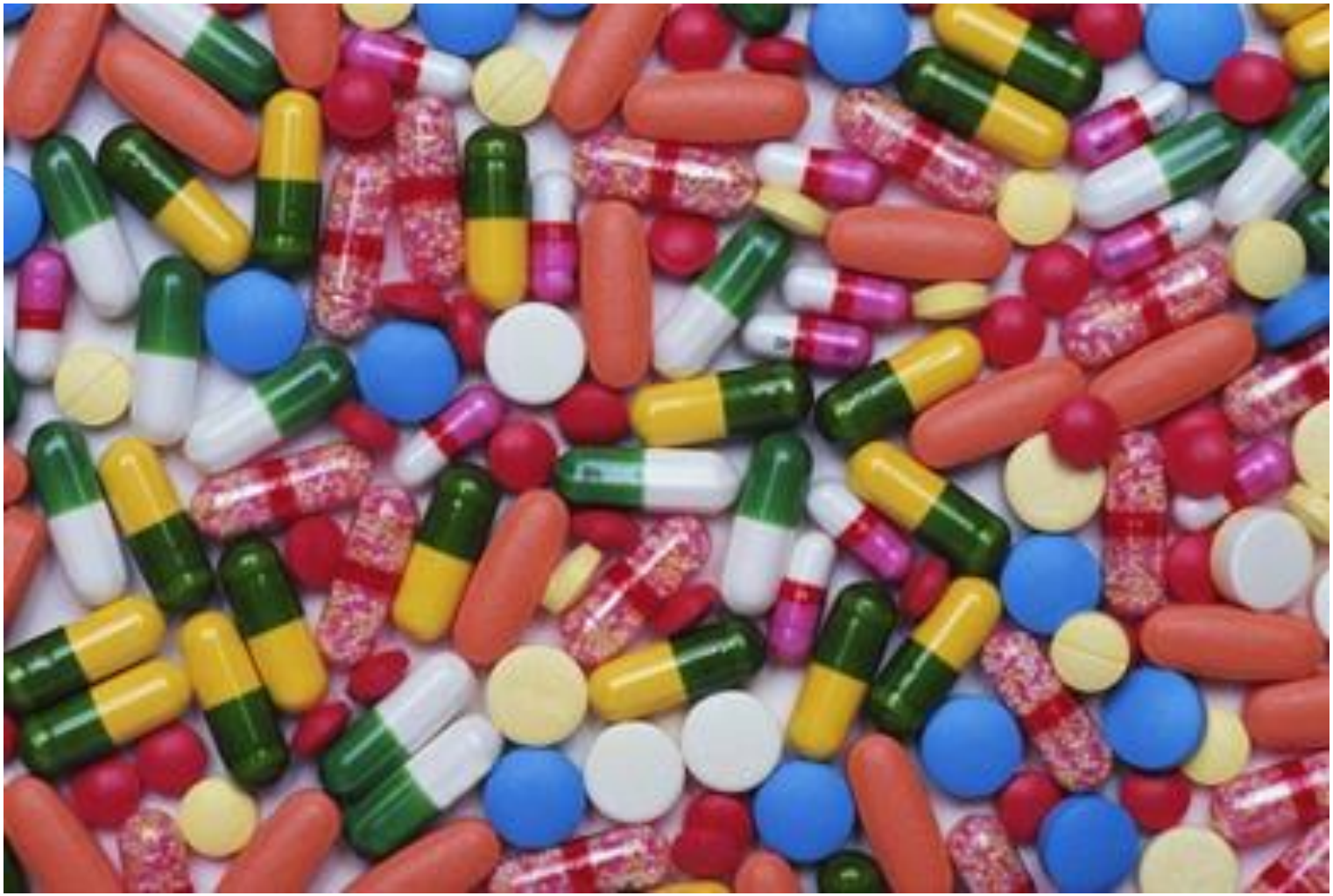
Among the 766 patients 75 years or older, of whom 673 had a nonhigh clinical probability, using the age-adjusted cutoff instead of the 500 µg/L cutoff increased the proportion of patients in whom PE could be excluded on the basis of D-dimer from 43 of 673 patients (6.4% [95% CI, 4.8%-8.5%) to 200 of 673 patients (29.7% [95% CI, 26.4%-33.3%), without any additional false-negative findings.

Righini et al., JAMA 2014

Situations associées à une élévation des D-dimères

- Maladies artérielles thromboemboliques
  - Infarctus du myocarde
  - ACV
  - Ischémie aigue d'un membre
  - FA
  - Thrombus intracardiaque
- Maladies thromboemboliques veineuses
  - TPP
  - Embolie pulmonaire
- CIVD
- Prééclampsie, éclampsie
- Fibrinolyse anormale ; agents fibrinolytiques
- Insuffisance cardiaque
- Infection, sepsis, inflammation, SIRS (systemic inflammatory response)
- Chirurgie, trauma
- Maladie hépatique sévère
- Cancer
- Maladie rénale
  - Syndrome néphrotique
  - IRA
  - IRC et maladie cardiaque sous-jacente
- Grossesse normale
- Malformations veineuses
- Âge plus de 75 ans

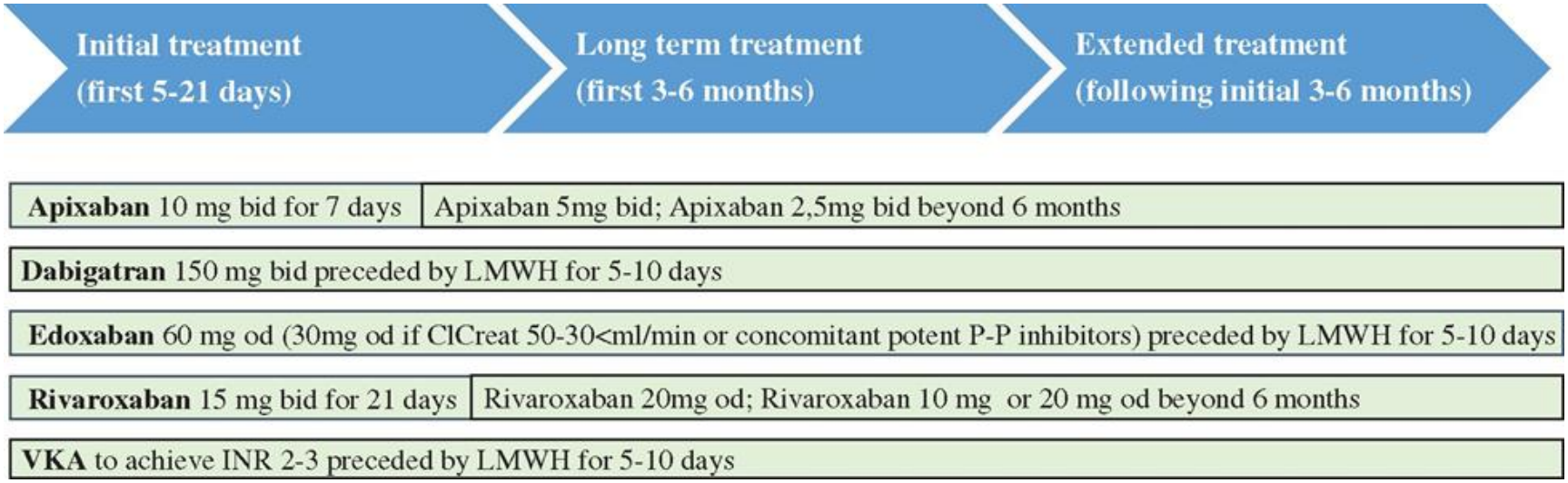




	Dosage	Interval
Lovenox® Enoxaparin	1.0 mg/kg or 1.5 mg/kg[a]	Every 12 hours Once daily[a]
Innohep® Tinzaparin	175 U/kg	Once daily
Fragmine® Dalteparin	100 IU/kg[b] or 200 IU/kg[b]	Every 12 hours[b] Once daily[b]
Fraxiparine®, Fraxodi® Nadroparin[c]	86 IU/kg or 171 IU/kg	Every 12 hours Once daily
Arixtra® Fondaparinux	5 mg (body weight <50 kg); 7.5 mg (body weight 50–100 kg); 10 mg (body weight >100 kg)	Once daily

ESC guidelines, Eur Heart J 2014

In the absence of contraindications, DOACs should be preferred as first-line anticoagulant therapy in non-cancer patients with proximal DVT.



Whether isolated distal DVT should be treated with anticoagulation is still debated.

Mazzolai et al., Eur Heart J 2018

Type d'anticoagulation et durée

Recommendations	Class[a]	Level[b]
Therapeutic anticoagulation for ≥ 3 months is recommended for all patients with PE.[347]	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.[331,340,341]	I	B
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.[358]	I	B
Oral anticoagulant treatment with a VKA for an indefinite period is recommended for patients with antiphospholipid antibody syndrome.[359]	I	B
Patients in whom extension of anticoagulation beyond 3 months should be considered[c,d]		
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE and no identifiable risk factor.[330,331,347,351–353]	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 antiphospholipid antibody syndrome.[330,352,353]	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.[330,331,352]	IIa	C
NOAC dose in extended anticoagulation[e]		
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.[352,353]	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.[355–357]	IIb	B
Follow-up of the patient under anticoagulation		
In patients who receive extended anticoagulation, it is recommended that their drug tolerance and adherence, hepatic and renal[f] function, and bleeding risk be reassessed at regular intervals.[259]	I	C

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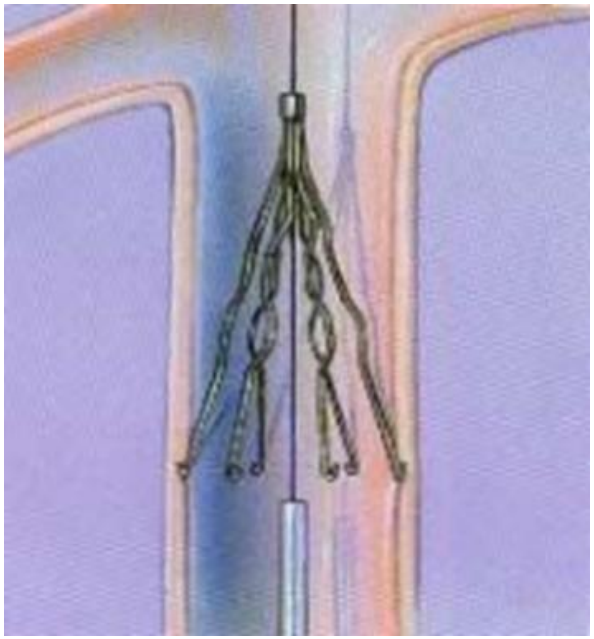
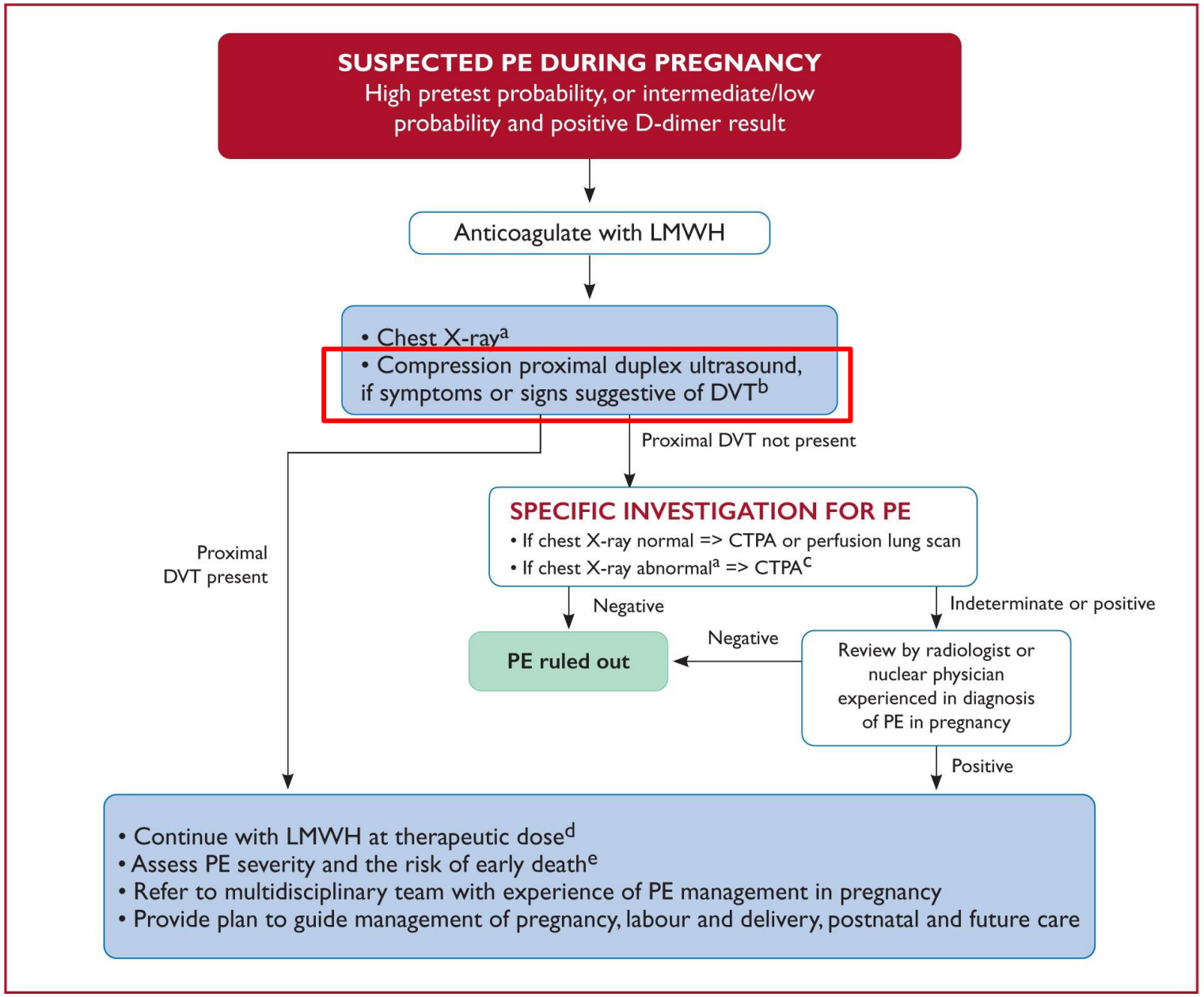


Si contre-indication absolue à l'anticoagulation chez patient avec TVP proximale nouvellement diagnostiquée

Mazzolai et al., Eur Heart J 2018



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EP et grossesse

Recommendations	Class[a]	Level[b]
Diagnosis		
Formal diagnostic assessment with validated methods is recommended if PE is suspected during pregnancy or in the post-partum period.[388,391]	I	B
D-dimer measurement and clinical prediction rules should be considered to rule out PE during pregnancy or the post-partum period.[388,391]	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.[388]	IIa	B
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.[385,386]	IIa	C
Treatment		
A 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.[408,410]	I	B
Thrombolysis or surgical embolectomy should be considered for pregnant women with high-risk PE.[421]	IIa	C
Insertion of a spinal or epidural needle is not recommended, unless ≥24 h have passed since the last therapeutic dose of LMWH.	III	C
Administration of LMWH is not recommended within 4 h of removal of an epidural catheter.	III	C
NOACs are not recommended during pregnancy or lactation.	III	C

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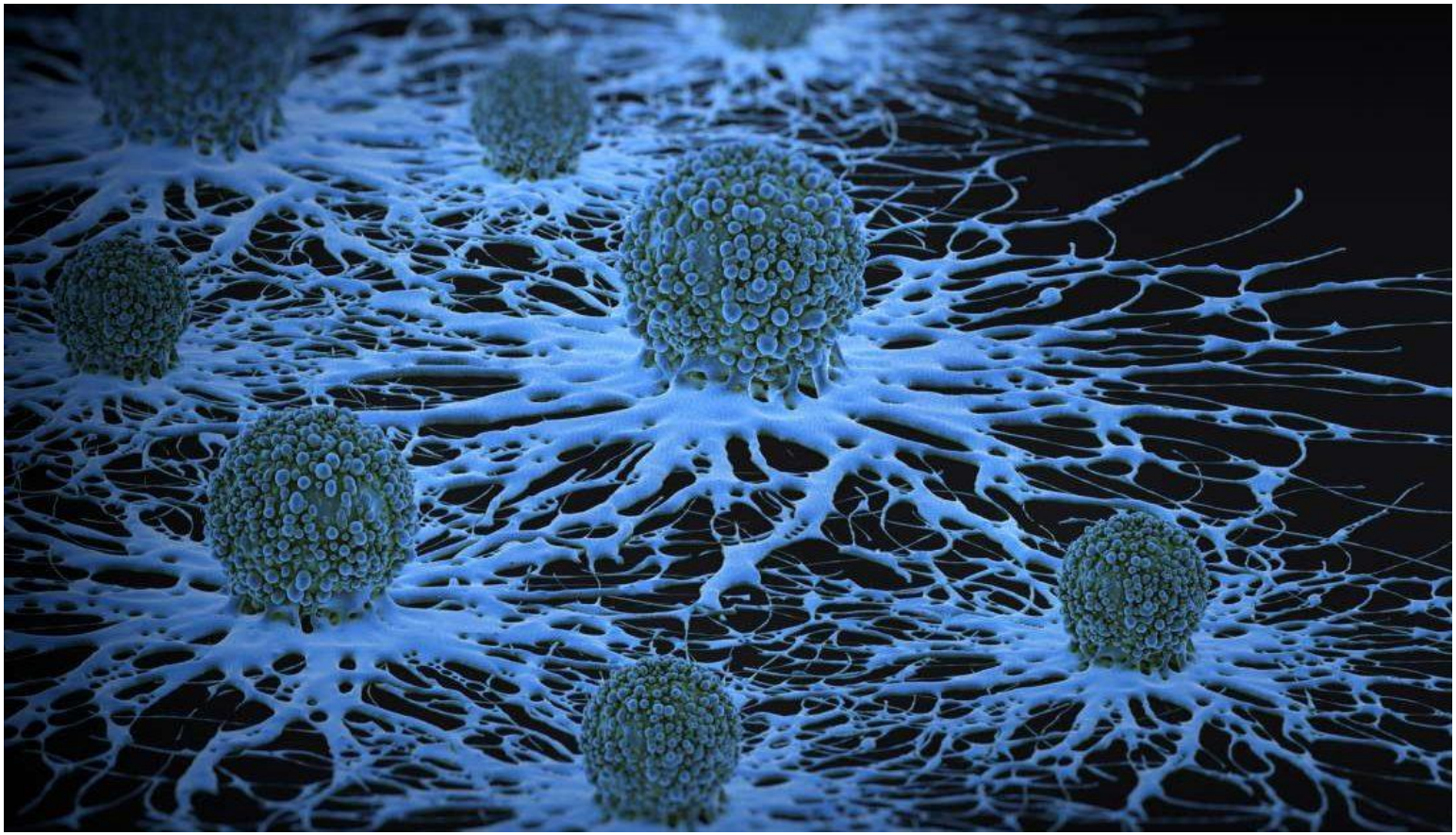

EP et cancer

Recommendations	Class[a]	Level[b]
For patients with PE and cancer, weight-adjusted subcutaneous LMWH should be considered for the first 6 months over VKAs.[360–363]	IIa	A
Edoxaban should be considered as an alternative to weight-adjusted subcutaneous LMWH in patients without gastrointestinal cancer.[366]	IIa	B
Rivaroxaban should be considered as an alternative to weight-adjusted subcutaneous LMWH in patients without gastrointestinal cancer.[367]	IIa	C
For patients with PE and cancer, extended anticoagulation (beyond the first 6 months)[c] should be considered for an indefinite period or until the cancer is cured.[378]	IIa	B
In patients with cancer, management of 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.[376,377]	IIa	B

Kc Poumon, colon, prostate

Myélome, T. cérébrale, Kc pancréas

Risque x 4 (x 6 si chimioT)

- AOD si pas de risque élevé de saignement GI ou génito-urinaire
- AVK si Cl créat < 20 ml/min

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AMBULATOIRE
Service
Ambulatoire
Accueil
ZONE DE DISCRETION

Quid de la prise en charge ambulatoire de l'EP?

- Sélection +++ des patients
- Faible risque (PESIs I ou II)
- 13 à 51 % des EP

Author	Design	Inclusion criteria	Main exclusion criteria	Patients included	Treatment
Aujesky[217]	Open-label Randomized Non-inferiority 19 centres (ED) Discharge within 24 hours vs. inpatient therapy	Age ≥18 years Confirmed acute PE PESI Class I or II	BP <100 mm Hg Pain needing opioids Active bleeding or high risk Extreme obesity CrCl <30 ml/min HIT history Barriers to home treatment	344 (of 1557 screened)	*Both arms:* enoxaparin s.c. twice daily; overlap with VKA (starting 'early')
Otero[349]	Open-label Randomized 9 centres Discharge after 3–5 days vs. inpatient therapy	Age ≥18 years Confirmed acute PE Low-risk by Uresandi clinical prediction rule[350]	Haemodynamic instability Troponin T ≥0.1 ng/ml RV dysfunction (TTE) High bleeding risk Severe comorbidity O_2 saturation <93% COPD, asthma Extreme obesity	132 (of 1016 screened)	*Both arms:* LMWH s.c. overlap with VKA (starting day 10)
Zondag[347]	Prospective cohort 12 centres (ED) All treated as outpatients, discharge within 24 hours	Age ≥18 years Confirmed acute PE	Haemodynamic instability Active bleeding or high risk Oxygen requirement CrCl <30 mL/min Hepatic failure HIT history Barriers to home treatment	297 (of 581 screened)	Nadroparin s.c. once daily; overlap with VKA (starting day 1)
Agterof[237]	Prospective cohort 5 centres (ED) Discharge within 24 hours	Age ≥18 years Confirmed acute PE NT-proBNP <500 pg/mL	Haemodynamic instability Active bleeding or high risk Severe comorbidity Pain with i.v. analgesia Oxygen requirement Creatinine >150 µmol/L Barriers to home treatment	152 (of 351 screened)	LMWH s.c. once daily; overlap with VKA (starting 'early')

ESC guidelines, Eur Heart J 2014

Critères HESTIA

Si tous les critères sont absents : un traitement ambulatoire est envisageable.
Si un critère est présent : le traitement ambulatoire n'est pas envisageable.

1. Hémodynamique instable ? *
2. Thrombolyse ou embolectomie nécessaire ?
3. Saignement actif ou haut risque hémorragique ? **
4. Oxygénothérapie ?
5. EP diagnostiquée durant un traitement anticoagulant ?
6. Raison sociale ou médicale justifiant un traitement en milieu hospitalier ?
7. Nécessité d'un traitement antalgique intraveineux ?
8. Clairance de la créatinine < 30mL/min ?
9. Insuffisance hépatique sévère ?
10. Enceinte ?
11. Thrombocytopénie ?

** TAS<100mmHg avec FC>100/min.*

*** Saignement gastro-intestinal dans les 14 jours, AVC dans les 4 semaines, intervention chirurgicale dans les 2 semaines, trouble de la crase sanguine, ou thrombocytopénie < 75g/L, HTA non contrôlée (TAS > 180 mmHg ou TAD > 110 mmHgH).*

Zondag et al., J Thromb Haemost 2011

Ne peut être traité en ambulatoire…

- Risque élevé : PESIs $\geq$ 3, voire PESIs $\geq$ 1
- Etat de choc, hypotension
- Dysfonction VD (TDM et/ou EDC)
- Troponine T $\geq$ 0,1 ng/ml, NtProBNP > 500 ng/
- SaO2 < 93%, O2 dépendance

- Douleurs nécessitant morphiniques
- Saignement actif ou risque hémorragique élevé
- Antécédent de thrombopénie induite par l'héparine

- Comorbidité sévère
- Obésité extrême
- Cl créatinine < 30 ml/min
- BPCO, asthme
- Insuffisance hépatique

- Thrombus flottant fémoro-ilio-cave
- EP sous anticoagulant

- Barrières à un traitement à domicile dont désaccord du patient et non organisation d'un parcours de soin dès le retour à domicile

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La majorité des TVP peut être traitée en ambulatoire.

Bilan étiologique MTEV

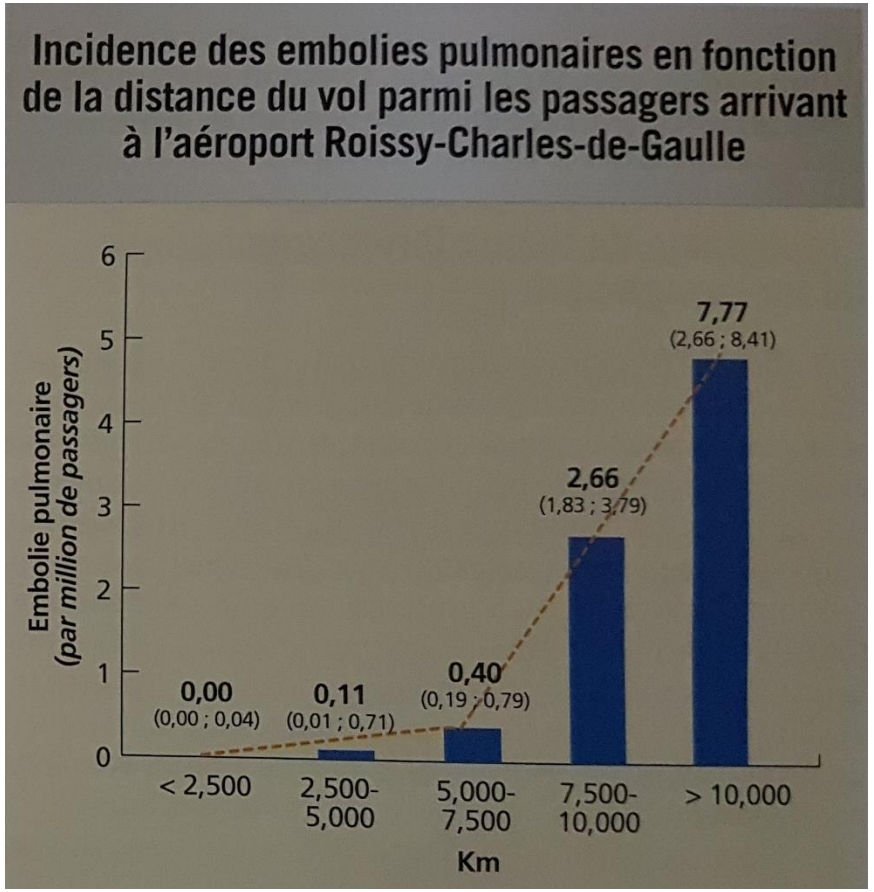
Interrogatoire, examen clinique ++

MTEV provoquée	Pas d'exploration complémentaire
1er épisode non provoqué de TVP proximale ou d'EP < 50 ans	SAPL (ACC lupique, anticardiolipine, anti-β2-glycoprotéine 1)
1er épisode non provoqué de TVP proximale ou d'EP < 50 ans + ATCD MTEV familial 1er degré	Thrombophilie constitutionnelle (TC)
MTEV récidivante (dont 1 épisode non provoqué < 50 ans)	TC, SAPL
MTEV non provoquée < 40 ans femme	TC si désir grossesse
MTEV non provoquée > 50 ans	NFS, B coag, BH, Rx thorax, hémogramme, dépistage cancer (Hemoccult, frottis CV, mammographie, PSA) Si point d'appel cancer : cibler Si récidive dans l'année ou sous traitement ou EP bilatérale : dépistage cancer par TDM
Hémolyse intravasculaire	Hémoglobinurie paroxystique nocturne
Thrombocytose ou polyglobulie	Sd MP (mutation JAK2, progéniteurs hématopoïétiques)

Quel bilan de thrombophilie constitutionnelle?

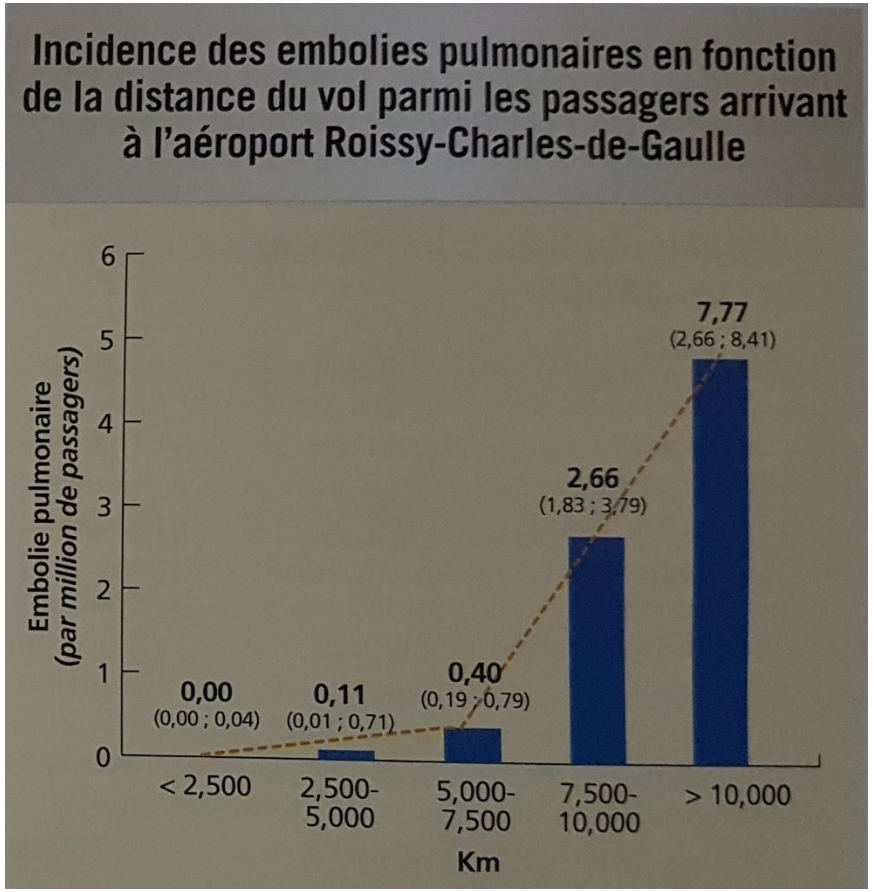
- Déficit en antithrombine
- Déficit en protéine C et S
- Mutations Leiden du facteur V
- Entre 3 et 6 mois après MTEV
- Si +, recherche suggérée chez apparentés 1er degré asymptomatiques


AIR AUSTRAL
ÎLE DE RÉUNION


Incidence des embolies pulmonaires en fonction de la distance du vol parmi les passagers arrivant à l'aéroport Roissy-Charles-de-Gaulle
Embolie pulmonaire (par million de passagers)
0
1
2
3
4
5
6
0,00 (0,00 ; 0,04)
0,11 (0,01 ; 0,71)
0,40 (0,19 ; 0,79)
2,66 (1,83 ; 3,79)
7,77 (2,66 ; 8,41)
< 2,500
2,500-5,000
5,000-7,500
7,500-10,000
> 10,000
Km


AIR AUSTRAL
ÎLE DE RÉUNION


MAGIC SYSTEM
Bouger Bouger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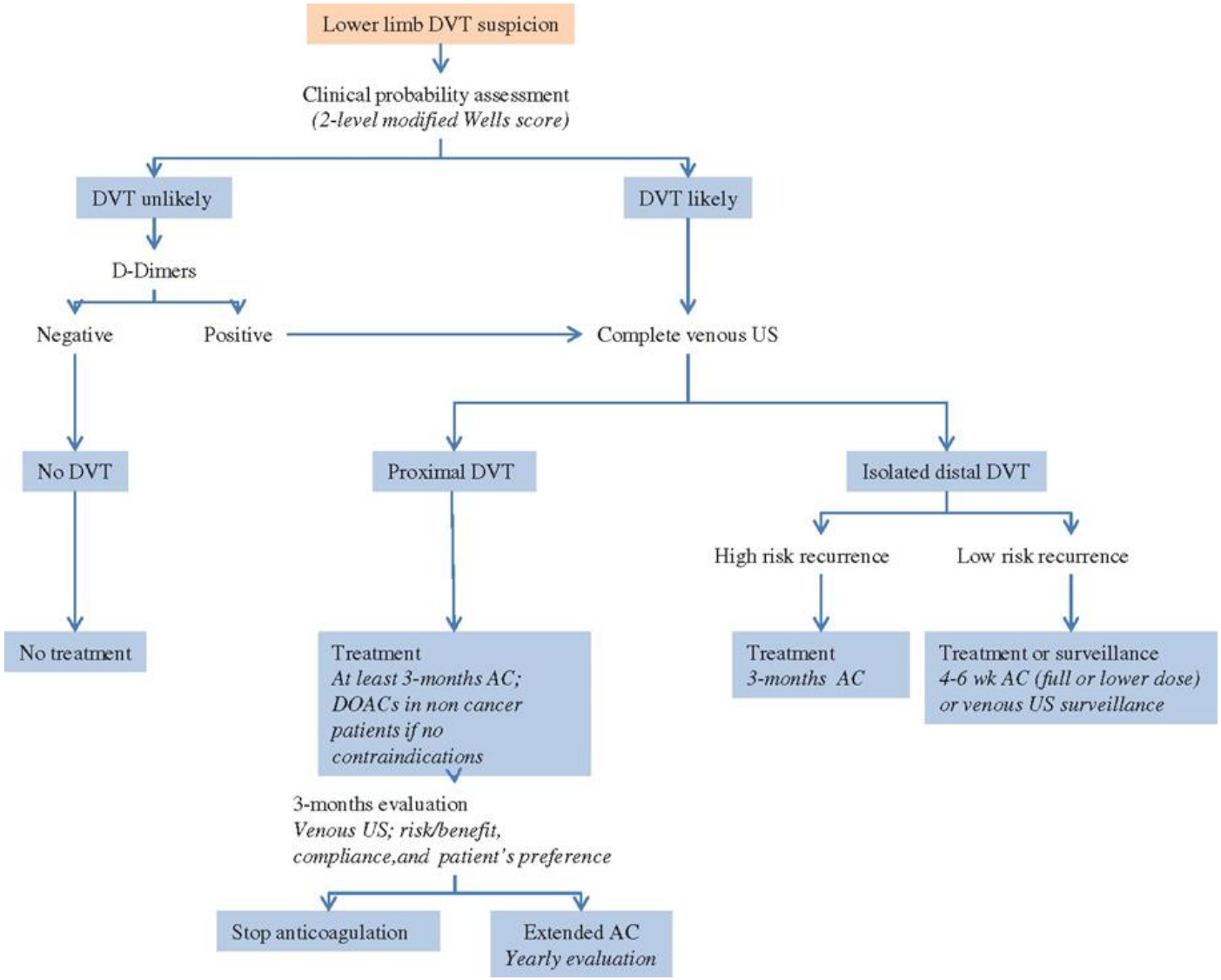

Mazzolai et al., Eur Heart J 2018

Merci!