Embolie Pulmonaire: mise à jour des recommandations

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2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC)

Endorsed by the European Respiratory Society (ERS)

European Heart Journal Advance Access published August 29, 2014

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European Heart Journal
doi:10.1093/eurheartj/ehu283

ESC GUIDELINES

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Histoire naturelle de l'EP

- Mortalité à 30 jours (toute cause): 9 – 11%
- Mortalité à 3 mois: 9 – 17%

⇨Diagnostic précoce et rigoureux

⇨Evaluation du pronostic

⇨Stratégie thérapeutique adaptée

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Buts de la prise en charge initiale

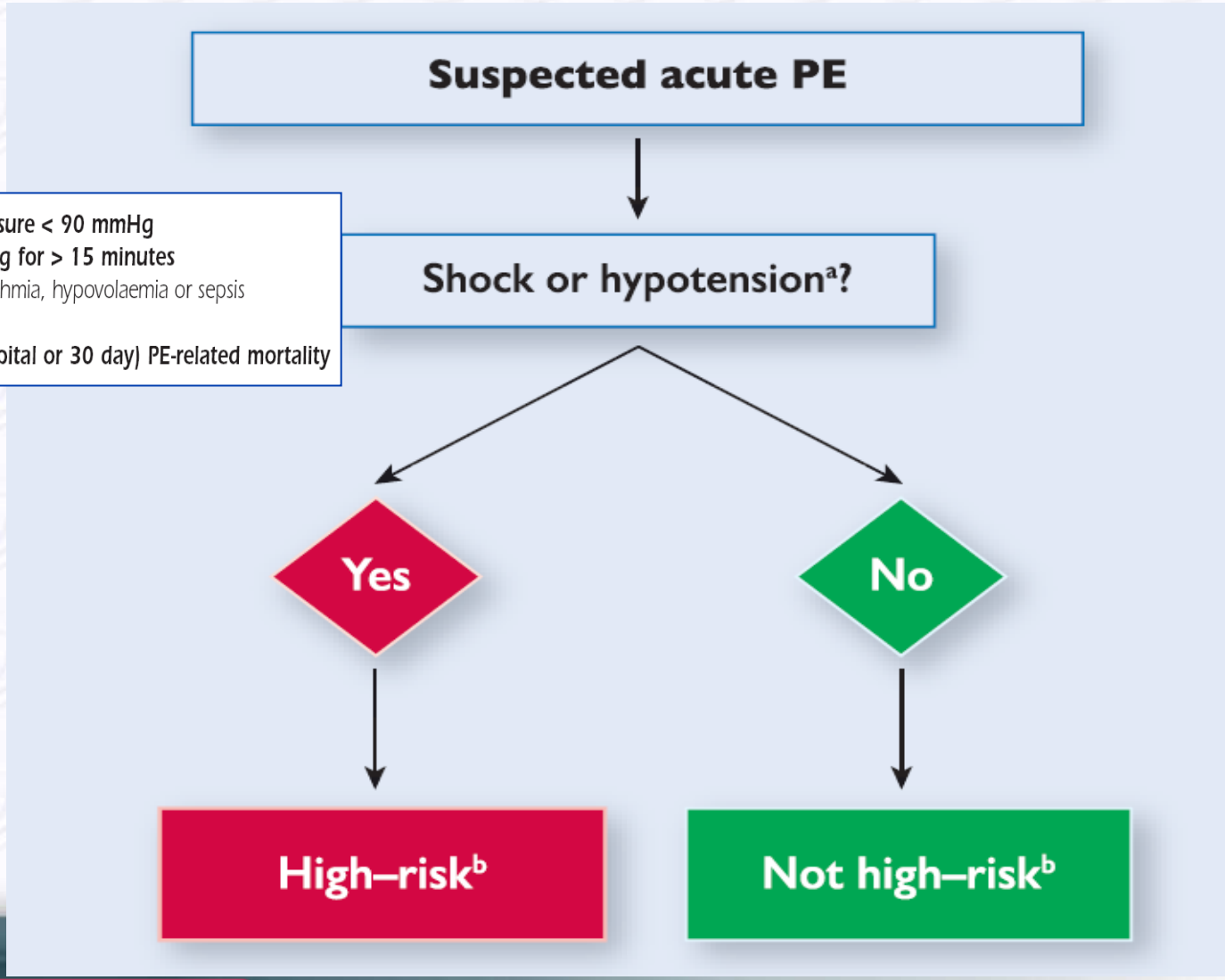
1. Analyser la gravité et confirmer le diagnostic.
2. Mettre en place le traitement initial.
3. Définir le lieu et conditions de prise en charge initiale.
4. Traitement ultérieur et durée du traitement

Relevant *new* aspects 2014

1. Recently identified predisposing factors
2. Simplification of clinical prediction rules
3. Age-adjusted D-dimer cut-offs
4. Sub-segmental pulmonary embolism (PE)
5. Incidental, clinically unsuspected PE
6. Advanced risk stratification of intermediate-risk PE
7. Initiation of treatment with vitamin K antagonists
8. Treatment and secondary prophylaxis of venous thromboembolism with non-Vitamin-K-dependent oral anticoagulants (NOACs)
9. Efficacy and safety of reperfusion treatment for patients at intermediate risk
10. Early discharge and home (outpatient) treatment of PE
11. Current diagnosis and treatment of CTEPH
12. Formal recommendations for the management of PE in pregnancy and of PE in patients with cancer.

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

Initial risk stratification of acute PE



* Defined as a systolic blood pressure < 90 mmHg
or a pressure drop of ≥ 40 mmHg for > 15 minutes
if not caused by new-onset arrhythmia, hypovolaemia or sepsis

** Defined as risk of early (in-hospital or 30 day) PE-related mortality

[a]Defined as systolic blood pressure <90 mmHg, or a systolic pressure drop by ≥40 mmHg, for >15 minutes, if not caused by new-onset arrhythmia, hypovolaemia, or sepsis.
[b]Based on the estimated PE-related in-hospital or 30-day mortality.

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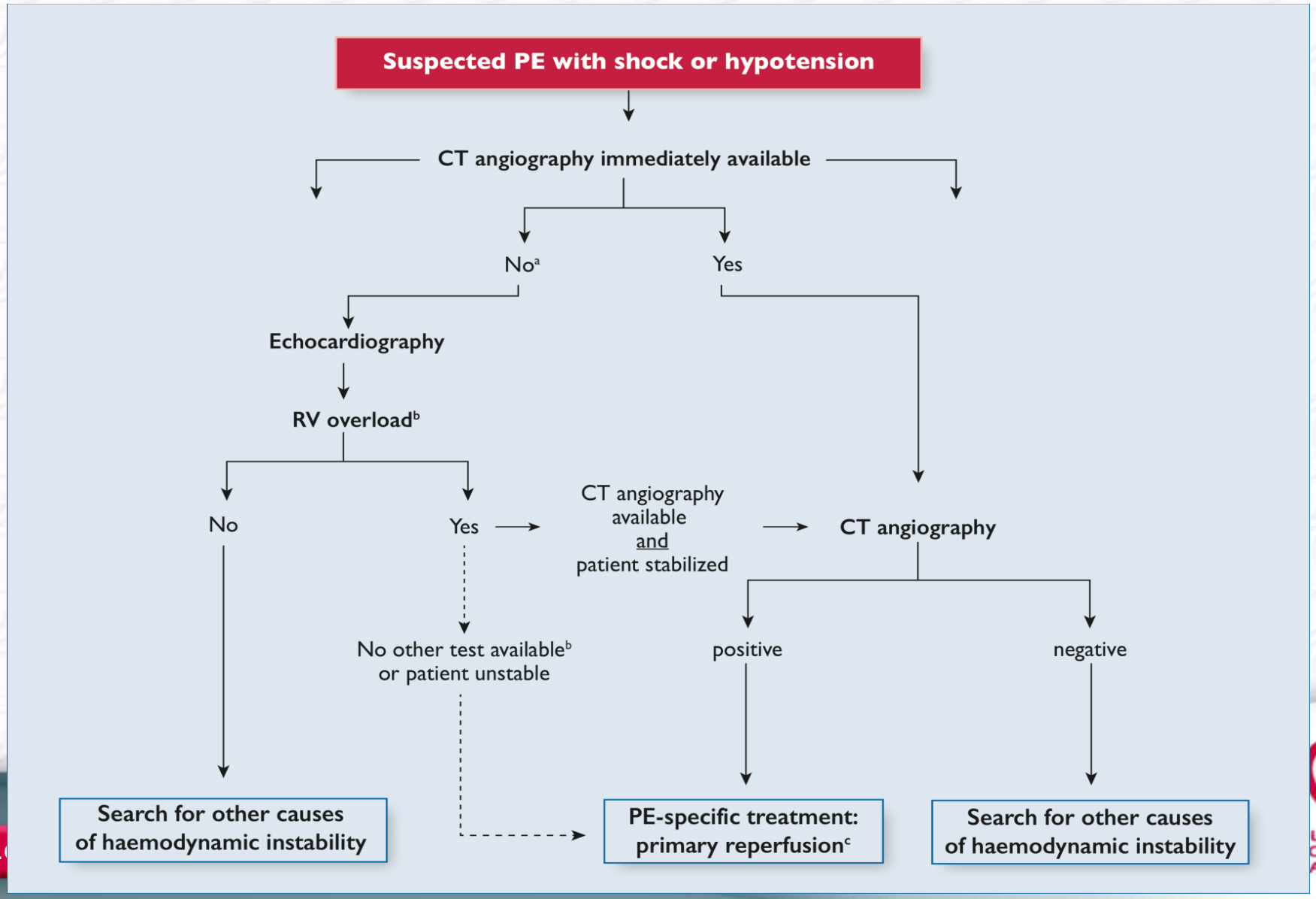
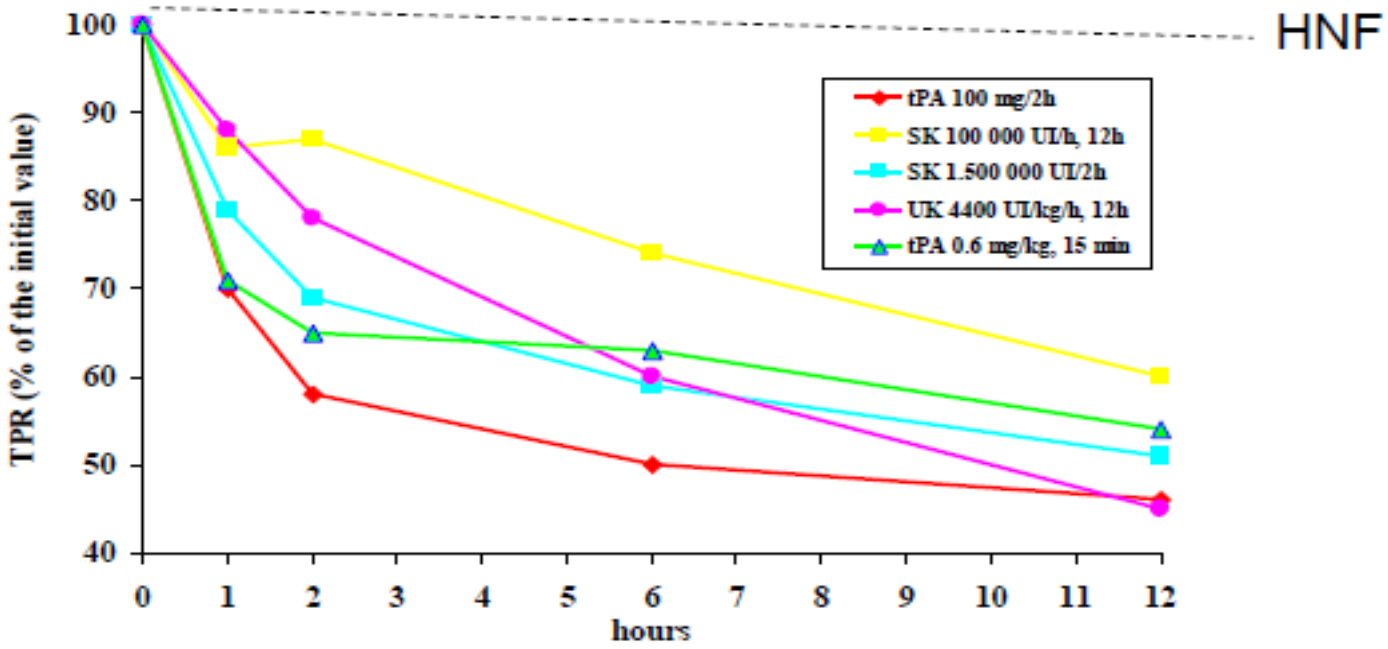
Diagnostic algorithm: high-risk PE



Traitement de l'embolie pulmonaire grave

- Fibrinolyse
  - Intérêt hémodynamique
    - ***Pour :***



Meyer 92, Sors 94, Meneveau 97, Meneveau 98

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

Recommendations for diagnosis

Suspected PE with shock or hypotension		
In suspected high-risk PE, as indicated by the presence of shock or hypotension, emergency CT angiography or bedside transthoracic echocardiography (depending on availability and clinical circumstances) is recommended for diagnostic purposes.	I	C
In patients with suspected high-risk PE and signs of RV dysfunction who are too unstable to undergo confirmatory CT angiography, bedside search for venous and/or pulmonary artery thrombi with CUS and/or TOE may be considered to further support the diagnosis of PE if immediately available.	IIb	C
Pulmonary angiography may be considered in unstable patients admitted directly to the catheterization laboratory, in case coronary angiography has excluded an acute coronary syndrome and PE emerges as a probable diagnostic alternative.	IIb	C

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

Recommendations for acute phase treatment

PE with shock or hypotension (high-risk)		
It is recommended to initiate intravenous anticoagulation with UFH without delay in patients with high-risk PE.	I	C
Thrombolytic therapy is recommended.	I	B
Surgical pulmonary embolectomy is recommended for patients in whom thrombolysis is contraindicated or has failed.[c]	I	C
Percutaneous catheter-directed treatment should be considered as an alternative to surgical pulmonary embolectomy for patients in whom full-dose systemic thrombolysis is contraindicated or has failed.[c]	IIa	C

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Approved thrombolytic regimens for pulmonary embolism	
Streptokinase	250 000 IU as a loading dose over 30 minutes, followed by 100 000 IU/h over 12–24 hours
	Accelerated regimen: 1.5 million IU over 2 hours
Urokinase	4400 IU/kg as a loading dose over 10 min, followed by 4400 IU/kg per hour over 12–24 hours
	Accelerated regimen: 3 million IU over 2 hours
rtPA	100 mg over 2 hours; or
	0.6 mg/kg over 15 minutes (maximum dose 50 mg)

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

Contraindications to thrombolytic therapy
Absolute contraindications:[a]
• Haemorrhagic stroke or stroke of unknown origin at any time
• Ischaemic stroke in the preceding 6 months
• Central nervous system damage or neoplasms
• Recent major trauma/surgery/head injury in the preceding 3 weeks
• Gastrointestinal bleeding within the last month
• Known bleeding risk
Relative contraindications
• Transient ischaemic attack in the preceding 6 months
• Oral anticoagulant therapy
• Pregnancy, or within one week postpartum
• Non-compressible puncture site
• Traumatic resuscitation
• Refractory hypertension (systolic blood pressure >180 mm Hg)
• Advanced liver disease
• Infective endocarditis
• Active peptic ulcer

Traitement symptomatique de l'EP grave

- Expansion volémique modérée (500 ml)
- Oxygénothérapie.
- Ventilation mécanique: Indications très rares: troubles de conscience et arrêt cardiaque. Faible VT, pas de PEP
- Noradrénaline
  - ↑ contractilité myocardique (ß1 +)
  - Vasoconstriction périphérique (α1 +) : ↑ PA systémique ⇒↑ débit coronaire droit
  - Si hypotension artérielle systémique
- Dopamine et dobutamine
  - ↑ IC sous dobu chez l'homme (*Jardin et al Crit Care Med 1985)*

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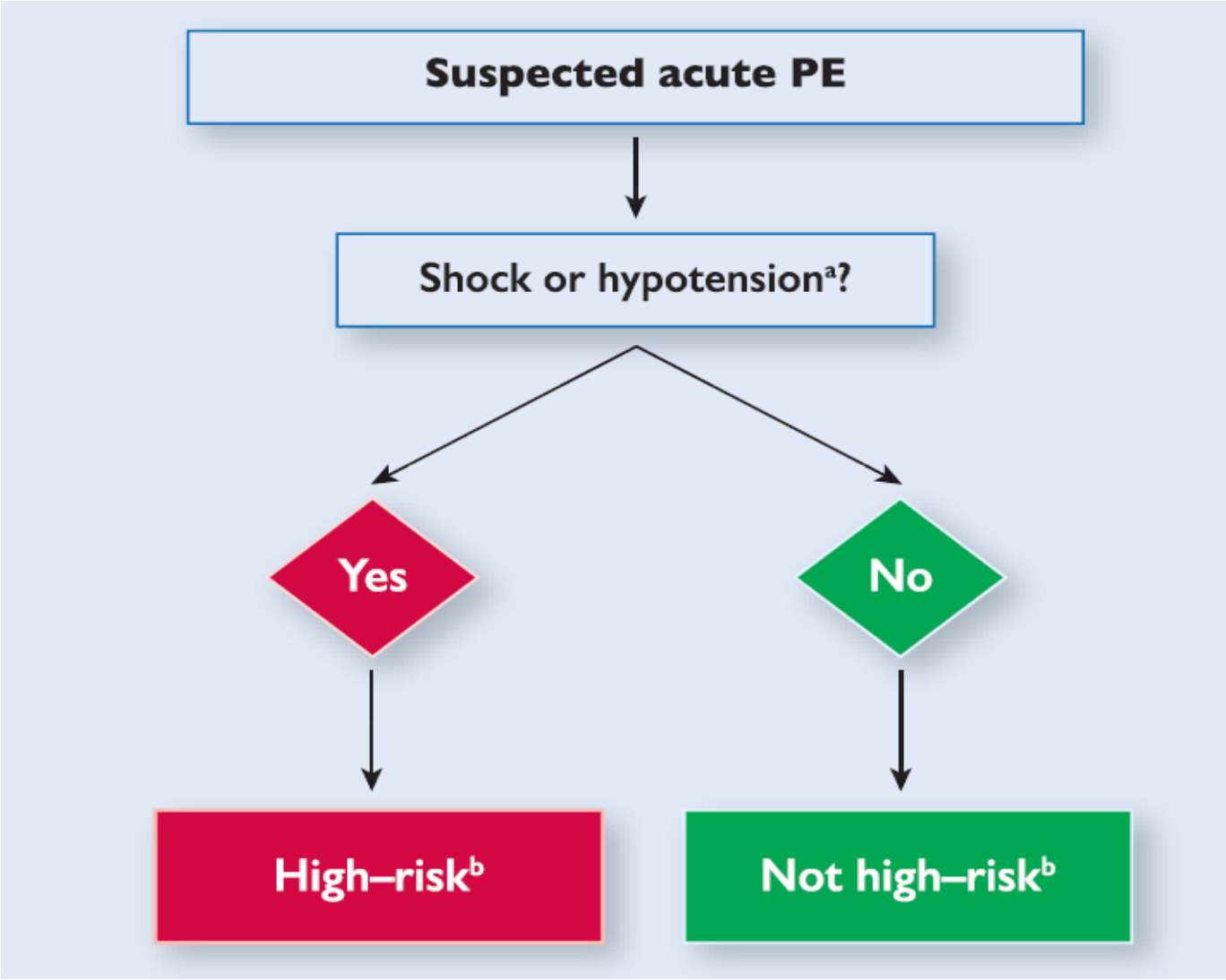
Initial risk stratification of acute PE



[a]Defined as systolic blood pressure <90 mmHg, or a systolic pressure drop by ≥40 mmHg, for >15 minutes, if not caused by new-onset arrhythmia, hypovolaemia, or sepsis.
[b]Based on the estimated PE-related in-hospital or 30-day mortality.

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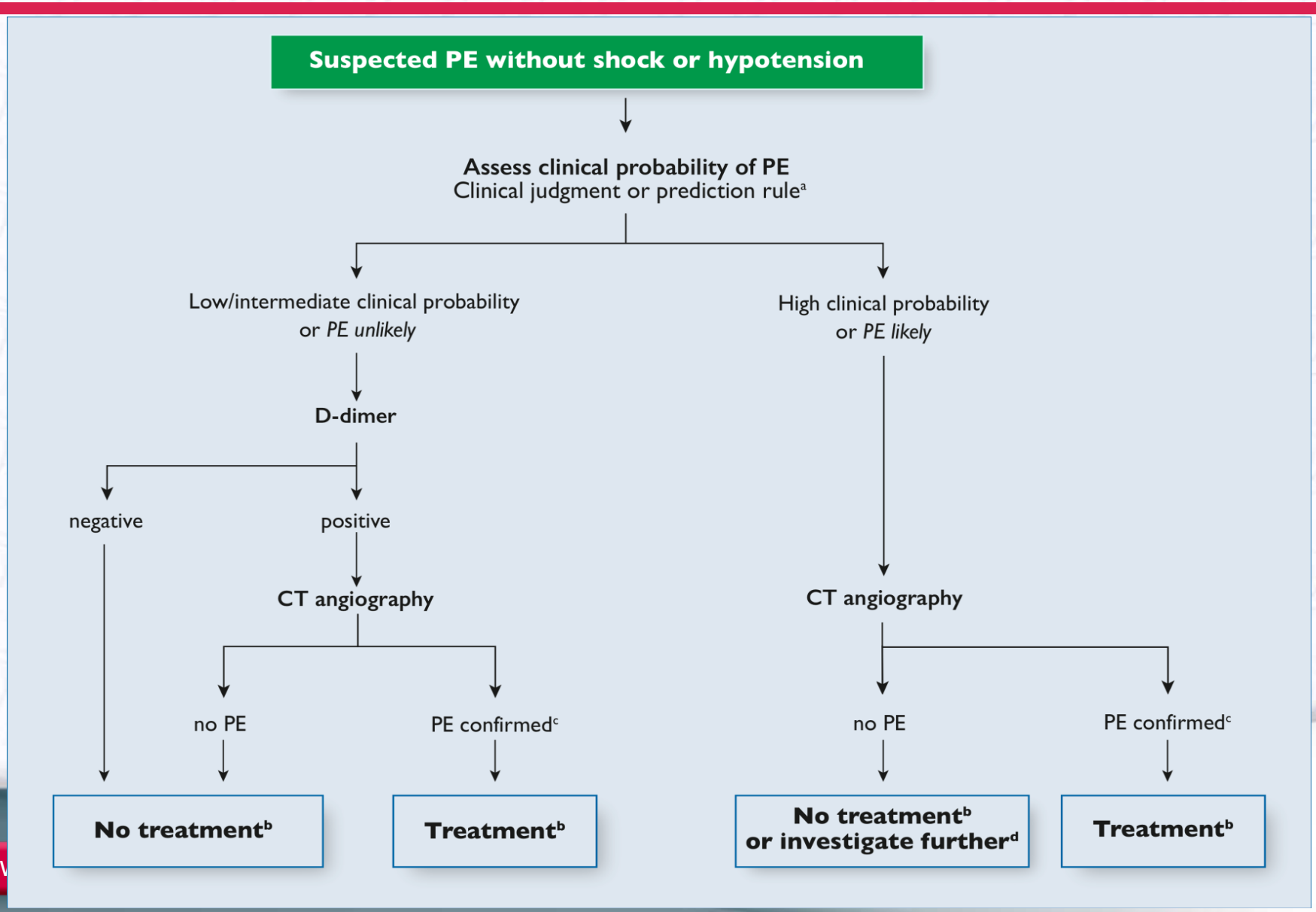
Diagnostic algorithm: not high-risk PE



Clinical prediction rules for pulmonary embolism		
	Clinical decision rule points	
Wells rule	Original version	Simplified version
Previous PE or DVT	1.5	1
Heart rate ≥100 b.p.m.	1.5	1
Surgery or immobilization within the past 4 weeks	1.5	1
Haemoptysis	1	1
Active cancer	1	1
Clinical signs of DVT	3	1
Alternative diagnosis less likely than PE	3	1
Clinical probability		
Three-level score		
Low	0–1	N/A
Intermediate	2–6	N/A
High	≥7	N/A
Two-level score		
PE unlikely	0–4	0–1
PE likely	≥5	≥2

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Clinical prediction rules for pulmonary embolism (cont.)		
	Clinical decision rule points	
Revised Geneva score	Original version	Simplified version
Previous DVT or PE	3	1
Heart rate 75–94 b.p.m. ≥95 b.p.m.	 3 5	 1 2
Surgery or fracture within the past month	2	1
Haemoptysis	2	1
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
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

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Clinical prediction rules for pulmonary embolism (cont.)		
	Clinical decision rule points	
Revised Geneva score	Original version	Simplified version
Previous DVT or PE	3	1
Heart rate 75–94 b.p.m. ≥95 b.p.m.	 3 5	 1 2
Surgery or fracture within the past month	2	1
Haemoptysis	2	1
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
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

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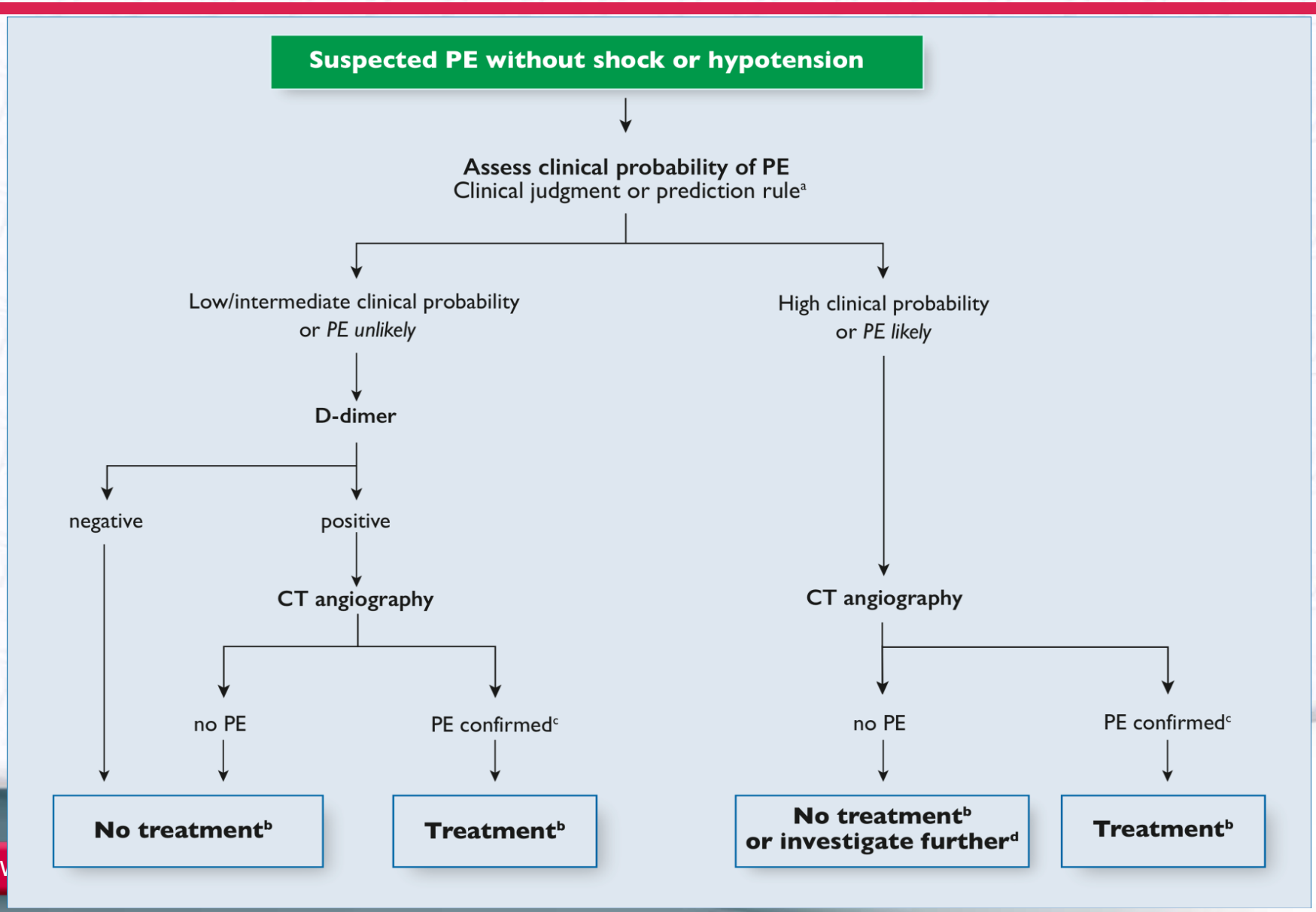

Age-Adjusted D-Dimer Cutoff Levels to Rule Out Pulmonary Embolism:The ADJUST-PE Study. *Righini et al, JAMA 2014*

- < 50 years, PE was excluded in those with a D-dimer value lower than 500 µg/L.
- > 50 years or older, the D-dimer test result was considered negative in those with a D-dimer value lower than their age multiplied by 10.

Table 3. Study Results According to D-Dimer Assays

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	1/8	0 0.1 (0.0-0.7)	337	1/331	0.3 (0.1-1.7)

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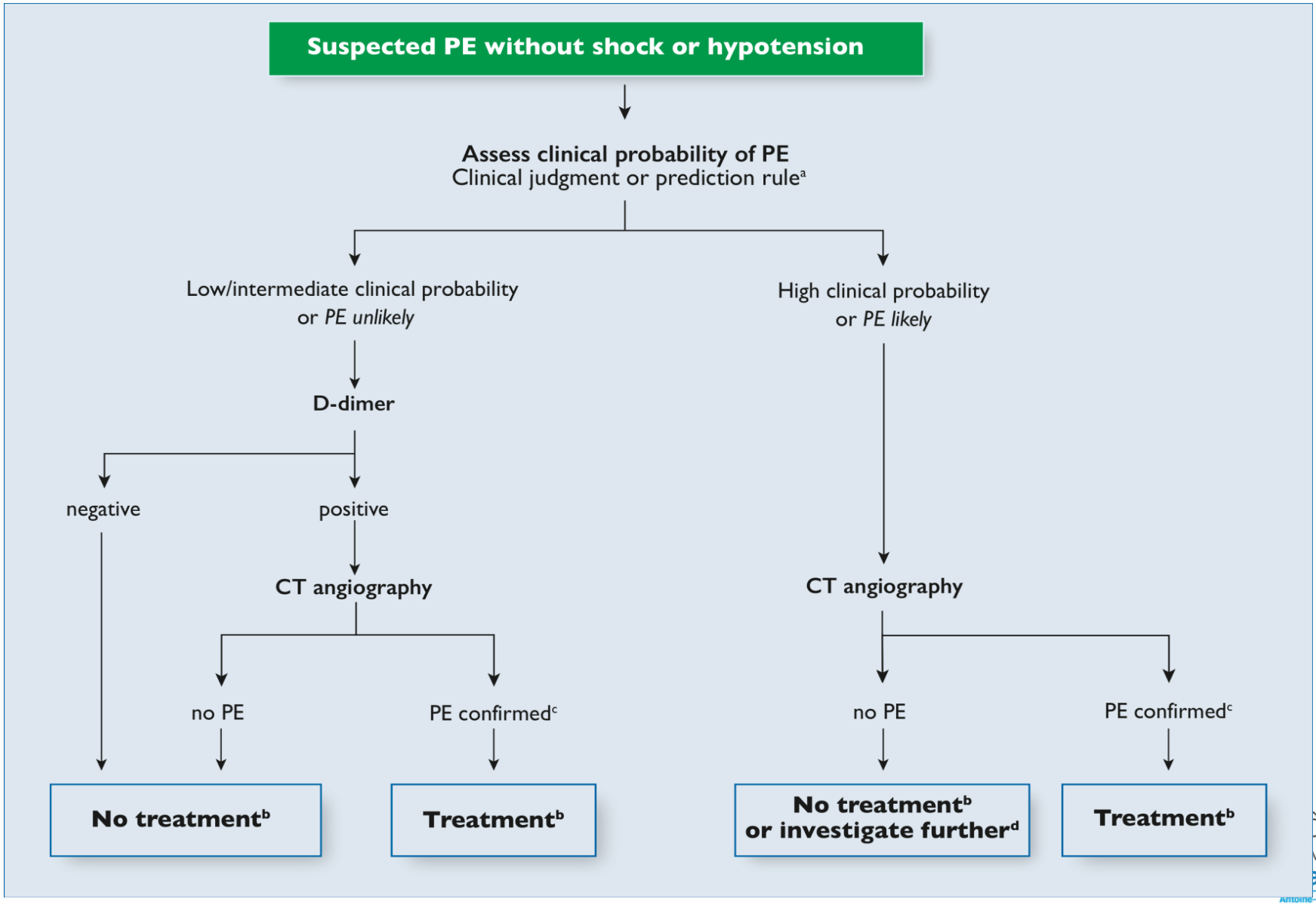
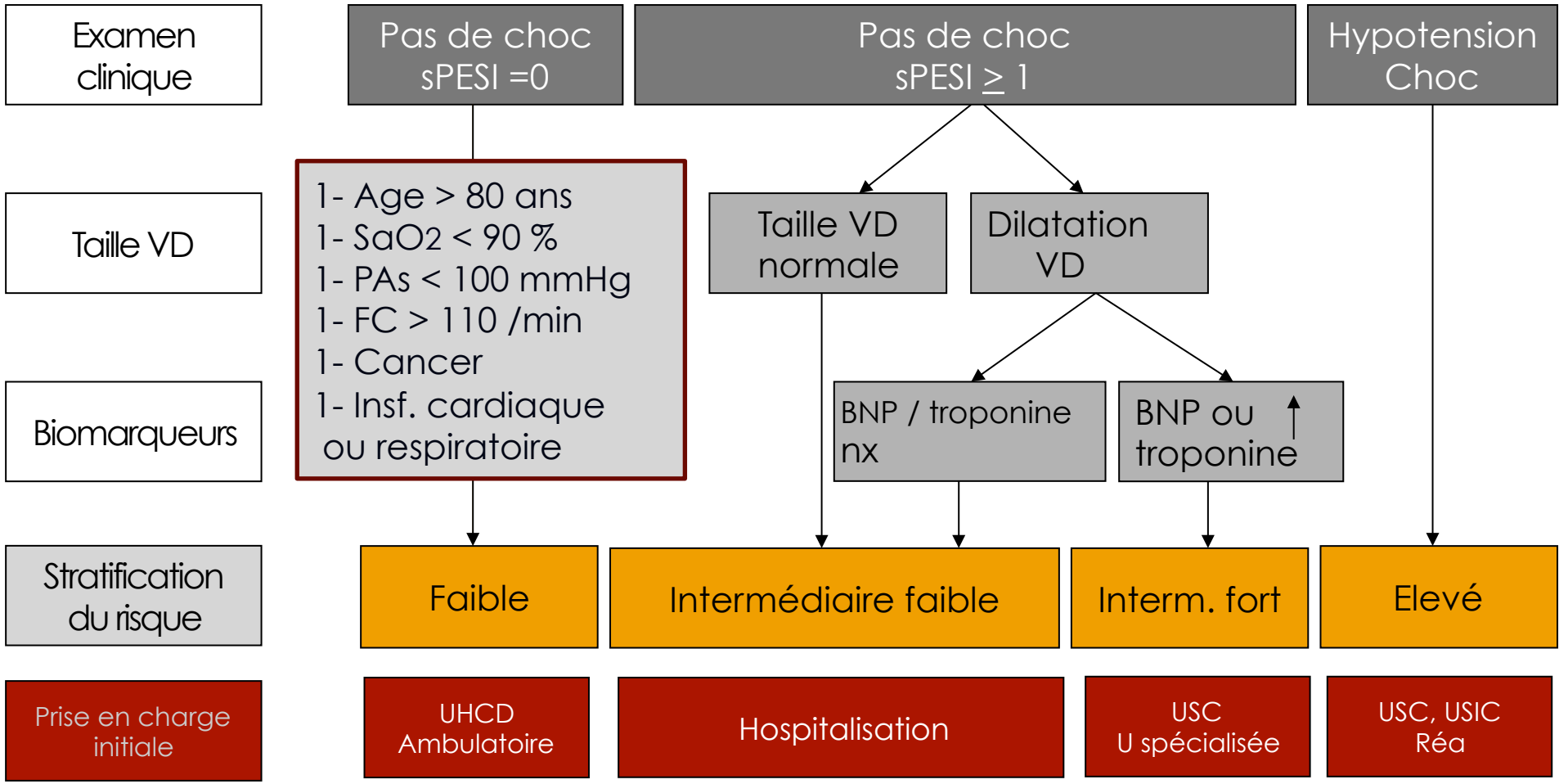
Diagnostic algorithm: not high-risk PE



Phase initiale de l' EP

Lieu et conditions de prise en charge



Recommendations for diagnosis

Suspected PE with shock or hypotension		
In suspected high-risk PE, as indicated by the presence of shock or hypotension, emergency CT angiography or bedside transthoracic echocardiography (depending on availability and clinical circumstances) is recommended for diagnostic purposes.	I	C
In patients with suspected high-risk PE and signs of RV dysfunction who are too unstable to undergo confirmatory CT angiography, bedside search for venous and/or pulmonary artery thrombi with CUS and/or TOE may be considered to further support the diagnosis of PE if immediately available.	IIb	C
Pulmonary angiography may be considered in unstable patients admitted directly to the catheterization laboratory, in case coronary angiography has excluded an acute coronary syndrome and PE emerges as a probable diagnostic alternative.	IIb	C

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Recommendations for diagnosis

Suspected PE without shock or hypotension		
The use of validated criteria for diagnosing PE is recommended.	I	B
Clinical evaluation		
It is recommended to base the diagnostic strategy on clinical probability assessed either by clinical judgement or a validated prediction rule.	I	A
D-dimer		
Plasma D-dimer measurement 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, preferably using a highly sensitive assay.	I	A
In low clinical probability or PE-unlikely patients, normal D-dimer level using either a highly or moderately sensitive assay excludes PE.	I	A
Further testing may be considered in intermediate probability patients with a negative moderately sensitive assay.	IIb	C
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	B

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Recommendations for diagnosis

CT angiography[c]		
Normal CT angiography safely excludes PE in patients with low or intermediate clinical probability or PE-unlikely.	I	A
Normal CT angiography may safely exclude PE in patients with high clinical probability or PE-likely.	IIa	B
CT angiography showing a segmental or more proximal thrombus confirms PE.	I	B
Further testing to confirm PE may be considered in case of isolated subsegmental clots.	IIb	C
Scintigraphy		
Normal perfusion lung scintigram excludes PE.	I	A
High probability V/Q scan confirms PE.	IIa	B
A non-diagnostic V/Q scan may exclude PE when combined with a negative proximal CUS in patients with low clinical probability or PE-unlikely.	IIa	B

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Recommendations for diagnosis

Lower limb CUS		
Lower limb CUS in search of DVT may be considered in selected patients with suspected PE to obviate the need for further imaging tests if the result is positive.	IIb	B
CUS showing a proximal DVT in a patient with clinical suspicion of PE confirms PE.	I	B
If CUS shows only a distal DVT, further testing should be considered to confirm PE.	IIa	B
Pulmonary angiography		
Pulmonary angiography may be considered in cases of discrepancy between clinical evaluation and results of non-invasive imaging tests.	IIb	C
MRA		
MRA should not be used to rule out PE.	III	A

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Recommendations for diagnosis

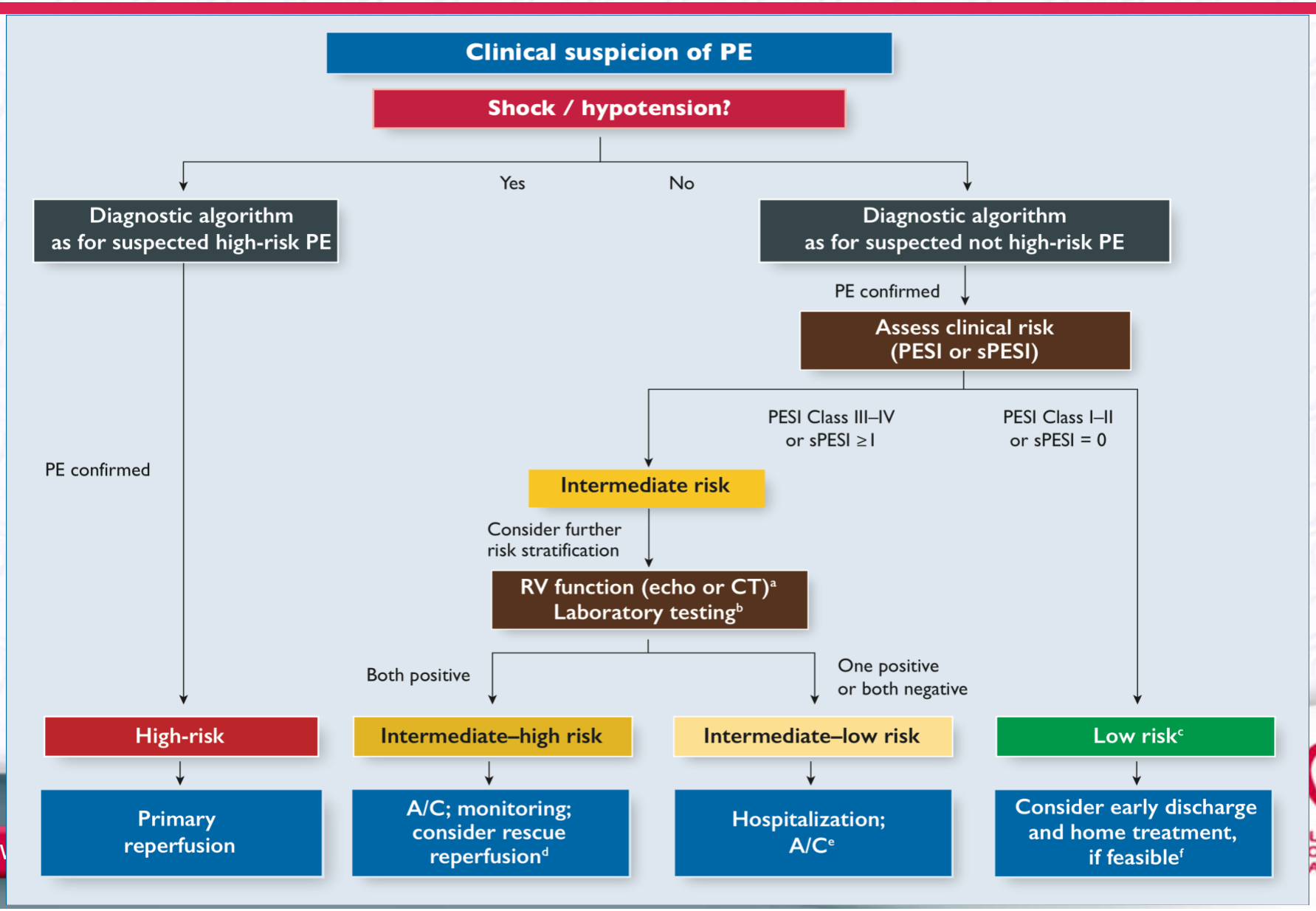
Lower limb CUS		
Lower limb CUS in search of DVT may be considered in selected patients with suspected PE to obviate the need for further imaging tests if the result is positive.	**IIb**	**B**
CUS showing a proximal DVT in a patient with clinical suspicion of PE confirms PE.	**I**	**B**
If CUS shows only a distal DVT, further testing should be considered to confirm PE.	**IIa**	**B**
Pulmonary angiography		
Pulmonary angiography may be considered in cases of discrepancy between clinical evaluation and results of non-invasive imaging tests.	**IIb**	**C**
MRA		
MRA should not be used to rule out PE.	**III**	**A**

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

Diagnostic: cas particuliers

- En cas de thrombi sous-segmentaire isolés visualisés à l'angioscanner, d'autres examens doivent être discutés avant de confirmer le diagnostic d'EP (IIb-C).
- En cas de suspicion d'EP, dans certains cas, un écho-doppler veineux des M Infs peut être réalisé: s'il existe une TVP proximale, le diagnostic est établi sans autre examen (I-B)
- L'IRM ne doit pas être utilisée pour éliminer une EP (III-A)

Risk-adjusted management algorithm



Original and simplified pulmonary embolism severity index (PESI)

Parameter	Original version	Simplified version
Age	Age in years	1 point (if age >80 years)
Male sex	+10 points	–
Cancer	+30 points	1 point
Chronic heart failure	+10 points	1 point
Chronic pulmonary disease	+10 points	
Pulse rate ≥110 b.p.m.	+20 points	1 point
Systolic blood pressure <100 mmHg	+30 points	1 point
Respiratory rate >30 breaths per minute	+20 points	–
Temperature <36 °C	+20 points	–
Altered mental status	+60 points	–
Arterial oxyhaemoglobin saturation <90%	+20 points	1 point

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

Original and simplified pulmonary embolism severity index (PESI)

Parameter	Original version	Simplified version
	Risk strata[a]	
	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%) 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%)	0 points = 30-day mortality risk 1.0% (95% CI 0.0%–2.1%) ≥1 point(s) = 30-day mortality risk 10.9% (95% CI 8.5%–13.2%)

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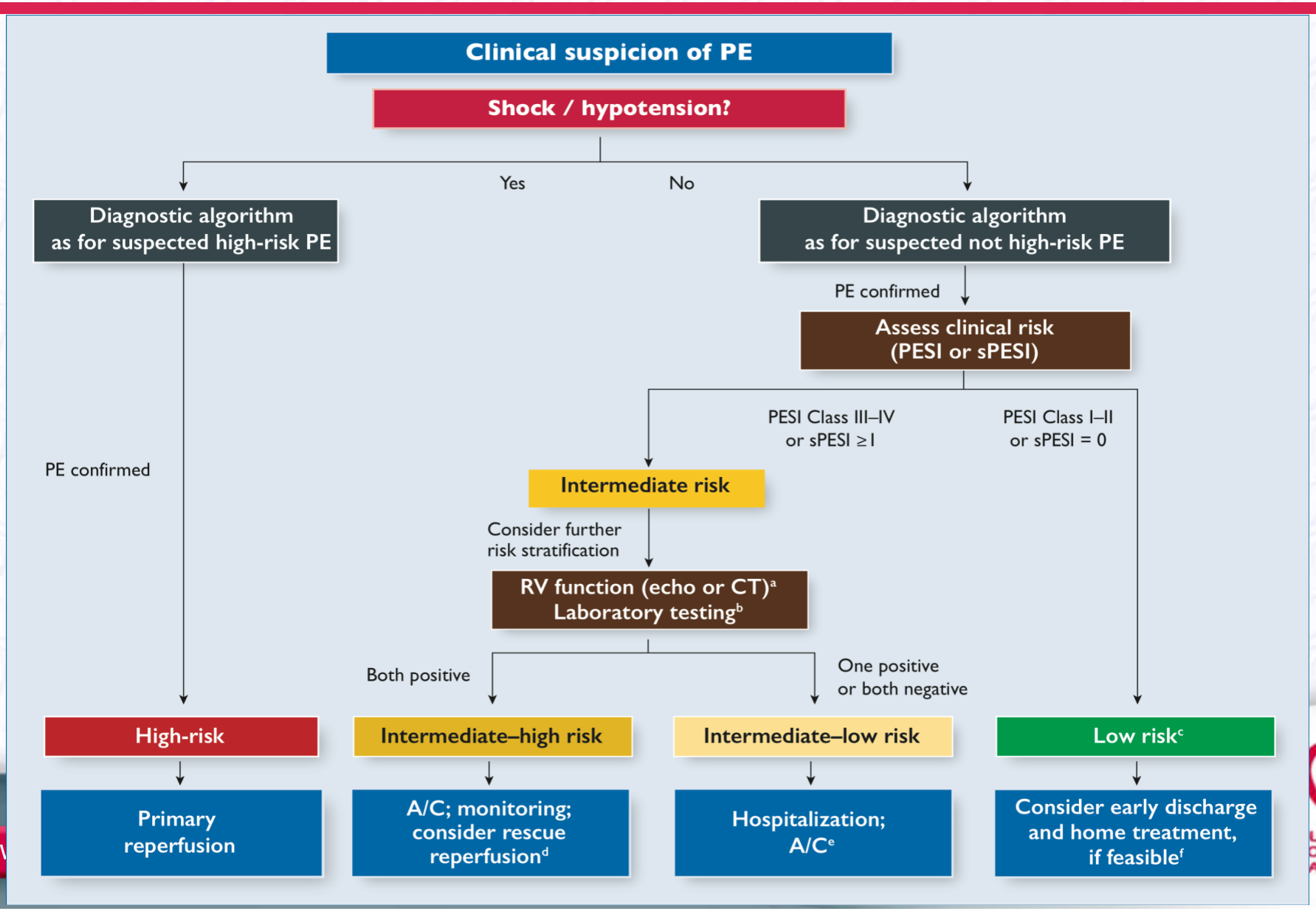
Risk-adjusted management algorithm



EP: prise en charge ambulatoire

- Le score PESI permet d'identifier cliniquement des patients à faible risque de mortalité et de complication
- Prise en charge ambulatoire de patients ayant une EP et un score de PESI « faible risque » est au moins aussi efficace et sûre que la prise en charge conventionnelle (1 essai randomisé / 344 pts. *Aujezsky Lancet 2011*)
- Mais, le score ne fait pas tout. Il est recommandé :
  - ⇨ Diagnostic de certitude
  - ⇨ EDUCATION+++
  - ⇨ Evaluation des facteurs de risque de saignement, de l'environnement social
  - ⇨ Mise en place de structures de référence

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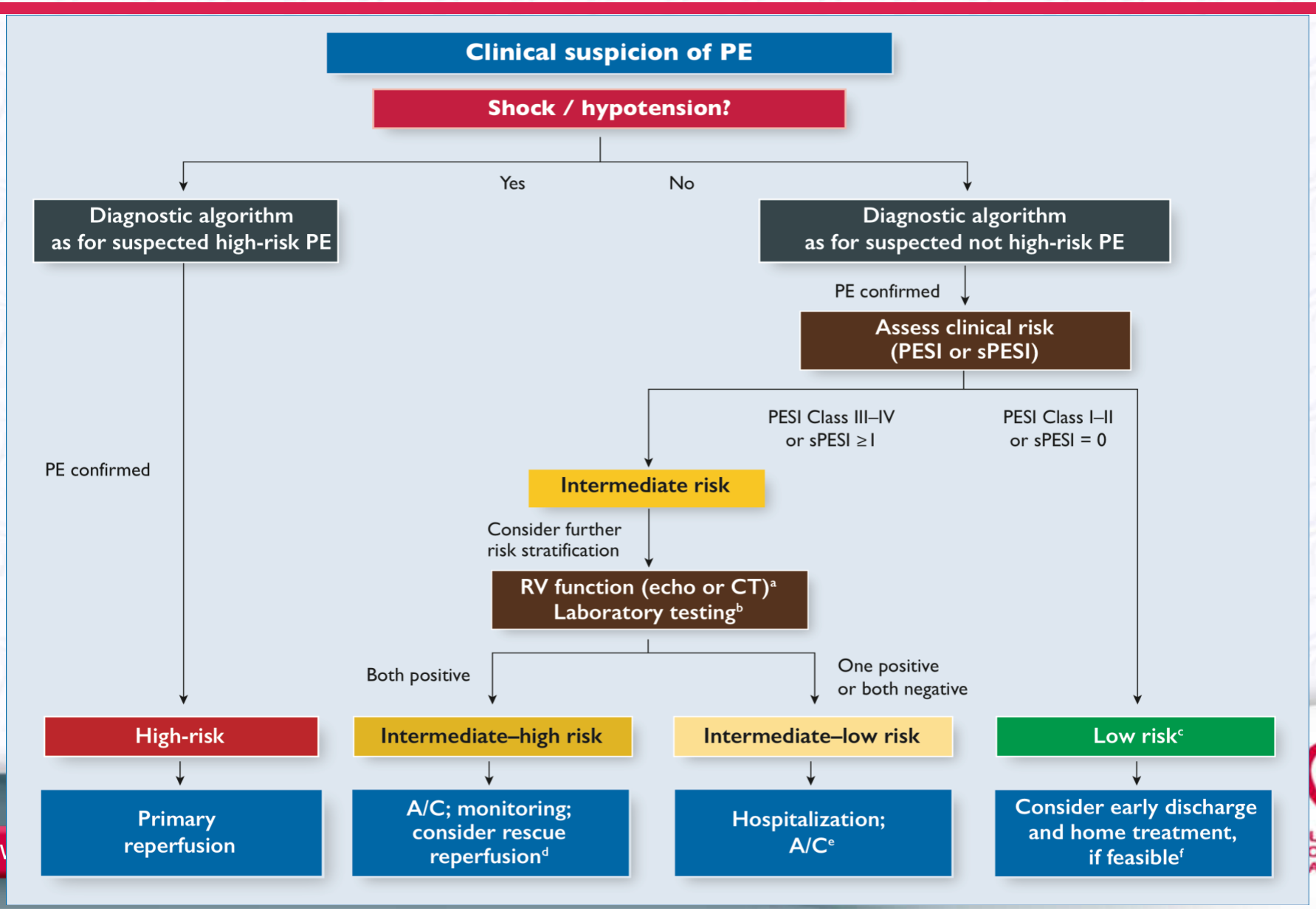
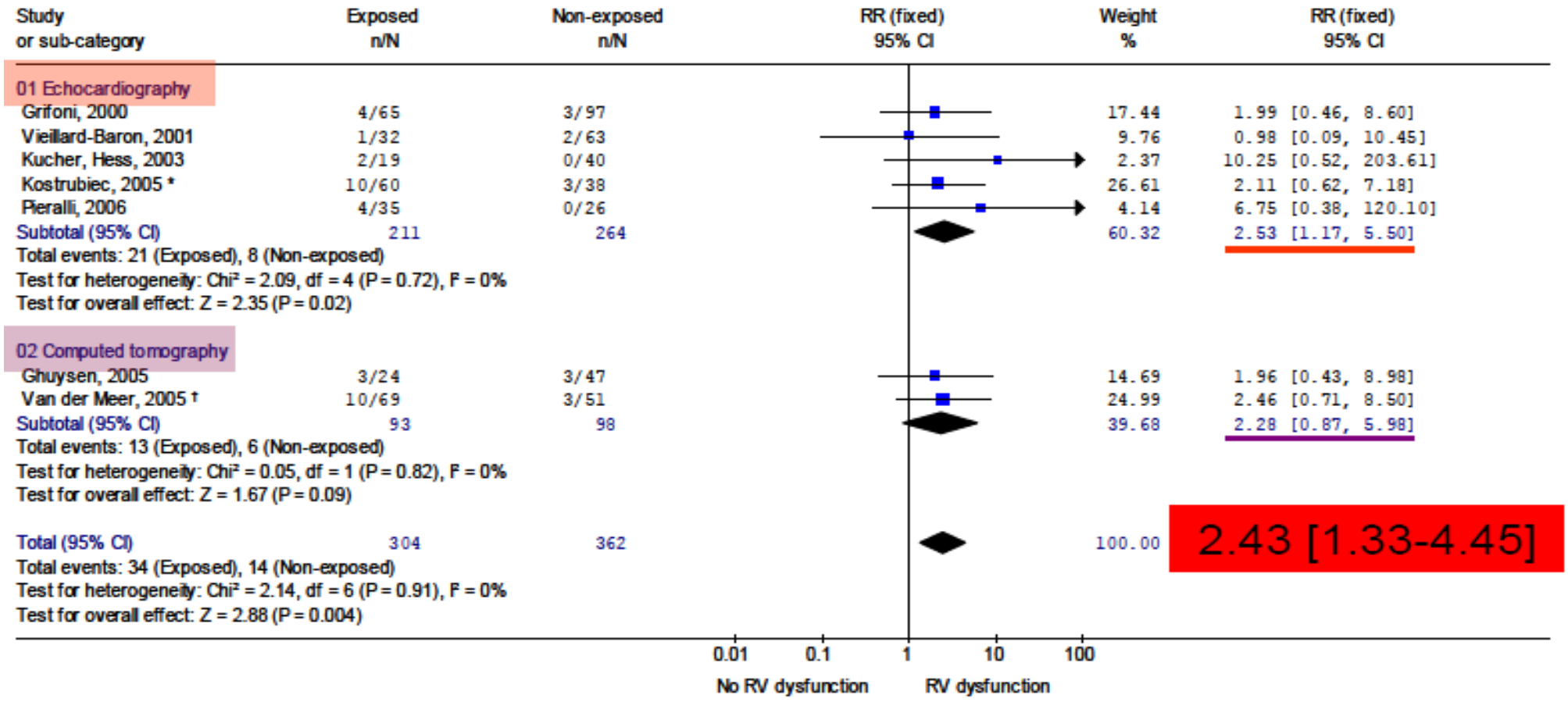
Risk-adjusted management algorithm



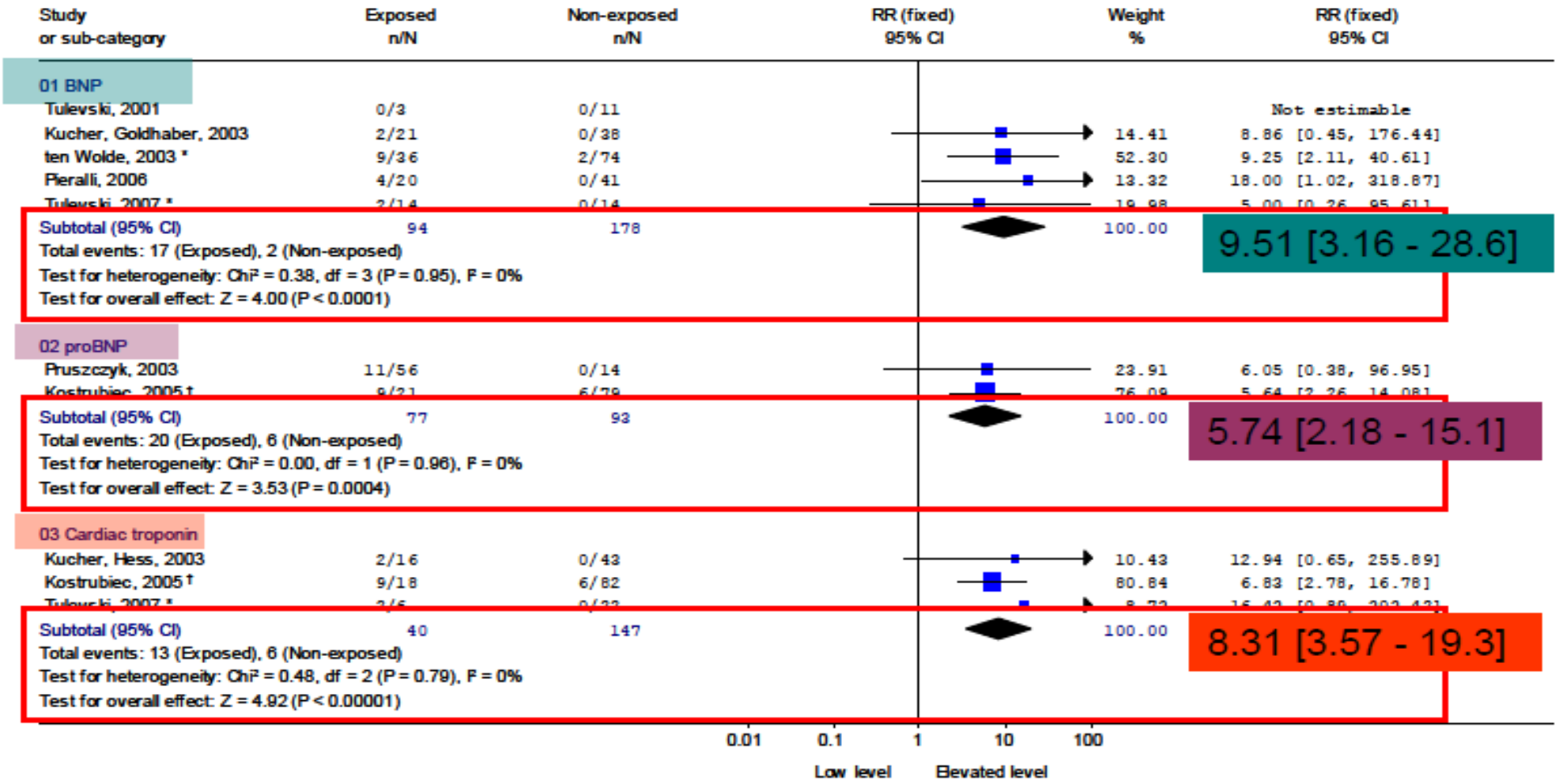
Mortalité précoce: Valeur pronostique de la dysfonction du VD chez les patients ayant une EP sans choc

Dysfonction droite : synthèse imagerie



Sanchez et al, Eur Heart J 2008

Biomarqueurs : synthèse



Sanchez et al,Eur Heart J 2008

From: Acute Pulmonary EmbolismRisk Stratification in Acute Pulmonary Embolism: External Validation of an Integrated Risk Stratification Model

Chest. 2013;144(5):1539-1545. doi:10.1378/chest.12-2938

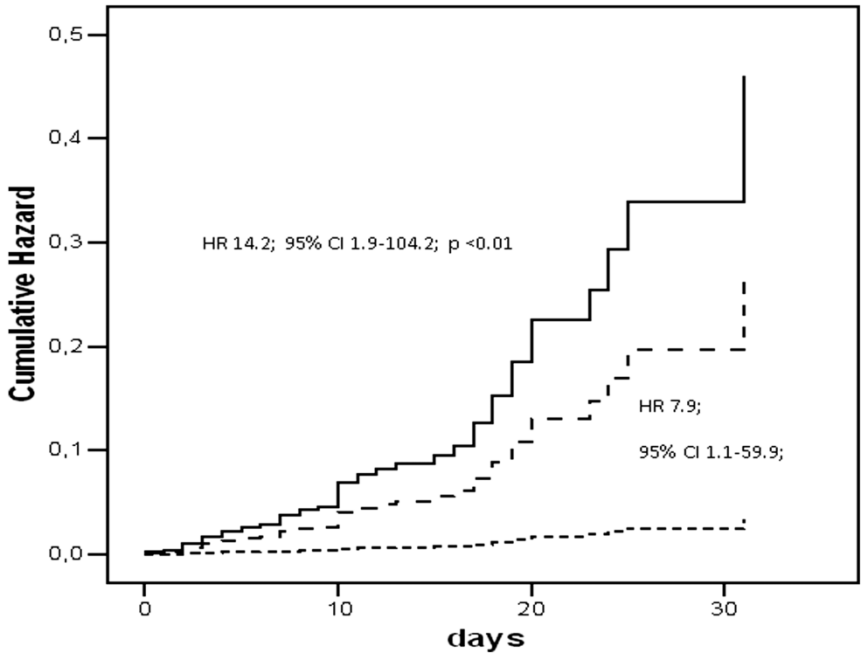


Figure Legend:

Adjusted cumulative hazard for in-hospital death or clinical deterioration in hemodynamically stable patients with acute pulmonary embolism and echocardiography performed within 48 h and troponin level measured on hospital admission. The solid line represents patients with right ventricular dysfunction by echocardiography and elevated troponin levels, the dashed line represents patients with right ventricular dysfunction or elevated troponin levels, and the dotted line represents patients without right ventricular dysfunction and normal troponin levels. HR = hazard ratio.

Fibrinolyse dans l'EP de gravité intermédiaire

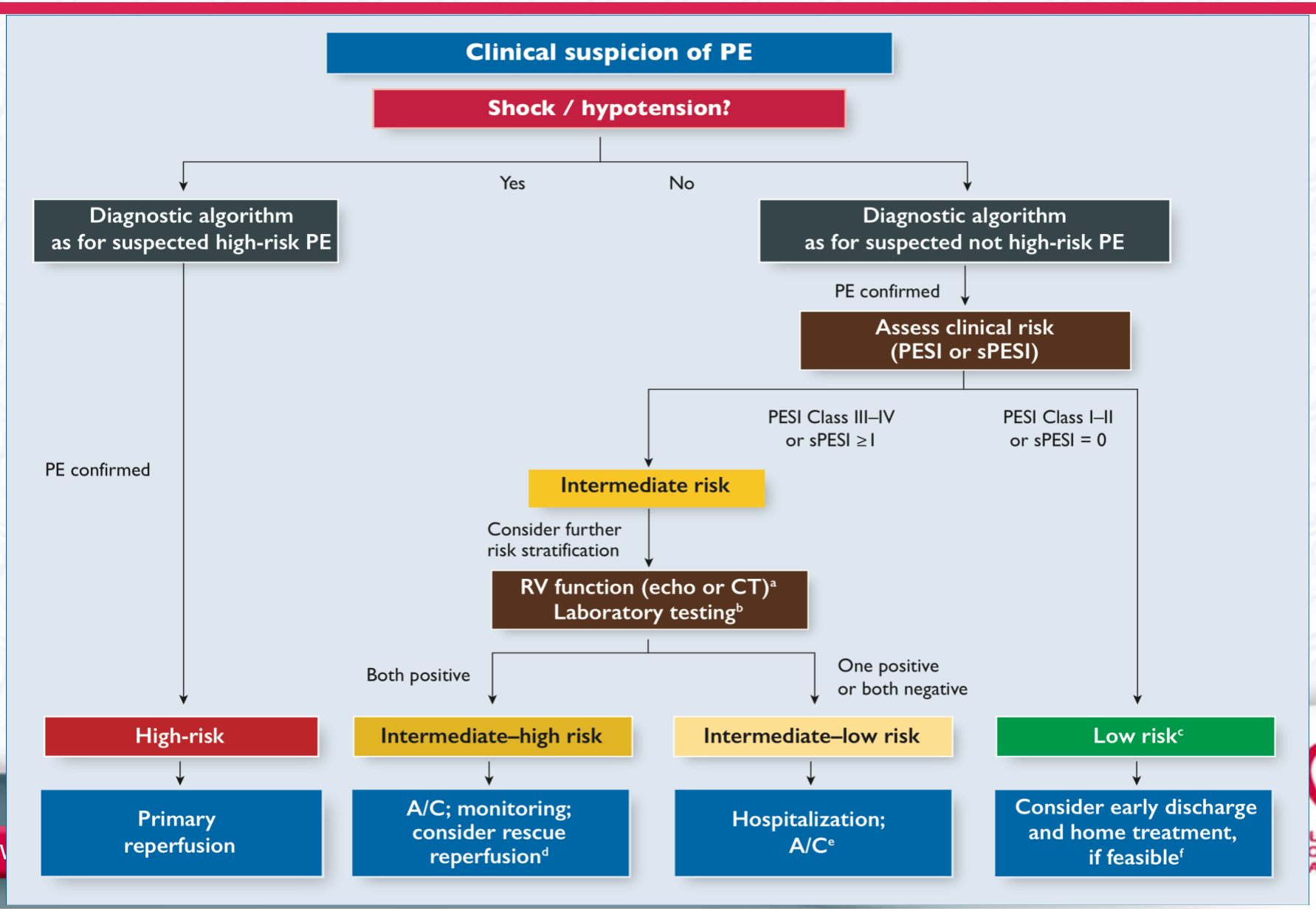
Meta-analyse, 6 études ayant inclus des malades **stables**

(EP non exclusivement sub-massive)

	Thrombolyse (n = 246)	Héparine (n = 248)	Odds Ratio
Récidives	2.0%	2.8%	0.76 (0.28-2.08)
Décès	3.3%	2.4%	1.16 (0.44-3.05)
Hémorragie	2.4%	3.2%	0.67 (0.24-1.86)

Wan et al. Circulation 2004; 110: 744-9:

Risk-adjusted management algorithm



Pulmonary Embolism Thrombolysis Study

an investigator-initiated, investigator-sponsored trial

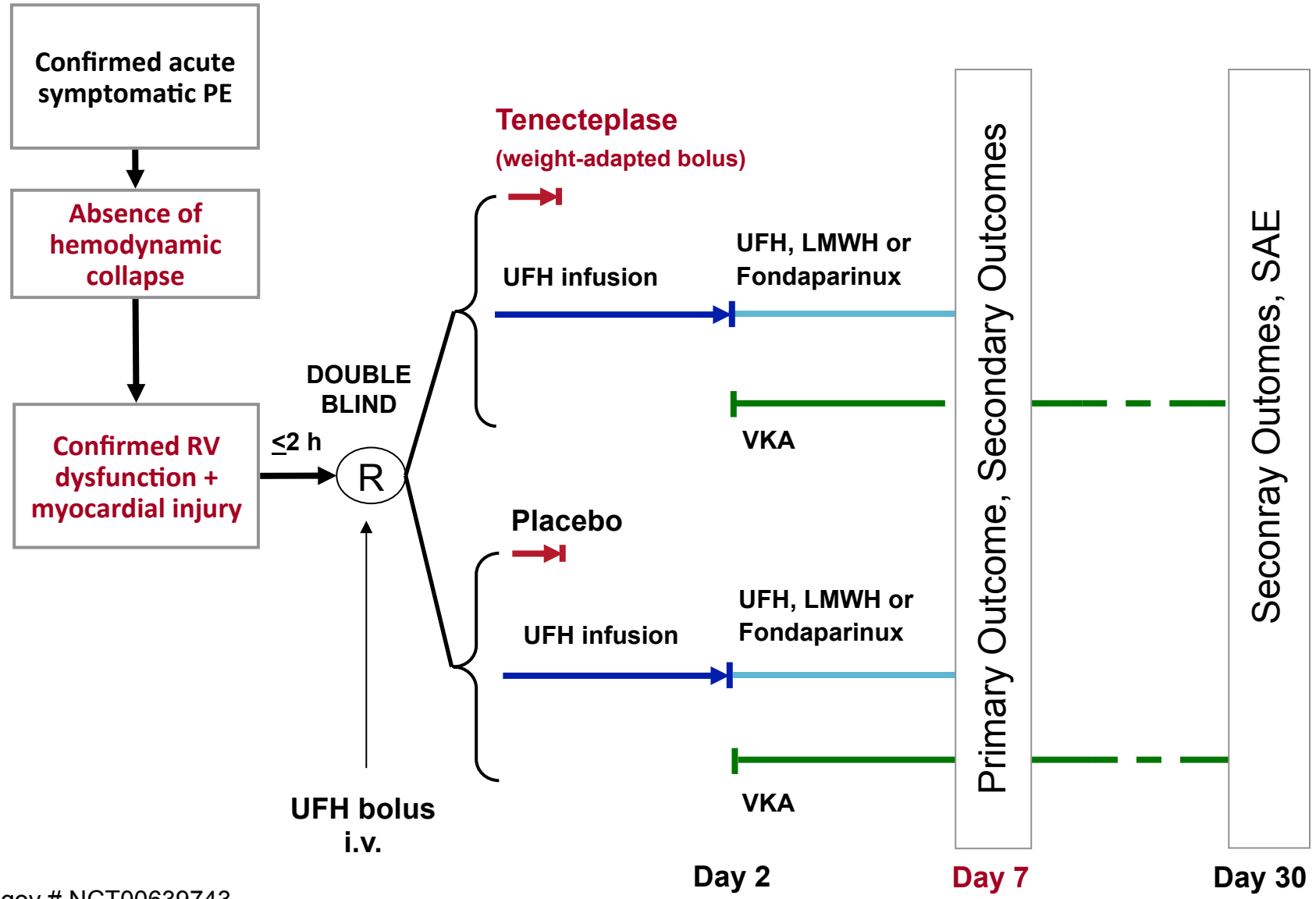
The PEITHO Investigators

ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

Bundesministerium für Bildung und Forschung

ClinicalTrials.gov # NCT00639743
EudraCT # 2006-005328-18

PEITHO: Overview of study design

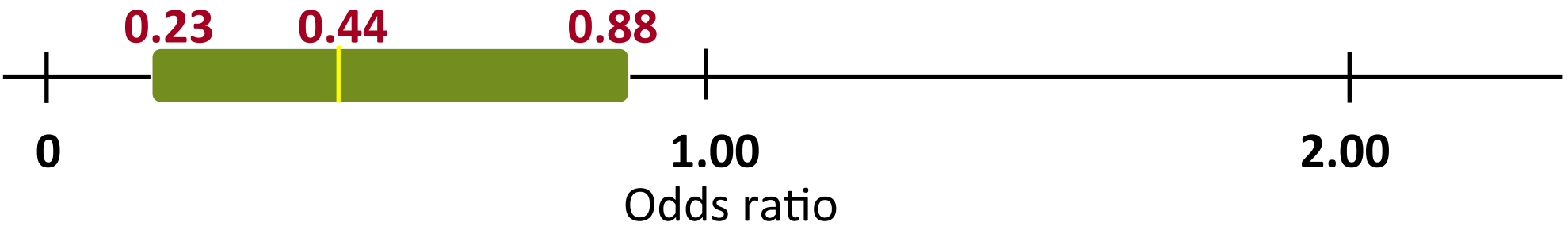


ClinicalTrials.gov # NCT00639743
EudraCT # 2006-005328-18

S Konstantinides for the PEITHO Steering Committee. Am Heart J 2012;163:33-38.e1

PEITHO: Primary efficacy outcome

	Tenecteplase (n=506)		Placebo (n=499)		*P* value
	n	(%)	n	(%)	
All-cause mortality or hemodynamic collapse within 7 days of randomization	13	(2.6)	28	(5.6)	0.015



Thrombolysis superior

ITT population

PEITHO: Secondary efficacy outcomes

	Tenecteplase (n=506)		Placebo (n=499)		*P* value
	n	(%)	n	(%)	
All-cause mortality within 7 days	6	(1.2)	9	(1.8)	0.43
Hemodynamic collapse within 7 days	8	(1.6)	25	(5.0)	0.002

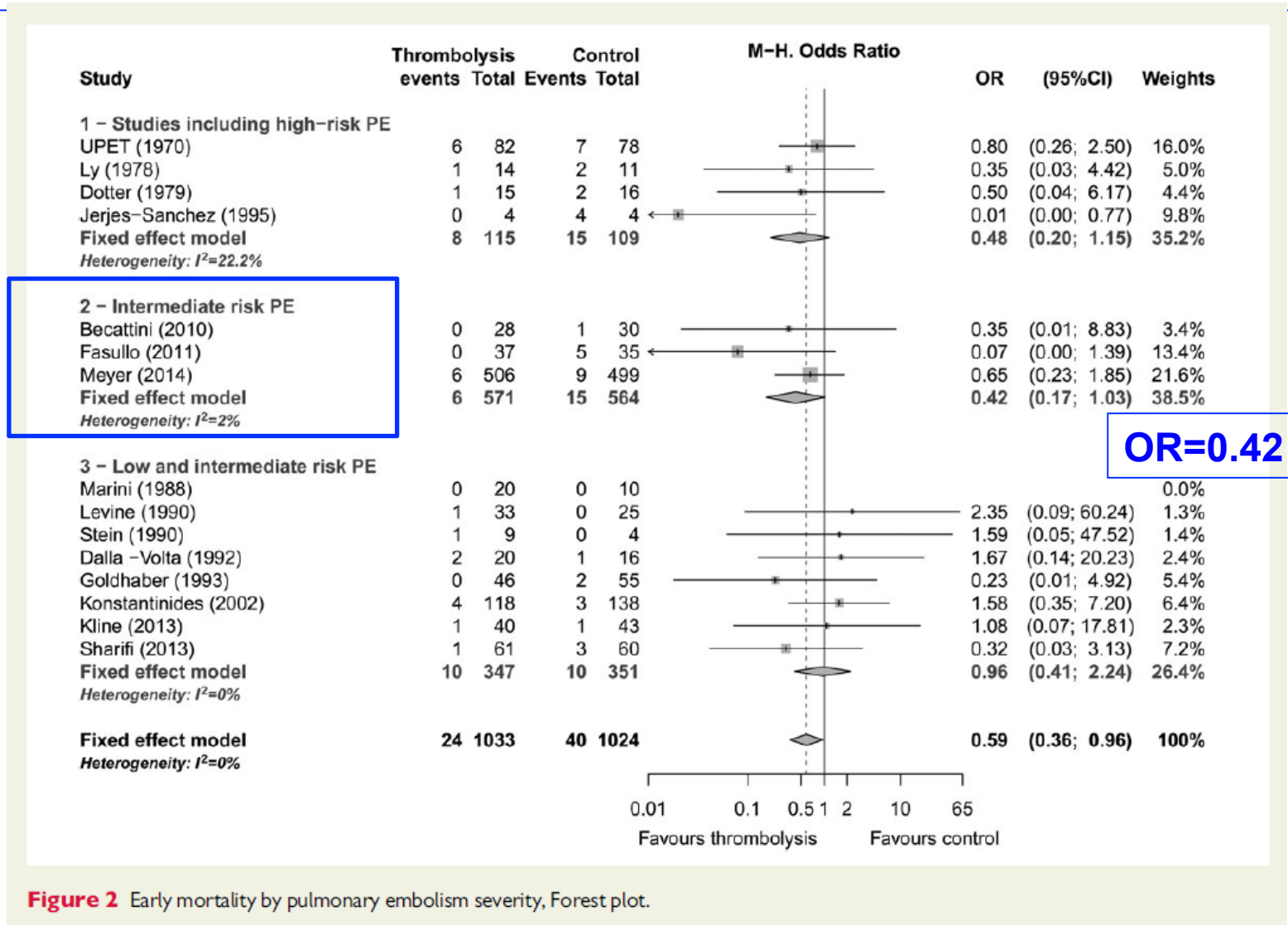
ITT population

PEITHO: Secondary efficacy outcomes

	Tenecteplase (n=506)		Placebo (n=499)		*P* value
	n	(%)	n	(%)	
All-cause mortality within 7 days	**6**	**(1.2)**	**9**	**(1.8)**	**0.43**
Hemodynamic collapse within 7 days	**8**	**(1.6)**	**25**	**(5.0)**	**0.002**
Need for CPR	1		5		
Hypotension / blood pressure drop	8		18		
Catecholamines	3		14		
Resulted in death	1		6		

ITT population

Systemic thrombolytic therapy for acute pulmonary embolism: a systematic review and meta-analysis. *Marti et al, EHJ 2015*



OR=0.42 [0.17-1.03]

Figure 2 Early mortality by pulmonary embolism severity, Forest plot.

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Systemic thrombolytic therapy for acute pulmonary embolism: a systematic review and meta-analysis. *Marti et al, EHJ 2015*

Table 3 Safety outcomes, subgroup analyses

	All studies			Alteplase	Tenecteplase	Other thrombolytics	Group difference
	OR (95% CI)	*P*-value	I^2 (%)	OR (95% CI)	OR (95% CI)	OR (95% CI)	*P*-value
Major bleeding	2.91 (1.95 to 4.36)	<0.001	25	1.07 (0.43 to 2.62)	5.02 (2.72 to 9.26)	2.16 (1.03 to 4.54)	0.02
Fatal/intracranial haemorrhage	3.18 (1.25 to 8.11)	0.008	0	1.09 (0.27 to 4.40)	7.32 (1.64 to 32.63)	NA	0.07

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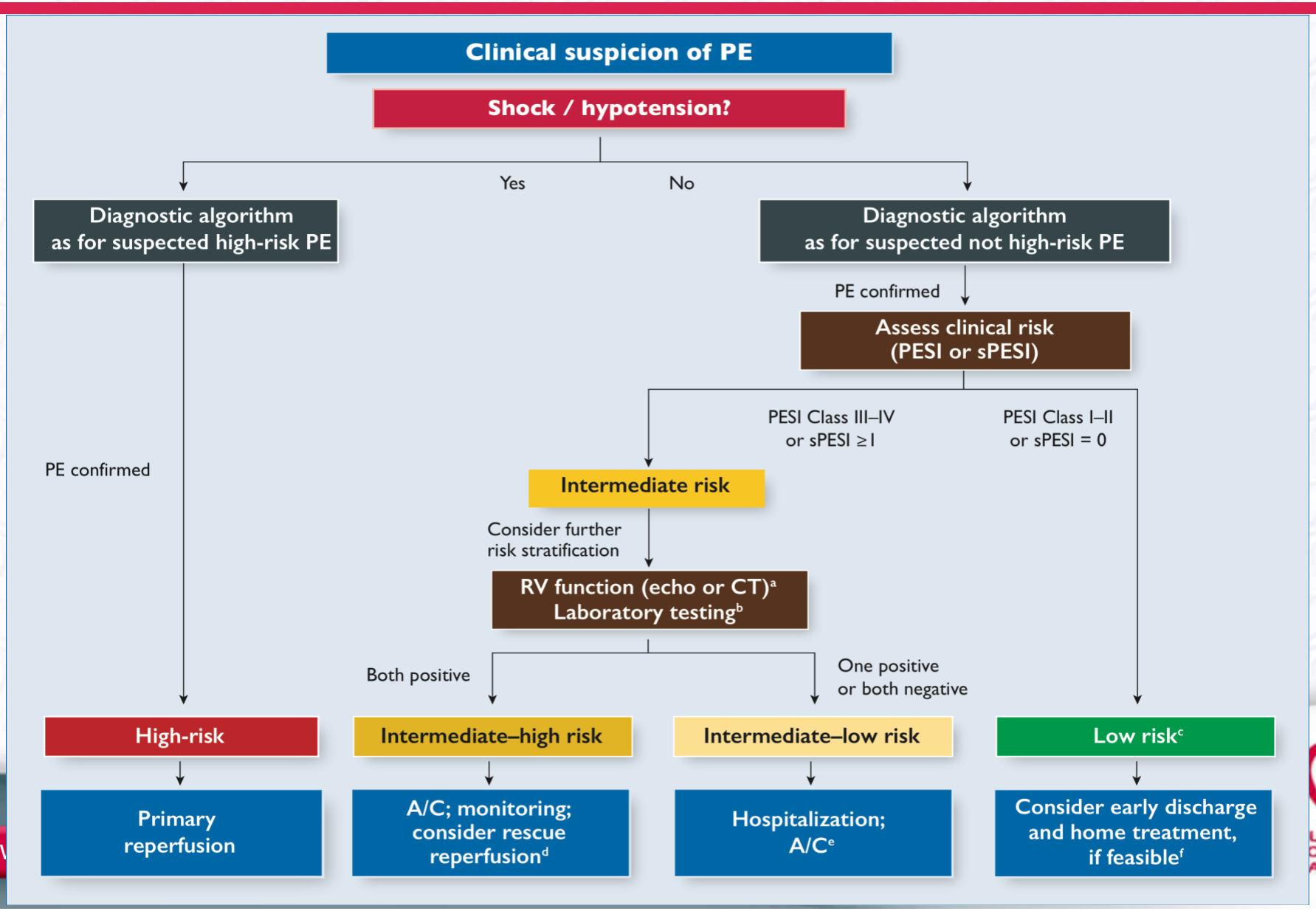
Risk-adjusted management algorithm



Acute phase treatment

Recommendations	Class	Level
PE without shock or hypotension (intermediate or low risk)		
Reperfusion treatment		
Routine use of primary systemic thrombolysis is not recommended in patients without shock or hypotension.	III	B
Close monitoring is recommended in patients with intermediate-high risk PE to permit early detection of haemodynamic decompensation and timely initiation of rescue reperfusion therapy.	I	B
Thrombolytic therapy should be considered for patients with intermediate-high-risk PE and clinical signs of haemodynamic decompensation.	IIa	B
Surgical pulmonary embolectomy may be considered in intermediate-high-risk patients if the anticipated risk of bleeding under thrombolytic treatment is high.	IIb	C
Percutaneous catheter-directed treatment may be considered in intermediate-high-risk patients if the anticipated risk of bleeding under thrombolytic treatment is high.	IIb	B

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

Acute phase treatment

Recommendations	Class	Level
PE without shock or hypotension (intermediate or low risk)		
Anticoagulation - combination of parenteral treatment with VKA		
Initiation of parenteral anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE while diagnostic work-up is ongoing.	I	C
LMWH or fondaparinux is the recommended form of acute phase parenteral anticoagulation for most patients.	I	A
In parallel to parenteral anticoagulation, treatment with a VKA is recommended, targeting an INR of 2.5 (range 2.0-3.0).	I	B

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

Acute phase treatment

Recommendations	Class	Level
PE without shock or hypotension (intermediate or low risk)		
Anticoagulation - new oral anticoagulants		
As an alternative to the combination of parenteral anticoagulation with a VKA, anticoagulation with rivaroxaban (15 mg twice daily for 3 weeks, followed by 20 mg once daily) is recommended.	I	B
As an alternative to the combination of parenteral anticoagulation with a VKA, anticoagulation with apixaban (10 mg twice daily for 7 days, followed by 5 mg twice daily) is recommended.	I	B
As an alternative to VKA treatment, administration of dabigatran (150 mg twice daily, or 110 mg twice daily for patients >80 years of age or those under concomitant verapamil treatment) is recommended following acute-phase parenteral anticoagulation.	I	B
As an alternative to VKA treatment, administration of edoxaban is recommended following acute-phase parenteral anticoagulation.	I	B
New oral anticoagulants (rivaroxaban, apixaban, dabigatran, edoxaban) are not recommended in patients with severe renal impairment.	III	A

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

Drug	Trial	Design	Treatments and dosage	Duration	Patients	Efficacy outcome (results)	Safety outcome (results)
Dabigatran	RE-COVER[293]	Double-blind, double-dummy	Enoxaparin/dabigatran (150 mg b.i.d.)[a] vs. enoxaparin/warfarin	6 months	2539 patients with acute VTE	Recurrent VTE or fatal PE: 2.4% under dabigatran vs. 2.1% under warfarin	Major bleeding: 1.6% under dabigatran vs. 1.9% under warfarin
	RE-COVER II[294]	Double-blind, double-dummy	Enoxaparin/dabigatran (150 mg b.i.d.)[a] vs. enoxaparin/warfarin	6 months	2589 patients with acute VTE	Recurrent VTE or fatal PE: 2.3% under dabigatran vs. 2.2% under warfarin	Major bleeding: 15 patients under dabigatran vs. 22 patients under warfarin

Drug	Trial	Design	Treatments and dosage	Duration	Patients	Efficacy outcome (results)	Safety outcome (results)
Rivaroxaban	EINSTEIN-DVT[295]	Open-label	Rivaroxaban (15 mg b.i.d. for 3 weeks, then 20 mg o.d.) vs. enoxaparin/warfarin	3, 6, or 12 months	3449 patients with acute DVT	Recurrent VTE or fatal PE: 2.1% under rivaroxaban vs. 3.0% under warfarin	Major or CRNM bleeding 8.1% under rivaroxaban vs. 8.1% under warfarin
	EINSTEIN-PE[296]	Open-label	Rivaroxaban (15 mg b.i.d. for 3 weeks, then 20 mg o.d.) vs. enoxaparin/warfarin	3, 6, or 12 months	4832 patients with acute PE	Recurrent VTE or fatal PE: 2.1% under rivaroxaban vs. 1.8% under warfarin	Major or CRNM bleeding: 10.3% under rivaroxaban vs. 11.4% under warfarin
Apixaban	AMPLIFY[297]	Double-blind, double-dummy	Apixaban (10 mg b.i.d. for 7 days, then 5 mg b.i.d.) vs. enoxaparin/warfarin	6 months	5395 patients with acute DVT or PE	Recurrent VTE or fatal PE: 2.3% under apixaban vs. 2.7% under warfarin	Major bleeding: 0.6% under apixaban vs. 1.8% under warfarin
Edoxaban	Hokusai-VTE[298]	Double-blind, double-dummy	LMWH/edoxaban (60 mg o.d.; 30 mg o.d. if creatinine clearance 30–50 ml/min or body weight <60 kg) vs. UFH or LMWH/warfarin	Variable, 3–12 months	8240 patients with acute DVT and/or PE	Recurrent VTE or fatal PE: 3.2% under edoxaban vs. 3.5% under warfarin	Major or CRNM bleeding: 8.5% under edoxaban vs. 10.3% under warfarin

Traitement standard: pour tous? NON

- Patient porteur d'un cancer actif:
  - ⇨ Pas de relais AVK
  - ⇨ HBPM à dose thérapeutique, au moins 6 mois
  - ⇨ Pas d'indication des anticoagulants oraux directs (non évalués dans cette indication)

Lee (CLOT Investigators) N Engl J Med 2003

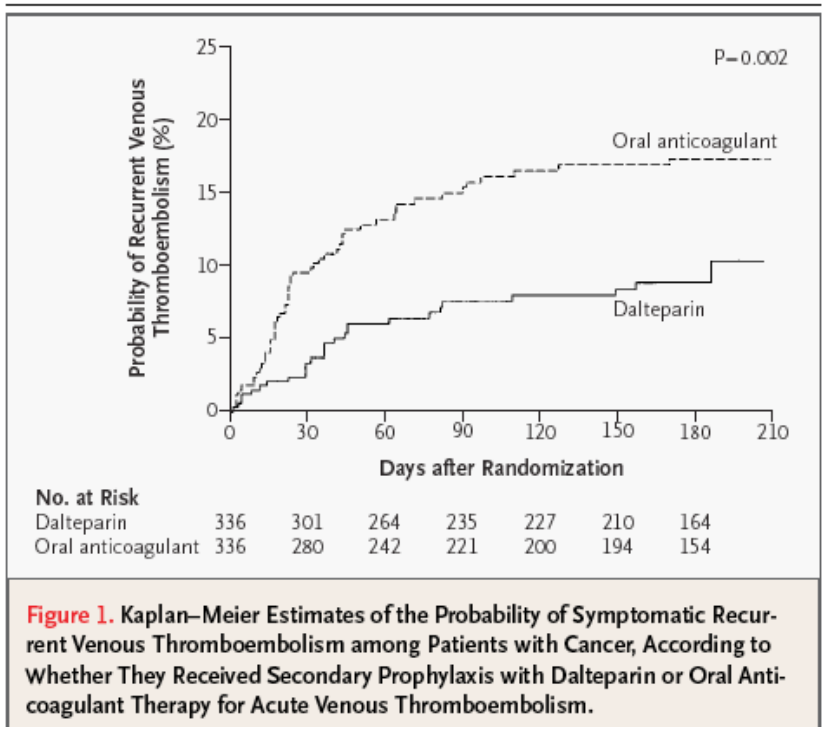


Figure 1. Kaplan–Meier Estimates of the Probability of Symptomatic Recurrent Venous Thromboembolism among Patients with Cancer, According to Whether They Received Secondary Prophylaxis with Dalteparin or Oral Anticoagulant Therapy for Acute Venous Thromboembolism.

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Traitement standard: pour tous? NON

- Patient porteur d'un cancer actif:
  - ⇨ Pas de relais AVK
  - ⇨ HBPM à dose thérapeutique, au moins 6 mois
  - ⇨ Pas d'indication des anticoagulants oraux directs (non évalués dans cette indication)

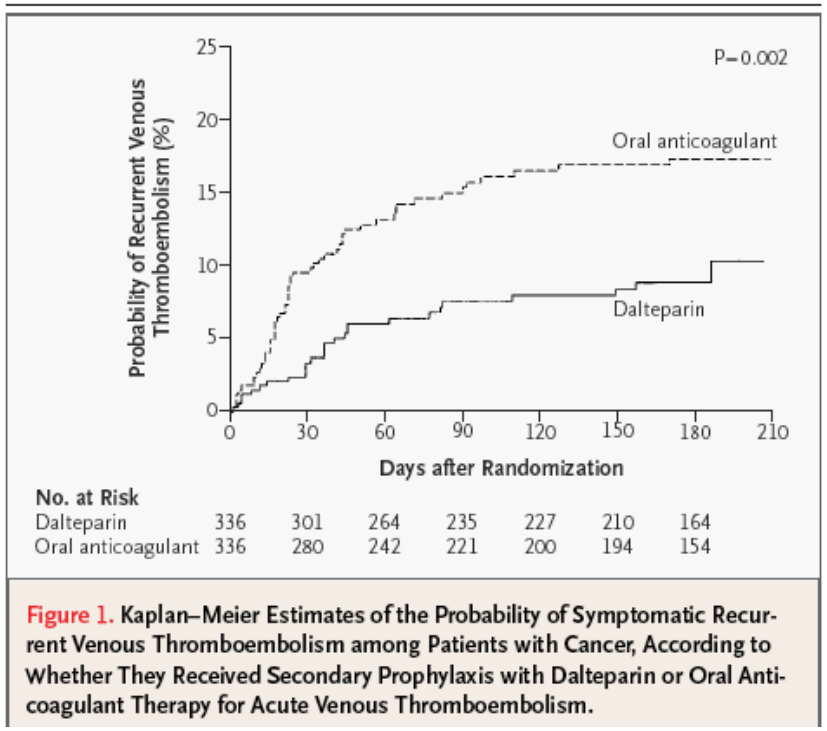

Figure 1. Kaplan–Meier Estimates of the Probability of Symptomatic Recurrent Venous Thromboembolism among Patients with Cancer, According to Whether They Received Secondary Prophylaxis with Dalteparin or Oral Anticoagulant Therapy for Acute Venous Thromboembolism.

Lee (CLOT Investigators) N Engl J Med 2003

Grossesse:

⇨Pas de relais AVK

⇨HBPM à dose thérapeutique, pendant toute la grossesse et 6semaines PP, pour un traitement de 6 mois.

⇨Pas d'indication des anticoagulants oraux directs

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Durée du traitement d'une EP et/ou TVP

- Facteur majeur de décision:
  - ⇨ « provoqué », par un facteur favorisant
    - ⇨Persistant (ex: cancer)
    - ⇨Temporaire (chirurgie, hospitalisation, COP,…)
  - ⇨ « Idiopathique » (quelque soit la thrombophilie)

- Durée:
  - ⇨« provoqué », par un facteur favorisant
    - Persistant: tant que le facteur persiste
    - Temporaire: 3 mois
  - ⇨« Idiopathique » (quelque soit la thrombophilie)
    - Au moins 6 mois
    - Traitement prolongé, en fonction du rapport bénéfice-risque
    - Résultats de l'étude PADIS en attente

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Recommendations for duration of anticoagulation after pulmonary embolism

Recommendations	Class[a]	Level[b]	Ref[c]
For patients with PE secondary to a transient (reversible) risk factor, oral anticoagulation is recommended for 3 months.	I	B	358
For patients with unprovoked PE, oral anticoagulation is recommended for at least 3 months.	I	A	363, 372–374
Extended oral anticoagulation should be considered for patients with a first episode of unprovoked PE and low bleeding risk .	IIa	B	375
Anticoagulation treatment of indefinite duration is recommended for patients with a second episode of unprovoked PE.	I	B	360

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

Recommendations	Class[a]	Level[b]	Ref[c]
PE without shock or hypotension (intermediate-or low-risk)[d]			
Anticoagulation: combination of parenteral treatment with VKA			
Initiation of parenteral anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE while diagnostic work-up is in progress.	I	C	352
LMWH or fondaparinux is the recommended form of acute phase parenteral anticoagulation for most patients.	I	A	273, 274, 281, 353
In parallel to parenteral anticoagulation, treatment with a VKA is recommended, targeting an INR of 2.5 (range 2.0–3.0).	I	B	352, 354
Anticoagulation: new oral anticoagulants			
As an alternative to the combination of parenteral anticoagulation with a VKA, anticoagulation with rivaroxaban (15 mg twice daily for 3 weeks, followed by 20 mg once daily) is recommended.	I	B	296

Why use only validated criteria for diagnosing PE?

Roy PM et al., Ann Intern Med 2006;144:157-164

Table 3. **Patient Outcomes at 3 Months after Exclusion of Pulmonary Embolism***

Diagnostic Work-up	Patients Receiving Appropriate Management (n = 418)	Patients Receiving Inappropriate Management (n = 506)	*P* Value
Total thromboembolic events, n (%)	5 (1.2)	39 (7.7)	<0.001
Nonfatal thromboembolic event, n	2	10	0.045
Unexplained sudden death, n	3	29	<0.001

Conclusion

- Diagnostic selon les recommandations
- Evaluation du risque de mortalité
  - Lieu de prise en charge et type de traitement
- Education thérapeutique
- Mise en place de schémas de suivi, discussion de la durée de traitement

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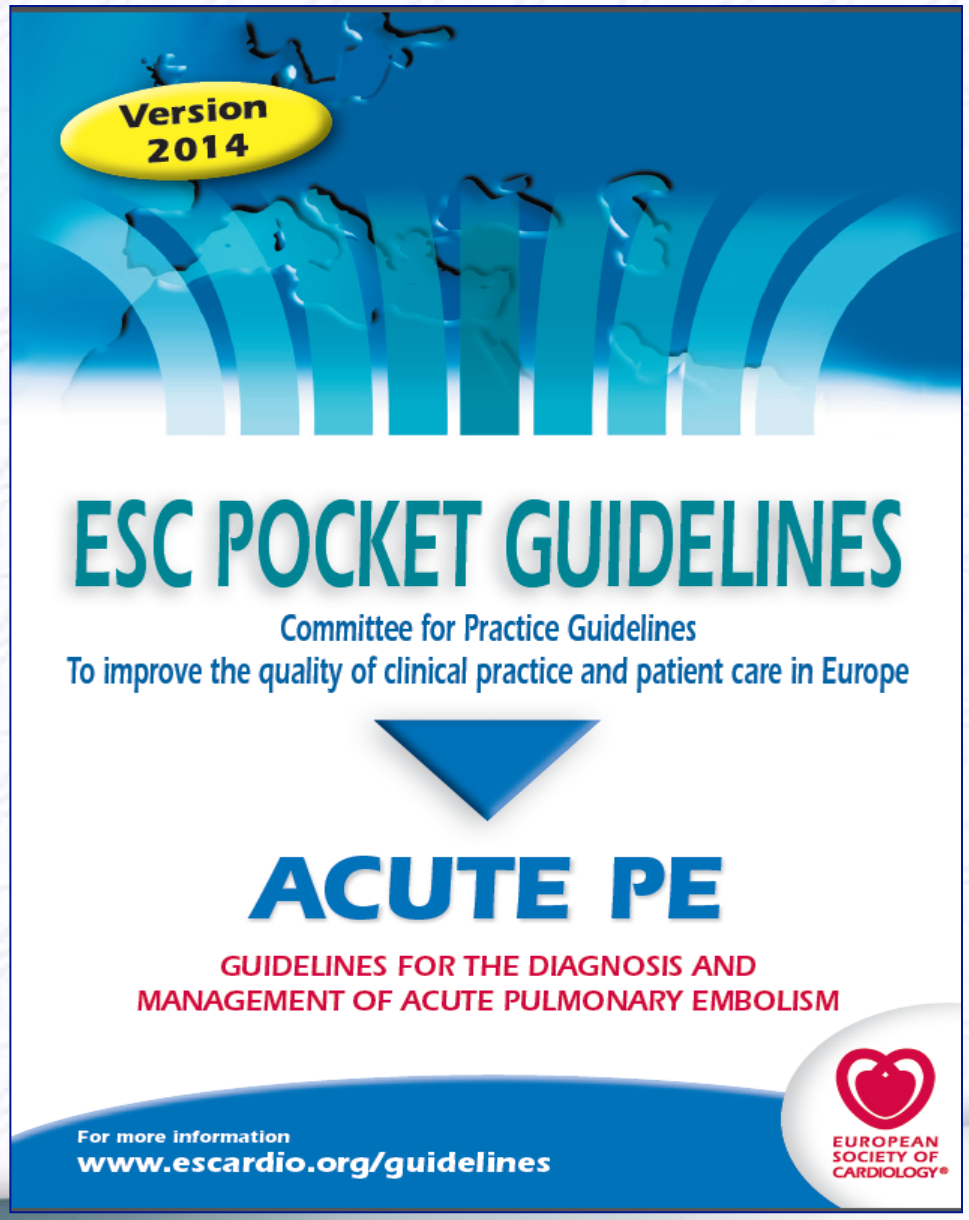

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European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

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Bilan de thrombophilie

- Pas de bilan de thrombophilie en cas de
  - **TVS**
  - **1er épisode de TVP ou EP après 60 ans**
  - **1er épisode de TVP distale**
- Bilan en cas de
  - 1er épisode de TVP distale chez les **patients à risque** (ex : patients lupiques)
  - **1er épisode de MTE idiopathique avant 60 ans**
  - Épisode de MTE chez la **femme à l'âge de procréation**
  - **Récidive** de MTE avec un 1er épisode avant l'âge de 60 ans

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Recommendations for PE in pregnancy

Suspicion of PE in pregnancy warrants formal diagnostic assessment with validated methods.	I	C
D-dimer measurement may be performed in order to avoid unnecessary irradiation, as a negative result has a similar clinical significance as in non-pregnant patients.	IIb	C
Venous compression ultrasonography may be considered in order to avoid unnecessary irradiation, as a diagnosis of proximal DVT confirms PE.	IIb	C
Perfusion scintigraphy may be considered to rule out suspected PE in pregnant women with normal chest X-ray.	IIb	C
CT angiography should be considered if the chest X-ray is abnormal or if lung scintigraphy is not readily available.	IIa	C
A weight-adjusted dose of LMWH is the recommended therapy during pregnancy in patients without shock or hypotension.	I	B

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

Probabilité clinique

Age	> 65 ans	+1
ATCD	*perso EP ou TVP*	+2
	Chirurgie ou immobilisation	+3
	cancer actif	+2
Symptômes		
	Hémoptysie	+2
	Douleur spontanée mollet	+3
Signes cliniques		
	FC *75-94 /min*	+3
	FC ≥ 95/min	+5
	Signes de TVP	+4
	Œdème et douleur provoquée	

Score révisé de Genève

PC faible	≤ 4
PC moyenne	5-8
PC forte	≥ 9

Probabilité d'EP	Prévalence EP	Dérivation	Validation
Faible	< 10 %	9%	8%
Moyenne	-	27,5	28,5%
Forte	> 60 %	71,7%	73,2%

Le Gal G et al. Ann Intern Med 2006

Embolie pulmonaire : Probabilité clinique

- Haute probabilité:
  - → Facteur de risque présent
  - → Tableau clinique évocateur
  - → Absence d'autre diagnostic
- Faible probabilité:
  - → Signes cliniques et anomalies des examens simples présents, mais pouvant être expliqués par un autre diagnostic
  - → Absence de facteur de risque
- Probabilité intermédiaire

Hyers Am J Respir Crit Care Med 1999; 159:1-14

Dosage des D- Dimères au cours de la grossesse

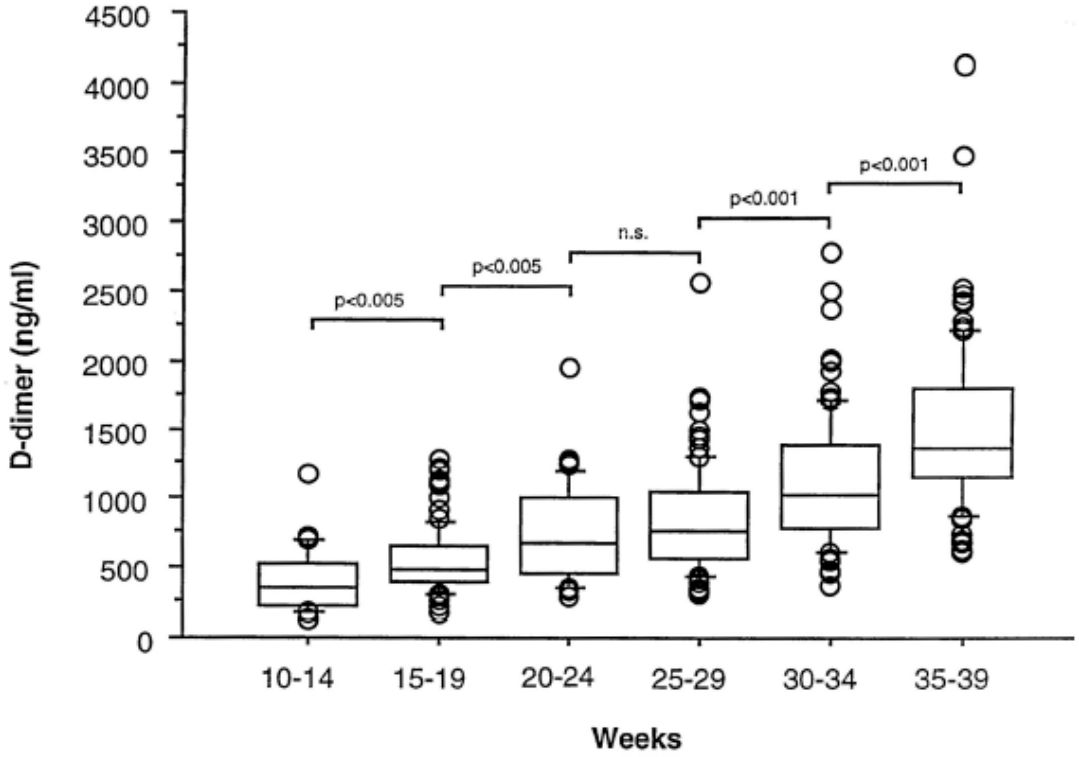
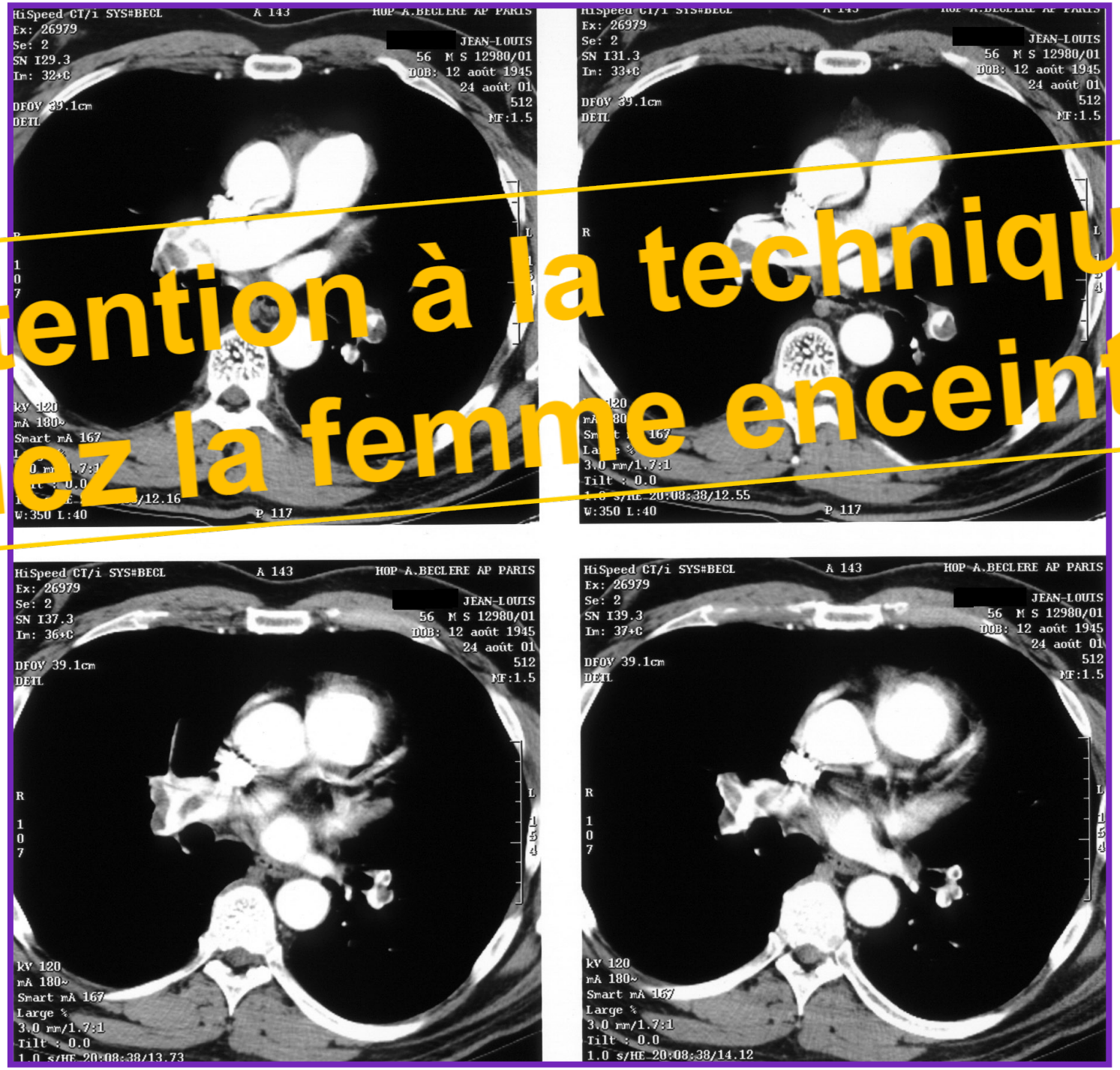


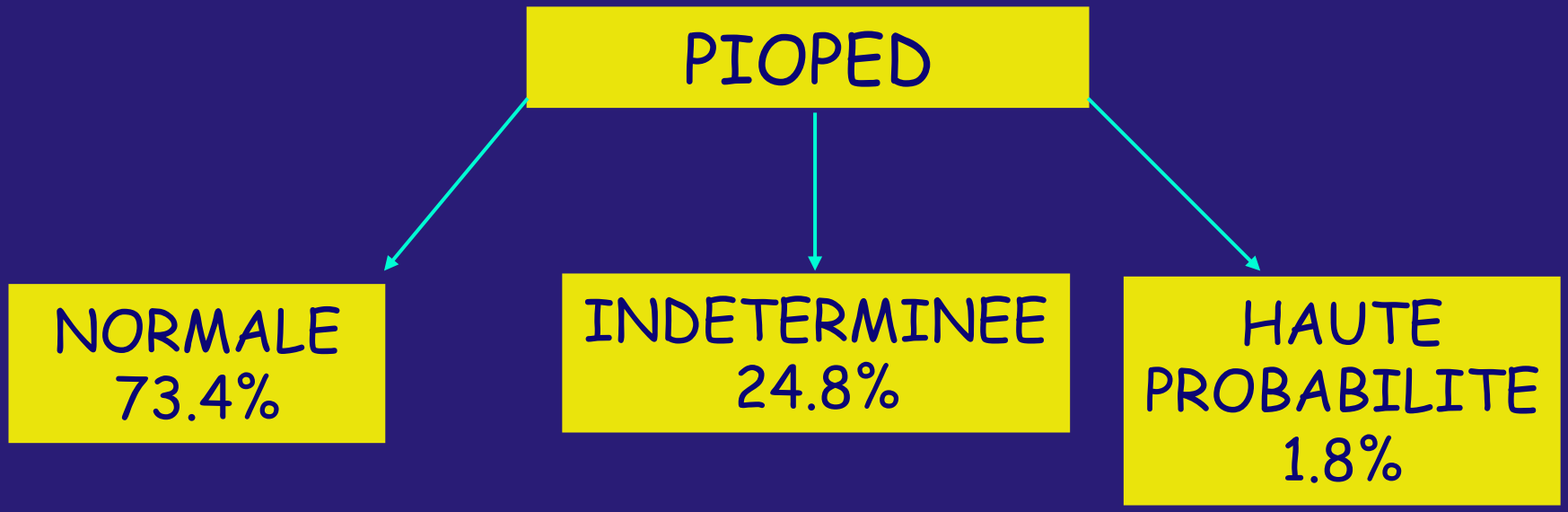
Fig 2. Box plots of D-dimer values as a function of pregnancy periods. The box represents 50% of the values, the horizontal bar inside the median, and the lower and the upper bars the 10th and 90th percentiles respectively.

Patrick Chabloz, British Journal of Haematology, 2001, 115, 150-152



Attention à la technique chez la femme enceinte

SCINTIGRAPHIE PULMONAIRE ET GROSSESSE
MEILLEURE RENTABILITE



Grossesse: fréquence supérieure de scintigraphie normale

WS Chan Arch Intern Med 2002; 162: 1170-5

Table 14 Estimated radiation absorbed in procedures used for diagnosing PE (adapted from Bajc *et al.* (2009)[430] and Chunilal *et al.* (2009)).[431]

Test	Estimated foetal radiation exposure (mSv)	Estimated maternal radiation exposure to breast tissue (mSv)
Chest X-ray	<0.01	0.01
Perfusion lung scan with technetium-99m labelled albumin		
Low dose: 40 MBq	0.11–0.20	0.28–0.50
High dose: 200 MBq	0.20–0.60	1.20
Ventilation lung scan	0.10–0.30	<0.01
Computed tomographic angiography	0.24–0.66	10–70

mSv = milisievert; PE = pulmonary embolism

The upper limit with regard to the danger of injury to the fetus is considered to be 50 mSv (50 000 μGy)

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