สาขาวิชาศัลยศาสตร์หลอดเลือด คณะแพทยศาสตร์ศิริราชพยาบาล
ร่วมกับ สมาคมแพทย์โรคหลอดเลือดแห่งประเทศไทย

Interhospital conference:

VENOUS DISEASE

How to manage PE

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17th December 2020

Management in pulmonary embolism

Pulmonary embolism → Diagnosis → Pulmonary severity score and risk of early death → Tx strategy → Chronic Tx & prevention recurrence

- Clinical
- D-dimer
- CTA
- V/Q scintigraphy
- Pulmonary angiography
- MRA
- Compression U/S
- CTV

- Clinical parameter
- RV insufficiency
- Lab

- High risk
- Intermediate risk
- Low risk

- Assessment VTE recurrence
- Cancer

Outline

Diagnostic and treatment strategy

Chronic treatment and prevent recurrence

ESC
European Society of Cardiology

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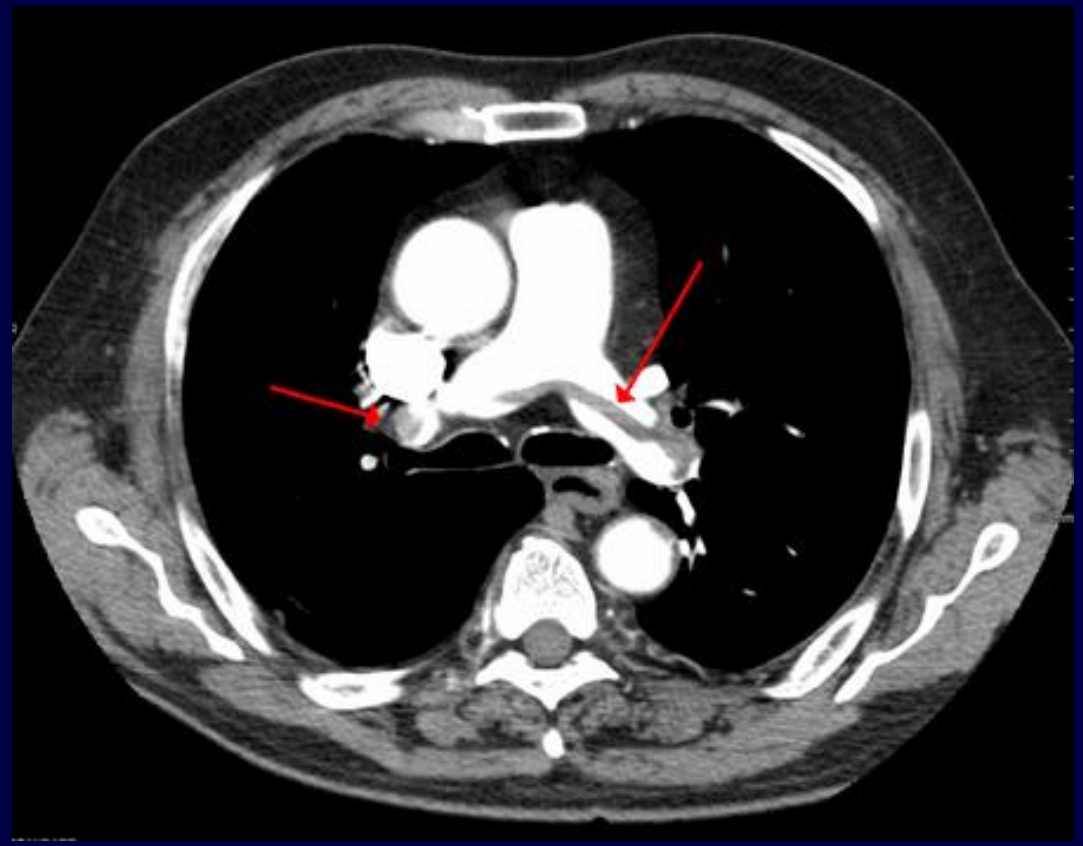
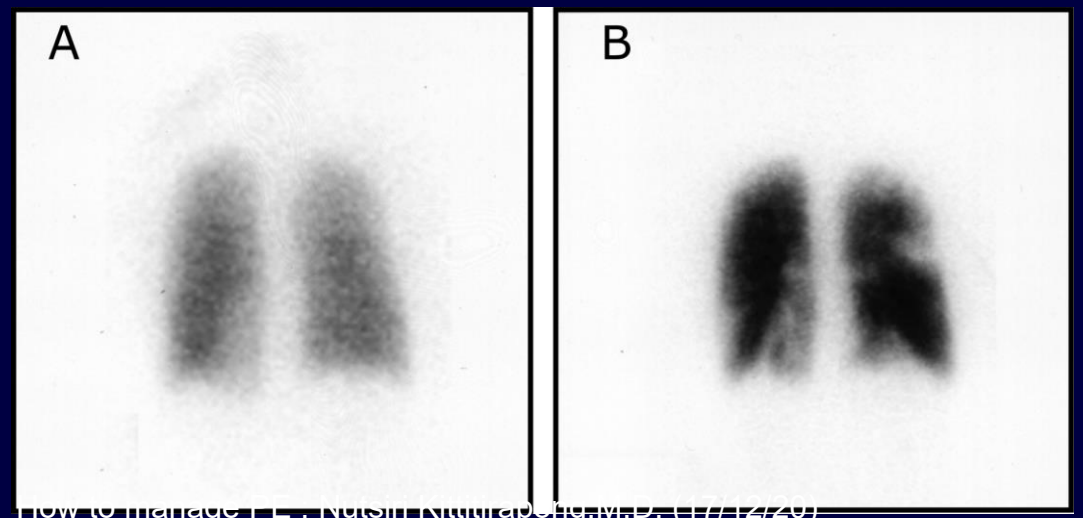
ESC GUIDELINES

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

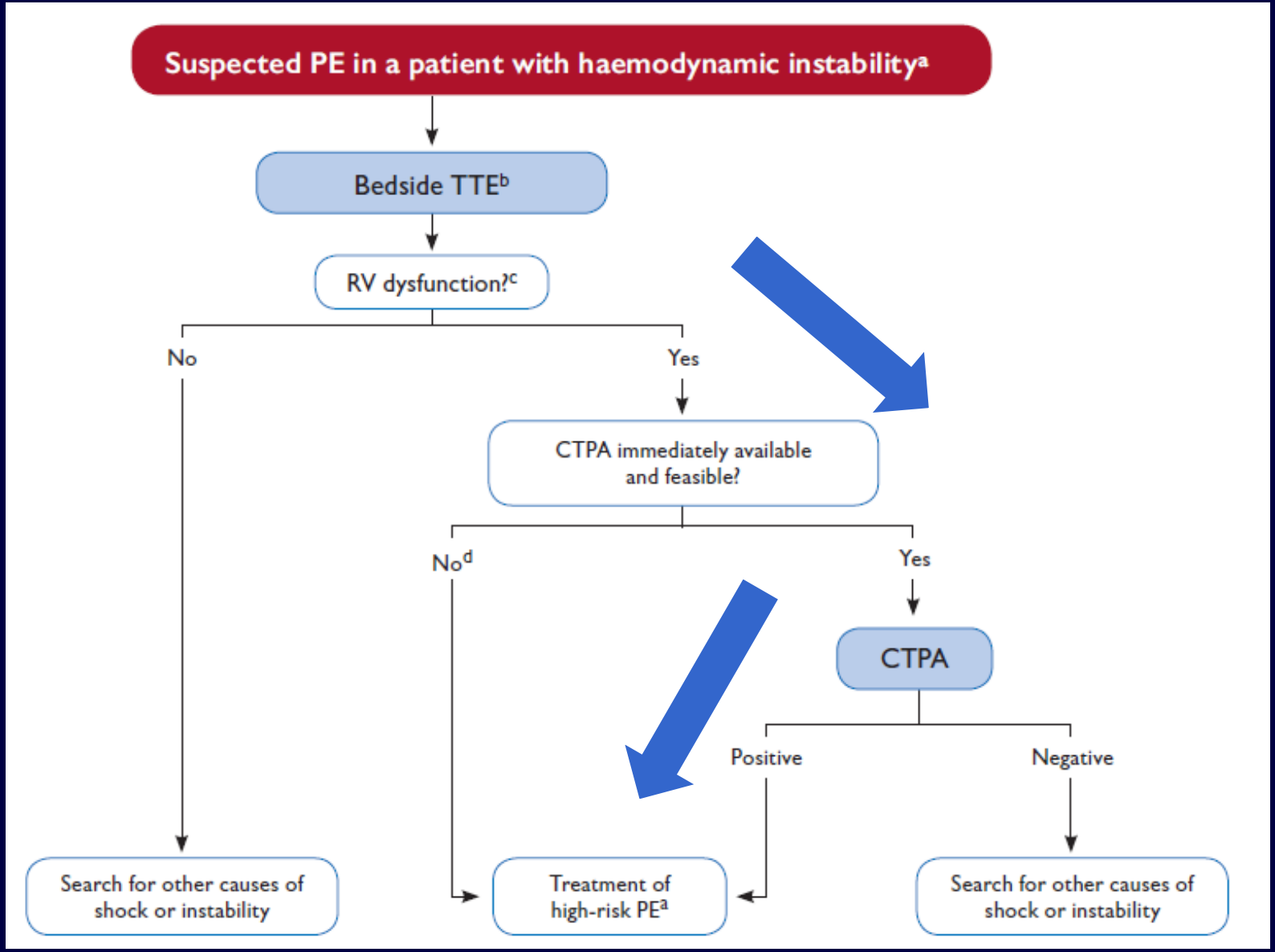
The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC)



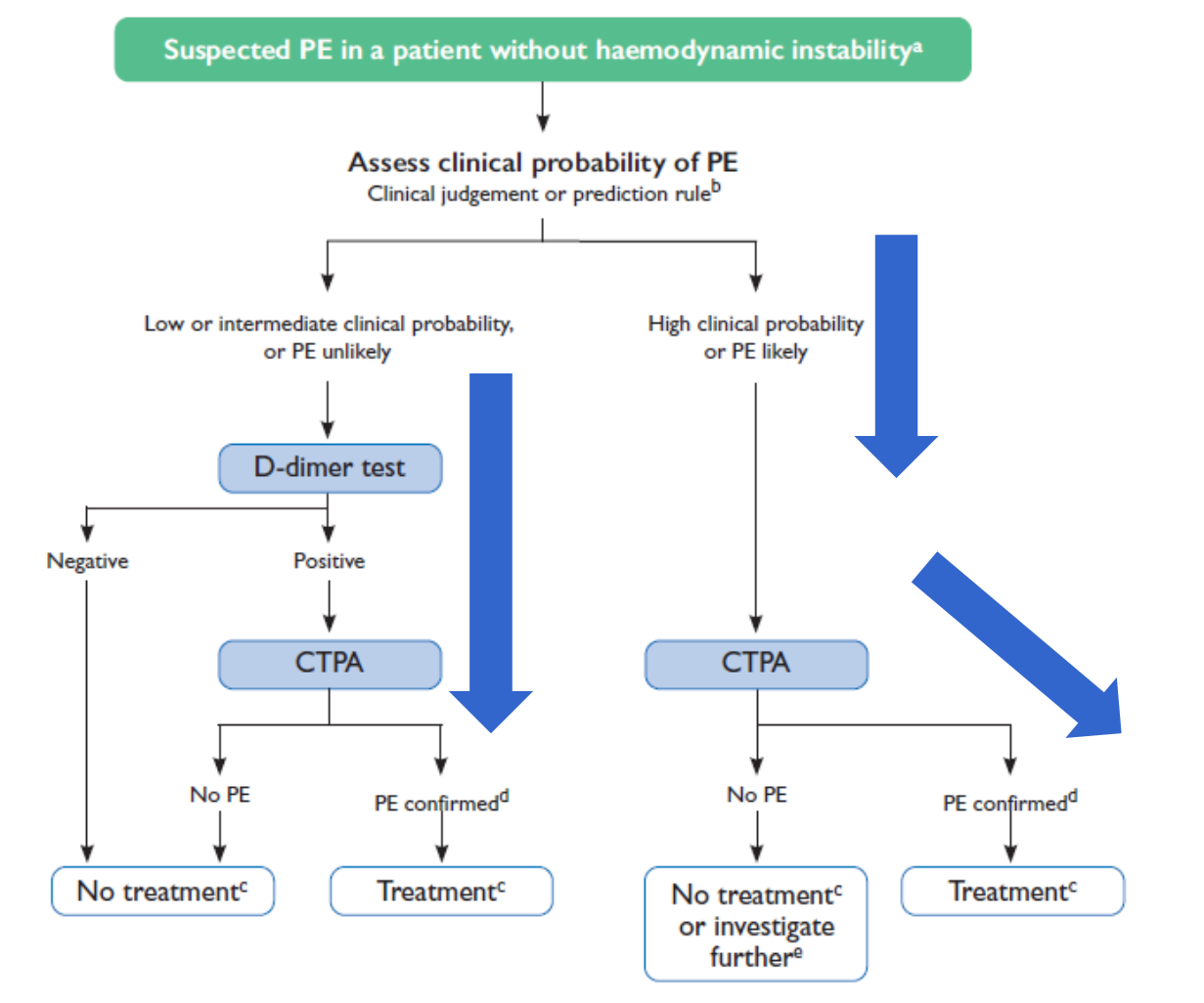


Diagnostic strategy

Diagnostic strategy



Diagnostic strategy



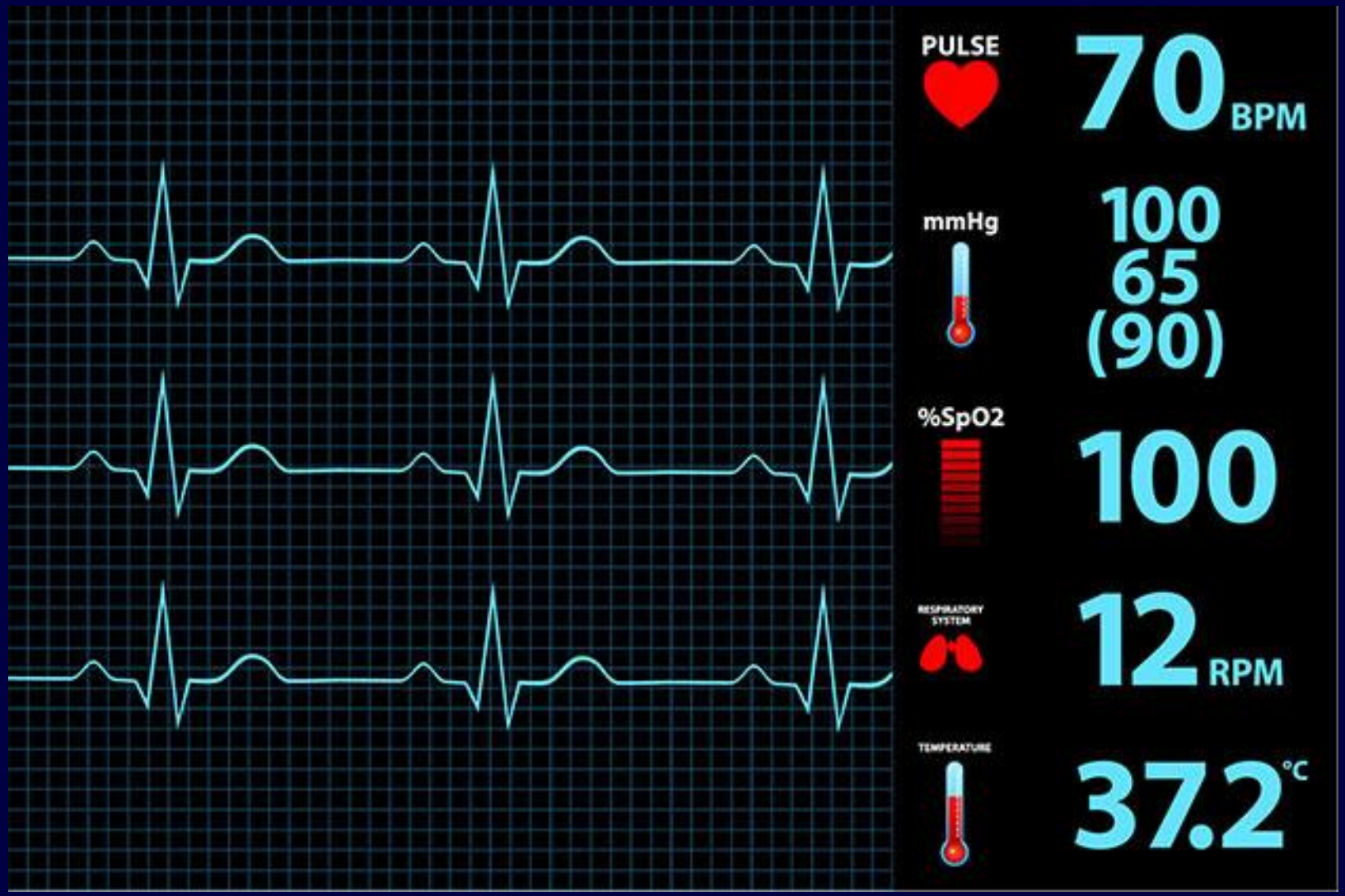
Supplementary Table 1 The Wells clinical prediction rule for pulmonary embolism

Items	Clinical decision rule points	
	Original version[1]	Simplified version[2]
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
Alterative 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

Table 5 The revised Geneva clinical prediction rule for pulmonary embolism

Items	Clinical decision rule points	
	Original version[91]	Simplified version[87]
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
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

b.p.m. = beats per minute; DVT = deep vein thrombosis; PE = pulmonary embolism.



Prognostic assessment strategy

Prognostic assessment strategy

Table 8 **Classification of pulmonary embolism severity and the risk of early (in-hospital or 30 day) death**

Early mortality risk		Indicators of risk			
		Haemodynamic instability[a]	Clinical parameters of PE severity and/or comorbidity: PESI class III–V or sPESI ≥I	RV dysfunction on TTE or CTPA[b]	Elevated cardiac troponin levels[c]
High		+	(+)[d]	+	(+)
Intermediate	Intermediate–high	-	+[e]	+	+
	Intermediate–low	-	+[e]	One (or none) positive	
Low		-	-	-	Assesment optional; if assessed, negative

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Hemodynamic instability

Table 4 **Definition of haemodynamic instability, which delineates acute high-risk pulmonary embolism (one of the following clinical manifestations at presentation)**

(1) Cardiac arrest	(2) Obstructive shock[68–70]	(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, lasting longer than 15 min 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)	

BP = blood pressure.

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Intermediate	Intermediate–high	-	+[e]	+	+
	Intermediate–low	-	+[e]	One (or none) positive	
Low		-	-	-	Assesment optional; if assessed, negative

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Risk assessment (severity)

- To assess a patient's overall mortality risk and early outcome
  - Pulmonary Embolism Severity Index (PESI)
  - simplified version (sPESI)

- Strength of the PESI and sPESI : **identification of patients at low risk for 30 day mortality** (PESI classes I and II)

Table 7 Original and simplified Pulmonary Embolism Severity Index

Parameter	Original version[226]	Simplified version[229]
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 BP <100 mmHg	+30 points	1 point
Respiratory rate >30 breaths per min	+20 points	–
Temperature <36°C	+20 points	–
Altered mental status	+60 points	–
Arterial oxyhaemoglobin saturation <90%	+20 points	1 point
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%)	**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%)

BP = blood pressure; b.p.m. = beats per minute; CI = confidence interval.
[a]Based on the sum of points.

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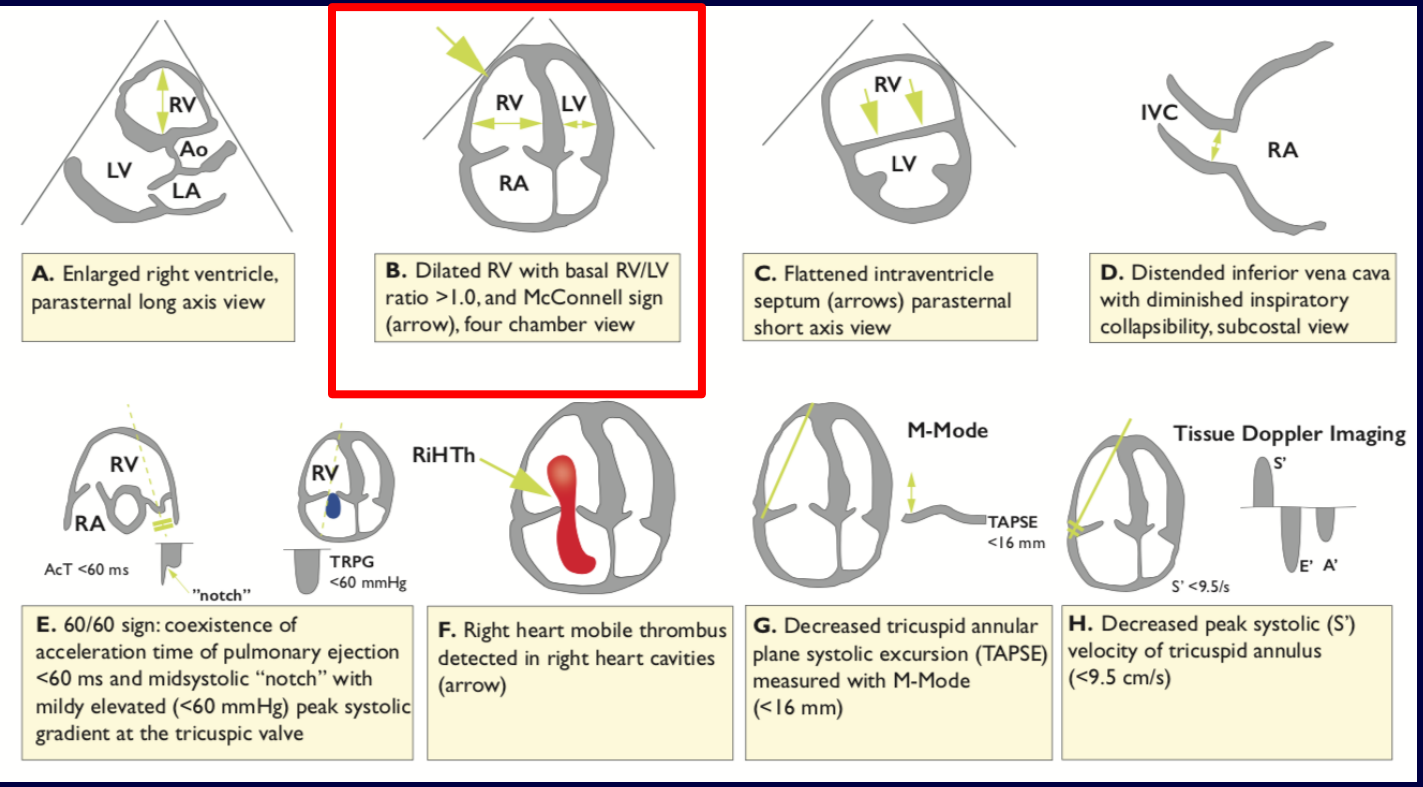
RV dysfunction on TTE or CTPA

Elevated cardiac troponin levels



- Elevation of further laboratory biomarkers
  - NT-proBNP ≥ 600 ng/L
  - H-FABP ≥ 6 ng/mL
  - copeptin ≥ 24 pmol/L

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Prognostic assessment strategy

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Intermediate	Intermediate–high	-	+[e]	+	+
	Intermediate–low	-	+[e]	One (or none) positive	
Low		-	-	-	Assesment optional; if assessed, negative

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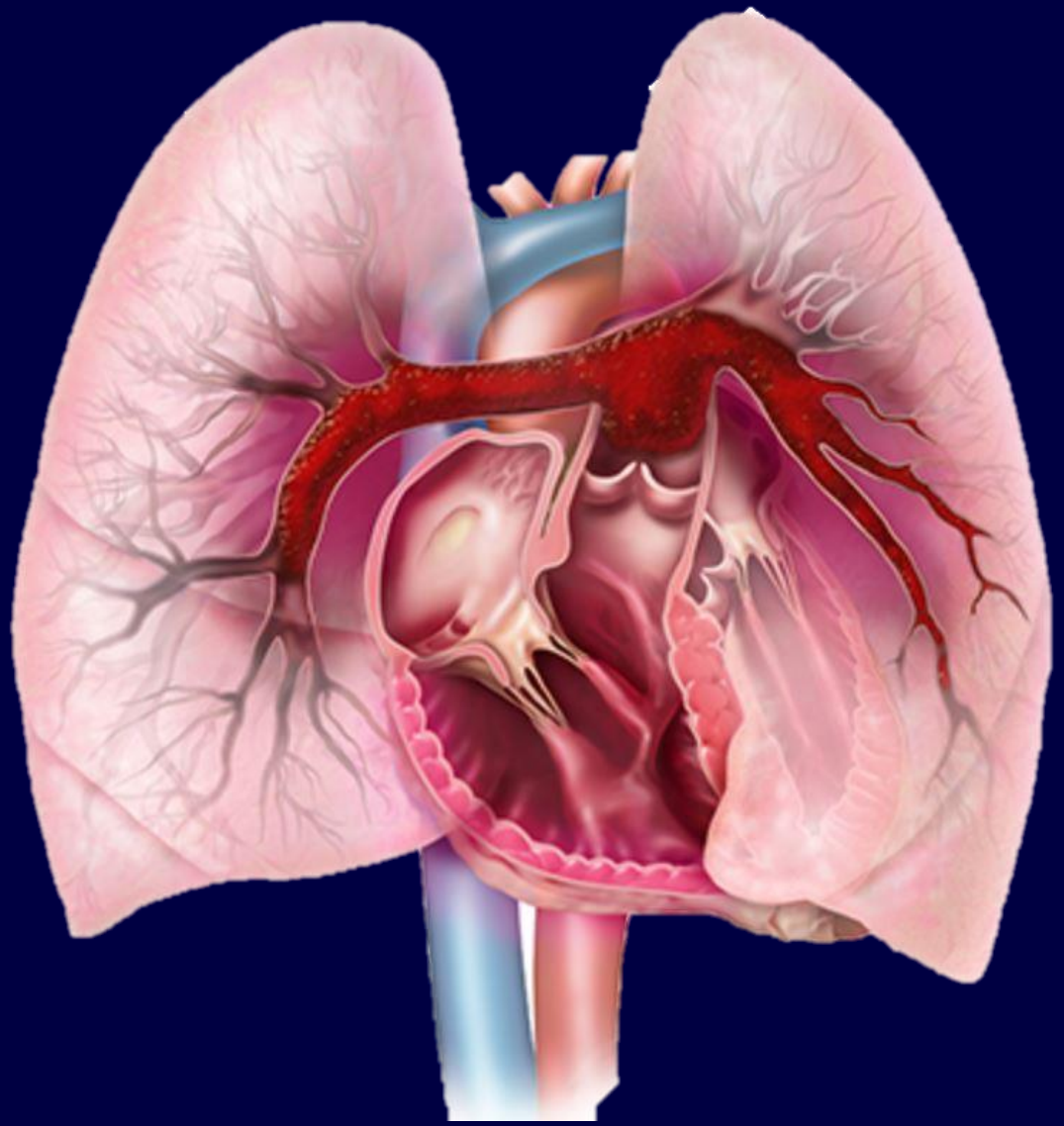
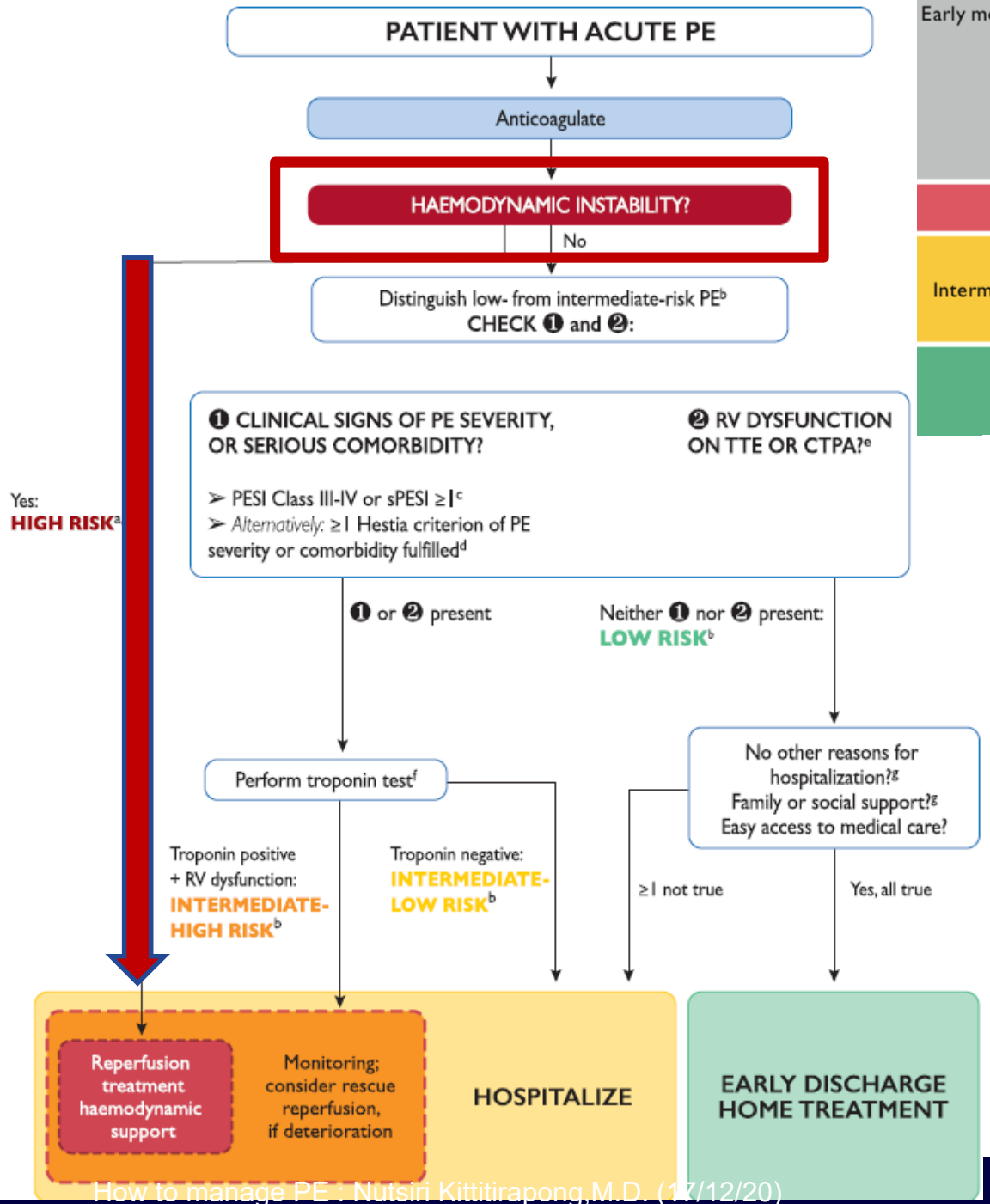


Treatment Strategy

- High risk
- Intermediate risk
- Low risk

High risk PE



Early mortality risk		Indicators of risk			
		Haemodynamic instability[a]	Clinical parameters of PE severity and/or comorbidity: PESI class III–V or sPESI ≥1	RV dysfunction on TTE or CTPA[b]	Elevated cardiac troponin levels[c]
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Respiratory rate >30 breaths per min	+20 points	–
Temperature <36°C	+20 points	–
Altered mental status	+60 points	–
Arterial oxyhaemoglobin saturation <90%	+20 points	1 point

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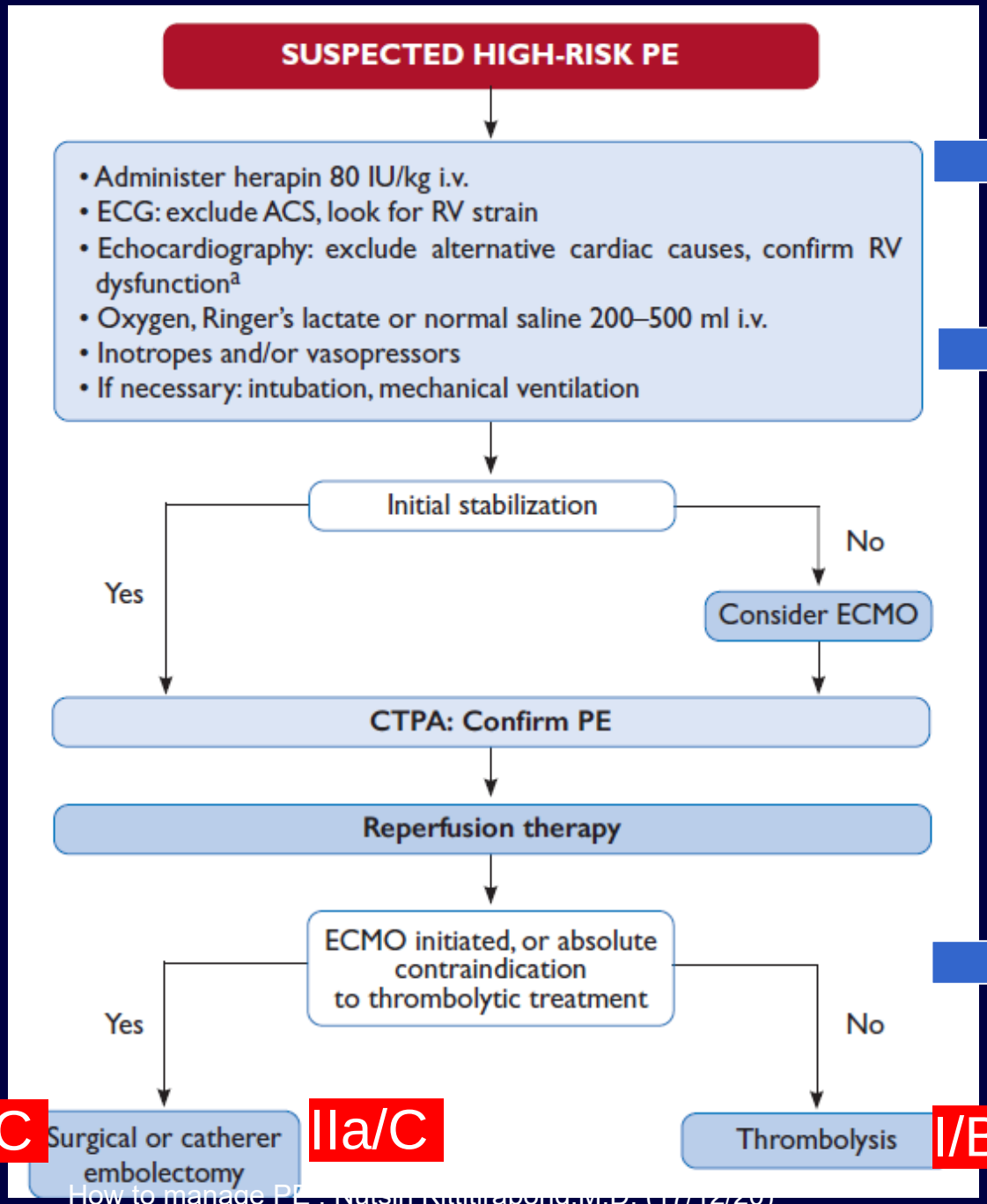

Acute phase: UFH (Reperfusion Tx) I/C

Norepinephrine/ Dobutamine IIa/C

Veno-arterial ECMO/
extracorporeal life support
(Combination with surgical thrombectomy)
IIb/C

I/C IIa/C I/B

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After reperfusion Tx

Supplementary Table 5 Low-molecular weight heparins and fondaparinux

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

- As patients in this risk category were excluded from the phase III NOAC trials
  - higher initial dose
    - apixaban 1 wk
    - rivaroxaban 3 wk
  - Heparin 5 d before switching to dabigatran or edoxaban

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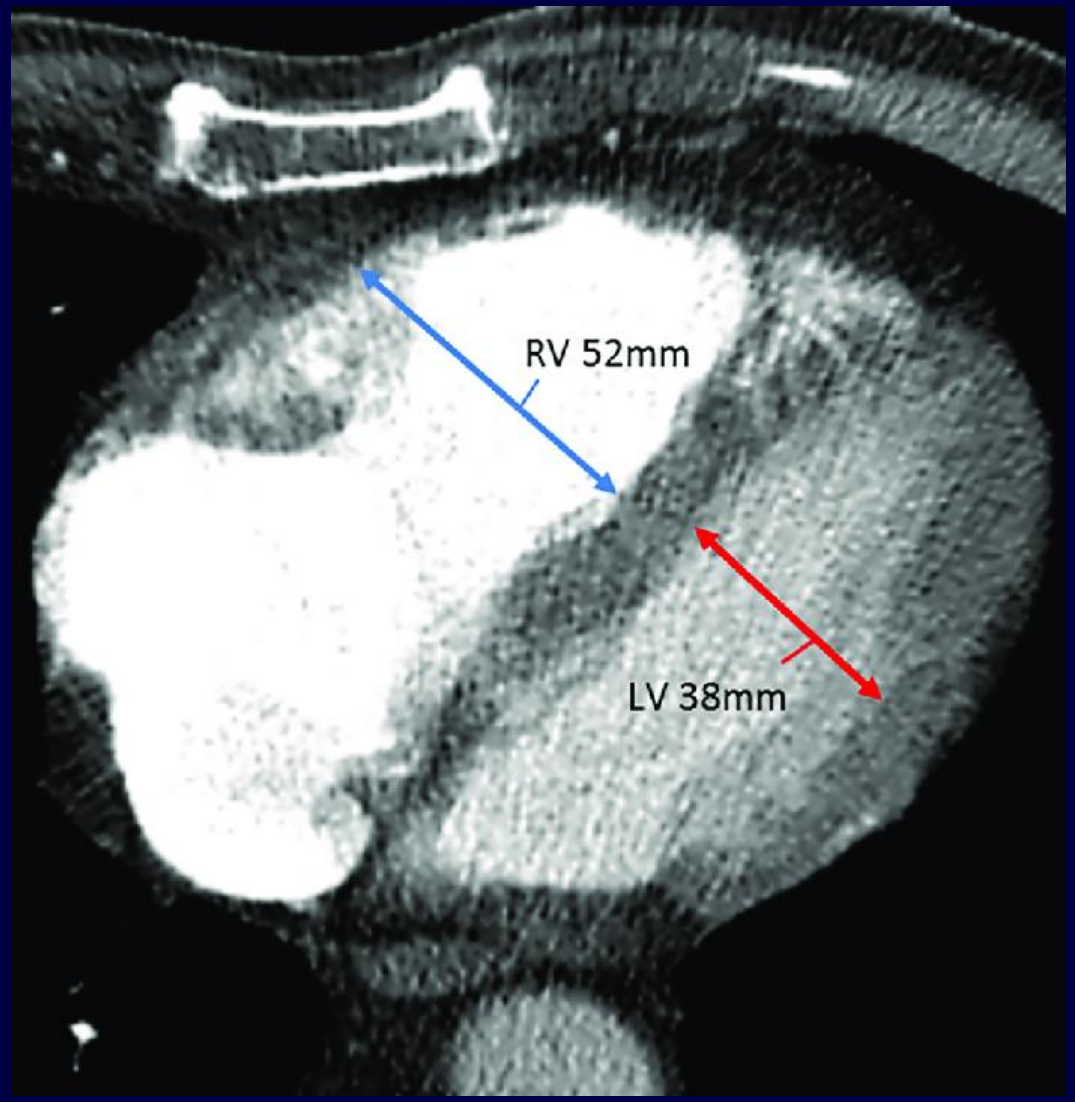
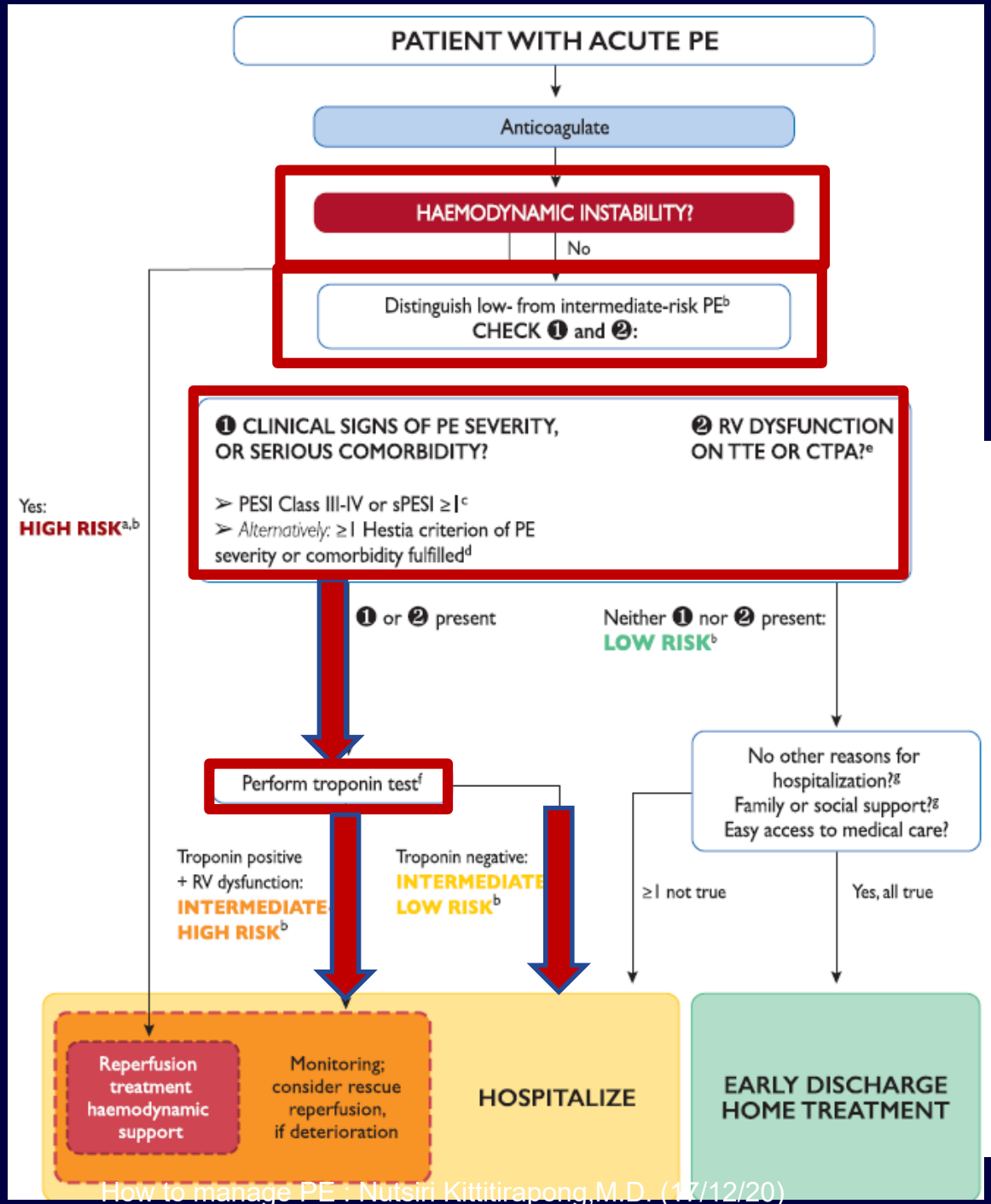
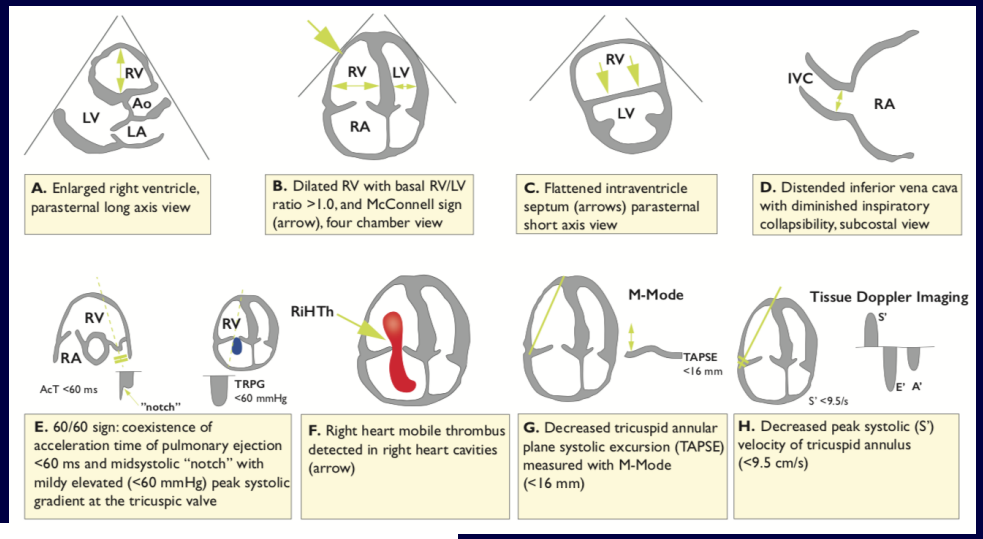


Intermediate risk PE





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BP = blood pressure; b.p.m. = beats per minute; CI = confidence interval.
[a]Based on the sum of points.

Intermediate risk PE

- Admit
- Monitored over the first hours or days
  - Risk of early haemodynamic decompensation and circulatory collapse
- Anticoagulant
  - Parenteral (LMWH > UFH I/A)
    - LMWH over the first 2 – 3 days and ensure that they remain stable before switching to oral anticoagulation.
    - UFH is recommended in renal impairment(CrCl) ≤ 30 mL/min/ severe obesity/ need reperfusion Tx
  - Oral (NOAC > VKA IA)
- Intermediate high risk PE: I/C for reperfusion Tx (Catheter-based or Surgical thrombectomy IIa/C)

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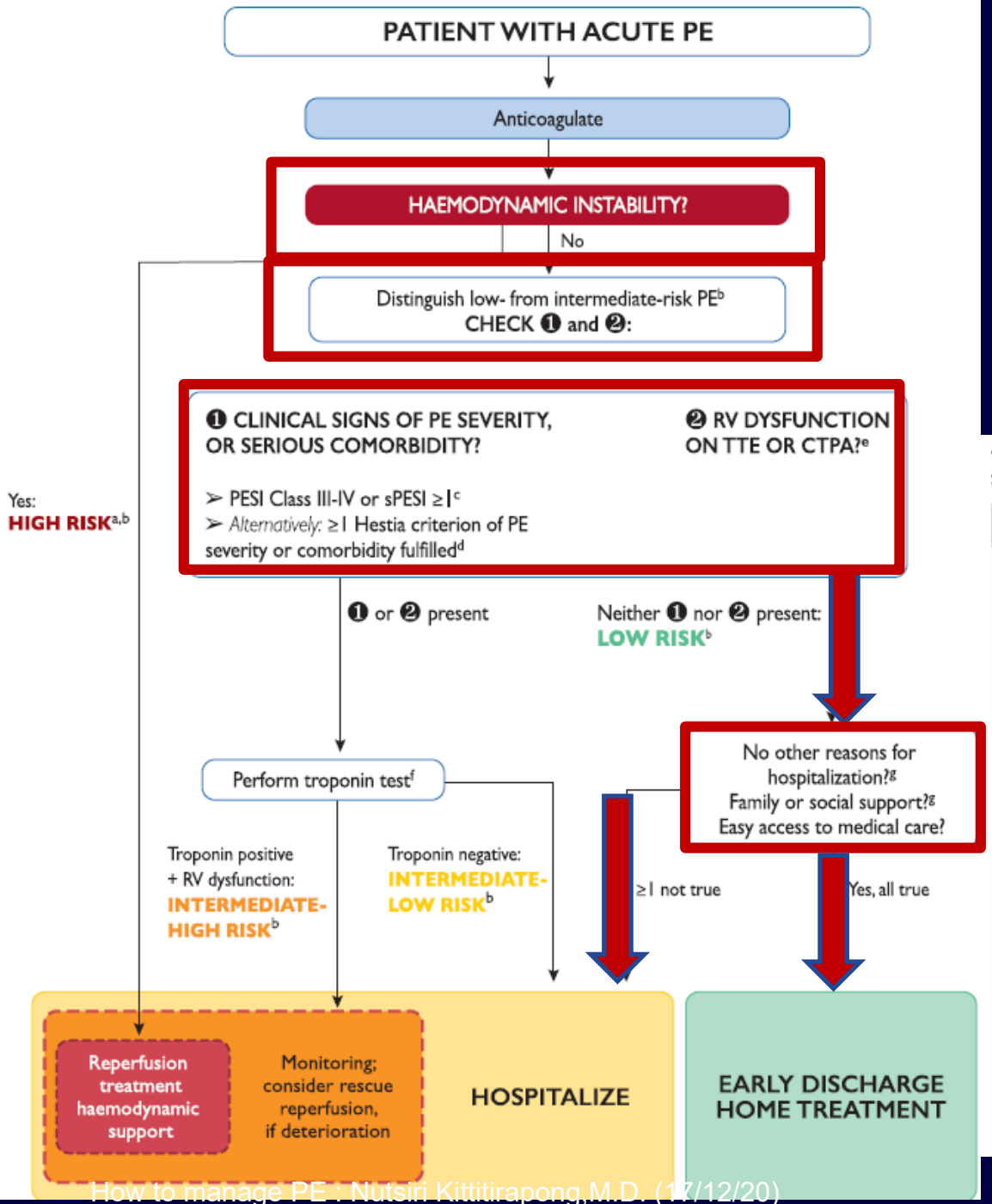
Low risk PE



Supplementary Table 12 Hestia exclusion criteria for outpatient management

Criterion/question
Is the patient haemodynamically unstable?[a]
Is thrombolysis or embolectomy necessary?
Active bleeding or high risk of bleeding?[b]
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?
Medical or social reason for treatment in the hospital for >24 h (infection, malignancy, or no support system)?
Does the patient have a CrCl of <30 mL/min?[c]
Does the patient have severe liver impairment?[d]
Is the patient pregnant?
Does the patient have a documented history of heparin-induced thrombocytopenia?

Hestia exclusion criteria for outpatient management of pulmonary embolism (from Zondag *et al.*[32]). If the answer to one or more of the questions is 'yes', then the patient cannot be treated at home.

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BP = blood pressure; b.p.m. = beats per minute; CI = confidence interval.
[a]Based on the sum of points.

Low risk PE

Early discharge of a patient with acute PE and continuation of anticoagulant treatment at home should be considered if **three sets of criteria are fulfilled**: IIb/A

- The risk of early PE-related death or serious complications is LOW
- There is no serious comorbidity or aggravating condition(s) that would mandate hospitalization
- Proper outpatient care and anticoagulant treatment can be provided, considering the patient's (anticipated) compliance, and the possibilities offered by the healthcare system and social infrastructure.

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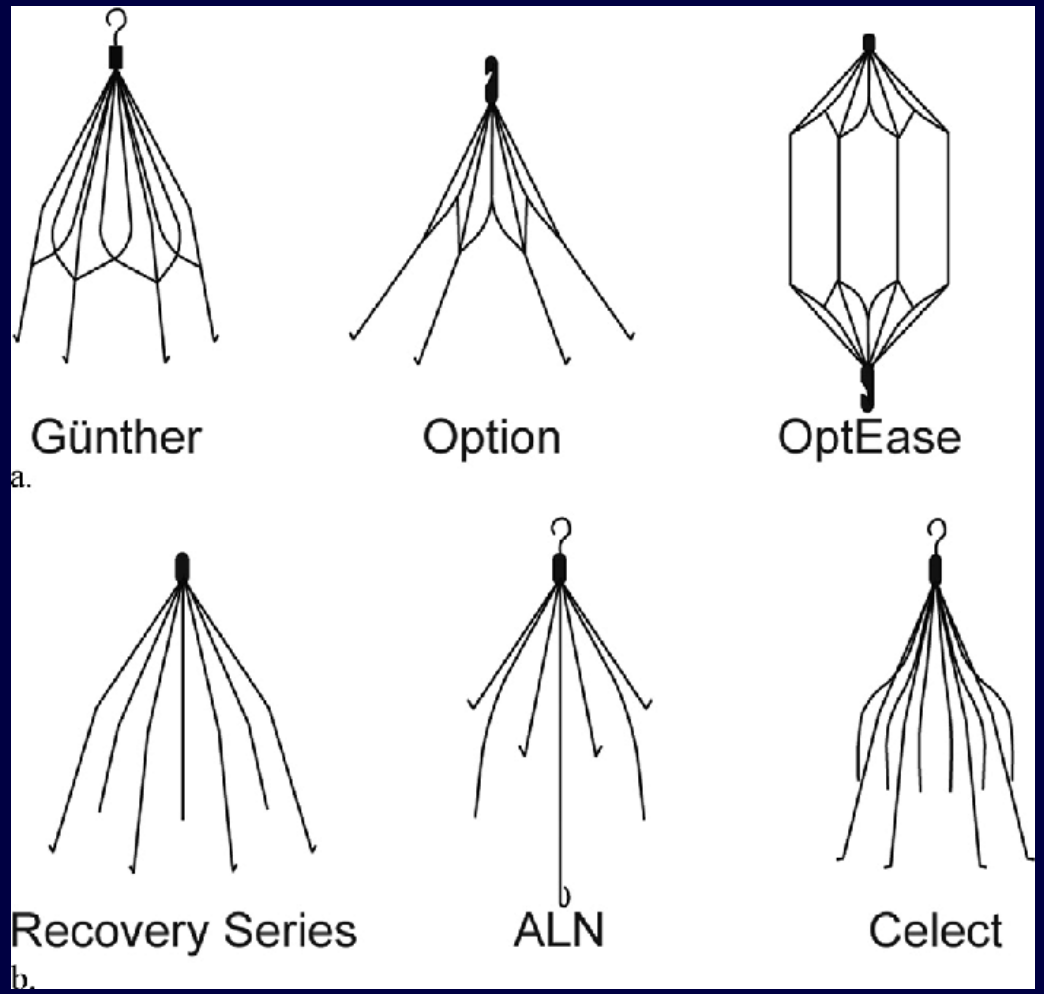
Specific conditions: Subsegmental PE

Supplementary Table 9 **Management of pulmonary embolism in specific clinical situations**

Clinical setting	Suggested management[a]	Comments
Subsegmental PE	Single subsegmental PE in an outpatient without cancer and without proximal DVT: • Clinical surveillance. Single subsegmental PE in a hospitalized patient, a patient with cancer, or if associated with confirmed proximal DVT: • Anticoagulant treatment. Multiple subsegmental PE: • Anticoagulant treatment.	• Poor interobserver agreement for the diagnosis of subsegmental PE; diagnosis to be confirmed by an experienced thoracic radiologist. • Suggestion based on indirect evidence, only limited data available.
Incidental PE	If single subsegmental PE: • Proceed as above. In all other cases: • Anticoagulant treatment.	• Suggestion based on retrospective cohort data.

In patients with cancer, incidental PE should be managed in the same manner as symptomatic PE, whether it involves segmental or more proximal branches, multiple subsegmental vessels, or a single subsegmental vessel in association with detectable DVT.

IVC filter



6.9 Recommendations for inferior vena cava filters

Recommendations	Class[a]	Level[b]
IVC filters should be considered in patients with acute PE and absolute contraindications to anticoagulation.	IIa	C
IVC filters should be considered in cases of PE recurrence despite therapeutic anticoagulation.	IIa	C
Routine use of IVC filters is not recommended.[302–304]	III	A

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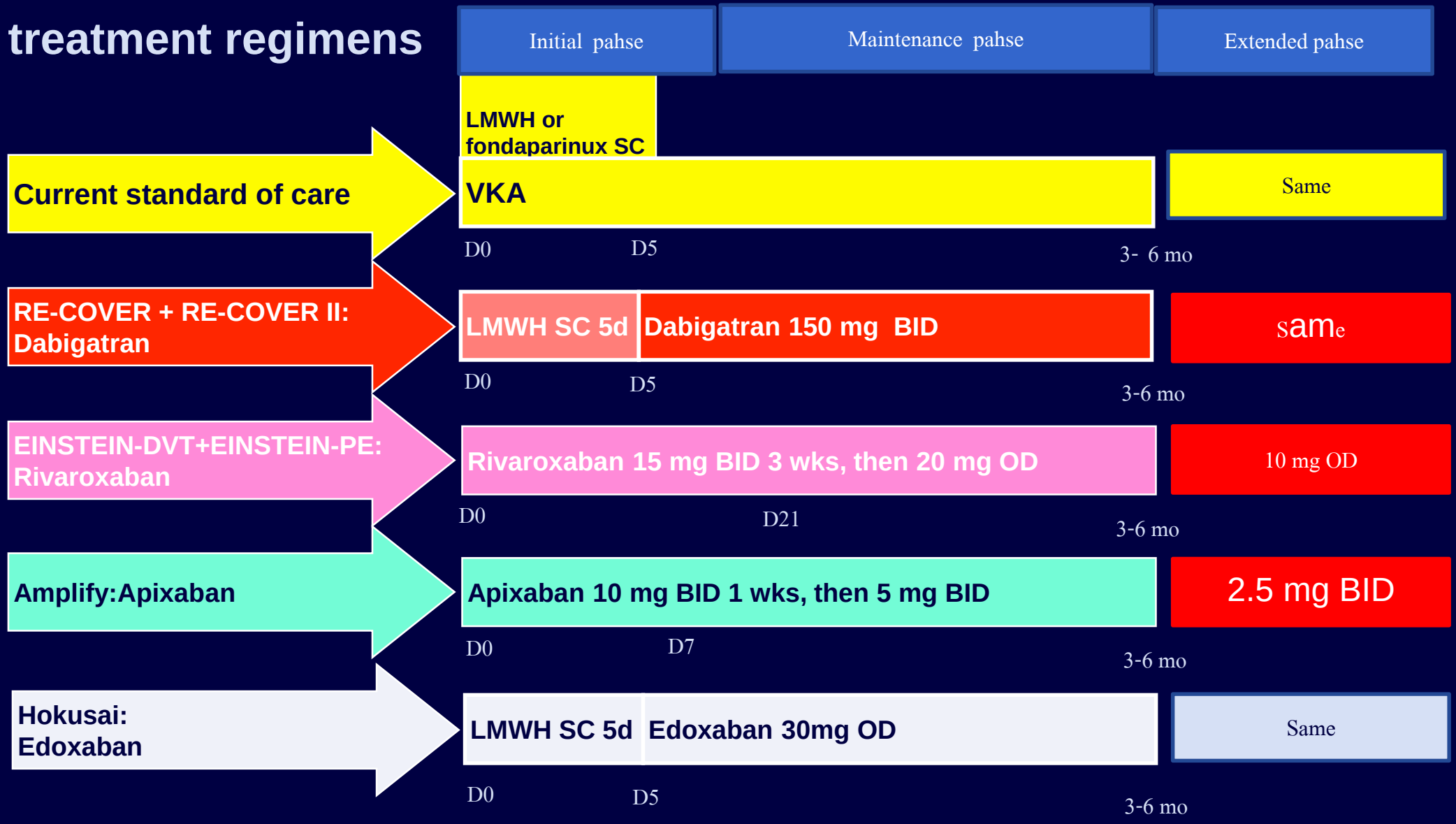
Outline

Diagnostic and treatment strategy

Chronic treatment and prevent recurrence

Current VTE treatment regimens



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ASA/Sulodexide

Recommendations for the regimen and duration of anticoagulation after pulmonary embolism

Recommendations	Class[a]	Level[b]
Therapeutic anticoagulation for ≥ 3 months is recommended for all patients with PE.[347]	I	A

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Table 11 Categorization of risk factors for venous thromboembolism based on the risk of recurrence over the long term

Estimated risk for long-term recurrence[a]	Risk factor category for index PE[b]	Examples[b]
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

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

3 Months

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Table 11 Categorization of risk factors for venous thromboembolism based on the risk of recurrence over the long-term

Beyond 3 months

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

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

Table 11 Categorization of risk factors for venous thromboembolism based on the risk of recurrence over the long term

Estimated risk for long-term recurrence[a]	Risk factor category for index PE[b]	Examples[b]
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

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

Beyond 3 months I/B

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Recommendations for the regimen and the duration of anticoagulation after pulmonary embolism in patients with active 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

ESC guideline 2019. European Heart Journal (2020) 41, 543–603

Conclusion

PE is one of the life-threatening conditions

Early diagnosis, proper management and intervention can prevent mortality and morbidity

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Interhospital conference:

VENOUS DISEASE

How to manage PE

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