Initial assessment and how to approach to patients suspected to PTE

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EPIDEMIOLOGY

In the United States, the Surgeon General estimates that there are 100,000 to 180,000 deaths annually from PE and has declared that PE is **the most common preventable cause of death among hospitalized patients**

- The hospital mortality rate from acute PE is 2–5% once the diagnosis of embolism is confirmed and appropriate therapy initiated

- In patients who initially present with hemodynamic impairment and those with recurring PE despite therapy, in whom mortality rates are much higher.
- the majority of deaths related to embolism appear to arise from a failure to prevent the disease in at-risk patients and from a failure to make the diagnosis in those afflicted.

clinical presentations

Dyspnea at rest or with exertion	(73 percent)
Pleuritic pain	(66 percent)
Cough	(37 percent)
Orthopnea	(28 percent)
Calf or thigh pain and/or swelling	(44 percent)
Wheezing	(21 percent)
Hemoptysis	(13 percent)

transient or persistent arrhythmias (eg, atrial fibrillation)	**<10%**
presyncope	<10%
syncope	<10%
hemodynamic collapse	<10%
Hoarsness(Ortner syndrome)	rare

Tachypnea	(54 percent)
Calf or thigh swelling, erythema, edema, tenderness, palpable cords	(47 percent)
Tachycardia	(24 percent)
Rales	(18 percent)
Decreased breath sounds	(17 percent)
An accentuated pulmonic component of the second heart sound	(15 percent)
Jugular venous distension	(14 percent)
Fever, mimicking pneumonia	(3 percent)

- Although upper extremity DVT (UEDVT) embolizes less commonly than lower extremity DVT, symptoms of UEDVT (arm pain or tightness) should also raise the suspicion of PE

INITIAL APPROACH

Assess hemodynamic stability

- Hemodynamically unstable PE, ie, high-risk or "massive" PE
- Hemodynamically stable PE

Determining the pretest probability of pulmonary embolism

1) Wells score and Modified Wells score

2) Modified Geneva score

3) Years algorithm

Wells criteria and modified Wells criteria: clinical assessment for pulmonary embolism

Clinical symptoms of DVT (leg swelling, pain with palpation)	3.0
Other diagnosis less likely than pulmonary embolism	3.0
Heart rate >100	1.5
Immobilization (≥3 days) or surgery in the previous four weeks	1.5
Previous DVT/PE	1.5
Hemoptysis	1.0
Malignancy	1.0
Probability	**Score**
Traditional clinical probability assessment (Wells criteria)	
High	>6.0
Moderate	2.0 to 6.0
Low	<2.0
Simplified clinical probability assessment (Modified Wells criteria)	
PE likely	>4.0
PE unlikely	≤4.0

DVT: deep vein thrombosis; PE: pulmonary embolism.

Data from van Belle A, Buller HR, Huisman MV, et al. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. JAMA 2006; 295:172.

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.

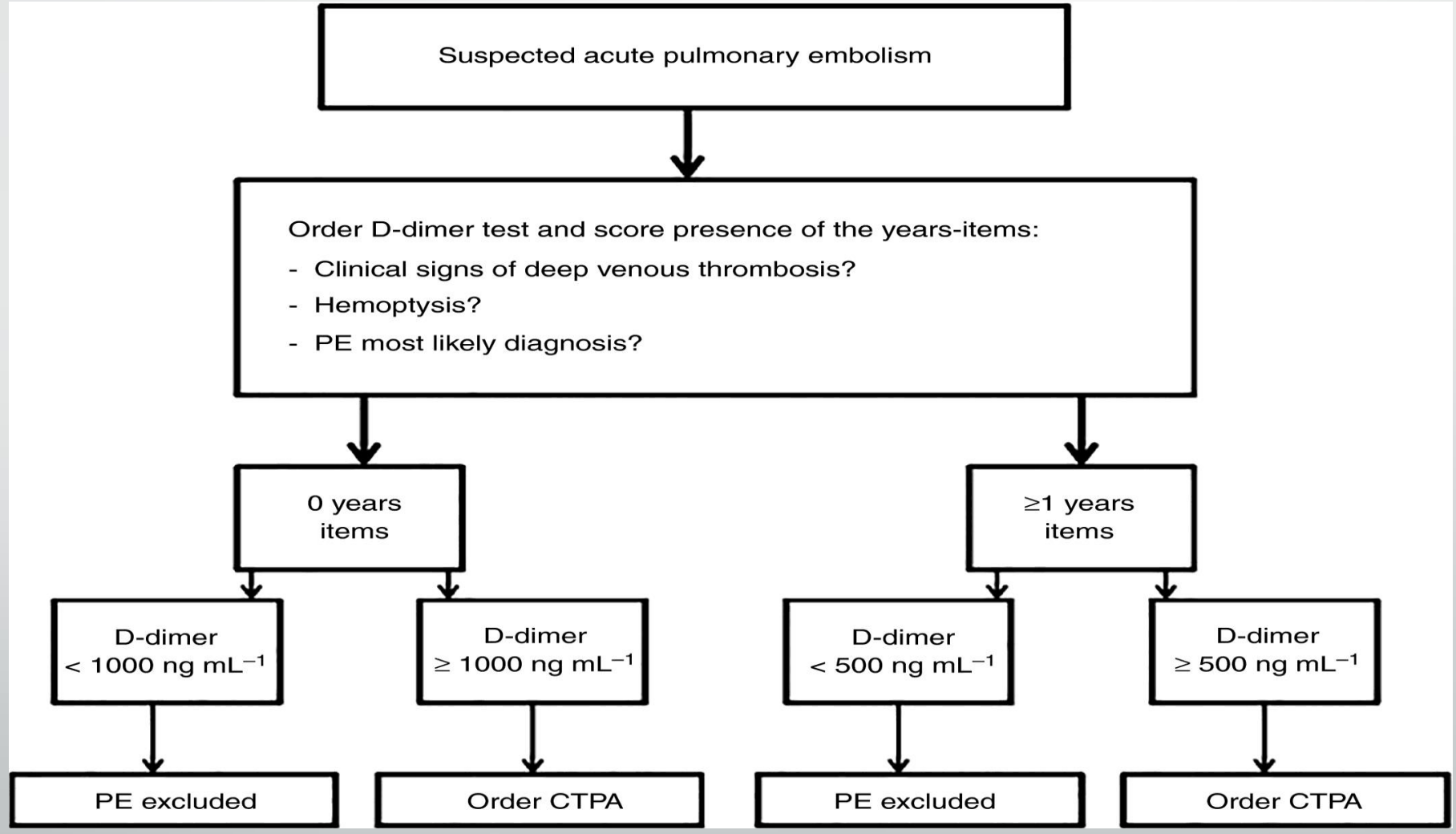
wells score vs Geneva score

- main difference between two rules is that the Wells score used “no alternative diagnosis” as a major score items. “No alternative diagnosis” can discriminate the PE patients which not included the high PE risk, such as surgery, previous DVT/PE, and malignancy

- Wells criteria have best validated in outpatients presenting with suspected PE. However, one study of hospitalized patients, reported a sensitivity and specificity of 72 and 62 percent, respectively
- they may not be as accurate in older or critically ill patients

- two-tiered system: patients are likely (score >4) or unlikely (score ≤4)
- three-tiered classification of low, intermediate, and high probability
- Low (score <2)
- Intermediate (score 2 to 6)
- high probability (score >6)

YEARS algorithm



wells score vs YEARS

- A retrospective study compared the Wells score with the YEARS algorithm and found that the YEARS algorithm was more sensitive (97 versus 74 percent) but less specific (14 versus 34 percent) for the diagnosis of PE

D-dimer

- Elevated plasma D-dimer levels indicate that coagulation has been activated, fibrin clot has formed, and clot degradation by plasmin has occurred.
- The sensitivity of the D-dimer is >80% for DVT (including isolated calf DVT) and >95% for PE.
- their specificity is low, usually between 40 and 60 percent
- a normal D-dimer can be used to rule out PE in patients with a low or intermediate probability of PE.
- D-dimer testing is best used in conjunction with clinical probability assessment

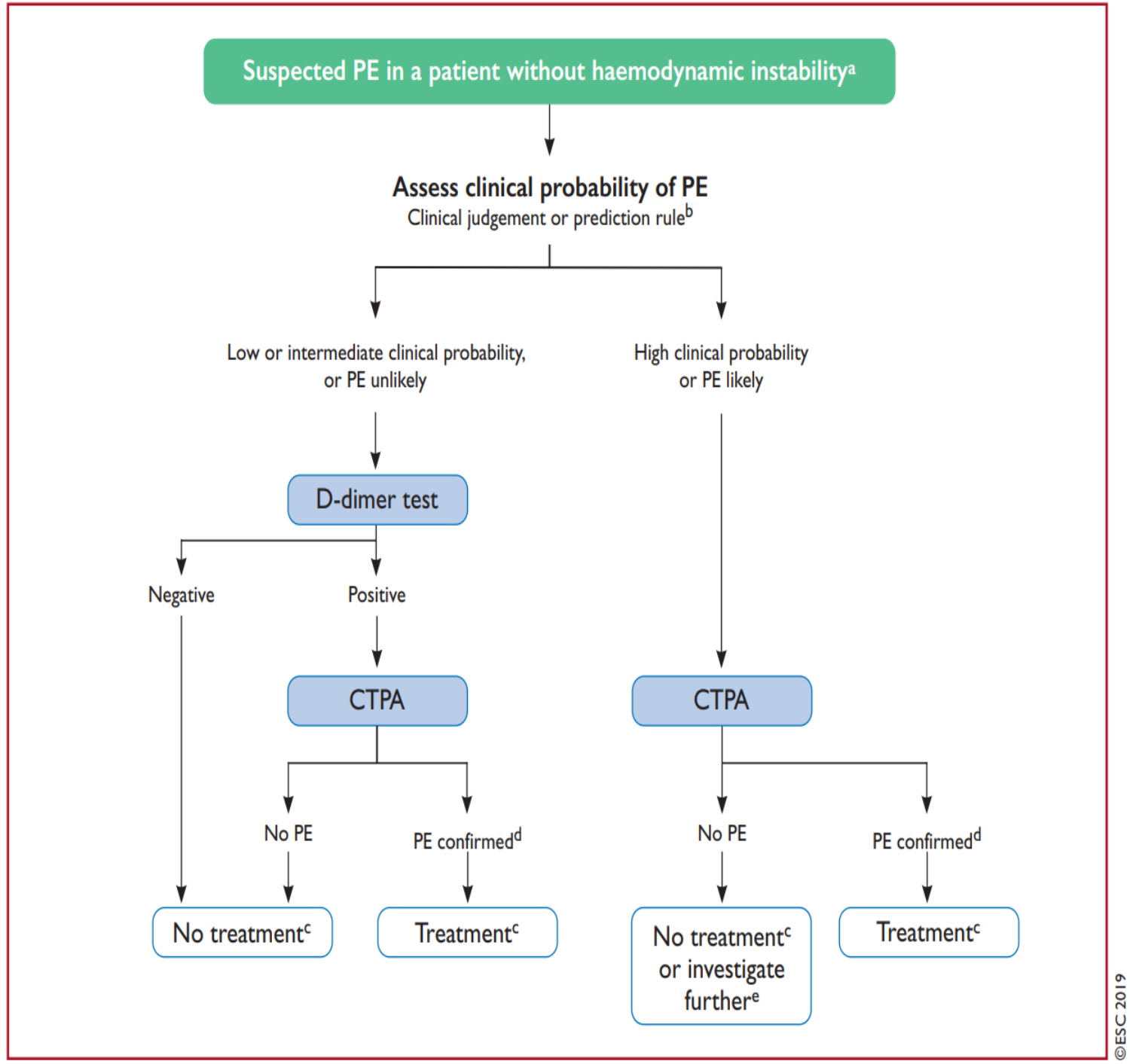
D-Dimer elevation

- myocardial infarction(arterial thrombosis)
- Pneumonia(Prognostic assessment in coronavirus disease 2019 (COVID-19)
- sepsis,
- cancer
- postoperative state/trauma
- second or third trimester of pregnancy.
- age >50 years
- renal dysfunction [estimated glomerular filtration rate <60 mL/min/1.73 m^2])
- Liver disease

Adjusted D-dimer

- D-dimer levels rise with age
- Age (if over 50 years) x 10 = cutoff value in ng/mL (fibrinogen equivalent units)

- low probability or low intermediate probability for PE.
- They should not be used in those with high-probability or intermediate-high-probability for PE.


Suspected PE in a patient without haemodynamic instability[a]
Assess clinical probability of PE
Clinical judgement or prediction rule[b]
Low or intermediate clinical probability, or PE unlikely
High clinical probability or PE likely
D-dimer test
Negative
Positive
CTPA
CTPA
No PE
PE confirmed[d]
No PE
PE confirmed[d]
No treatment[c]
Treatment[c]
No treatment[c] or investigate further[e]
Treatment[c]
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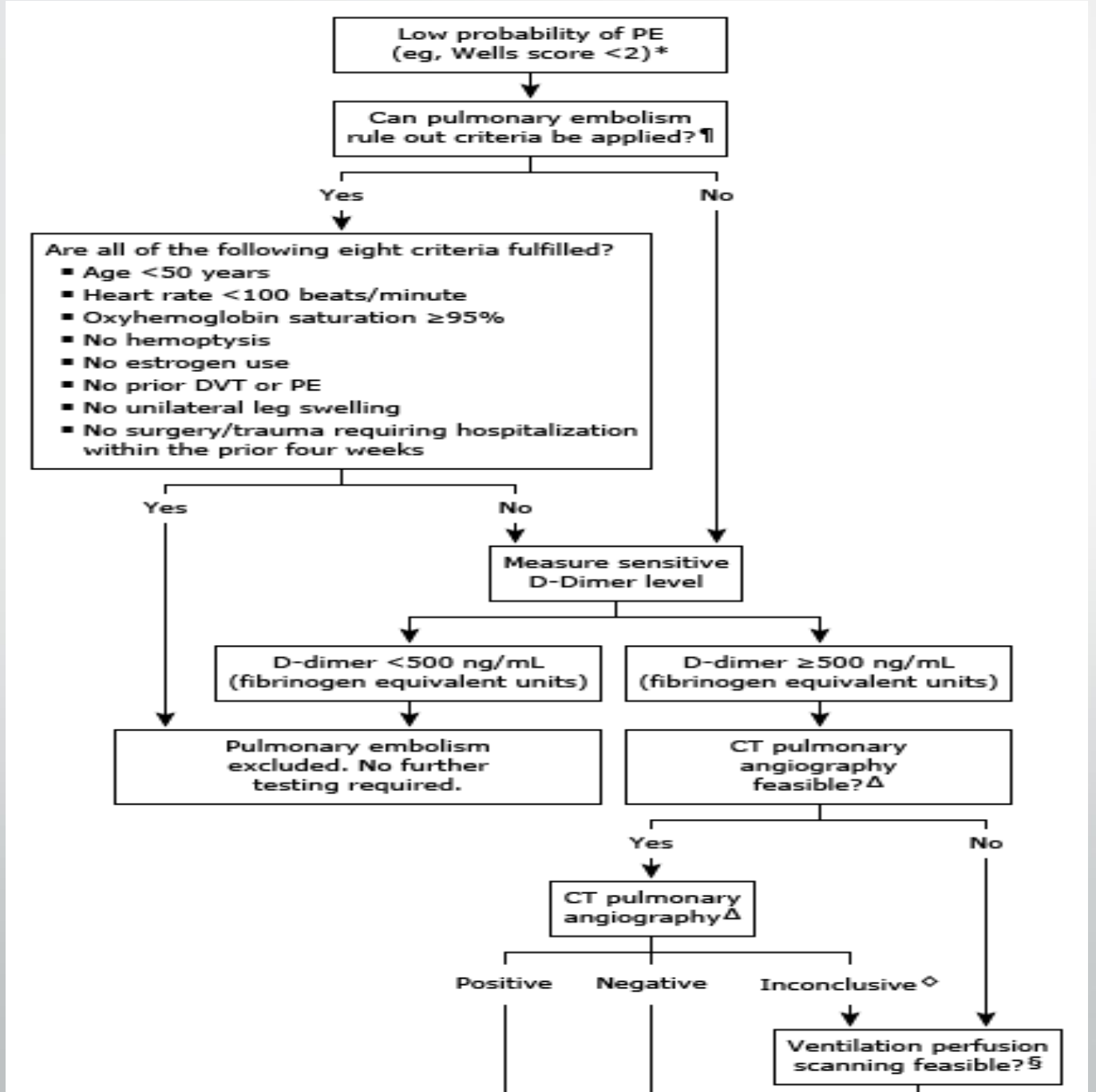
Low probability of PE (eg, Wells score <2)*
Can pulmonary embolism rule out criteria be applied?¶
Yes
No
Are all of the following eight criteria fulfilled?
Age <50 years
Heart rate <100 beats/minute
Oxyhemoglobin saturation ≥95%
No hemoptysis
No estrogen use
No prior DVT or PE
No unilateral leg swelling
No surgery/trauma requiring hospitalization within the prior four weeks
Yes
No
Measure sensitive D-Dimer level
D-dimer <500 ng/mL (fibrinogen equivalent units)
D-dimer ≥500 ng/mL (fibrinogen equivalent units)
Pulmonary embolism excluded. No further testing required.
CT pulmonary angiography feasible?Δ
Yes
No
CT pulmonary angiographyΔ
Positive
Negative
Inconclusive◇
Ventilation perfusion scanning feasible?§

The pulmonary embolism rule out criteria (PERC rule)*[1]

Age <50 years
Heart rate <100 bpm
Oxyhemoglobin saturation ≥95%
No hemoptysis
No estrogen use
No prior DVT or PE
No unilateral leg swelling
No surgery/trauma requiring hospitalization within the prior four weeks

- **PERC rule** — identify patients with a **low** clinical probability of PE in whom the risk of unnecessary testing outweighs the risk of PE

- In patients with a low probability of PE who fulfill all eight criteria, the likelihood of PE is sufficiently low that further testing is not indicated

- **Computed tomography pulmonary angiography**
- first-choice diagnostic imaging modality because it is sensitive and specific for the diagnosis of PE

- cTPA may be relatively contraindicated in patients with a history of moderate to severe iodinated contrast allergy or renal insufficiency (eGFR <30 mL/min per 1.73 m^2)
- Most studies report that CTPA is >90 percent sensitive and specific for the diagnosis of PE

- cTPA is traditionally considered most accurate for the detection of large, main, lobar, and segmental PE, and less accurate for the detection of smaller, peripheral subsegmental PE

- there is a risk of PE in those with a negative CTPA and a high clinical suspicion for PE (up to 5 percent when a ≤64 detector row multidetector CT [MDCT] is used), such that further testing may need to be considered

- **Ventilation perfusion scan** — V/Q scanning is mostly reserved for patients in whom CTPA is contraindicated or inconclusive, or when additional testing is needed.

- A normal chest radiograph is usually required prior to V/Q scanning

PIOPED, V/Q scans were reported as one of the following

- Normal
- Low-probability PE
- Intermediate-probability PE
- High-probability PE

Most patients have indeterminate scans, which is the major limitation of V/Q scanning since an indeterminate scan is insufficient to either confirm or exclude the diagnosis of PE,

- the proportion of patients whose scans fall into a nondiagnostic category is much higher in patients with COPD

- sing chest CTPA or *single-photon emission computed tomography* (SPECT)-V/Q

Table 6 Imaging tests for diagnosis of pulmonary embolism

	Strengths	Weaknesses/limitations	Radiation issues[a]

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 breastfeeding women
		  ○ contraindicated in severe renal failure
		• Tendency to overuse because of easy accessibility
		• Clinical relevance of CTPA diagnosis of subsegmental PE unknown
			• Radiation effective dose 3–10 mSv[b]
			• Significant radiation exposure to young female breast tissue

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 if PE excluded	• Lower radiation than CTPA, effective dose ~2 mSv[b]
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 if PE excluded • No validation in prospective management outcome studies	• Lower radiation than CTPA, effective dose ~2 mSv[b]
Pulmonary angiography	• Historical gold standard	• Invasive procedure • Not readily available in all centres	• Highest radiation, effective dose 10–20 mSv[b]

CTPA = computed tomographic pulmonary angiography; mGy = milligray; mSv = millisieverts; PE = pulmonary embolism; SPECT = single-photon emission computed tomography; V/Q = ventilation/perfusion (lung scintigraphy).

[a]In this section, effective radiation dose is expressed in mSv [dose in mSv = absorbed dose in mGy × radiation weighting factor (1.0 for X-rays) × tissue weighting factor]. This reflects the effective doses of all organs that have been exposed, that is, the overall radiation dose to the body from the imaging test. Compare with *Table 12*, in which the absorbed radiation dose is expressed in mGy to reflect the radiation exposure to single organs or to the foetus.

[b]For comparison, the whole-body effective dose of a chest X-ray examination is 0.1 mSv.[141]

HEMODYNAMICALLY UNSTABLE PATIENTS

A small percentage of patients with PE present with hemodynamic instability or shock (approximately 8 percent, high-risk or "massive" PE)

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.

The most useful initial test in this situation is bedside TTE, which will yield evidence of acute RV dysfunction

In a highly unstable patient, echocardiographic evidence of RV dysfunction is sufficient to prompt immediate reperfusion without further testing

TEE direct visualization of thrombi in the pulmonary artery and its main branches, especially in patients with RV dysfunction. TEE should be cautiously performed in hypoxaemic patients

Moreover, bedside CUS can detect proximal DVT

As soon as the patient is stabilized using supportive treatment, final confirmation of the diagnosis by CT angiography should be sough

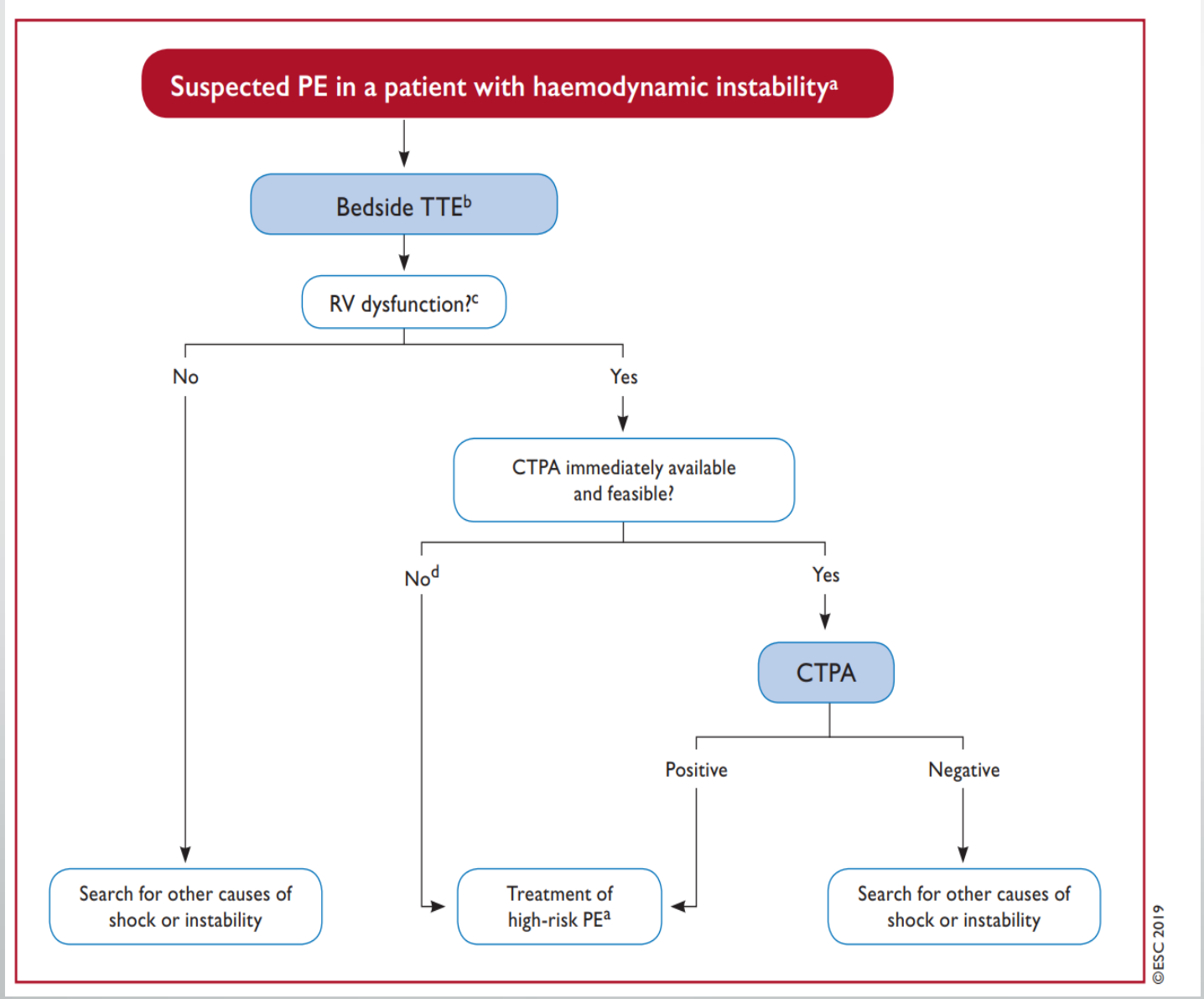
Suspected PE in a patient with haemodynamic instability[a]
Bedside TTE[b]
RV dysfunction?[c]
No
Yes
CTPA immediately available and feasible?
No[d]
Yes
CTPA
Positive
Negative
Search for other causes of shock or instability
Treatment of high-risk PE[a]
Search for other causes of shock or instability
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Table 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

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