



The Elusive Pulmonary Embolism: ED Diagnosis and Management

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Pathophysiology

- Gas exchange abnormalities
 - Right to left shunt
 - Hypoxemia
 - Increases a-A gradient
 - V/Q mismatch
 - Increased Dead Space
 - Respiratory alkalosis

Pathophysiology

- Hemodynamic abnormalities
 - Often related to size of the emboli
 - Increased vascular resistance
 - RV
 - Dilation
 - Hypokinesis
 - Tricuspid regurgitation
 - Myocardial ischemia

Evaluation and Diagnosis

- Initial step: Assessing clinical probability
- Risk of having the disease
 - Risk of acute adverse event
 - Need anticoagulation now
 - Select patient for diagnostic work-up

- ### Challenge
- Clinical symptoms aren't accurate
 - No feature has good enough sensitivity and specificity to rule in or rule out
 - Non-imaging tests aren't good enough
 - ABG
 - CXR
 - ECG

ECG

- Tachycardia
- Complete or Incomplete RBBB
- Signs of R heart strain

Risk Factors

- Inherited
 - Factor V Leiden
 - Prothombin gene mutation
 - Low protein C, S
 - Family hx of VTE
- Acquired
 - Age
 - Smoking
 - Obesity
 - Immobility
 - Malignancy
 - OCP
 - Atherosclerosis
 - Trauma
 - Infection

Signs and Symptoms

- Symptoms
 - Dyspnea
 - Chest pain
 - Cough
 - Hemoptysis
 - Syncope
 - Palpitations
 - Wheezing
 - Leg pain
- Signs
 - Tachycardia
 - Tachypnea
 - Hypoxemia
 - Fever
 - Diaphoresis
 - Signs of DVT
 - JVD
 - Hypotension

CXR

- Most often normal
- May show collapse, consolidation, effusions, elevated hemidiaphragm
- Uncommon
 - Westermark's sign
 - Dilation of vessels proximal to embolism
 - Hampton's hump
 - Pleural based opacity

Clinical probability

- Combining everything together
- Methods
 - Clinical gestalt
 - Prediction rules

Prediction rules

Prediction rules

- These scores are not more accurate than clinical judgment
- More reproducible
- Allow classification into distinct categories
- Note the Geneva Rule
 - Required an Arterial blood gas

Lancet 2002;360:1914-20
Arch Intern Med 2000;160:512-6

Prediction Rules

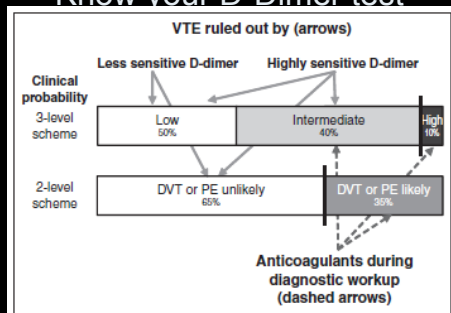
Table 3. Clinical decision rules for pulmonary embolism

Wells score ²⁸		Geneva score ²⁹		Pisa model ³⁰	
Characteristic	Score	Characteristic	Points	Characteristic	Points
Recent pulmonary embolism or deep vein thrombosis	1.5	Previous pulmonary embolism or deep vein thrombosis	2	Male sex	0.83
Hypoxia <100 mm Hg on room air	1.5	Heart rate >100 beats per minute	1	Age 65-72 years	0.34
Recent surgery or immobilization	1.5	Recent surgery	3	72 or more years	0.60
Unilateral signs of deep vein thrombosis	3	Age 60-79	1	Preceding disease	-0.89
Alternative diagnosis less likely than pulmonary embolism	3	Age 80 or older	2	Cardiomegaly	-0.89
Haemoptysis	1	PFO ³¹	1	Pulmonary thromboembolism (past)	0.69
Diarr	1	<35 mm Hg	2	Symptoms	
		36-39.9 mm Hg	1	Dyspnea (moderate)	1.29
		40-44.9 mm Hg	4	Chest pain	0.64
		45-49.9 mm Hg	3	Hemoptysis	0.88
		50-54.9 mm Hg	2	Fever >38°C	-1.27
		55-59.9 mm Hg	1		
		60-64.9 mm Hg	1	ECG signs of acute right ventricular overload	1.33
		65-69.9 mm Hg	1	Chest radiograph	
		70-74.9 mm Hg	1	Oliguria	3.86
		75-79.9 mm Hg	1	Absence of hilar artery	3.60
		80-84.9 mm Hg	1	Ascites	3.57
		85-89.9 mm Hg	1	Conduction system disease	-1.23
		90-94.9 mm Hg	1	Pulmonary edema	-2.83
		95-99.9 mm Hg	1	Constable	-1.26
		100-104.9 mm Hg	1		
		105-109.9 mm Hg	1		
		110-114.9 mm Hg	1		
		115-119.9 mm Hg	1		
		120-124.9 mm Hg	1		
		125-129.9 mm Hg	1		
		130-134.9 mm Hg	1		
		135-139.9 mm Hg	1		
		140-144.9 mm Hg	1		
		145-149.9 mm Hg	1		
		150-154.9 mm Hg	1		
		155-159.9 mm Hg	1		
		160-164.9 mm Hg	1		
		165-169.9 mm Hg	1		
		170-174.9 mm Hg	1		
		175-179.9 mm Hg	1		
		180-184.9 mm Hg	1		
		185-189.9 mm Hg	1		
		190-194.9 mm Hg	1		
		195-199.9 mm Hg	1		
		200-204.9 mm Hg	1		
		205-209.9 mm Hg	1		
		210-214.9 mm Hg	1		
		215-219.9 mm Hg	1		
		220-224.9 mm Hg	1		
		225-229.9 mm Hg	1		
		230-234.9 mm Hg	1		
		235-239.9 mm Hg	1		
		240-244.9 mm Hg	1		
		245-249.9 mm Hg	1		
		250-254.9 mm Hg	1		
		255-259.9 mm Hg	1		
		260-264.9 mm Hg	1		
		265-269.9 mm Hg	1		
		270-274.9 mm Hg	1		
		275-279.9 mm Hg	1		
		280-284.9 mm Hg	1		
		285-289.9 mm Hg	1		
		290-294.9 mm Hg	1		
		295-299.9 mm Hg	1		
		300-304.9 mm Hg	1		
		305-309.9 mm Hg	1		
		310-314.9 mm Hg	1		
		315-319.9 mm Hg	1		
		320-324.9 mm Hg	1		
		325-329.9 mm Hg	1		
		330-334.9 mm Hg	1		
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		370-374.9 mm Hg	1		
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		380-384.9 mm Hg	1		
		385-389.9 mm Hg	1		
		390-394.9 mm Hg	1		
		395-399.9 mm Hg	1		
		400-404.9 mm Hg	1		
		405-409.9 mm Hg	1		
		410-414.9 mm Hg	1		
		415-419.9 mm Hg	1		
		420-424.9 mm Hg	1		
		425-429.9 mm Hg	1		
		430-434.9 mm Hg	1		
		435-439.9 mm Hg	1		
		440-444.9 mm Hg	1		
		445-449.9 mm Hg	1		
		450-454.9 mm Hg	1		
		455-459.9 mm Hg	1		
		460-464.9 mm Hg	1		
		465-469.9 mm Hg	1		
		470-474.9 mm Hg	1		
		475-479.9 mm Hg	1		
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		570-574.9 mm Hg	1		
		575-579.9 mm Hg	1		
		580-584.9 mm Hg	1		
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		610-614.9 mm Hg	1		
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		620-624.9 mm Hg	1		
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		735-739.9 mm Hg	1		
		740-744.9 mm Hg	1		
		745-749.9 mm Hg	1		
		750-754.9 mm Hg	1		
		755-759.9 mm Hg	1		
		760-764.9 mm Hg	1		
		765-769.9 mm Hg	1		
		770-774.9 mm Hg	1		
		775-779.9 mm Hg	1		
		780-784.9 mm Hg	1		
		785-789.9 mm Hg	1		
		790-794.9 mm Hg	1		
		795-799.9 mm Hg	1		
		800-804.9 mm Hg	1		
		805-809.9 mm Hg	1		
		810-814.9 mm Hg	1		
		815-819.9 mm Hg	1		
		820-824.9 mm Hg	1		
		825-829.9 mm Hg	1		
		830-834.9 mm Hg	1		
		835-839.9 mm Hg	1		
		840-844.9 mm Hg	1		
		845-849.9 mm Hg	1		
		850-854.9 mm Hg	1		
		855-859.9 mm Hg	1		
		860-864.9 mm Hg	1		
		865-869.9 mm Hg	1		
		870-874.9 mm Hg	1		
		875-879.9 mm Hg	1		
		880-884.9 mm Hg	1		
		885-889.9 mm Hg	1		
		890-894.9 mm Hg	1		
		895-899.9 mm Hg	1		
		900-904.9 mm Hg	1		
		905-909.9 mm Hg	1		
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		950-954.9 mm Hg	1		
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		965-969.9 mm Hg	1		
		970-974.9 mm Hg	1		
		975-979.9 mm Hg	1		
		980-984.9 mm Hg	1		
		985-989.9 mm Hg	1		
		990-994.9 mm Hg	1		
		995-999.9 mm Hg	1		
		1000-1004.9 mm Hg	1		
		1005-1009.9 mm Hg	1		
		1010-1014.9 mm Hg	1		
		1015-1019.9 mm Hg	1		
		1020-1024.9 mm Hg	1		
		1025-1029.9 mm Hg	1		
		1030-1034.9 mm Hg	1		
		1035-1039.9 mm Hg	1		
		1040-1044.9 mm Hg	1		
		1045-1049.9 mm Hg	1		
		1050-1054.9 mm Hg	1		
		1055-1059.9 mm Hg	1		
		1060-1064.9 mm Hg	1		
		1065-1069.9 mm Hg	1		
		1070-1074.9 mm Hg	1		
		1075-1079.9 mm Hg	1		
		1080-1084.9 mm Hg	1		
		1085-1089.9 mm Hg	1		
		1090-1094.9 mm Hg	1		
		1095-1099.9 mm Hg	1		
		1100-1104.9 mm Hg	1		
		1105-1109.9 mm Hg	1		
		1110-111			

D-Dimer

- High sensitive=ELISA
 - Automated turbidimetric assay
 - Sensitivity>95%
 - Cut-off value usually >500ug/L
- New D-Dimer tests
 - Vidas D-dimer
 - ELISA test
 - Tunaquant
 - Immunoturbimetric test

Know your D-Dimer test



Vasc Med 2010;15:399-406

Clinical Prediction Rules

Wells' score for DVT ¹		Wells' score for PE ²		Revised Geneva score for PE ³	
Items	Points	Items	Points	Items	Points
Cancer	+1	Previous PE or DVT	+1.5	Age > 65 years	+1
Paralysis or recent plaster cast	+1	Heart rate > 100/min	+1.5	Previous DVT or PE	+3
Bed rest > 3 days or surgery < 4 weeks	+1	Recent surgery or immobilization	+1.5	Surgery (under general anaesthesia) or fracture (of the lower limb) within 1 month	+2
Pain on palpation of deep veins	+1	Clinical signs of DVT	+3	Active malignancy (solid or haematological malignancy, currently active or considered as cured since < 1 year)	+2
Swelling of entire leg	+1	Alternative diagnosis less likely than PE	+3	Unilateral lower limb pain	+3
Diameter difference on affected calf > 3 cm	+1	Haemoptysis	+1	Haemoptysis	+2
Pitting oedema (affected side only)	+1	Cancer	+1	Heart rate 75-94 bpm	+3
Dilated superficial veins (affected side)	+1			Heart rate > 95 bpm	+5
Alternative diagnosis at least as probable as DVT	-2			Pain on lower limb deep vein palpation and unilateral edema	+4
Clinical probability					
Low	0	Initial rule Low	< 2	Low	0-3
Intermediate	1-2	Intermediate	2-6	Intermediate	4-10
High	≥ 3	High	≥ 6	High	≥ 11
Dichotomized rule					
Unlikely					
Likely					
≤ 4					
> 4					

Vasc Med 2010;15:399-406

Geneva score

- Not as dependent on prevalence of disease
- Studies most often with a high sensitivity D-dimer

Does everyone need a D-dimer?

- PERC score
 - Age < 50
 - HR < 100
 - O2 Sat on Room Air >94%
 - No Prior History of DVT/PE
 - No Recent Trauma or Surgery
 - No Hemoptysis
 - No Exogenous Estrogen
 - No Clinical Signs Suggesting DVT

PERC score cautions

- Defines a <2% risk group
- Not accurate in populations with a high prevalence of disease

Diagnostic Modality

- Multi-detector CT
 - Original algorithms included compression ultrasound
 - 3rd generation CT
 - Sensitivity 99.1% (95%CI 97.3-99.7)
 - Risk of 3 months AE in negative scan
 - 1.5% (95% CI 0.9-2.7%)
 - Addition benefit of compression ultrasound is minimal in PE unlikely patients

Lancet 2008;371:1343-52

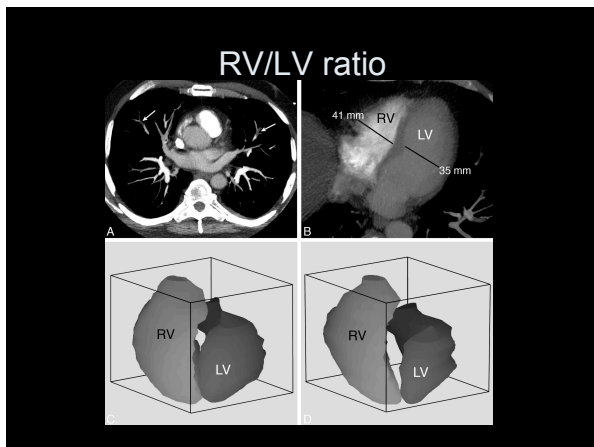
JAMA 2007; 298:2743-53

11/11/2008 205:170.6

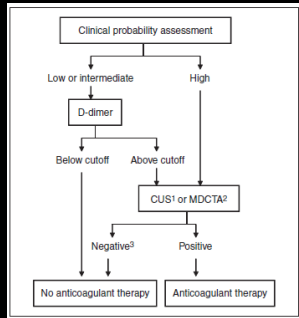
MDCT: additional information

- Provides prognostic information
- Assess Right Ventricle size
- Parameters associated with poor outcome
 - PA obstructive index >50%
 - RV/LV ratio >1.5

[Acta Radiol.](#) 2010;51(3):271-6.




Clinical Algorithm



Risk Assessment


Outcome

- 3 month mortality
 - SBP <90mmHg
 - As high as 58.3%
 - SBP ≥ 90mmHg
 - 15.1%



METHODS OF RISK-STRATIFY


<u>Clinical data</u>	<u>RV on Echo</u>	<u>Blomarkers</u>
Vital signs	Hypokinesia	Troponin
Age	Dilation	BNP
Comorbidity	Septum	Pro-BNP
	RVSP	D-dimer



BEST PREDICTORS OF **IN-HOSPITAL** DEATH, SHOCK OR INTUBATION

	<u>Sens</u>	<u>Spec</u>
Echocardiography + RV dilation or hypokinesia (N=714)	86%	39%
Troponin I + >0.4 ng/mL or T>0.04 ng/mL (N=115)	60%	85%
Pulse Oximetry + <95%, breathing room air (N=303)	90%	64%
BNP + <90 pg/mL (N=73)	85%	75%

Konstantinides S, 2002; Kline JA, 2003; Grifoni S, 2000; Konstantinides S, 1997; Kucher, 2003; Galle 2001



PREDICTORS OF 6 MONTH MORBIDITY OR DISABILITY

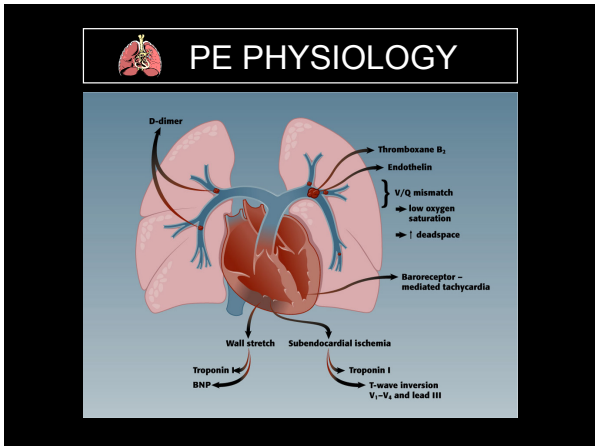
	<u>Sens</u>	<u>Spec</u>
Echocardiography +	61%	57%
Pulse Oximetry (94.5%)	65%	67%
Troponin T (>0.1 ng/mL)	20%	92%
Any one of previous 3	71%	62%
BNP (90 pg/mL)	55%	81%
Panel OR BNP>90	80%	57%

Kline et al., Crit Care Med, IN PRESS 2006


PE severity index (PESI)

Age, per yr	Age, in yr
Male sex	10
Cancer	30
Heart failure	10
Chronic lung disease	10
Clinical findings	
Pulse ≥ 110 /min	20
Systolic blood pressure ≥ 100 mmHg	30
Respiratory rate ≥ 30 /min	20
Temperature ≥ 36 C	20
Altered mental status*	60
Arterial oxygen saturation $\geq 90\%$ †	20

- ### PESI
- 65 class I, very low risk
– 1.1% 30 day mortality
 - 66–85 class II, low risk
 - 86–105 class III intermediate risk
 - 106–125 class IV, high risk
 - 125 class V, very high risk
– 24.5% 30 day mortality



Treatment



BACKGROUN D

Massive or major PE: Thrombolytic therapy is indicated

Submassive (non-massive) PE: Thrombolytic therapy may be indicated in the presence of RV dysfunction

Low Risk PE: absence of all other features

Task Force Report Eur Heart J 2000 21:1301

AHA

- **Recommendations for Initial Anticoagulation for Acute PE**
 - Therapeutic anticoagulation with subcutaneous LMWH, intravenous or subcutaneous UFH or subcutaneous fondaparinux should be given to patients with objectively confirmed PE and no contraindications to anticoagulation (*Class I; Level of Evidence A*).
 - Therapeutic anticoagulation during the diagnostic workup should be given to patients with intermediate or high clinical probability of PE and no contraindications to anticoagulation (*Class I; Level of Evidence C*).

Circulation. 2011;123:1788-1830

How to assess bleeding risk

Hemorrhages bleeding risk score ^a		RIETE bleeding risk score ^b	
Prior bleed	2 points	Recent major bleed	2 points
Hepatic or renal disease	1 point	Creatininaemia > 1.2 mg dL ⁻¹ (110 μmol L ⁻¹)	1.5 point
Alcohol abuse	1 point	Haemoglobin < 13 (men) or 12 (women) g dL ⁻¹	1.5 point
Malignancy	1 point	Malignancy	1 point
Age >75 years	1 point	Clinically overt PE	1 point
Uncontrolled hypertension	1 point	Age >75 years	1 point
Anaemia	1 point		
Excessive risk of fall	1 point		
Stroke	1 point		
Reduced platelet count or function	1 point		
Prior bleed	2 points		

Rate of bleeding: 0-2.5% score of 1, > 5 =12.3%

Rate of bleeding: 0=0.3%, >4=7.4%

Duration of therapy

- First PE secondary to a transient risk factor
 - Treat 3 months
- Idiopathic PE
 - At least 3 months
- Re-eval at 3 months
 - Some advocate following D-dimer levels

New treatments

- Direct Thrombin Inhibitor
 - Dabigatran
- Anti-Xa agents
 - Rivoraxoban
 - Apixaban
 - Edoxaban

Conclusion

- PE has a high mortality rate and is difficult to diagnose
- Clinical rules provide a reproducible way to risk stratify
 - Diagnostic algorithm
 - Prognosis
- Treatment is based on classification
 - Anticoagulation
 - Thrombolytics
